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Tourniquet use for knee replacement surgery (Review)

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[Intervention Review]

Tourniquet use for knee replacement surgery

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ABSTRACT

Background

Many surgeons prefer to perform total knee replacement surgery with the aid of a tourniquet. A tourniquet is an occlusive device that restricts distal blood flow to help create a bloodless field during the procedure. A tourniquet may be associated with increased risk of pain and complications.

Objectives

To determine the benefits and harms of tourniquet use in knee replacement surgery.

Search methods

We searched MEDLINE, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) up to 26 March 2020. We searched clinicaltrials.gov, the World Health Organization trials portal, and several international registries and joint registries up to March 2020.

Selection criteria

We included randomised controlled trials (RCTs) comparing knee replacement with use of a tourniquet versus without use of a tourniquet and non-randomised studies with more than 1000 participants. Major outcomes included pain, function, global assessment of success, health-related quality of life, serious adverse events (including venous thromboembolism, infection, re-operation, and mortality), cognitive function, and survival of the implant. Minor outcomes included blood loss, economic outcomes, implant stability, and adverse events.

Data collection and analysis

Two review authors screened abstracts and full texts, extracted data, performed risk of bias assessments, and assessed the certainty of the evidence using the GRADE approach.

Main results

We included 41 RCTs with 2819 participants. Trials included from 20 to 199 participants. Mean age ranged between 58 and 84 years. More than half of the RCTs had unclear risk of selection bias and unclear risk of performance and detection bias due to absence of blinding of participants and surgeons.

Major outcomes

Pain: at postoperative day 1, pain (on a scale from zero to 10, with higher scores indicating worse pain) was ranked at 4.56 points after surgery without a tourniquet and at 1.25 points (MD) higher (95% CI 0.32 higher to 2.19 higher) with a tourniquet (8 studies; 577 participants), for an absolute difference of 12.5% higher pain scores (95% CI 3.2% higher to 21.9% higher) and a relative difference of 19% higher pain scores (95% CI 3.4% higher to 49% higher) with a tourniquet. Evidence for these findings was of moderate certainty, downgraded due to risk of bias. Knee replacement with a tourniquet probably led to higher postoperative pain scores at day 1, although this difference may or may not be noticeable to patients (based on a minimal clinically important difference (MCID) of 1.0).

Function: at 12 months, tourniquet use probably makes little or no difference to function, based on an MCID of 5.3 for Knee Society Score (KSS) and 5.0 for Oxford Knee Score (OKS). Mean function (on a scale from 0 to 100, with higher scores indicating better outcomes) was 90.03 points after surgery without a tourniquet and was 0.29 points worse (95% CI 1.06 worse to 0.48 better) on a 0 to 100 scale, absolute difference was 0.29% worse (1.06% worse to 0.48% better), with a tourniquet (5 studies; 611 participants). This evidence was downgraded to moderate certainty due to risk of bias.

Global assessment of success: low-certainty evidence (downgraded due to bias and imprecision) indicates that tourniquet use may have little or no effect on success. At six months, 47 of 50 (or 940 per 1000) reported overall successful treatment after surgery without a tourniquet and 47 of 50 (or 940 per 1000) with a tourniquet (risk ratio (RR) 1.0, 95% CI 0.91 to 1.10) based on one study with 100 participants.

Health-related quality of life: at six months, tourniquet may have little or no effect on quality of life. The 12-Item Short Form Survey (SF-12) score (mental component from zero to 100 (100 is best)) was 54.64 after surgery without a tourniquet and 1.53 (MD) better (95% CI 0.85 worse to 3.91 better) with a tourniquet (1 study; 199 participants); absolute difference was 1.53% better (0.85% worse to 3.91% better). Evidence was of low certainty, downgraded due to risk of bias and small number of participants.

Serious adverse events: the risk of serious adverse events was probably higher with tourniquet; 26 of 898 (29 per 1000) reported events following surgery without a tourniquet compared to 53 of 901 (59 per 1000) with a tourniquet (RR 1.73, 95% CI 1.10 to 2.73) in 21 studies (1799 participants). Twenty-nine more per 1000 patients (95% CI 3 to 50 more per 1000 patients) had a serious adverse event with a tourniquet. Forty-eight (95% CI 20 to 345) participants would need to have surgery without a tourniquet to avoid one serious adverse event. This evidence was downgraded to moderate certainty due to risk of bias.

Cognitive function: one study reported cognitive function as an outcome; however the data were incompletely reported and could not be extracted for analysis.

Survival of implant: it is uncertain if tourniquet has an effect on implant survival due to very low certainty evidence (downgraded for bias, and twice due to very low event rates); 2 of 107 (19 per 1000) required revision surgery in the surgery with a tourniquet group compared to 1 of 107 (9 per 1000) without a tourniquet group at up to two years' follow-up (RR 1.44, 95% CI 0.23 to 8.92). This equates to a 0.4% (0.7% lower to 7% more) increased absolute risk in surgery with a tourniquet.

Authors' conclusions

Moderate certainty evidence shows that knee replacement surgery with a tourniquet is probably associated with an increased risk of serious adverse events. Surgery with a tourniquet is also probably associated with higher postoperative pain, although this difference may or may not be noticeable to patients. Surgery with a tourniquet does not appear to confer any clinically meaningful benefit on function, treatment success or quality of life. Further research is required to explore the effects of tourniquet use on cognitive function and implant survival, to identify any additional harms or benefits.

If a tourniquet continues to be used in knee replacement surgery, patients should be informed about the potential increased risk of serious adverse events and postoperative pain.

PLAIN LANGUAGE SUMMARY

What are the benefits and risks of using a tourniquet in knee replacement surgery?

Why is this question important?

Knee replacement is a common operation that involves replacing a damaged, worn, or diseased knee with an artificial joint made of metal and plastic.

Most surgeons prefer to carry out knee replacement surgery with the aid of a tourniquet - a tight band placed around the thigh that restricts blood flow to the knee.

Potential benefits of using a tourniquet include limiting blood loss during surgery and making it easier to conduct the operation. However, a tourniquet may increase the risk of pain and complications for patients after surgery. We reviewed evidence from research studies to find out about the benefits and risks of using a tourniquet in knee replacement surgery.

How did we identify and evaluate the evidence?

First, we searched for relevant, robust studies in the medical literature. We then compared the results and summarised the evidence from all studies. Finally, we assessed how certain the evidence was. To do this, we considered factors such as the way studies were conducted, study size, and consistency of findings across studies. Based on our assessments, we categorised the evidence as being of very low, low, moderate, or high certainty.

What did we find?

We found 41 studies that involved 2819 people (944 men and 1777 women) who were randomly assigned to have surgery with a tourniquet, or surgery without. This type of study, known as a randomised controlled trial, provides the most robust evidence about the effects of a treatment.

Studies were conducted in hospitals in Australia, Asia, Europe, and the USA. Each study involved between 20 and 166 people who were between 58 and 84 years of age. They were followed for between one day and two years after surgery.

Five studies were publicly funded, and one study received funding from a medical equipment manufacturing company. The other 35 studies did not receive specific funding or did not state who funded them.

The studies provided low to moderate evidence that:

- pain on the first day after surgery is probably worse with a tourniquet. On average, on a scale of 0 to 10 (higher scores = worse pain), people operated on with a tourniquet rated their pain as 5.81. People operated on without a tourniquet rated their pain as 4.56 (average difference: 1.25 points);

- knee function one year after surgery is probably similar with or without a tourniquet. On average, on a scale of 0 to 100 (higher scores = better functioning), people operated on with a tourniquet rated their knee function as 89.74. People operated on without a tourniquet rated their knee function as 90.03 (average difference: 0.29 points);

- satisfaction with treatment may be similar with or without a tourniquet. Six months after the operation, 94% of people operated on with or without a tourniquet were 'extremely' or 'very' satisfied with their treatment;

- there may be little or no difference in health-related quality of life with or without a tourniquet. On average, on a scale of 0 to 100 (higher scores = better quality of life), people operated on with a tourniquet rated their quality of life as 54.64. People who had surgery without a tourniquet rated their quality of life as 56.17 (average difference: 1.53 points); and

- serious adverse events such as blood clots in the leg or lung, infection, or re-operation other than to replace the artificial joint are probably more likely to occur with a tourniquet. Five per cent of people operated on with a tourniquet reported serious adverse events compared to 2.9% of people operated on without a tourniquet.

We do not know if using a tourniquet affects chances of needing a second operation to replace an artificial joint because available evidence is of very low certainty.

No studies investigated the effects of surgery with a tourniquet on people’s ability to process thoughts (cognitive function).

What does this mean?

Knee replacement with a tourniquet is probably slightly less beneficial, and is associated with greater risks, than surgery without a tourniquet.

How up-to-date is this review?

Evidence in this Cochrane Review is current to March 2020.

Summary of findings 1. Knee replacement with tourniquet compared to knee replacement without tourniquet

Participants: patients undergoing knee replacement surgery

Settings: hospitals around the world performing knee replacement surgery

Intervention: surgery performed with a tourniquet for all or part of the procedure

Comparator: surgery performed without a tourniquet

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk without tourniquet	Risk with tourniquet				
Pain Visual analogue scale (VAS) for pain from zero to 10 (higher scores indicate more pain) Follow-up day 1 postoperative pain scores	Mean pain was 4.56	MD 1.25 worse pain (0.32 worse to 2.19 worse)	-	577 (8 RCTs)	⊕⊕⊕⊖ MODERATE[a]	Knee replacement with a tourniquet led to higher postoperative pain scores at day 1, although this difference may or may not be noticeable to patients [b] Absolute difference 12.5% worse (3.2% worse to 21.9% worse) Relative difference 19% worse (3.4% worse to 49% worse)[c]
Function Similar 0 to 100 scales (100 is best) were used to measure the same conceptual functional outcome: Knee Injury and Osteoarthritis Outcome Score Activities of Daily Living (KOOS-ADL); Knee Society Score (KSS); Hospital for Special Surgery Score (HSS) Follow-up 12 months	Mean function was 90.03	MD 0.29 worse function (1.06 worse to 0.48 better)[d]	-	611 (5 RCTs)	⊕⊕⊕⊖ MODERATE[a]	Knee replacement with tourniquet probably has little or no meaningful effect on function [b] Absolute difference 0.29% worse (1.06% worse to 0.48% better) Relative difference 0.57% worse (2.07% worse to 0.94% better)[c]
Global assessment of success Participants reporting overall successful treatment and satisfaction[e]	940 per 1000	940 per 1000	RR 1.0 (0.91 to 1.10)	100 (1 RCT)	⊕⊕⊖ LOW[a,f]	Number of participants reporting success may not differ Absolute difference 0% (8.5% worse to 9.4% better)

Follow-up 6 months		(855 to 1034)				Relative difference 0% (9% worse to 10% better)
Health-related quality of life SF-12 mental component from zero to 100 (100 is best) Follow-up 6 months	Mean health-related quality of life was 54.64	MD 1.53 better (0.85 worse to 3.91 better)		199 (1 RCT)	⊕⊕⊖ LOW[a,f]	Knee replacement with tourniquet may have little or no meaningful effect on health-related quality of life[b] Absolute difference 1.53% better (0.85% worse to 3.91% better) Relative difference 3% better (2% worse to 7% better)[c]
Serious adverse events	29 per 1000	59 per 1000 (32 to 79)	RR 1.73 (1.10 to 2.73)	1799 (21 RCTs)	⊕⊕⊕⊖ MODERATE[a]	Knee replacement with tourniquet probably has a meaningful effect on risk of serious adverse events Absolute difference 2.1% more (0.29% more to 5.00% more)[g] Relative difference 73% (10% more to 173% more) Number needed to harm (NNTH) is 48 (20 to 345) participants to have surgery with a tourniquet for 1 serious adverse event (venous thromboembolism, infection, or re-operation)
Cognitive function	-	-	-	-	-	No studies with adequate data
Survival of the implant Risk of revision At 1 year	9 per 1000	13 per 1000 (2 to 83)	RR 1.44 (0.23 to 8.92)	214 (3 RCTs)	⊕⊕⊕⊖ VERY LOW[a,f,h]	It is uncertain if knee replacement has an effect on survival of implant at 1 year Absolute difference 0.4% more (0.7% less to 7% more) in the surgery with a tourniquet group Relative difference 44% more (77% lower to 892% more) in the surgery with a tourniquet group

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: confidence interval; MD: mean difference; RCT: randomised controlled trial; RR: risk ratio.

GRADE Working Group grades of evidence.
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded by one level due to risk of bias. Many studies had unclear risk of allocation concealment and unclear risk of participant blinding.

[b]We assumed that clinically important improvement was 1 point or 10% absolute improvement for pain on a VAS (0 to 10) (Dworkin 2008; Kelly 2001; Wall 2017); 5.3 points or 5.3% absolute improvement in KSS for function (Chean Lee 2017), and 10 points or 10% absolute improvement for health-related quality of life.

[c]Relative changes calculated relative to baseline in the surgery with a tourniquet group (i.e. absolute change (mean difference) divided by mean at baseline in the surgery without a tourniquet group from Liu 2017 b (values were 6.54 points on a 0 to 10 point VAS scale for pain and 51.3 on a 0 to 100 point KSS scale for function) and Goel 2019 (values were 54.64 on a 0 to 100 point SF-12 mental component score for continuous outcomes).

[d]The mean difference was calculated by multiplying the SMD by the baseline SD (4.8) of the control group (Liu 2017 b).

[e]Participant satisfaction was derived from one study (Huang 2017). Satisfaction was defined as the number of participants who were 'extremely' or 'very' satisfied with their treatment.

[f]Downgraded by one level due to imprecision. Small total number of participants. Not enough information to calculate effect estimate precisely.

[g]Confidence intervals around absolute risk demonstrated an effect equal to or greater than 0.29%, which was deemed to be highly clinically relevant given the seriousness of the outcome. The total number of events was low; however, this was expected, and we did not downgrade for imprecision, as this was is in line with previous literature on SAEs (Benjamin 2016), which reported an incidence of VTE of 2.4% in patients undergoing TKR. Our results therefore do not indicate a 'low' total number of events for this outcome of interest.

[h]Downgraded again due to very serious imprecision (only three events reported across the studies).

BACKGROUND

Description of the condition

Knee replacement surgery is widely regarded as an established and effective surgical procedure performed for relief of pain from end-stage arthritis (Skou 2016). During knee replacement surgery, joint surfaces are removed and are replaced with artificial components. All of the knee joint surface can be replaced (total knee replacement - TKR), part of the joint can be replaced (partial knee replacement; e.g. unicondylar, patellofemoral), or a redo of an existing knee replacement can be performed (revision knee replacement). TKR is by far the most common type of knee replacement, with more than 106,000 performed in the UK in 2018 (National Joint Registry 2018; Scottish Arthroplasty Project 2019).

A 2010 survey found that 95% of surgeons in the USA use a tourniquet for knee replacement surgery (Zhang 2014), and the UK's National Joint Registry (NJR) reported that 93% of knee replacements were done with a tourniquet in 2003 (National Joint Registry 2004). A UK-based survey conducted in 2016 demonstrated that 90% of surgeons prefer to use a tourniquet when undertaking TKR (Gibbs 2016). This preference is similar to that in other European countries; the Swedish Joint Registry reported that 90% of cases were performed with a tourniquet (The Swedish Knee Arthroplasty Register 2012).

Description of the intervention

A thigh tourniquet is an occlusive device that squeezes the upper leg and restricts distal blood flow. Using a tourniquet may help create a bloodless field during the procedure (Alcelik 2012).

Two broad types of thigh tourniquet are used for TKR surgery.

1. Inflatable/pneumatic: a cuff placed around the thigh is filled with compressed gas. Pressure in the cuff is maintained by a microprocessor and can be adjusted (Kumar 2016).
2. Non-inflatable: a rubber or elasticated cloth ring is placed around the thigh. A device that achieves the required pressure is applied and cannot be adjusted unless it is replaced with a new device (Kumar 2016).

Before the tourniquet is applied, the leg can be elevated or exsanguinated (using a bandage or similar device), to help reduce the amount of pooled blood within the leg (Chiu 2012).

A thigh tourniquet can be used for the duration of the procedure or for part of the procedure (e.g. during cementation of the components only).

How the intervention might work

The tourniquet is designed to apply pressure to the thigh above the internal pressure of local blood vessels (limb occlusion pressure), thereby restricting both arterial and venous blood flow distally (Alcelik 2012; Gibbs 2016).

Why it is important to do this review

The effects of using a tourniquet in knee replacement surgery have already been reported in the following four systematic reviews: Alcelik 2012; Smith 2010; Tai 2011; and Zhang 2014. However, 21 additional randomised controlled trials have since been published: Alexandersson 2019; Ayik 2020; Dong 2019 Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Harston 2015; Huang 2017; Jawhar 2015; Jawhar 2020; Kumar 2015; Liu 2014; Liu 2017; Liu 2017 b; Mori 2016; Ozkunt 2018; Vertullo 2017; Wu 2018; Zhang 2016; Zhou 2017. These newer trials have explored additional outcomes of interest including pain, function, and serious adverse events, and combining data derived from these studies will help to identify the benefits and risks of using a tourniquet.

Potential benefits of using a tourniquet

Surgical field of view

Using a tourniquet may improve the surgical field of view by limiting intraoperative blood loss (Zhang 2014).

Cementation

Most TKR components are cemented in place to hold and stabilise them in the correct position on the bone. Cement, which is initially soft when it is inserted, interdigitates into the porous bone, forming a strong bond with the bone as it sets. Some surgeons believe that using a tourniquet helps reduce bleeding from the porous bone ends and allows the soft cement to bond more effectively, thereby improving long-term survival of the knee implant components (Grewal 1992; Pfitzner 2016).

Blood loss

One previous systematic review showed that intraoperative blood loss was reduced when a tourniquet was used (Alcelik 2012). However, when another group reviewed overall blood loss (Zhang 2014), they found no difference between intervention groups.

Potential risks of using a tourniquet

Pain and function

A tourniquet may cause pain, both during and after surgery (Abdel-Salem 1995). In addition to pain, a tourniquet may cause bruising and swelling of the thigh muscles, which it squeezes. These muscles are important for mobilisation, thus inhibiting postoperative function and recovery.

Venous thromboembolism (VTE)

A tourniquet causes both arterial and venous stasis within the lower leg for the duration that it is inflated (typically over an hour). Thus it is possible that use of a surgical tourniquet might increase the risk of postoperative venous thromboembolism (VTE) (Tai 2011; Wauke 2002; Zhang 2014). Systematic reviews have shown that a tourniquet may increase the risk of VTE (Zhang 2014), although another review found that this increased risk was not statistically significant (Tai 2011).

Systemic emboli

VTE may not be the only thromboembolic risk associated with using a tourniquet. Systemic emboli can occur following deflation of a tourniquet (Berman 1998). Transoesophageal echocardiography has demonstrated shower-like echogenic materials circulating from the lower limbs to the right atrium, ventricle, and pulmonary artery after release of a thigh tourniquet, as well as macroscopic emboli in the central circulation (Berman 1998). As the carotid arteries are the first branches from the aortic arch in a straight-line orientation, some of these clots may enter the cerebral circulation. Transcranial Doppler ultrasound studies show 60% prevalence of echogenic material in the circle of Willis after a tourniquet is

released and have revealed that microemboli can occur even in the absence of a patent foramen ovale (connection between left and right sides of the circulation within the heart) (Sulek 1999). The most likely route for emboli in these circumstances is through the pulmonary capillaries or the opening of other pulmonary vessels (Sulek 1999). The critical time is immediately after release of the tourniquet, when there is potential haemodynamic instability and evidence to suggest a five-fold increase in the amount of embolic material (Huh 2012; Parmet 1998). The presence of cerebral emboli that can cause cerebral damage may explain the higher than expected prevalence of postoperative cognitive deficit following TKR surgery, which in published reports varies from 41% to 75% at seven days to 18% to 45% at three months postoperatively (Deo 2011).

Other effects

Alcelik 2012 concluded that minor complications are more common when a tourniquet is used; similarly, Zhang 2014 showed increased complications, including infection, blister, haematoma, wound oozing, bruising, nerve palsy, and re-operation in the surgery with a tourniquet group.

OBJECTIVES

To determine the benefits and harms of tourniquet use in knee replacement surgery.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised

We included studies in which participants are randomised to intervention groups and studies in which allocation to interventions is quasi-randomised (i.e. not strictly random, for example, by date of birth, hospital record number, or alternation).

Non-randomised

Randomised studies, particularly in the field of this review, are unlikely to include more than 1000 participants. To help improve estimates of potential risks (e.g. adverse events of the intervention, many of which may be rare events (VTE approximately < 5% (Zhang 2014)), we aimed to include observational cohort studies and unselected case series of 1000 or more participants, which include concurrent comparison groups (e.g. published data from joint replacement registries). The minimum sample of 1000 was based on a previous work (Gurung 2015), which recommended this number when risks for rare events are estimated.

To minimise selection bias within non-randomised studies, we aimed to include only studies that use statistical adjustment for baseline case mix (e.g. multi-variable analyses to adjust for age, co-morbidity, and type of knee replacement (total or partial, primary, or revision)).

Types of participants

We included participants who underwent knee replacement surgery for any indication, regardless of age. All types of knee replacement, including total replacement, partial replacement, and revision surgery, were included in this review.

Types of interventions

We included studies of all types of thigh tourniquet (inflatable or non-inflatable) used for the duration or for part of knee replacement surgery. Comparators could be:

1. placebo: this may include a sham tourniquet, for example, one that is applied but is not inflated;
2. no tourniquet; or
3. alternative measures to improve the surgical field of view or to reduce intraoperative blood loss (e.g. this may include tranexamic acid).

Types of outcome measures

Major outcomes

According to the Outcome Measures in Rheumatology (OMERACT) core outcome set (Bellamy 1997), pain, function/disability, global assessment of success, and health-related quality of life are major outcomes. We prioritised them according to previous evidence on the hierarchy of patient-reported outcomes (Juhl 2012).

1. Pain

Measured using mean pain or mean change in pain on a visual analogue scale (VAS), a numerical rating scale, or another scale.

2. Function

Measured with instruments such as Knee Society Score (KSS), Western Ontario and McMaster Universities Arthritis Index (WOMAC), Knee Injury and Osteoarthritis Outcome Score (KOOS), Oxford Knee Score (OKS). We will extract all available function scores and will present total scores in the primary analysis and subscores as additional analyses when available.

3. Global assessment of success

As reported by the participant (e.g. proportion of participants reporting overall successful treatment and participant satisfaction).

4. Health-related quality of life

Measured with instruments such as the 36-Item Short Form Survey (SF-36) or EuroQoL Group Quality of Life Questionnaire based on 5 dimensions (EQ-5D).

5. Serious adverse events (SAEs)

A serious adverse event is an adverse event that fulfils one of more of the following criteria: results in death, is immediately life-threatening, requires hospitalisation or prolongation of existing hospitalisation, or is an important medical condition. We screened studies to report the following SAEs: number of deaths, infection (joint or wound), nerve damage, ischaemia, VTE, systemic embolic events, and re-operation, excluding revisions for implant failure.

6. Cognitive function

Measured with instruments such as Mini-Mental State Examination (MMSE), Oxford Cognitive Screen (OCS), and Montreal Cognitive Assessment (MoCA).

7. Survival of the implant

Measured as revision rate. The preferred marker of implant failure will be revision surgery. The outcome included in this review is revision risk.

We prioritised the major outcomes in numerical order, as given above.

Minor outcomes

Following discussion between the senior review authors, we prioritised the minor outcomes in numerical order as shown below.

1. Blood loss

a. Total blood loss during surgery (intraoperative blood loss)
b. Postoperative blood loss measured from drainage systems and blood transfusion rates
c. Overall blood loss

2. Economic outcomes

a. Resource usage: direct healthcare and societal costs to facilitate a cost-effectiveness analysis
b. Duration of surgery: surgery start and finish times when available
c. Length of hospital stay

3. Implant stability

Validated methods such as radiostereometric analysis (RSA).

4. Adverse events

We report adverse events that are not classified as serious adverse events based on the criteria above.

Timing of outcome assessment

Studies are likely to report the outcomes discussed at several time points. We therefore planned to group these assessments into three categories: short-term (up to and including three months), medium-term (after three months and up to and including 12 months), and long-term follow-up (longer than one year).

The greatest effect of the intervention on pain was likely to be seen in the very early postoperative phase. Therefore we have made day 1 the time point for this primary outcome. We have also reported pain scores at later time points up to six weeks, when we anticipated pain levels would be lower and any differences would be fewer.

The primary time point for SAE, function, health-related quality of life, global assessment of success, and cognitive function is within 12 months of surgery, and the primary time point for revision surgery is any revision surgery performed within the follow-up period of the study. For studies included in this review, it was 24 months.

Search methods for identification of studies

Electronic searches

This current review includes randomised controlled trials (RCTs) published between 1946 and 26 March 2020 and non-randomised studies published between 1946 and 26 March 2020.

We searched the following databases for randomised trials.

1. Cochrane Central Register of Controlled Trials, via Cochrane Library (Appendix 1).
2. OVID MEDLINE, 1946 to 26 March 2020 (Appendix 2).
3. OVID Embase, 1974 to 26 March 2020 (Appendix 3).
4. ClinicalTrials.gov for ongoing trials (Appendix 4).
5. World Heath Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal (www.who.int/ictrp/en/; Appendix 5).

We also searched the following databases for non-randomised studies.

- OVID MEDLINE, 1946 to 26 March 2020 (Appendix 6).
- OVID Embase, 1974 to 26 March 2020 (Appendix 7).

Searching other resources

We checked the reference lists of all primary studies and review articles for additional references.

In addition, we searched the following established joint registry programmes for relevant published reports and used the contacts below to identify any missing joint registry programmes.

Australasia

1. Australian Orthopaedic Association National Joint Replacement Registry (aoanjrr.sahmri.com/)
2. New Zealand National Joint Register (https://nzoa.org.nz/nzoa-joint-registry)

Europe

1. Danish Knee Arthroplasty Register (https://www.sundhed.dk/sundhedsfaglig/kvalitet/kliniske-kvalitetsdatabaser/planlagt-kirugi/knaealloplastikregister/)
2. European Arthroplasty Register (https://www.efort.org/about-us/nore/)
3. Scottish Arthroplasty Project (www.arthro.scot.nhs.uk/)
4. Slovak National Arthroplasty Register (sar.mfn.sk/the-slovak-arthroplasty-register.348.html)
5. Swedish Knee Arthroplasty Register (www.myknee.se/en/)
6. National Joint Registry of England and Wales (www.njrcentre.org.uk/njrcentre/default.aspx)
7. Norwegian Arthroplasty Register (nrlweb.ihelse.net/eng/)
8. Portugese Arthroplasty Register (www.rpa.spot.pt/)
9. RIPO Bologna, Italy (ripo.cineca.it/)
10. Romanian Arthroplasty Register (www.rne.ro/?lang=en)

North America

1. American Joint Replacement Registry (www.ajrr.net/)
2. Canadian Joint Replacement Register (www.cihi.ca/en/types-of-care/specialized-services/joint-replacements/canadian-joint-replacement-registry)
3. Health East Joint Replacement Registry (www.healtheast.org/orthopaedics/registry.html)
4. Kaiser Permanente National Implant Registries (www.kpimplantregistries.org/)

We searched for errata or retractions from included studies published in full text on PubMed (www.ncbi.nlm.nih.gov/pubmed), and we reported in the review the date this was done.

Data collection and analysis

Selection of studies

Two review authors (IA and PW) independently screened titles and abstracts of all studies for potential inclusion that we identified as a result of the search. We coded them as 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve'. After retrieving the full-text study reports/publications, two review authors (IA and PW for RCTs, IA and AC for non-randomised studies) independently screened them and identified studies for inclusion; we also identified and recorded reasons for exclusion of ineligible studies. We resolved any disagreement through discussion, or, if required, we consulted a third review author (MU). We identified and excluded duplicates and collated multiple reports of the same study, so that each study, rather than each report, is the unit of interest in the review. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram and Characteristics of excluded studies section. Search strategies can be seen in the appendices (Appendix 1; Appendix 2; Appendix 3; Appendix 4; Appendix 5; Appendix 6; Appendix 7).

Data extraction and management

We used a data collection form for study characteristics and outcome data that has been piloted on at least one study in the review. One review author (IA) extracted study characteristics from the included studies. A second review author (PW) cross-checked study characteristics for accuracy against the trial report. We extracted the following study characteristics.

1. Methods: study design, total duration of study, details of any 'run-in' period, number of study centres and locations, study setting, withdrawals, and dates of study.
2. Participants: number (N), mean age, age range, sex, disease duration, inclusion criteria, and exclusion criteria.
3. Interventions: type of surgery, number of participants in tourniquet group, and number of participants in comparator group (sham/no tourniquet/other).
4. Outcomes: major and minor outcomes specified and collected, and time points reported.
5. Characteristics of the design of the trial, as outlined in the Assessment of risk of bias in included studies section below.
6. Notes: funding for trial and notable declarations of interest of trial authors.

Two review authors (IA and AC) independently extracted outcome data from the included studies. We extracted the number of events and the number of participants in each treatment group for dichotomous outcomes, and we extracted means and standard deviations and number of participants in each treatment group for continuous outcomes. For non-randomised trials, we aimed to extract adjusted outcome measures.

We aimed to use non-randomised studies to extract outcomes of interest that are rare (e.g. VTE, implant failure rate).

We noted in the Characteristics of included studies table if outcome data were not reported in a usable way, and when data were transformed or estimated from a graph. We resolved disagreements by reaching consensus or by involving a third review author (MU). One review author (IA) transferred data into the Review Manager 5 file (RevMan 2014). We double-checked that data were entered correctly by comparing data presented in the review with data presented in study reports.

Our a priori decision rules to extract data in the event of multiple outcome reporting in trials are as follows.

1. When trialists report both final values and change from baseline values for the same outcome, we extracted change from baseline values.
2. When trialists report both unadjusted and adjusted-for-baseline values for the same outcome, we extracted unadjusted baseline values.
3. When trialists report data analysed based on the intention-to treat (ITT) sample and another sample (e.g. per protocol, as treated), we extracted ITT-analysed data.
4. When trials do not include a measure of overall pain but include one or more other measures of pain, for the purpose of pooling data we combined overall pain with other types of pain in the following hierarchy: unspecified pain, pain at rest, pain with activity, daytime pain.
5. When trialists report multiple pain outcome measures, for the purposes of pooling data we extracted one measure using the following hierarchy: visual analogue scale, numerical or cognitive rating scale, McGill Pain Questionnaire, or another scale.
6. When trialists report multiple measures of function or disability, for the purposes of pooling data we extracted a single measure using the following hierarchy: Oxford Knee Score (OKS), Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Society Score (KSS), Western Ontario and McMaster Universities Arthritis Index (WOMAC), or an other scale.

Assessment of risk of bias in included studies

Randomised studies

Two review authors (IA and PW) independently assessed risks of bias for each study, using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions, version 6.1* (Higgins 2020a). We resolved disagreements by discussion or by consultation with another review author (MU). We assessed risks of bias according to the following domains.

1. Random sequence generation (only for randomised studies).
2. Allocation concealment (only for randomised studies).
3. Blinding of participants and personnel.
4. Blinding of outcome assessment.
5. Incomplete outcome data.
6. Selective outcome reporting.
7. Other potential bias (e.g. discrepancies between groups for co-morbidities that could act as confounding factors, such as clotting disorders; differences in application of co-interventions, such as postoperative rehabilitation).

We graded each potential source of bias as high, low, or unclear, and we provided a quote from the study report together with a justification for our judgement in the 'Risk of bias' table. We summarised risk of bias judgements across different studies for

each of the domains listed. We considered blinding separately for different key outcomes when necessary (e.g. for unblinded outcome assessment, risk of bias for all-cause mortality may be different than for a participant-reported pain scale). We also considered the impact of missing data by key outcomes.

When information on risk of bias relates to unpublished data or correspondence with a trialist, we noted this in the 'Risk of bias' table.

When considering treatment effects, we aimed to take into account the risk of bias for studies that contributed to that outcome.

We presented the figures generated by the 'Risk of bias' tool to provide summary assessments of risks of bias.

Non-randomised studies

We planned to use ROBINS-I (Risk Of Bias In Non-randomised Studies of Interventions), a tool for assessing risk of bias in non-randomised studies (Sterne 2016). This approach involved three stages for each study.

Stage 1

To specify the research question, list confounding domains and co-interventions, and specify the outcomes being examined. Confounding factors that may influence outcome include:

1. co-morbidities such as vascular disease;
2. previous VTE disease;
3. prothrombotic conditions such as malignancy;
4. use and type of VTE prophylaxis (such as low molecular weight heparin, aspirin, or intermittent calf pump);
5. type of implant used;
6. use of cement; and
7. basic participant demographics, including age, body mass index (BMI), and American Society of Anesthesiologists (ASA) grade.

Stage 2

Risk of bias assessment for a specific result.

Stage 3

Overall risk of bias 'triangulated' across all studies. This tool evaluated the following area of bias.

1. Confounding.
2. Selection bias.
3. Bias in measurement classification of interventions.
4. Bias due to deviations in intended interventions.
5. Bias due to missing data.
6. Bias in measurement of outcomes.
7. Bias in selection of the reported result.

Studies would be reported as having low risk of bias, moderate risk of bias, serious risk of bias, or critical risk of bias. A 'no information' category will be used to describe the risk of bias where there is insufficient information to permit a judgement for the study.

Assessment of bias in conducting the systematic review

We conducted the review according to the published protocol and reported any deviations from it in the Differences between protocol and review section of the review.

Measures of treatment effect

We used risk ratios (RRs) with 95% confidence intervals (CIs) to report categorical outcomes. We analysed continuous data as mean differences (MDs) or as standardised mean differences (SMDs), depending on whether the same scale was used to measure an outcome, along with 95% CIs. We then translated the SMD back to a common scale by multiplying SMD by baseline standard deviation (SD) for the control group from the most representative study (Higgins 2020b). We entered data presented as a scale with a consistent direction of effect across studies.

In the Effects of interventions section under Results and in the 'Comments' column of the 'Summary of findings' table, we provide the absolute per cent difference, the relative per cent change from baseline, and the number needed to treat for an additional beneficial outcome (NNTB); we calculated the NNTB only when the outcome showed a clinically significant difference.

For dichotomous outcomes, such as serious adverse events, we calculated the NNTB from the control group event rate and the risk ratio, using the Visual Rx NNT calculator (Cates 2008). We will calculate the NNTB for continuous measures using the Wells calculator (available at the CMSG Editorial office; musculoskeletal.cochrane.org/).

For dichotomous outcomes, we calculated the absolute per cent change from the difference in risks between intervention and control groups using GRADEpro (GRADEpro 2015), and we expressed this as a percentage. For continuous outcomes, we calculated the absolute risk difference as improvement in the intervention group minus improvement in the control group, in the original units.

We calculated the relative per cent change for dichotomous data as the RR minus 1, expressed as a percentage. For continuous outcomes, we calculated the relative difference in change from baseline as the absolute benefit divided by the baseline mean of the control group.

Unit of analysis issues

We anticipated most studies to use a simple parallel-group design. However, if we found any other design (e.g. cluster-randomised), we planned to use generic inverse variance methods to combine data. For analysis, we planned to use details of intraclass correlation coefficients (ICCs) and cluster sizes for trials of this type, if reported effects had not been adjusted for clustering.

When multiple trial arms are reported in a single trial, we included only the relevant arms.

We preferred trials that reported a unit of analysis at the participant level, to maintain independence of the outcome variable. When studies reported outcomes in patients undergoing bilateral total knee replacement surgery, the unit of analysis was presented at a joint level (e.g. each individual knee; Kumar 2015; Liu 2017; Liu 2017 b). For these studies, we extracted outcomes only if they were reported as specifically related to each individual knee (e.g.

pain, function, global assessment of success, SAEs (infection, VTE, re-operation, nerve damage), survival of implant, intraoperative blood loss (per knee), duration of surgery). In these studies, trial authors made direct comparisons between one knee and the other; as a result, outcomes were knee-specific and therefore could be included in the meta-analysis.

Dealing with missing data

We contacted investigators or study sponsors to verify key study characteristics and to obtain missing numerical outcome data when possible (e.g. when a study is identified as an abstract only, when data are not available for all participants). When this was not possible, and when missing data were thought to introduce serious bias, we explored the impact of including such studies in the overall assessment of results by performing a sensitivity analysis**.** We described any assumptions and imputations for handling missing data and we explored the effect of imputation by conducting sensitivity analyses.

For dichotomous outcomes (e.g. number of withdrawals due to adverse events), we calculated the withdrawal rate using the number of participants randomised to the group as the denominator.

For continuous outcomes (e.g. mean change in pain score), we calculated MD or SMD based on the number of participants analysed at that time point. If the number of participants analysed was not presented for each time point, we aimed to use the number of randomised participants in each group at baseline.

When possible, we aimed to compute missing SDs from other statistics such as standard errors, confidence intervals, or P values, according to the methods recommended in the *Cochrane Handbook for Systematic Reviews of Interventions, version 6.1 (* Deeks 2020). If we could not estimate standard deviations, we aimed to impute them (e.g. from other studies in the meta-analysis).

Assessment of heterogeneity

We assessed clinical and methodological diversity in terms of participants, interventions, outcomes, and study characteristics for included studies, to determine whether a meta-analysis was appropriate. We assessed statistical heterogeneity by visually inspecting the forest plot to assess for obvious differences in results between studies, and by using I^2 and Chi^2 statistical tests.

As recommended in the *Cochrane Handbook for Systematic Reviews of Interventions*, *version 6.1* (Deeks 2020), I^2 value of 0% to 40% indicates 'might not be important'; 30% to 60% may represent 'moderate heterogeneity'; 50% to 90% may represent 'substantial heterogeneity'; and 75% to 100% represents 'considerable heterogeneity'. We considered the importance of I^2 to depend on the magnitude and direction of effects and on the strength of evidence for heterogeneity (e.g. P value from Chi^2 test, confidence interval for I^2). If we identified substantial heterogeneity, we reported this and investigated possible causes by following the recommendations provided in Section 9.6 of the *Cochrane Handbook for Systematic Reviews of Interventions, version 6.1 (* Deeks 2020).

Assessment of reporting biases

We aimed to create and examine a funnel plot to explore possible small-study biases. In interpreting funnel plots, we examined the different possible reasons for funnel plot asymmetry, as outlined in Section 13 of the *Cochrane Handbook for Systematic Reviews of Interventions, version 6.1 (* Page 2020), and we related this information to results of the review. If we were able to pool more than 10 trials, we decided to undertake formal statistical tests to investigate funnel plot asymmetry and to follow the recommendations provided in Section 13 of the *Cochrane Handbook for Systematic Reviews of Interventions, version 6.1* (Page 2020). For continuous data, we tested asymmetry by using a weighted linear regression of the standardised mean against its standard error (Egger 1997). For dichotomous data, we used a weighted linear regression based upon the odds ratio against its variance (Harbord 2009). In both cases, we considered a P value below 0.05 as evidence that publication bias was present. We performed analyses using the "meta" R package (Schwarzer 2007).

To assess outcome reporting bias, we checked trial protocols against published reports. For studies published after 1 July 2005, we screened the Clinical Trial Register at the International Clinical Trials Registry Platform of the World Health Organization for the a priori trial protocol (apps.who.int/trialssearch). We evaluated whether selective reporting of outcomes was present.

Data synthesis

We pooled outcomes of clinically and methodologically homogeneous studies, when meaningful, using a random-effects model. We performed analysis using Review Manager 5 (RevMan 2014), and we produced forest plots for all analyses. We aimed to pool outcomes of non-randomised studies only if the studies were clinically homogeneous, using a random-effects model, which allows for different study variances. We aimed to use log-RR data (with corresponding standard errors (SEs) on the log scale) and aimed to pool outcomes using the generic inverse variance method. We aimed to use non-randomised studies to analyse only outcomes that are rare (e.g. VTE, implant failure rate). We planned to assess clinical homogeneity based on participants, interventions (procedures performed with a tourniquet), outcomes (VTE and implant failure), and study characteristics, including study design. Two review authors (IA and PW) determined if at least three of these features are matching between each study, to pool the data.

Subgroup analysis and investigation of heterogeneity

We planned to carry out the following subgroup analyses.

1. Different surgical procedures that may affect outcome (e.g. total versus partial knee replacement, primary versus knee replacement and revision knee replacement).
2. Different types of tourniquet that may affect outcome (e.g. inflatable, non-inflatable).

Types of surgical procedures vary in complexity, and this may impact both the duration of tourniquet use and the risk of complications.

We planned to use the following outcomes in subgroup analyses.

1. Pain.
2. Function.

3. Adverse events.

We planned to use the formal test for subgroup interactions in Review Manager 5 (RevMan 2014), and we used caution in interpreting subgroup analyses, as advised in Section 10 of the *Cochrane Handbook for Systematic Reviews of Interventions, version 6.1* (Deeks 2020).

Sensitivity analysis

If studies differed markedly from most other studies (different outcomes), and if we deemed it necessary to exclude them, we conducted sensitivity analyses to report whether the overall effect changed when these studies were removed.

When we identified sufficient studies, we performed sensitivity analyses to assess the impact of selection bias, performance bias, and detection bias on major outcomes.

Interpreting results and reaching conclusions

We followed the guidelines provided in Chapter 15 of the *Cochrane Handbook for Systematic Reviews of Interventions, version 6.1* when interpreting results (Schunemann 2020b), and we were aware of distinguishing lack of evidence of effect from lack of effect. We based our conclusions only on findings from the quantitative or narrative synthesis of included studies for this review. We avoided making recommendations for practice, and our implications for research suggest priorities for future research and outline remaining uncertainties in this area.

Summary of findings and assessment of the certainty of the evidence

'Summary of findings' table

We created a 'Summary of findings' (SoF) table using the following outcomes:

1. Pain
2. Function
3. Global assessment of success
4. Health-related quality of life
5. Serious adverse events
6. Cognitive function
7. Survival of the implant

The comparison in the SoF table was: *tourniquet versus no tourniquet.*

Two review authors (IA and PW) independently assessed the quality of the evidence. We used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of a body of evidence as it relates to the studies which contribute data to the meta-analyses for the pre-specified outcomes. We used methods and recommendations from Chapter 14 of the *Cochrane Handbook for Systematic Reviews of Interventions, version 6.1* (Schunemann 2020a), and used GRADEpro software to prepare the SoF tables (GRADEpro 2015). We justified all decisions to downgrade the quality of studies using footnotes, and made comments to aid the reader's understanding of the review where necessary.

The planned minimum clinically important difference (MCID) was 1 point or 10% absolute improvement for pain on a VAS (0-10) (Dworkin 2008; Kelly 2001; Wall 2017); 5.3 points or 5.3% absolute improvement in KSS for function (Chean Lee 2017) and 10 points or 10% absolute improvement for health-related quality of life (Karjalainen 2019).

RESULTS

Description of studies

Results of the search

Randomised controlled trials

The database search was performed on March 2020. Results of the search can be seen in Figure 1. The search returned 1290 citations through databases (CENTRAL 539; MEDLINE 340; Embase 411) and a further 150 citations from trial registries (Clinical trials.gov 42; WHO 108). No further citations were obtained from grey literature (e.g. unpublished studies, registry data). After duplicates were removed, title and abstracts were screened for eligibility, leaving 53 full texts for further assessment. In total, 41 studies met the inclusion criteria of this review and were included for further analysis: Abdel-Salem 1995; Aglietti 2000; Alexandersson 2019; Ayik 2020; Clarke 2001; Dong 2019; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Harston 2015; Huang 2017; Jawhar 2015; Jawhar 2020; Juelsgaard 2001; Kato 2002; Kiss 2005; Kumar 2015; Ledin 2012; Li 2008; Li 2009; Liu 2014; Liu 2017; Liu 2017 b; Matziolis 2004; Molt 2014; Mori 2016; Ozkunt 2018; Pfitzner 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Vertullo 2017; Wakankar 1999; Wauke 2002; Wu 2018; Yavarikia 2010; Zhang 2010; Zhang 2016; Zhou 2011; Zhou 2017. Eleven studies were excluded following full-text screening. Reasons for exclusion were:

Figure 1. Study flow diagram: search for randomised controlled trials.

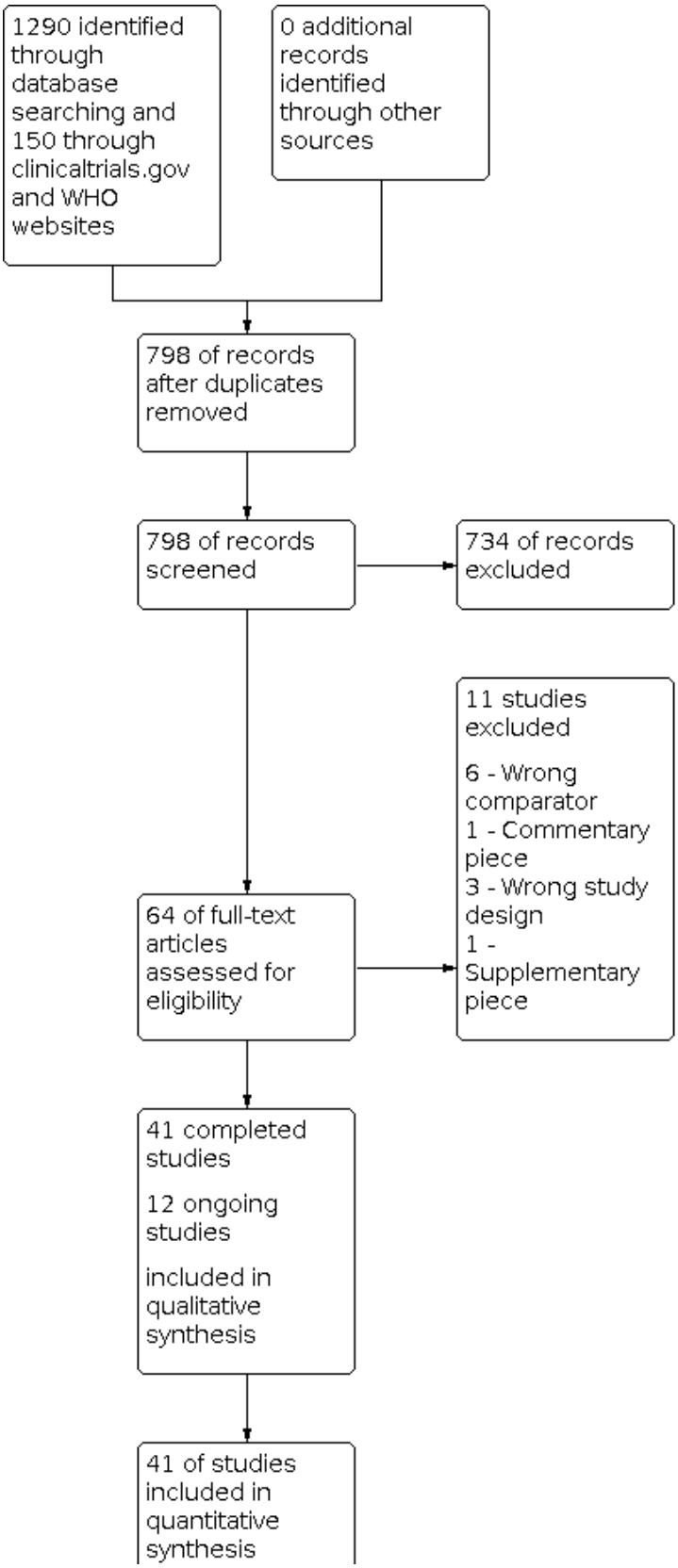
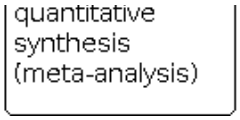


Figure 1. (Continued)



1. wrong comparator (n = 6): Brin 2015; Dennis 2016; Friedrich 1990 Husted 2005; Nielsen 2016; Padala 2004;
2. commentary piece (n = 1): Dorr 2014;
3. wrong study design (n = 3): Harvey 1997; Huang 2015; Nicolaiciuc 2019b; and
4. supplementary piece (n = 1): Mourikis 2009.

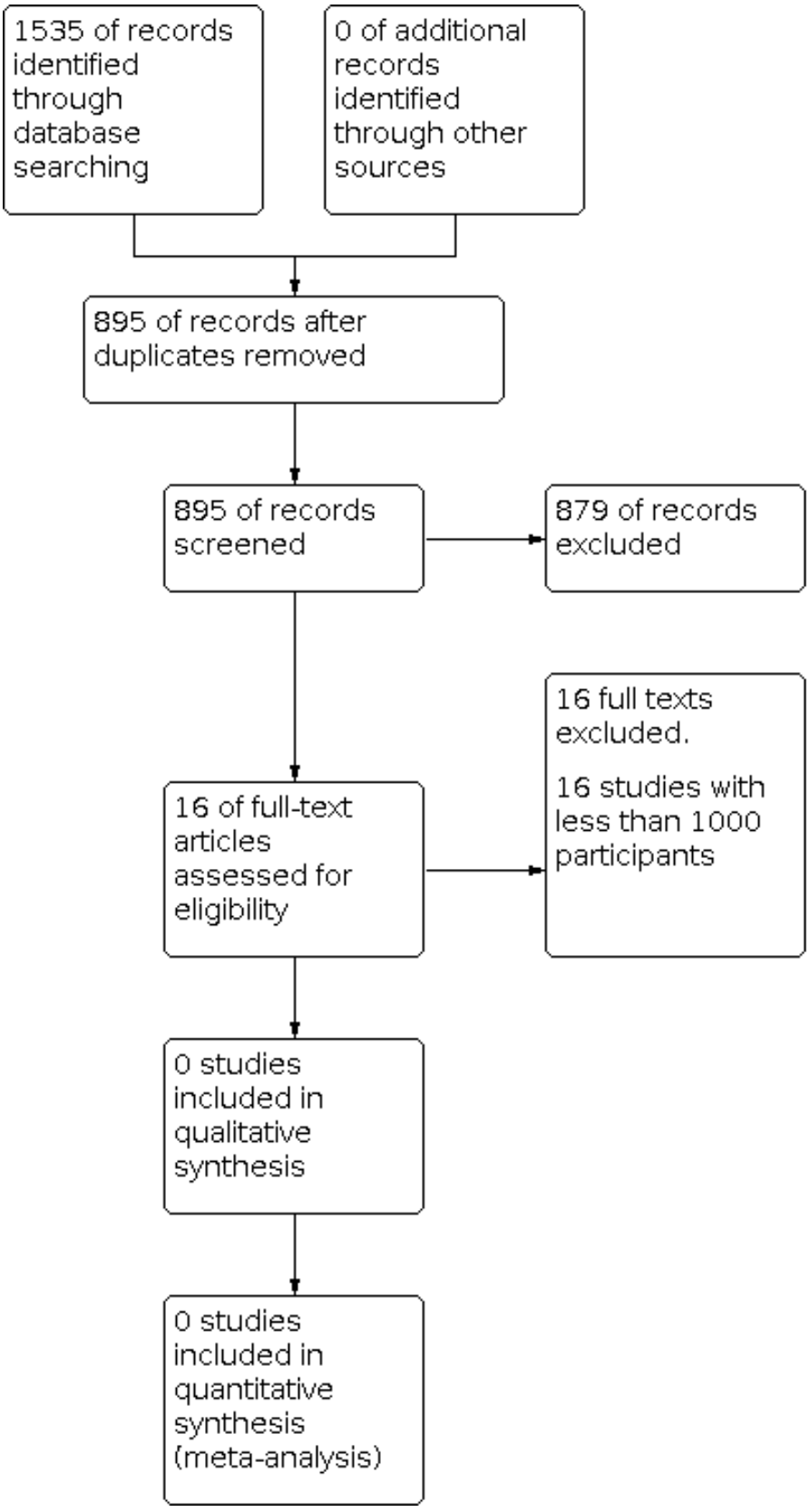
We identified 12 ongoing studies meeting the inclusion criteria and presented their characteristics in the Characteristics of ongoing studies table. All of these studies were in the recruitment phase or the follow-up period: Duncan 2019; Forsmo 2018; Gill 2018; Kange 2017; Liebensteiner 2016; Pei 2016; Pei 2016 (b); Shen 2018; Singh 2019; Vasquez 2019; Wall 2016; Wang 2016.

We identified a study protocol or registration for 13 studies (Alexandersson 2019; Dong 2019; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Harston 2015; Huang 2017; Jawhar 2015; Jawhar 2020; Molt 2014; Wu 2018; Zhou 2017); however, despite contacting authors, we could gather no study protocols nor registrations for 28 studies (Abdel-Salem 1995; Aglietti 2000; Ayik 2020; Clarke 2001; Juelsgaard 2001; Kato 2002; Kiss 2005; Kumar 2015; Ledin 2012; Li 2008; Li 2009; Liu 2014; Liu 2017; Liu 2017 b; Matziolis 2004; Mori 2016; Ozkunt 2018; Pfitzner 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Vertullo 2017; Wakankar 1999; Wauke 2002; Yavarikia 2010; Zhang 2010; Zhang 2016; Zhou 2011).

Non-randomised studies

The search for non-randomised studies was performed in March 2020 and returned 1535 citations through database screening (MEDLINE 656, Embase 879). No further citations were found through searching grey literature. After duplicates were removed, 895 citations underwent title and abstract screening. Once complete, 16 full texts were assessed for eligibility. All 16 were excluded, as the sample size was less than 1000, which was a pre-specified inclusion criterion (Ajnin 2020; Bakker 2019; Barros 2017; Burg 2009; Fakuda 2007; Hasanain 2018; Jarolem 1995; Kheir 2018; Matziolis 2011; Mutlu 2015; Nicolaiciuc 2019; Nishiguchi 2008; Schimizu 2016; Schnettler 2017; Stroh 2011; Zhang 2019). We also searched registry databases; only the Swedish Registry reported tourniquet use but provided no data on SAEs or revision rates. The search results are summarised in Figure 2.

Figure 2. Study flow diagram: search for non-randomised studies.



Included studies

We have provided a full description of the 41 included studies in the Characteristics of included studies table; we have presented a summary of trial features and participant characteristics in Table 1.

Trial design, settings, and characteristics

The 41 included studies were randomised controlled trials (RCTs); no quasi-randomised studies were identified or included. Thirty-seven studies were two-arm single-centre RCTs comparing knee replacement performed with a tourniquet versus without a tourniquet (Abdel-Salem 1995; Aglietti 2000; Alexandersson 2019; Ayik 2020; Dong 2019; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Harston 2015; Jawhar 2015; Jawhar 2020; Juelsgaard 2001; Kato 2002; Kiss 2005; Kumar 2015; Ledin 2012; Li 2008; Li 2009; Liu 2014; Liu 2017; Liu 2017 b; Matziolis 2004; Molt 2014; Mori 2016; Pfitzner 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Vertullo 2017; Wakankar 1999; Wauke 2002; Wu 2018; Zhang 2010; Zhang 2016; Zhou 2011; Zhou 2017). Four studies included three arms in the study design. Clarke 2001 compared surgery performed without a tourniquet versus surgery performed with a tourniquet inflated at low pressure (225 mmHg) and surgery performed with a tourniquet inflated at high pressure (300 mmHg). Huang 2017 compared surgery performed with a tourniquet and multiple doses of tranexamic acid against surgery performed with a tourniquet only and surgery performed without multiple doses of tranexamic acid and with no tourniquet. Ozkunt 2018 and Yavarikia 2010 compared surgery performed without a tourniquet against surgery performed with a tourniquet inflated for the entire procedure and surgery performed with the tourniquet inflated only for implantation of the prosthesis.

With regards to anaesthetic protocol, 14 studies used general anaesthesia for all participants (Abdel-Salem 1995; Clarke 2001; Dong 2019; Huang 2017; Kato 2002; Liu 2014; Liu 2017; Liu 2017 b; Ozkunt 2018; Vandenbussche 2001; Wakankar 1999; Wauke 2002; Zhou 2017; Wu 2018). Eight studies reported using spinal anaesthesia (Aglietti 2000; Ayik 2020; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Ledin 2012; Mori 2016; one study reported using intrathecal anaesthesia (Harston 2015); one study reported using either general anaesthesia or regional anaesthesia with a block (Zhang 2016); and two studies reported using epidural anaesthesia (Kiss 2005; Kumar 2015). Two studies used different methods of anaesthesia between the two groups; one study compared hypotensive epidural anaesthesia in surgery without a tourniquet versus spinal anaesthesia in surgery with a tourniquet (Juelsgaard 2001), and one study compared epinephrine-augmented hypotensive epidural anaesthesia in surgery without a tourniquet versus normotensive epidural anaesthesia in surgery with a tourniquet (Kiss 2005). Fourteen studies did not explicitly state the anaesthetic protocol used (Alexandersson 2019; Jawhar 2015; Jawhar 2020; Li 2008; Li 2009; Matziolis 2004; Molt 2014; Pfitzner 2014; Tai 2012; Tetro 2001; Vertullo 2017; Yavarikia 2010; Zhang 2010; Zhou 2011).

Chemical thromboprophylaxis regimens were started in 25 studies, 14 studies reported using heparin-based anticoagulation (Abdel-Salem 1995; Alexandersson 2019; Ayik 2020; Kiss 2005; Ledin 2012; Li 2009; Molt 2014; Ozkunt 2018; Tetro 2001; Vandenbussche 2001; Wauke 2002; Wu 2018; Yavarikia 2010; Zhang 2010), seven studies reported using rivaroxiban (Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Liu 2017; Liu 2017 b; Zhang 2016; Zhou 2017), and one study used aspirin (Goel 2019). In three studies, the exact method was not clearly stated (Clarke 2001; Huang 2017; Wakankar 1999).

Follow-up in the included studies ranged from within hours of the operation, in Aglietti 2000, Ejaz 2015, Jawhar 2015, and Kato 2002, to two years in Abdel-Salem 1995, Dong 2019, Ejaz 2015 b, Ledin 2012, and Molt 2014.

Six studies reported sources of study funding. Two were supported by institutional grants (Harston 2015; Matziolis 2004), and one was supported by an industrial grant (Liu 2014), Ledin 2012 was supported by a grant from the Swedish Research Council, Wu 2018 was supported by a science and technology department of Sichaun Province Grant, and Zhou 2017 received funding from a health industry special scientific research projects of China grant. The remainder of the studies did not report a source of funding or did not receive any further financial support.

The included studies were carried out in 16 different countries: Australia (Liu 2014; Vertullo 2017), Austria (Kiss 2005), China (Dong 2019; Huang 2017; Li 2008; Li 2009; Liu 2017; Liu 2017 b; Zhang 2010; Zhang 2016; Zhou 2011; Zhou 2017), Denmark (Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Jawhar 2015; Juelsgaard 2001), France (Vandenbussche 2001), Germany (Jawhar 2015; Jawhar 2020; Matziolis 2004; Pfitzner 2014), India (Kumar 2015), Iran (Yavarikia 2010), Italy (Aglietti 2000), Japan (Kato 2002; Mori 2016; Wauke 2002), Kingston (Tetro 2001), Sweden (Alexandersson 2019; Harston 2015; Ledin 2012; Molt 2014), Taiwan (Tai 2012), Turkey (Ayik 2020; Ozkunt 2018), the United Kingdom (Abdel-Salem 1995; Clarke 2001; Wakankar 1999), and the USA (Goel 2019).

Participants

All participants were recruited from a secondary care hospital at which orthopaedic surgeons offered total knee replacement surgery. In total, 2819 participants were allocated to surgery without a tourniquet (n = 1466) or to surgery with a tourniquet (n = 1461). The number of participants per trial ranged from 20 to 199. When studies reported age and body mass index (BMI), mean age in the tourniquet group was 69.0 and mean age in the non-tourniquet group was 68.2. Mean BMI in the tourniquet group was 27.7 and in the non-tourniquet group 27.8. A total of 944 male participants and 1777 female participants were reported in the studies included in this review.

Inclusion criteria were comparable between groups when participants were listed for knee replacement surgery. In most cases, surgery was performed to treat end-stage osteoarthritis; however, in five studies, patients with rheumatoid arthritis were also included (Li 2008; Li 2009; Tetro 2001; Zhang 2016; Zhou 2017).

The main exclusion criteria included a history of diabetes (Abdel-Salem 1995; Ayik 2020; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Li 2008; Li 2009; Liu 2017; Liu 2017 b; Matziolis 2004; Vandenbussche 2001; Wakankar 1999), neurovascular or peripheral vascular disease (Abdel-Salem 1995; Ayik 2020; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Jawhar 2020; Kumar 2015; Li 2008; Li 2009; Liu 2014; Liu 2017; Liu 2017 b; Matziolis 2004; Tai 2012; Tetro 2001; Vertullo 2017; Zhang 2010; Zhang 2016), previous open knee surgery (Aglietti 2000; Alexandersson 2019; Ayik 2020; Clarke 2001; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Harston 2015; Huang 2017; Liu 2017 b; Molt 2014; Vandenbussche 2001; Zhou 2017), neoplastic disease or malignancy (Aglietti 2000;

Jawhar 2015; Jawhar 2020; Ledin 2012; Li 2008; Li 2009; Liu 2017; Molt 2014; Wakankar 1999; Zhang 2010), treatment with anticoagulant medication (Aglietti 2000; Ayik 2020; Clarke 2001; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Huang 2017; Jawhar 2015; Jawhar 2020; Juelsgaard 2001; Liu 2017; Liu 2017 b; Mori 2016; Pfitzner 2014; Wu 2018; Zhou 2017), or coagulation disorder (Aglietti 2000; Jawhar 2015; Jawhar 2020; Kiss 2005; Li 2008; Li 2009; Liu 2017; Matziolis 2004; Mori 2016; Pfitzner 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Wakankar 1999; Yavarikia 2010; Zhang 2010; Zhang 2016; Zhou 2011; Zhou 2017). Patients were also excluded if they had BMI greater than 35 (Alexandersson 2019; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Molt 2014; Wu 2018), American Society of Anesthesiologists (ASA) grade greater than IV (Huang 2017), anaemia (defined as haemoglobin < 10) (Huang 2017; Li 2008; Li 2009; Zhang 2010), known infection within the knee (Jawhar 2020 Liu 2014; Liu 2017; Molt 2014; Tetro 2001; Wu 2018; Zhang 2010), or a history of cardiovascular disease (Dong 2019; Jawhar 2015; Juelsgaard 2001; Kiss 2005; Kumar 2015; Ledin 2012; Li 2009; Liu 2017; Liu 2017 b; Ozkunt 2018; Tai 2012; Wu 2018; Zhou 2017). Fourteen studies excluded participants undergoing bilateral knee surgery (Alexandersson 2019; Dong 2019; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Huang 2017; Ledin 2012; Li 2009; Tetro 2001; Wakankar 1999;Vandenbussche 2001;Zhang 2016;Zhou 2017).

A postoperative antibiotic regimen was clearly provided in 13 studies and regimens were comparable amongst studies (Abdel-Salem 1995; Alexandersson 2019; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Kumar 2015; Ledin 2012; Li 2008; Ozkunt 2018; Wakankar 1999; Yavarikia 2010; Zhang 2016). The duration of illness was unspecified in all studies included in this review. For further details on eligibility criteria and participant characteristics in the included studies, see Characteristics of included studies.

Mean preoperative pain scores were reported in six studies and were comparable between groups. Mean preoperative pain score in the tourniquet group was 6.53 (0.75) and in the non-tourniquet group 6.54 (0.76) in a study by Liu 2017 b. Zhang 2016 reported mean preoperative pain score of 3.87 (1.19) in the tourniquet group and 3.62 (0.91) in the non-tourniquet group; Alexandersson 2019 reported a mean preoperative pain score of 1.84 (2.44) in the tourniquet group and 1.71 (1.93) in the non-tourniquet group; Ayik 2020 reported a mean preoperative pain score of 6 (0.8) in the tourniquet group and 7 (0.75) in the non-tourniquet group; Dong 2019 reported a mean pain score of 2.14 (0.83) in the tourniquet group and 2.22 (0.81) in the non-tourniquet group; and Goel 2019 reported a mean pain score of 5.19 (2.54) in the tourniquet group and 5.74 (2.48) in the non-tourniquet group.

Mean preoperative knee function scores were reported in seven studies and were comparable between the two groups. Huang 2017 reported a mean preoperative Hospital for Special Surgery (HSS) score of 45.1 (11.8) in the surgery with a tourniquet group and 45.9 (11.2) in the surgery without a tourniquet group. This is similar to Zhou 2011, which reported preoperative figures of 47.7 (11.8) and 49.6 (12.3) for the two groups. Three studies reported KSS scores preoperatively: Liu 2014 reported a score of 51.2 (5) in the tourniquet group and 51.3 (4.8) in the non-tourniquet group; Ozkunt 2018 reported a preoperative KSS score of 63 (5.68) in the surgery with a tourniquet group and 82 (6.21) in the non-tourniquet group; and Ayik 2020 reported a mean KSS score of 42 (16) in the tourniquet group and 43 (15) in the non-tourniquet group. Jawhar 2020 reported a mean preoperative OKS score of 39 in the tourniquet group and 40 in the non-tourniquet group. Goel 2019 reported mean preoperative KOOS scores; the mean score for activities of daily living was 50.69 (19.70) in the tourniquet group and 50.59 (17.56) in the non-tourniquet group.

Interventions

Details of interventions are provided in the Characteristics of included studies section.

Number of surgeons

Seventeen studies clearly stated that a single surgeon performed all procedures (Abdel-Salem 1995; Aglietti 2000; Ayik 2020; Huang 2017; Kato 2002; Kumar 2015; Liu 2017; Liu 2017 b; Matziolis 2004; Ozkunt 2018; Pfitzner 2014; Vandenbussche 2001; Vertullo 2017; Zhang 2010; Zhang 2016; Zhou 2017; Wu 2018). In three studies, two surgeons performed all procedures (Goel 2019; Molt 2014; Mori 2016); in two studies, three surgeons performed all procedures (Juelsgaard 2001; Ledin 2012); in one study, four surgeons performed all procedures (Li 2009); and in one study, seven surgeons were responsible for performing all procedures (Alexandersson 2019).

Types of knee replacement

All procedures were primary total knee replacement surgery. None of the included studies reported outcomes in patients undergoing revision or partial knee replacement surgery. Although the types of total knee replacement components differed between studies, all prostheses were implanted following cementation; in most studies, a posterior cruciate retaining implant was used. When reported, seven studies resurfaced the patella in all cases and six studies did not resurface the patella in all cases. All surgery was open surgery performed predominantly via a para-patellar approach.

Tourniquet pressures

Thirty-six studies reported tourniquet pressure in the protocol. Seven studies reported tourniquet pressure of 250 mmHg (Clarke 2001; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Mori 2016; Wu 2018; Yavarikia 2010); ten studies reported tourniquet pressure of 100 mmHg above the patient's systolic blood pressure (Ayik 2020; Dong 2019; Harston 2015; Huang 2017; Kumar 2015; Li 2008; Li 2009; Tai 2012; Wauke 2002; Zhang 2010); three studies reported tourniquet pressure of 125 mmHg above systolic blood pressure (Liu 2017; Liu 2017 b; Tetro 2001; and nine studies reported tourniquet pressure of 300 to 350 mmHg (Alexandersson 2019; Juelsgaard 2001; Kato 2002; Kiss 2005; Liu 2014; Molt 2014; Vandenbussche 2001; Vertullo 2017; Pfitzner 2014). Studies reported tourniquet pressure of 0.8 bar (Aglietti 2000), 360 to 380 mmHg (Jawhar 2015; Jawhar 2020), 275 mmHg (Ledin 2012), 400 mmHg (Matziolis 2004), 13.3 kPa (Zhang 2016, 225 or 300 mmHg (dependent on surgeon preference) (Goel 2019), and twice the systolic blood pressure (Wakankar 1999).

Rehabilitation regimens

Postoperatively, when studies specifically reported rehabilitation regimens, participants were allowed to mobilise under supervision on day 2 in eight studies (Abdel-Salem 1995; Ayik 2020; Clarke 2001; Kiss 2005; Kumar 2015; Li 2009; Liu 2017 b; Vandenbussche 2001) and on day 1 in six studies (Alexandersson 2019; Huang 2017; Tai 2012; Tetro 2001; Yavarikia 2010; Zhou 2011). Continuous passive motion was used in five studies (Abdel-Salem 1995; Kiss 2005; Li 2008; Liu 2017; Vandenbussche 2001).

Outcomes

Major outcomes

Pain

Eighteen studies reported pain scores as an outcome measure. All studies reported pain using a 10-point visual analogue scale (VAS), with higher scores indicating more pain. Eight studies reported pain on the first postoperative day (Abdel-Salem 1995; Dong 2019; Kumar 2015; Li 2008; Liu 2014; Liu 2017; Tai 2012; Alexandersson 2019); six studies reported pain on day 2 (Dong 2019; Kumar 2015; Li 2008; Liu 2017; Pfitzner 2014; Tai 2012); 10 studies reported pain on day 3 (Alexandersson 2019; Dong 2019; Ejaz 2014; Kumar 2015; Ledin 2012; Liu 2014; Liu 2017; Pfitzner 2014; Tai 2012; Zhang 2016); six studies reported pain scores at two weeks (Dong 2019; Kumar 2015; Li 2008; Liu 2017; Tai 2012; Zhang 2016); and seven studies reported pain scores at four to six weeks postoperatively (Alexandersson 2019; Ayik 2020; Goel 2019; Kumar 2015; Liu 2017; Ozkunt 2018; Zhang 2016). One study reported a change in pain score at one and six weeks postoperatively (Wakankar 1999; however, these investigators did not report baseline values. One study reported that pain was collected as an outcome but did not include any data in the results section (Vandenbussche 2001). One study reported pain graphically without any raw values, and we were unable to extract the data (Zhou 2017).

Function

Ten studies reported function scores as an outcome measure (Abdel-Salem 1995;Ayik 2020; Ejaz 2014; Goel 2019; Huang 2017; Jawhar 2020; Liu 2014; Liu 2017 b; Ozkunt 2018; Zhou 2017). One study reported HSS score at 12 months (Abdel-Salem 1995), and two studies reported HSS score at six months (Huang 2017; Zhou 2017). Three studies reported KOOS: one at three months (Goel 2019), and two at 12 months postoperatively (Ejaz 2014; Goel 2019). Two studies reported in the methods that OKS scores will be collected for all participants (Jawhar 2020; Liu 2014; however, for one study, no data were provided in the results section (Liu 2014). Four studies reported KSS score: three at three months (Ayik 2020; Ozkunt 2018; Liu 2017 b), and one at 12 months postoperatively (Liu 2017 b).

Global assessment of success

One study with 100 participants reported global assessment of success in terms of patient satisfaction (Huang 2017). Investigators reported the satisfaction level of participants based on a six-point Likert scale ranging from extremely satisfied to very dissatisfied at discharge and at one, three, and six months after surgery. Results were reported as the number of patients who selected each option at each time point. Goel 2019 reported participant satisfaction based on a VAS at three months and at six months; however, study authors did not report what a 'satisfactory' score was, and so the data were not included in the analysis.

Health-related quality of life

One study with 122 participants reported SF-12 scores at six weeks and at eight months postoperatively (Goel 2019). One study with 99 participants reported EQ-5D index and VAS scores at six weeks, six months, and 12 months (Jawhar 2020; however, we did not pool these data with data from the other study because we could not access standard deviations of the mean scores despite contacting study authors.

Serious adverse events

In all, 21 studies reported serious adverse events as defined in the methods section (Abdel-Salem 1995; Alexandersson 2019; Ejaz 2015 b; Goel 2019; Huang 2017; Jawhar 2020; Kato 2002; Li 2008; Liu 2017; Liu 2017 b; Matziolis 2004; Molt 2014; Mori 2016; Tetro 2001; Vandenbussche 2001; Wakankar 1999; Wauke 2002; Wu 2018; Zhang 2010; Zhang 2016; Zhou 2017). 17 studies reported deep vein thrombosis (DVT) as an SAE (Abdel-Salem 1995; Ejaz 2015 b; Goel 2019; Huang 2017; Jawhar 2020; Li 2008; Liu 2017 b; Molt 2014; Mori 2016; Tetro 2001; Vandenbussche 2001; Wakankar 1999; Wauke 2002; Wu 2018; Zhang 2010; Zhang 2016; Zhou 2017); five reported pulmonary embolism (PE) (Huang 2017; Kato 2002; Mori 2016; Wauke 2002; Wu 2018); one reported incidence of stroke as an SAE (Molt 2014); two reported nerve damage (Matziolis 2004; Vandenbussche 2001); 12 reported infection (Abdel-Salem 1995; Alexandersson 2019; Goel 2019; Huang 2017; Jawhar 2020; Liu 2017; Liu 2017 b; Matziolis 2004; Tetro 2001; Vandenbussche 2001; Wu 2018; Zhou 2017); four reported re-operation for reasons other than revision surgery (Jawhar 2020; Li 2008; Matziolis 2004; Wakankar 1999); and two reported the number of deaths (Molt 2014; Wakankar 1999).

Cognitive function

One study with 129 participants reported MoCA scores at days 1, 2, 3, and 7 postoperatively (Dong 2019). However, investigators reported these data only graphically, and despite contacting them, we were unable to obtain mean and SD values.

Survival of implant

We could not estimate the risk of revision due to the small total number of events. Studies included in this review had follow-up limited to between one day and two years. Two studies with 164 participants reported the risk of revision surgery up to one year (Liu 2017; Liu 2017 b). However, investigators reported only two revisions; all were performed in the group that had total knee replacement with a tourniquet. One study with 50 participants reported risk of revision surgery up to two years (Ledin 2012). However, only one revision was performed, and this took place in the group that had total knee replacement without a tourniquet.

Minor outcomes

Blood loss

Fifteen studies reported intraoperative blood loss (Aglietti 2000; Dong 2019; Ejaz 2015 b; Harston 2015; Huang 2017; Juelsgaard 2001; Kato 2002; Li 2008; Li 2009; Tai 2012; Tetro 2001; Wu 2018; Zhang 2010; Zhang 2016; Zhou 2017), which was measured by volume in the suction tubing and weight of the sponges. Twelve studies reported postoperative blood loss (Aglietti 2000; Huang 2017; Juelsgaard 2001; Li 2008; Li 2009; Liu 2014; Ozkunt 2018; Vandenbussche 2001; Wauke 2002; Wu 2018; Zhang 2010; Zhou 2017), which was measured through volume in the drains. Eighteen studies reported overall blood loss (Abdel-Salem 1995; Aglietti 2000; Dong 2019; Goel 2019; Huang 2017; Juelsgaard 2001; Ledin 2012; Li 2008; Li 2009; Mori 2016; Pfitzner 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Wu 2018; Yavarikia 2010; Zhang 2010; Zhou 2017), which was measured as combined intraoperative and postoperative blood loss or by the formula described in Gross 1983. Seventeen studies reported the number of units of blood transfused to patients in each group (Alexandersson 2019; Clarke 2001; Ejaz 2015 b; Huang 2017; Kiss 2005; Ledin 2012;

Li 2008; Liu 2014; Matziolis 2004; Molt 2014; Ozkunt 2018; Tai 2012; Tetro 2001; Vandenbussche 2001; Wu 2018; Zhang 2016; Zhou 2017); three reported the volume of blood transfused in each group (Juelsgaard 2001; Kato 2002; Yavarikia 2010); nine reported the change in haemoglobin concentration as the change in concentration between the postoperative blood test and the preoperative sample (Alexandersson 2019; Kiss 2005; Li 2008; Matziolis 2004; Tai 2012; Tetro 2001; Yavarikia 2010; Wu 2018; Zhang 2016); and three reported a change in haematocrit concentration between preoperative and postoperative blood samples (Tai 2012; Yavarikia 2010; Zhou 2011).

Economic outcomes

None of the included studies reported resource usage.

Twelve studies reported length of stay measured in days from the date of admission to the date of discharge (Abdel-Salem 1995; Harston 2015; Huang 2017; Ledin 2012; Liu 2014; Molt 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Wu 2018; Zhang 2016; Zhou 2017). Twenty-seven studies reported duration of surgery measured in minutes (Aglietti 2000; Ayik 2020; Dong 2019; Ejaz 2015 b; Goel 2019; Harston 2015; Huang 2017; Jawhar 2015; Kato 2002; Kiss 2005; Ledin 2012; Li 2008; Li 2009; Liu 2014; Liu 2017; Liu 2017 b; Matziolis 2004; Molt 2014; Mori 2016; Tai 2012; Tetro 2001; Vandenbussche 2001; Wauke 2002; Wu 2018; Yavarikia 2010; Zhang 2016; Zhou 2017).

Implant stability

Two studies measured implant stability using radiostereometric (RSA) analysis (Ejaz 2014; Molt 2014). These studies reported maximum total point motion (MTPM) at eight weeks, at six months, at one year, and at two years.

Excluded studies

Randomised studies

Twelve studies were excluded following full-text screening.

Six studies used a study comparator that did not meet our inclusion criteria. Brin 2015 and Dennis 2016 used a tourniquet for a reduced duration as the comparator. Friedrich 1990 used different regimens of tourniquet inflation as a comparator. Husted 2005 compared surgery with a tourniquet inflated in a straight knee versus a tourniquet inflated in a fully flexed knee. Padala 2004 compared surgery with a tourniquet and drains versus surgery without a drain. Nielsen 2016 compared topical versus systemic tranexamic acid application.

Harvey 1997 Huang 2015 and Nicolaiciuc 2019b used a study design that did not meet our inclusion criteria.

Dorr 2014 was a commentary piece.

Mourikis 2009 was a supplementary piece for a study that did not meet our inclusion criteria.

Non-randomised studies

Sixteen non-randomised studies were excluded following full-text screening because they had a sample size less than 1000 (Ajnin 2020; Bakker 2019; Barros 2017; Burg 2009; Fakuda 2007; Hasanain 2018; Jarolem 1995; Kheir 2018; Matziolis 2011; Mourikis 2009; Mutlu 2015; Nicolaiciuc 2019; Nishiguchi 2008; Schimizu 2016; Schnettler 2017; Stroh 2011; Zhang 2019). We also searched registry reports; however, no registry report included data specifically related to tourniquet use and the outcomes of interest in this review.

Further details can be seen in Characteristics of excluded studies.

Ongoing studies

Following our search of trial registries, we identified 12 ongoing studies; for further details on study design, interventions, and outcomes, please see the Characteristics of ongoing studies section.

Risk of bias in included studies

The summary of risk of bias is presented in Figure 3 and Figure 4. Three trials met all methodological criteria for low risk of bias (Alexandersson 2019; Ayik 2020; Huang 2017). The other trials had sources of bias including unclear risk of selection bias, performance bias, and detection bias as blinding was not clearly stated in the methods nor in the protocol. The assessment of each domain of risk of bias for the included studies is summarised in the Characteristics of included studies section.

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

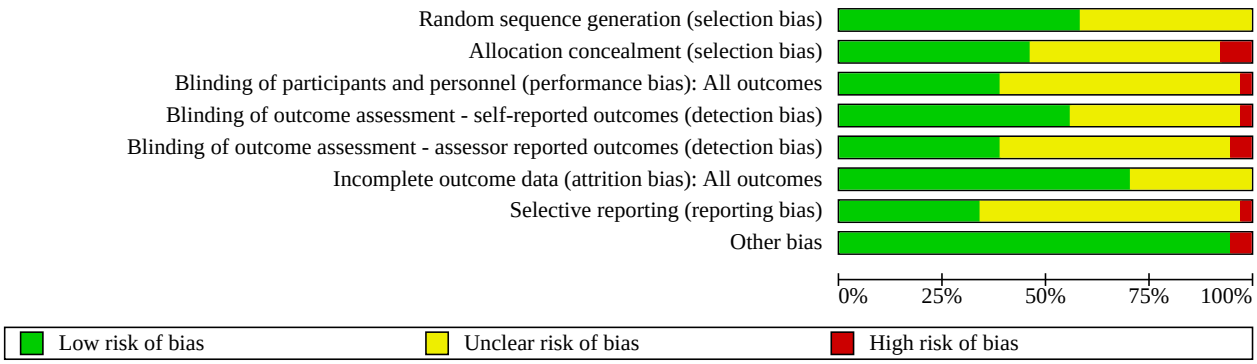


Figure 4. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

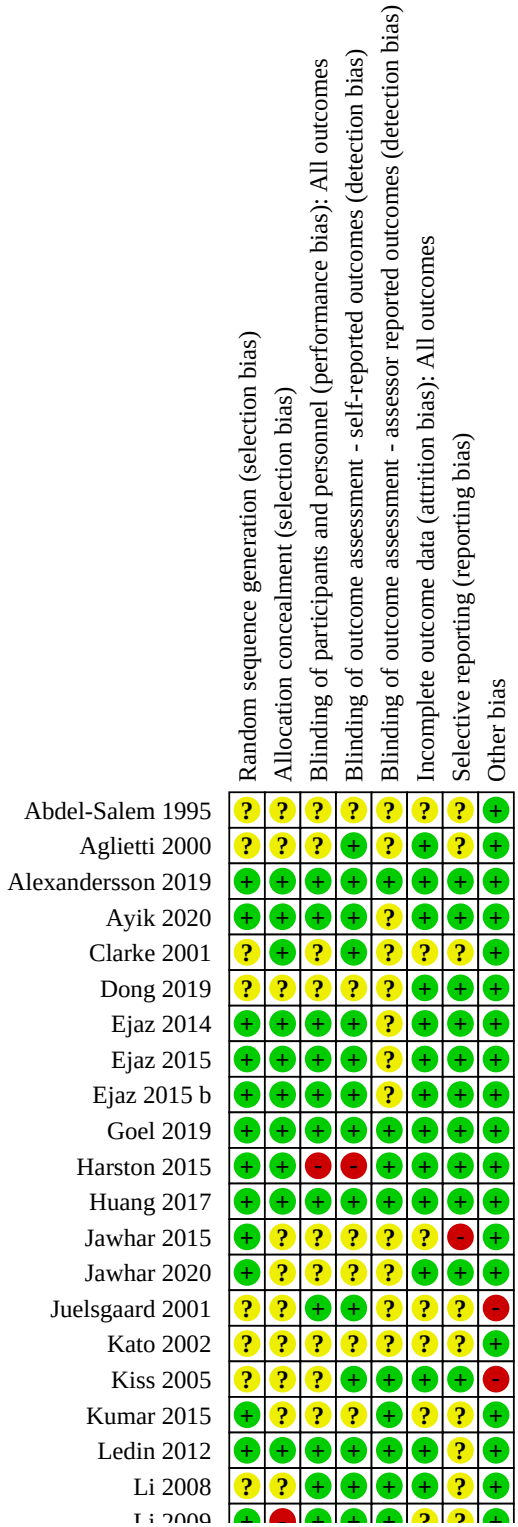
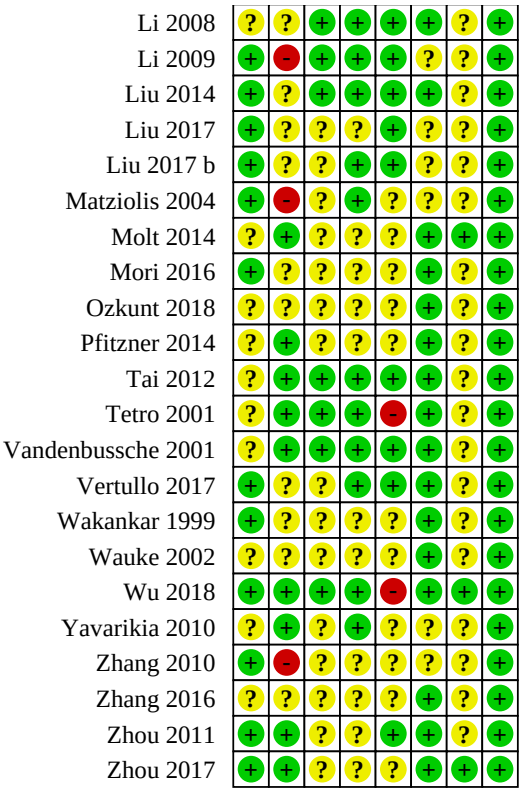


Figure 4. (Continued)



Allocation

Overall, 12 studies (29%) had low risk of selection bias due to both random sequence generation and allocation concealment (Alexandersson 2019; Ayik 2020; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Harston 2015; Huang 2017; Ledin 2012; Wu 2018; Zhou 2011; Zhou 2017). The remainder of studies (29 studies (71%)) had either unclear or high risk of bias for one of the two domains (Abdel-Salem 1995; Aglietti 2000; Clarke 2001; Dong 2019; Jawhar 2015; Jawhar 2020; Juelsgaard 2001; Kato 2002; Kiss 2005; Kumar 2015; Li 2008; Li 2009; Liu 2014; Liu 2017; Liu 2017 b; Matziolis 2004; Molt 2014; Mori 2016; Ozkunt 2018; Pfitzner 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Vertullo 2017; Wakankar 1999; Wauke 2002; Yavarikia 2010; Zhang 2010; Zhang 2016). Further details can be found below.

A total of 24 studies (59%) had low risk of selection bias as the random sequence generation was clearly stated as computer generated (Alexandersson 2019; Goel 2019; Harston 2015; Huang 2017; Jawhar 2015; Jawhar 2020; Liu 2014; Matziolis 2004; Vertullo 2017; Wu 2018; Zhou 2011; Zhou 2017) or block randomised (Ayik 2020; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Ledin 2012), or based on a random number list (Li 2009; Liu 2017; Liu 2017 b; Mori 2016; Wakankar 1999; Zhang 2010) or a coin toss (Kumar 2015). The remaining studies were deemed to have unclear risk due to failure to explicitly state their randomisation method (Abdel-Salem 1995; Aglietti 2000; Clarke 2001; Dong 2019; Juelsgaard 2001; Kato 2002; Kiss 2005; Li 2008; Mori 2016; Ozkunt 2018; Pfitzner 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Wauke 2002; Yavarikia 2010; Zhang 2016).

Nineteen of 41 studies (46%) were deemed to have low risk of selection bias due to allocation concealment. These studies used sealed envelopes (Alexandersson 2019; Ayik 2020; Clarke 2001; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Harston 2015; Huang 2017; Ledin 2012; Molt 2014; Pfitzner 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Wu 2018; Yavarikia 2010; Zhou 2011; Zhou 2017). Three studies were deemed at high risk due to an open random allocation schedule (Li 2009; Matziolis 2004; Zhang 2010); the remainder were deemed to have unclear risk due to failure to explicitly state allocation concealment methods (Abdel-Salem 1995; Aglietti 2000; Dong 2019; Jawhar 2015; Jawhar 2020; Juelsgaard 2001; Kato 2002; Kiss 2005; Kumar 2015; Li 2008; Liu 2014; Liu 2017; Liu 2017 b; Mori 2016; Ozkunt 2018; Vertullo 2017; Wakankar 1999; Wauke 2002; Zhang 2016).

Blinding

Performance bias

Due to the nature of the intervention, it was not possible for studies to blind the surgeons delivering the intervention. Despite this, it is unlikely that surgeons would want or would be able to alter their performance in these studies for main outcomes of interest. Duration of surgery is the most vulnerable outcome in this context. Sixteen studies (39%) were deemed to have low risk of performance bias as participants were blinded to the intervention (Alexandersson 2019; Ayik 2020; Goel 2019; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Huang 2017; Juelsgaard 2001; Ledin 2012; Li 2008; Li 2009; Liu 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Wu 2018). One study (4%) was deemed to have high risk as participants were aware of their treatment intervention (Harston

2015). Remaining studies (57%) were deemed to have unclear risk as blinding was not explicitly stated in the methods (Abdel-Salem 1995; Aglietti 2000; Clarke 2001; Dong 2019; Jawhar 2015; Jawhar 2020; Kato 2002; Kiss 2005; Kumar 2015; Liu 2017; Liu 2017 b; Matziolis 2004; Molt 2014; Mori 2016; Ozkunt 2018; Pfitzner 2014; Vertullo 2017; Wakankar 1999; Wauke 2002; Yavarikia 2010; Zhang 2010; Zhang 2016; Zhou 2011; Zhou 2017).

Detection bias

Detection bias was assessed for both self-reported outcomes (e.g. pain, function, global assessment of success, SAEs) and assessor-reported outcomes (e.g. implant stability, blood loss). Twenty-three (56%) studies were deemed to have low risk of detection bias for self-reported outcomes due to blinding of participants (Aglietti 2000; Alexandersson 2019; Ayik 2020; Clarke 2001; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Huang 2017; Juelsgaard 2001; Kiss 2005; Ledin 2012; Li 2008; Li 2009; Liu 2014; Liu 2017 b; Matziolis 2004; Tai 2012; Tetro 2001; Vandenbussche 2001; Vertullo 2017; Wu 2018; Yavarikia 2010); one study (2%) was deemed to have high risk as participants were not blinded and were responsible for self-reported outcomes (Harston 2015), Seventeen studies (42%) were deemed to have unclear risk of detection bias as how outcomes were reported was not explicitly stated in the methods (Abdel-Salem 1995; Dong 2019; Jawhar 2015; Jawhar 2020; Kato 2002; Kumar 2015; Liu 2017; Molt 2014; Mori 2016; Ozkunt 2018; Pfitzner 2014; Wakankar 1999; Wauke 2002; Zhang 2010; Zhang 2016; Zhou 2011; Zhou 2017).

Sixteen studies (39%) had low risk of detection bias for assessor-reported outcomes (e.g. duration of surgery, length of hospital stay, blood loss, RSA analysis) as the methods clearly stated that outcome assessors were blinded (Alexandersson 2019; Goel 2019; Harston 2015; Huang 2017; Kiss 2005; Kumar 2015; Ledin 2012; Li 2008; Li 2009; Liu 2014; Liu 2017; Liu 2017 b; Tai 2012; Vandenbussche 2001; Vertullo 2017; Zhou 2011). Twenty-three studies (56%) had unclear risk of detection bias for assessor-reported outcomes as it was not explicitly stated in the methods whether outcome assessors were blinded (Abdel-Salem 1995; Aglietti 2000; Ayik 2020; Clarke 2001; Dong 2019; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Jawhar 2015; Jawhar 2020; Juelsgaard 2001; Kato 2002; Matziolis 2004; Molt 2014; Mori 2016; Ozkunt 2018; Pfitzner 2014; Wakankar 1999; Wauke 2002; Yavarikia 2010; Zhang 2010; Zhang 2016; Zhou 2017). Two studies (5%) were deemed to have high risk as outcome assessors were not blinded (Tetro 2001; Wu 2018).

Incomplete outcome data

Twelve (29%) studies were deemed to have unclear risk of attrition bias due to incomplete reporting of attrition (Abdel-Salem 1995; Clarke 2001; Jawhar 2015; Juelsgaard 2001; Kato 2002; Kumar 2015; Li 2009; Liu 2017 Liu 2017 b; Matziolis 2004; Yavarikia 2010; Zhang 2010). These studies did not include CONSORT diagrams and did not clearly state the reasons for missing outcome data. The remainder of studies were deemed as having low risk of attrition bias. In these studies, no outcome data were missing or the missing outcome data were balanced in number across intervention groups with similar reasons for missing data across groups.

Selective reporting

Fourteen (34%) studies were deemed to have low risk of reporting bias (Alexandersson 2019; Ayik 2020; Dong 2019; Ejaz 2014; Ejaz 2015; Ejaz 2015 b; Goel 2019; Harston 2015; Huang 2017; Jawhar 2020; Kiss 2005; Molt 2014; Wu 2018; Zhou 2017). These studies reported all outcomes clearly specified in the trial registration document, protocol, or methods. The remaining studies were deemed to have unclear risk due to insufficient information to permit judgement. These studies were not registered at a clinical trials registry and had no accessible protocol. One study (3%) was deemed to have high risk as outcomes clearly stated in the protocol were not reported in the final study report (Jawhar 2015).

Other potential sources of bias

Two studies (5%) were deemed to have an additional source of bias related to study design. In both these studies, the comparators were different methods of anaesthesia used in the group that had a tourniquet and in the group that did not. Measured outcomes therefore could have been biased by additional differences in interventions other than those of interest. Juelsgaard 2001 investigated surgery with epidural anaesthesia without a tourniquet versus spinal anaesthesia with a tourniquet; blood loss and transfusion rate were the outcomes of interest. Kiss 2005 compared epinephrine-augmented hypotensive epidural anaesthesia without a tourniquet versus normotensive epidural anaesthesia with a tourniquet.

Effects of interventions

See: **Summary of findings 1** Knee replacement with tourniquet compared to knee replacement without tourniquet

The results described were derived when knee replacement with a tourniquet was compared to knee replacement without a tourniquet. None of the included studies reported the effect of tourniquet use on unicondylar or revision knee replacement surgery. All studies reported the effects of an inflatable tourniquet; no studies reported effects of a non-inflatable tourniquet.

Major outcomes

Pain

The primary endpoint for pain was day 1 postoperative pain scores, as this is the point at which the intervention is likely to have the greatest effect. Moderate-quality evidence based on eight studies of 577 participants shows that postoperative pain scores were statistically significantly higher on day 1 postoperatively in the surgery with a tourniquet group compared to the surgery without a tourniquet group (Abdel-Salem 1995; Alexandersson 2019; Dong 2019; Kumar 2015; Li 2008; Liu 2014; Liu 2017; Tai 2012). The mean pain score in the surgery without a tourniquet group was 4.56, and the mean pain score in the surgery with a tourniquet group was 5.81. The mean difference was 1.25 (95% confidence interval (CI) 0.32 to 2.19) (with higher pain scores in the surgery with a tourniquet group). The I^2 value was 94%; the most likely reason for this considerable heterogeneity is clinical diversity, which is explored in the discussion. Further details of the analysis can be seen in Analysis 1.1. Although the mean difference is above the threshold for clinical significance based on a minimum clinically important difference (MCID) for VAS for pain of one (Dworkin 2008; Kelly 2001; Wall 2017), the lower boundary of the confidence interval indicates that the results may or may not be clinical noticeable to the patient. The relative per cent change was 19% worse (3.4% worse to 49% worse) for pain scores in the surgery with a tourniquet group.

Postoperative pain levels can fluctuate and are likely to be higher in the the early postoperative phase; therefore, we analysed the data on different postoperative days.

Six studies involving 394 participants reported pain two days postoperatively (Dong 2019; Kumar 2015; Li 2008; Liu 2014; Pfitzner 2014; Tai 2012). Tourniquet use was associated with a mean difference of 0.37 (95% CI -0.03 to 0.76; I^2 = 48%) for higher pain scores compared to not using a tourniquet; however, this difference was not statistically significant.

Ten studies involving 807 participants reported postoperative pain at day 3 (Alexandersson 2019; Dong 2019; Ejaz 2014; Kumar 2015; Ledin 2012; Liu 2014; Liu 2017; Pfitzner 2014; Tai 2012; Zhang 2016). Using a tourniquet was associated with a significantly higher pain score when compared to not using a tourniquet. A mean difference of 0.78 (95% CI 0.34 to 1.23; I^2 = 87%) was noted for higher pain scores when a tourniquet was used compared to when a tourniquet was not used.

Six studies involving 562 participants reported postoperative pain at two weeks (Dong 2019; Kumar 2015; Li 2008; Liu 2017; Tai 2012; Zhang 2016). Using a tourniquet was associated with a statistically significantly higher postoperative mean pain score when compared to not using a tourniquet (mean difference (MD) 0.32, 95% CI 0.12 to 0.53; I^2 = 72%).

Six studies involving 637 participants reported postoperative pain at the six-week stage (Alexandersson 2019; Goel 2019; Kumar 2015; Liu 2017; Ozkunt 2018; Zhang 2016). There was no significant difference in pain scores between the two groups (MD 0.38, 95% CI -0.48 to 1.23; I^2 = 98%).

Four other studies reported pain as an outcome; however, these data were not included in the pooled results as we could not accurately extract the data from graphical plots, or because raw data were not available despite contact with study authors. Vandenbussche 2001 and Zhou 2017 reported pain scores that were significantly lower in the group without a tourniquet compared to the group with a tourniquet. Wakankar 1999 reported no significant difference between treatment groups. Wu 2018 reported that surgery with a tourniquet was associated with significantly higher pain scores at days 1, 2, and 3 postoperatively. There was no significant difference between the two groups at one month and at six months postoperatively.

Function

Nine studies investigated the effects of tourniquet use on knee function scores (Abdel-Salem 1995; Ayik 2020; Ejaz 2015 b; Goel 2019; Huang 2017; Jawhar 2015; Liu 2017 b; Ozkunt 2018; Zhou 2017). For all reported outcomes measuring function, higher score indicates better function.

Three studies reported change in HSS score. Abdel-Salem 1995 found no difference between the tourniquet group and the control group in HSS at one year postoperatively (mean HHS 23 in the tourniquet group versus 26 in the control group). Huang 2017 reported change in HSS at six months postoperatively with no significant difference between the two groups (mean HSS 45 in the tourniquet group versus 44.7 in the group without a tourniquet). Zhou 2017 reported no significant difference in change in HSS score at six months (mean HSS 43 in the tourniquet group versus 40.2 in the group without a tourniquet).

Liu 2017 b reported 12-month KSS scores and found no significant differences between the two groups. The mean KSS score in the surgery with a tourniquet group was 93.2, and it was 93.3 in the surgery without a tourniquet group. Investigators also found no significant differences in KSS score between the two groups at three months (90.3 in the tourniquet group and 90.2 in the no tourniquet group). Ozkunt 2018 found that using a tourniquet was associated with a significantly lower KSS score at three months compared to not using a tourniquet (mean KSS score in the surgery with a tourniquet group was 63, and it was 82 in the group without a tourniquet; P = 0.02). Ayik 2020 found no difference in KSS scores at three months between the two groups, with a mean KSS score of 79 in the tourniquet group and 76 in the group without a tourniquet.

Ejaz 2015 b reported the change in KOOS score up to 12 months postoperatively between the group with a tourniquet and the group without a tourniquet. These investigators found no significant difference between the two groups at 12 months postoperatively in any of the KOOS domains (pain, symptoms, activities of daily living, sports/recreation, and quality of life). However, at two months postoperatively, the group without a tourniquet was associated with significantly higher KOOS scores in all domains. Goel 2019 found no difference in KOOS scores between the two groups at three months postoperatively. In particular, the KOOS activities of daily living (ADL) mean score was 69.15 in the tourniquet group and 69.06 in the group without a tourniquet.

Four studies involving 425 participants reported three-month patient-reported functional outcome scores (Ayik 2020; Goel 2019; Liu 2017 b; Ozkunt 2018). There was no significant difference in these scores at three months between the two groups. The standardised mean difference between the two groups was a 0.64 lower function score in the tourniquet group (95% CI 1.52 lower to 0.25 higher) compared to the group without a tourniquet (standardised mean difference (SMD) -0.64, 95% CI -1.52 to 0.25; I^2 = 94%) (Analysis 1.2). The mean difference was calculated using a reference standard deviation (SD) from a selected study (Liu 2017 b); the mean difference was found to be 3.07 (95% CI 7.30 lower to 1.2 higher) lower function scores at three months (7.30 to 1.2) in the surgery with a tourniquet group. The absolute difference is 3.07% lower (7.3% lower to 1.2% higher) function scores at three months in the surgery with a tourniquet group. The relative difference is 5.98% (14.2% lower to 2.34% higher) lower function scores in the surgery with a tourniquet group.

Five studies involving 611 participants reported 12-month patient-reported functional outcome scores (Abdel-Salem 1995; Goel 2019; Huang 2017; Liu 2017 b; Zhou 2017). There was no significant difference in these scores at 12 months. The mean score in the tourniquet group was 89.5, and the mean score in the group without a tourniquet was 90.0. The standardised mean difference was 0.06 lower (95% CI 0.22 lower to 0.10 higher; I^2 = 0%) in the surgery with a tourniquet group compared to the group without a tourniquet (Analysis 1.3). The mean difference was translated back from the baseline SD in the control group of a selected paper (Liu 2017 b). The mean difference was found to be 0.29 points worse (1.06 worse to 0.48 better) in the tourniquet group. The absolute difference between the two groups was 0.29% worse for scores in the tourniquet group (1.06% worse to 0.48% better) than for scores in the surgery with a tourniquet group. Relative changes were calculated relative to baseline in the surgery with a tourniquet group (i.e. absolute change (mean difference) divided

by the mean at baseline in the surgery without a tourniquet group) from Liu 2017 b (values were 51.3 on a 0 to 100 point KSS score scale for function). The relative difference was 0.57% worse scores (2.07% worse to 0.94% better) in the surgery with a tourniquet group. The I^2 was reported as 0%, and the evidence was graded as low quality due to risk of bias and imprecision. All patient-reported functional outcome scores included were measured on a 0 to 100 scale, with higher scores indicating better outcomes. Previous studies have demonstrated an MCID of 5.9 for KSS and 5.0 for OKS, respectively (Chean Lee 2017; Clement 2014). Therefore none of the differences in patient-reported function were deemed to be clinically significant, as the minimum difference did not exceed the MCID.

We did not include Ejaz 2015 b in the meta-analysis as no raw data were available despite contact with study authors. We did not include Jawhar 2020 in the meta-analysis as study authors reported OKS and WOMAC scores. Both were different scales from those used for patient-reported functional scores included in the meta-analysis. Jawhar 2020 found no significant difference in OKS or WOMAC scores at six weeks or at six months.

Global assessment of success

Based on a single study, we found no evidence of clinically important between-group differences in the proportion of participants who were satisfied with their treatment. Huang 2017 reported the number of patients satisfied with their procedure at discharge, at one month, at three months, and at six months. We grouped the patients reporting that they were 'very satisfied' or 'extremely satisfied' with their procedure for this review. At three months, 47 out of 50 participants were satisfied with their procedure in the surgery with a tourniquet group and 46 out of 50 participants were satisfied with their procedure in the group without a tourniquet. The risk ratio was 1.02 (95% CI 0.92 to 1.14) (Analysis 1.4).

At six months, there was no significant difference in the number of participants satisfied with their procedure. At six months, 47 out of 50 participants were satisfied with their procedure in the surgery with a tourniquet group and 47 out of 50 participants were satisfied with their procedure in the group without a tourniquet. The risk ratio was 1.0 (95% CI 0.91 to 1.10) (Analysis 1.5). The relative per cent change was 0% (95% CI 10 fewer to 9.4 more) fewer satisfied following surgery with a tourniquet. The evidence was graded as moderate quality and was downgraded due to the low total number of events.

Health-related quality of life

Goel 2019 reported mean SF-12 scores at six months postoperatively. There was no significant difference in SF-12 scores between the two groups. The mean SF-12 mental component score in the tourniquet group was 54.64 (9.33). The mean score in the non-tourniquet group was 1.53 higher (95% CI 0.85 lower to 3.91 higher). This led to an absolute effect of 1.53% better (0.85% worse to 3.91% better) scores in the non-tourniquet group. Evidence was graded as low quality due to risk of bias and imprecision (Analysis 1.7).

There was no significant difference in SF-12 mental component scores at six weeks between the two groups. The mean difference was 2.58 (95% CI -0.09 to 5.25) higher scores in the non-tourniquet group (Analysis 1.6).

Jawhar 2020 reported EQ-5D at six weeks and at six months and found no significant differences between the two groups. The six-week EQ-5D score was 70 in both groups, and the six-month EQ-5D score was 74 in the surgery with a tourniquet group and 75 in the group without a tourniquet. We did not include this in the meta-analysis, as we could not access the standard deviations of mean scores despite contact with authors.

Serious adverse events

Based upon moderate-quality evidence from 21 studies involving 1799 participants, the risk of serious adverse events was significantly greater in the group that had surgery with a tourniquet compared to the group without a tourniquet (risk ratio (RR) 1.73, 95% CI 1.10 to 2.73) (Analysis 1.8) (Abdel-Salem 1995; Alexandersson 2019; Ejaz 2015 b; Goel 2019; Huang 2017; Jawhar 2020; Kato 2002; Li 2008; Liu 2017; Liu 2017 b; Matziolis 2004; Molt 2014; Mori 2016; Tetro 2001; Vandenbussche 2001; Wakankar 1999; Wauke 2002; Wu 2018; Zhang 2010; Zhang 2016; Zhou 2011). The absolute difference was 2.99% (0.29% more to 5.00% more) more SAEs in the surgery with a tourniquet group with a relative difference of 73% (10% more to 173% more) greater risk of SAE in the tourniquet group. The number needed to treat for additional harm (NNTH) is 48 (20 to 345) participants to have surgery with a tourniquet for one SAE. Confidence intervals around absolute risk demonstrate an effect equal or greater than 0.29%, which was deemed to be highly clinically relevant given the seriousness of the outcome.

Study authors consulted with key stakeholders including patients, lay members of the public, and surgeons and concluded that an RR of 1.73 and the precision of this estimate (95% confidence interval 1.1 to 2.73) were highly clinically relevant given the seriousness of the outcome; therefore this evidence was deemed clinically significant. The serious adverse events reported included deep vein thrombosis, pulmonary embolism, infection, re-operation, and mortality. When studies reported more than one SAE, we would include the results from only one SAE, as it is unclear whether one SAE led to the development of another. For example, Wauke 2002 reported two instances of DVT and one of PE in the surgery with tourniquet group. For the purposes of the meta-analysis, we reported this as two SAEs.

Two studies reported mortality at 30 days postoperatively (Molt 2014; Wakankar 1999). Molt 2014 reported that there was one death in the group that had surgery without a tourniquet and no deaths in the group with a tourniquet. Wakankar 1999 reported two deaths in the group without a tourniquet and one death in the tourniquet group. In both these studies, study authors concluded that the cause of mortality was not related to the treatment interventions.

Seventeen studies involving 1575 participants reported the incidence of venous thromboembolic events (VTEs) (pulmonary embolism and deep vein thrombosis) following total knee replacement surgery (Abdel-Salem 1995; Ejaz 2015 b; Goel 2019; Huang 2017; Jawhar 2015; Kato 2002; Li 2008; Liu 2017 b; Molt 2014; Tetro 2001; Vandenbussche 2001; Wakankar 1999; Wauke 2002; Wu 2018; Zhang 2016; Zhang 2010; Zhou 2011). Tourniquet use was associated with significantly higher risk of VTE compared to surgery without a tourniquet (RR 1.95, 95% CI 0.99 to 3.82; I^2 = 0%) (Analysis 1.9).

Sixteen studies involving 1499 participants reported incidences of symptomatic deep vein thrombosis following total knee replacement surgery (Abdel-Salem 1995; Ejaz 2015 b; Goel 2019; Huang 2017; Jawhar 2020; Li 2008; Liu 2017 b; Molt 2014; Tetro 2001; Vandenbussche 2001; Wakankar 1999; Wauke 2002; Wu 2018; Zhang 2016; Zhang 2010; Zhou 2011). Tourniquet use was associated with higher risk of symptomatic DVT; however, this difference was not significant (RR 1.83, 95% CI 0.92 to 3.65; I^2 = 0%). Mori 2016 reported both symptomatic and asymptomatic DVTs. When data from Mori 2016 were combined with data from the sixteen studies reporting symptomatic DVT, a significantly increased risk of DVT was evident in the group having surgery with a tourniquet (RR 2.05, 95% CI 1.35 to 3.13; I^2 = 0%) (Analysis 1.10).

Five studies involving 416 participants reported the incidence of pulmonary embolism following total knee replacement surgery (Huang 2017; Kato 2002; Mori 2016; Wauke 2002; Wu 2018). There was no significant difference in risk of pulmonary embolism between the two groups (RR 4.51, 95% CI 0.49 to 41.81; I^2 = 0%) (Analysis 1.11).

Three studies involving 157 participants reported the incidence of re-operation (without revision of components) following total knee replacement surgery (Li 2008; Matziolis 2004; Wakankar 1999). There was no significant difference in risk of re-operation between the two groups. Reasons for re-operation included revision of a superficial wound disorder and manipulation under anaesthesia to improve flexion and range of motion (RR 1.63, 95% CI 0.61 to 4.34; I^2 = 0%) (Analysis 1.13).

Nine studies involving 846 participants reported the incidence of wound infection following total knee replacement surgery (Abdel-Salem 1995; Goel 2019; Huang 2017; Liu 2017; Liu 2017 b; Matziolis 2004; Tetro 2001; Vandenbussche 2001; Zhou 2011). Tourniquet use was associated with significantly higher risk of developing wound infection when compared to use of control. The authors of these studies did not state whether these were superficial or deep infections, nor did they present the criteria used to diagnose the infection (RR 2.72, 95% CI 1.15 to 6.42; I^2 = 0%) (Analysis 1.12).

Cognitive function

One study involving 122 participants reported MoCA scores at days 1, 2, 3, and 7 postoperatively (Dong 2019). However, data were visible only graphically. We were unable to extract data accurately or to obtain data by contacting study authors. Study authors reported no difference in MoCA scores at day 7 postoperatively between the two groups.

Survival of the implant

Two studies involving 164 participants reported the risk of revision surgery up to one year (Liu 2017; Liu 2017 b), and one study involving 50 participants reported the risk of revision surgery up to two years (Ledin 2012). It is uncertain if knee replacement with a tourniquet has an effect on survival of the implant up to two years (RR 1.44, 95% CI 0.23 to 8.92; I^2 = 0%) (Analysis 1.14). There was an absolute difference of 0.4% more (0.7% lower to 7% more). The relative difference was 44% higher (77% lower to 892% higher) in the surgery with a tourniquet group. This evidence was graded as low quality due to risk of bias and serious imprecision.

Minor outcomes

Blood loss

Intraoperative blood loss

Fifteen studies involving 1187 participants reported intraoperative blood loss in patients who underwent knee replacement surgery with and without a tourniquet (Aglietti 2000; Dong 2019; Ejaz 2015 b; Harston 2015; Huang 2017; Juelsgaard 2001; Kato 2002; Li 2008; Li 2009; Tai 2012; Tetro 2001; Wu 2018; Zhang 2010; Zhang 2016; Zhou 2011). Surgery with a tourniquet was associated with significantly less intraoperative blood loss when compared to the control. The mean difference between the two groups was 147.05 mL (95% CI -190.97 to -103.12; I^2 = 99%) (Analysis 1.16).

Postoperative blood loss

Twelve studies involving 776 participants reported postoperative blood loss in patients who underwent knee replacement surgery with and without a tourniquet (Aglietti 2000; Huang 2017; Juelsgaard 2001; Li 2008; Li 2009; Liu 2014; Ozkunt 2018; Vandenbussche 2001; Wauke 2002; Wu 2018; Zhang 2010; Zhou 2011). Surgery with a tourniquet was associated with significantly greater postoperative blood loss when compared to the control. The mean difference between the two groups was 57.72 mL (95% CI 13.58 to 101.87; I^2 = 93%) (Analysis 1.17).

Overall blood loss

Eighteen studies involving 1500 participants reported overall blood loss in the two treatment groups (Abdel-Salem 1995; Aglietti 2000; Dong 2019; Goel 2019; Huang 2017; Juelsgaard 2001; Ledin 2012; Li 2008; Li 2009; Mori 2016; Pfitzner 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Wu 2018; Yavarikia 2010; Zhang 2010; Zhou 2011). There was no significant difference in overall blood loss among patients who underwent knee replacement surgery with a tourniquet and patients who underwent surgery without a tourniquet. The mean difference was 8.61 mL (95% CI -83.76 to 100.97; 18 studies; I^2 = 96%) (Analysis 1.18).

Blood transfusion risk

Eighteen studies involving 1285 participants reported blood transfusion risk in patients undergoing total knee replacement surgery with and without a tourniquet (Alexandersson 2019; Clarke 2001; Ejaz 2015 b; Huang 2017; Juelsgaard 2001; Kiss 2005; Ledin 2012; Li 2008; Liu 2014; Matziolis 2004; Molt 2014; Ozkunt 2018; Tai 2012; Tetro 2001; Vandenbussche 2001; Wu 2018; Zhang 2016; Zhou 2011). Although the risk of blood transfusion was higher in the tourniquet group compared to the control group, this difference was not significant (RR 1.20, 95% CI 0.86 to 1.67; I^2 = 29%) (Analysis 1.15).

Blood transfusion volume

Two studies reported blood transfusion volume rather than the number of patients receiving a blood transfusion (Kato 2002; Yavarikia 2010). Kato 2002 found that although the transfusion volume was greater in the control group, this difference was not significant (409 mL (150) versus 54 mL (151)). Yavarikia 2010 found no significant difference in blood transfusion volume between the two groups (248 mL (201) versus 239 mL (144 mL)).

Change in haemoglobin

Nine studies involving 713 participants reported change in haemoglobin among patients undergoing knee replacement surgery with and without a tourniquet (Alexandersson 2019; Kiss 2005; Li 2008; Matziolis 2004; Tai 2012; Tetro 2001; Wu 2018; Yavarikia 2010; Zhang 2016). There was no significant difference in change in haemoglobin (g/dL) between the two groups (MD -0.14, 95% CI -0.48 to 0.19; I^2 = 85%) (Analysis 1.19).

Economic outcomes

Duration of surgery

Twenty-seven studies involving 2070 participants reported duration of surgery in patients undergoing knee replacement with a tourniquet and without a tourniquet (Aglietti 2000; Ayik 2020; Dong 2019; Ejaz 2015 b; Goel 2019; Harston 2015; Huang 2017; Jawhar 2015; Kato 2002; Kiss 2005; Ledin 2012; Li 2008; Li 2009; Liu 2014; Liu 2017; Liu 2017 b; Matziolis 2004; Molt 2014; Mori 2016; Tai 2012; Tetro 2001; Vandenbussche 2001; Wauke 2002; Wu 2018; Yavarikia 2010; Zhang 2016; Zhou 2011). Tourniquets were associated with significantly reduced length of surgery when compared to the control. The mean difference was 3.7 minutes less in the surgery with a tourniquet group (95% CI -5.53 to -1.87; I^2 = 82%) (Analysis 1.21).

Length of hospital stay

Twelve studies involving 995 participants reported length of stay for patients undergoing knee replacement surgery with and without a tourniquet (Abdel-Salem 1995; Harston 2015; Huang 2017; Ledin 2012; Liu 2014; Molt 2014; Tai 2012; Tetro 2001; Vandenbussche 2001; Wu 2018; Zhang 2016; Zhou 2011). Surgery with a tourniquet was associated with significantly greater length of hospital stay when compared to surgery without a tourniquet. The mean difference was 0.34 days longer in the surgery with a tourniquet group (95% CI 0.03 to 0.64; I^2 = 78%) (Analysis 1.20).

Adverse events

None of the included studies reported any adverse events additional to those already described in the section on SAEs.

Implant stability

Two studies involving 130 participants assessed implant stability based on maximum total point motion (MTPM; higher values indicating greater implant movement and less stability) using radiostereometric analysis (RSA) (Ejaz 2014; Molt 2014). There was no significant difference in MTPM between the two groups at eight weeks (MD -0.06, 95% CI -0.13 to 0.01), at 12 months (MD 0.05, 95% CI -0.09 to 0.18) and at 24 months (MD 0.06, 95% CI -0.08 to 0.19) (Analysis 1.22; Analysis 1.23; Analysis 1.24).

Sensitivity analysis and assessment of heterogeneity

Heterogeneous study sensitivity analysis

Seven of the included studies were substantially different from the remainder. Huang 2017 compared the effects of tranexamic acid and tourniquet use in knee replacement. Both Juelsgaard 2001 and Kiss 2005 had different types of anaesthesia in in their comparator groups. Juelsgaard 2001 compared hypotensive epidural anaesthesia without a tourniquet versus spinal anaesthesia with a tourniquet. Kiss 2005 compared normotensive epidural anaesthesia with a tourniquet versus hypotensive epidural anaesthesia without a tourniquet. Kumar 2015, Liu 2017, and Liu 2017 b all included participants undergoing bilateral knee replacement surgery, with each knee acting as the unit of analysis. Mori 2016 reported the risk of deep vein thrombosis; however, these investigators performed an ultrasound on all participants, thereby potentially including patients with asymptomatic deep vein thrombosis.

A formal sensitivity analysis was performed by removing each of these studies from the outcomes included in this review.

Pain

With all studies included, the mean difference in day 1 pain scores was 1.25 (95% CI 0.32 to 2.19; I^2 = 94%).

After removal of Liu 2017, the difference between the two groups remained significant. Surgery with a tourniquet was associated with 1.32 (95% CI 0.20 to 2.43; I^2 = 95%) points higher on a 10-point scale.

After removal of Kumar 2015, the difference between the two groups remained significant. Surgery with a tourniquet was associated with 1.18 (95% CI 0.16 to 2.19; I^2 = 95%) points higher on a 10-point scale.

Function

With all studies included, the standardised mean difference for short-term function scores was -0.64 (95% CI -1.52 to 0.25; I^2 = 94%).

Removal of Liu 2017 led to no significant change in the results for short-term function scores. The SMD was -0.93 (95% CI -2.38 to 0.48; I^2 = 96%).

With all studies included, the standardised mean difference for medium-term function scores was -0.06 (95% CI -0.22 to 0.10; I^2 = 0%).

Removal of Liu 2017 led to no significant change in results for medium-term function scores. The SMD was -0.06 (95% CI -0.26 to 0.13; I^2 = 15%). Similarly, removal of Huang 2017 had no significant effect (SMD -0.03, 95% CI -0.2 to 0.14; I^2 = 0%).

Global assessment of success

Huang 2017 was the only study that reported global assessment of success.

Health-related quality of life

None of the above studies reported health-related quality of life.

Serious adverse events

With all studies included, the RR was 1.73 (95% CI 1.10 to 2.73; I^2 = 0%). When studies were removed, there remained a statistically significantly higher risk of SAEs in the group that had surgery with a tourniquet compared to the group that had surgery without a tourniquet. With removal of Huang 2017, the risk was 1.71 (95% CI 1.08 to 2.71; I^2 = 0%). Removal of Liu 2017 led to risk of 1.71 (95% CI 1.08 to 2.71; I^2 = 0%). Removal of Liu 2017 b led to risk of 1.86 (95% CI 1.14 to 3.02; I^2 = 0%). Finally, removal of Mori 2016 led to risk of 1.73 (95% CI 1.1 to 2.73; I^2 = 0%).

When the results of Mori 2016 (included asymptomatic DVTs) were included, the risk of developing a DVT was significantly higher in the

tourniquet group compared to the control group (RR 2.11, 95% CI 1.37 to 3.23; I^2 = 0%) compared to 2.05 (95% CI 1.35 to 3.13; I^2 = 0%) when this study was not included.

Cognitive function

None of the studies above reported cognitive function.

Survival of the implant

With all studies included, the risk ratio was 1.44 (95% CI 0.23 to 8.92; I^2 = 0%). Removal of Liu 2017 and Liu 2017 b led to no change in the overall significance of the results. The risk was 0.99 (95% CI 0.11 to 9.30; I^2 = 0%) when Liu 2017 was removed and 1.00 (95% CI 0.11 to 9.30; I^2 = 0%) when Liu 2017 b was removed.

Outcome analysis, which had 'substantial' or 'considerable' heterogeneity, included 'postoperative pain: day 1', 'postoperative pain: week 2', 'postoperative pain: week 6', 'blood loss: intraoperative', 'blood loss: postoperative', 'blood loss: overall', 'blood loss: change in haemoglobin', 'economic: length of hospital stay', and 'economic: duration of surgery'. The reasons for this heterogeneity are explored in the discussion.

Risk of bias sensitivity analysis

Pain

Selection bias sensitivity analysis

With all studies included, the mean difference in pain scores was 1.25 points (95% CI 0.32 to 2.19; I^2 = 94%) higher for pain scores in the surgery with a tourniquet group. When the seven studies with unclear risk of selection bias were removed (Abdel-Salem 1995; Dong 2019; Kumar 2015; Li 2008; Liu 2014; Liu 2017; Tai 2012), pain scores were still significantly higher in the surgery with a tourniquet group compared to the surgery without a tourniquet group (MD 1.65, 95% CI 0.93 to 2.37).

Performance bias sensitivity analysis

When four studies with unclear risk of performance bias were removed (Abdel-Salem 1995; Dong 2019; Kumar 2015; Liu 2017), pain scores remained significantly higher in the surgery with a tourniquet group (MD 0.79, 95% CI 0.01 to 1.56; I^2 = 66%) compared to a mean difference of 1.25 (95% CI 0.32 to 2.19; I^2 = 94%) when all studies were included.

Detection bias sensitivity analysis

When four studies with unclear risk of detection bias were removed (Abdel-Salem 1995; Dong 2019; Kumar 2015; Liu 2017), pain scores remained significantly higher in the surgery with a tourniquet group (MD 0.79, 95% CI 0.01 to 1.56; I^2 = 66%) compared to a mean difference of 1.25 (95% CI 0.32 to 2.19; I^2 = 94%) when all studies were included.

Function

Selection bias sensitivity analysis

When studies with unclear or high risk of selection bias at 12 months were removed (Abdel-Salem 1995; Liu 2017), there was still no significant difference in function (SMD -0.02, 95% CI -0.24 to 0.2; I^2 = 22%) compared to an SMD of -0.06 (95% CI -0.22 to 0.10; I^2 = 0%) when no studies were excluded.

Performance bias sensitivity analysis

When studies with unclear or high risk of performance bias were removed (Abdel-Salem 1995; Liu 2017; Zhou 2017), there was no significant difference in function at 12 months (SMD -0.13, 95% CI -0.36 to 0.11; I^2 = 0%) compared to an SMD of -0.06 (95% CI -0.22 to 0.10; I^2 = 0%) when no studies were excluded.

Detection bias sensitivity analysis

When studies with unclear or high risk of detection bias were removed (Abdel-Salem 1995; Liu 2017; Zhou 2017), there was no significant difference in function at 12 months (SMD -0.13, 95% CI -0.36 to 0.11; I^2 = 0%) compared to an SMD of -0.06 (95% CI -0.22 to 0.10; I^2 = 0%) when no studies were excluded.

Global assessment of success

Huang 2017 was the only study that reported this outcome. This study did not have unclear or high risk of detection bias, performance bias, or selection bias.

Health-related quality of life

Goel 2019 was the only study that reported this outcome. This study did not have unclear or high risk of detection bias, performance bias, or selection bias.

Serious adverse events

Selection bias sensitivity analysis

When 15 studies with unclear or high risk of selection bias were removed (Abdel-Salem 1995; Jawhar 2020; Kato 2002; Li 2008; Liu 2017; Liu 2017 b; Matziolis 2004; Molt 2014; Mori 2016; Tetro 2001; Vandenbussche 2001; Wakankar 1999; Wauke 2002; Zhang 2010; Zhang 2016), the risk of SAEs between groups was no longer statistically significant (RR 1.64, 95% CI 0.68 to 3.92; I^2 = 0%). When all studies were included, the RR was 1.73 (95% CI 1.10 to 2.73; I^2 = 0%).

Performance bias sensitivity analysis

When 13 studies with unclear or high risk of performance bias were removed (Abdel-Salem 1995; Jawhar 2020; Kato 2002; Liu 2017; Liu 2017 b; Matziolis 2004; Molt 2014; Mori 2016; Wakankar 1999; Wauke 2002; Zhang 2010; Zhang 2016; Zhou 2011), the difference in risk of SAEs between groups was no longer statistically significant (RR 1.78, 95% CI 0.74 to 4.26; I^2 = 0%). This differed from the results when all studies were included, which produced an RR of 1.73 (95% CI 1.10 to 2.73; I^2 = 0%).

Detection bias sensitivity analysis

When 13 studies with unclear or high risk of detection bias were removed (Abdel-Salem 1995; Ejaz 2015 b; Jawhar 2020; Kato 2002; Matziolis 2004; Molt 2014; Mori 2016; Tetro 2001; Wakankar 1999; Wauke 2002; Wu 2018; Zhang 2010; Zhang 2016), the difference in risk between groups was no longer statistically significant (RR 1.40, 95% CI 0.70 to 2.79; I^2 = 0%). Again, this differed from the results when all studies were included, which produced an RR of 1.73 (95% CI 1.10 to 2.73; I^2 = 0%).

Cognitive function

No data for this outcome were collected.

Survival of implant

Selection bias sensitivity analysis

When studies at high or unclear risk of selection bias were removed (Liu 2017; Liu 2017 b), there remained no significant difference in risk of revision surgery between the two groups (RR 0.33, 95% CI 0.01 to 7.81; I^2 = 0%). When all studies were included, the risk of revision surgery was found to be 1.44 (95% CI 0.23 to 8.92; I^2 = 0%).

Performance bias sensitivity analysis

When studies at high or unclear risk of performance bias were removed (Liu 2017; Liu 2017 b), there remained no significant difference in risk of revision surgery between the two groups (RR 0.33, 95% CI 0.01 to 7.81; I^2 = 0%). When all studies were included, the risk of revision surgery was found to be 1.44 (95% CI 0.23 to 8.92; I^2 = 0%).

Detection bias sensitivity analysis

When all studies were included, the risk of revision surgery was found to be 1.44 (95% CI 0.23 to 8.92; I^2 = 0%). No included studies were at high or unclear risk of detection bias.

Publication bias

Publication bias was assessed with the aid of funnel plots for all major outcomes. Funnel plots were symmetrical for postoperative pain, function, and survival of the implant. Formal statistical tests were performed when more than 10 trials were pooled (SAEs, blood loss, duration of surgery, length of hospital stay). There was no statistically significant sign of publication bias for serious adverse events, length of stay, or postoperative and overall blood loss (P > 0.05). There was evidence of publication bias for studies reporting intraoperative blood loss and duration of surgery (P < 0.05). Table 2 shows the results of publication bias testing.

DISCUSSION

Summary of main results

This review includes 41 randomised controlled trials involving 2819 participants, which investigated the effects of tourniquet use on total knee replacement surgery.

Eight studies reporting day 1 postoperative pain scores were included in this review. Moderate-quality evidence shows that surgery with a tourniquet was associated with statistically significantly higher pain scores when compared to surgery without a tourniquet. This difference may or may not be noticeable to patients, as the lower boundary of the confidence interval is below the minimum clinically important difference (MCID) for pain (Dworkin 2008). The evidence was downgraded due to risk of bias, as many studies had high or unclear risk of allocation concealment, blinding, and selection and detection bias. Five studies reported medium-term function scores. Moderate-quality evidence shows that surgery with a tourniquet confers little or no clinically important difference in knee function. Evidence was downgraded due to risk of bias, again because many studies had unclear or high risk of allocation concealment and blinding, leading to potential for selection and detection bias and likely overestimation of the effect. Low-quality evidence suggests that surgery with a tourniquet was associated with little or no clinically important difference in global assessment of success and health-related quality of life. The evidence was downgraded due to risk of bias and imprecision, as the studies included small numbers of participants.

Twenty-one studies reported serious adverse events. Moderate-quality evidence shows that surgery with a tourniquet was probably associated with higher risk of serious adverse events when compared to surgery without a tourniquet. Evidence was downgraded due to risk of bias. Serious adverse events included deep vein thrombosis, pulmonary embolism, infection, and re-operation for reasons other than implant loosening. Surgery with a tourniquet was associated with a significantly higher risk of deep vein thrombosis and infection when compared to surgery without a tourniquet. Studies found that surgery with a tourniquet was not associated with increased risk of pulmonary embolism and re-operation when compared to surgery without a tourniquet.

Very low-quality evidence suggests an uncertain effect of surgery with a tourniquet on risk of revision surgery when compared to surgery without a tourniquet. Evidence was downgraded due to risk of bias and serious imprecision, as total numbers in each arm were low (only three revision surgeries across both arms over two years). No data on cognitive function were extracted.

We also reported minor outcomes in this review, which were not included in our 'Summary of findings' table. This review found that surgery with a tourniquet was not associated with a significant effect on overall blood loss when compared to surgery without a tourniquet. Surgery with a tourniquet was associated with significantly increased length of hospital stay and a reduced duration of surgery when compared to surgery without a tourniquet. Use of a tourniquet was not associated with any meaningful difference in implant stability at two years. Studies reported no difference on radiostereometric analysis (RSA) analysis at eight weeks, at one year, and at two years. RSA analysis was utilised as a surrogate marker of implant stability; all included studies reported implant stability in patients undergoing cemented total knee replacement (TKR). None of the included studies reported any additional adverse events.

A sensitivity analysis was performed when studies that were substantially different from other studies were removed. Removal of these studies led to no difference in overall results for the major outcomes included in this review. When studies with unclear or high risk of bias were removed, there were no differences in the results reported for pain, function, global assessment of success, health-related quality of life, and survival of the implant. However, when these studies were removed, there was no longer a statistically significant difference in the risk of serious adverse events between the two groups.

Overall completeness and applicability of evidence

This review included 41 studies reporting outcomes for participants undergoing primary TKR surgery. Thirty-seven of these studies were single-centre studies that compared surgery with a tourniquet versus surgery without a tourniquet. More than 50% of the studies had high or unclear risk of bias. Reasons for increased risk of bias included unclear surgeon blinding and unclear allocation concealment and randomisation. Studies were conducted in 15 different countries, and all participants had features of osteoarthritis or rheumatoid arthritis requiring TKR. Participants in both groups were similar in terms of mean age, mean body mass index (BMI), gender distribution, and baseline pain and function scores. All included studies reported similar anticoagulation and anaesthetic regimens. Given that the inclusion criteria were similar

across all studies, the results of this review are applicable to similar patients undergoing primary TKR in clinical practice.

Measurement of pain varied across trials, with studies reporting pain from day 1 through six weeks. Our primary endpoint for pain was postoperative day 1, as this was when the intervention had the greatest effect. We also reported pain scores up to six weeks postoperatively. Regarding function, studies used different outcome measures. Given that function scores used similar scales in the same direction, we reported the standardised mean difference between the two groups. No data for cognitive function could be accurately extracted from the studies included in this review; as a result, no conclusions could be reached for this outcome. None of the included studies reported outcomes for patients undergoing revision surgery or unicondylar knee replacement with a tourniquet; therefore these results are not directly applicable to patients in clinical practice.

Many of the included studies reported only the minor outcomes included in this review (e.g. blood loss, economic outcomes). As a result, these studies were included in this review but were not included in the 'Summary of findings' table. This explains why out of 41 studies, only 21 studies were included in the 'Summary of findings' table.

It would have been interesting to explore the relationship between duration of tourniquet use and outcomes; however, the studies included in this review provided insufficient details on duration of tourniquet use and were not designed to measure a dose-response effect.

The included studies did not explore relationships between high- and low-risk patients for deep vein thrombosis (DVT) and surgery with a tourniquet. Twenty-five studies reported regimens for DVT prevention that included use of chemical thromboprophylaxis; however, the remaining studies did not. Therefore, an evidence gap is apparent when the association between DVT and surgery with a tourniquet in high- or low-risk patients and the impact of DVT prevention are explored.

Quality of the evidence

The quality of evidence for the outcomes included in this review was graded ‘high’ to ‘low’ based on the GRADE criteria.

Moderate quality

Pain, function, and serious adverse events were graded as moderate-quality evidence; they were downgraded due to risk of bias. Considerable heterogeneity was noted for pain scores at day 1; however this is likely to be due to differences in the types of anaesthetic and analgesic regimens used and in the exact timing of assessment, all of which led to clinical diversity. Furthermore, the direction of the clinical effect on pain was consistent across all studies and at other time points. We did not downgrade this outcome for inconsistency because the heterogeneity was expected. A random-effects model was used to incorporate heterogeneity amongst studies (Deeks 2020).

Low quality

Health-related quality of life and global assessment of success were graded as low-quality evidence. The reasons for downgrading were risk of bias and imprecision due to low total study numbers.

Very low quality

Implant survival was graded as very low-quality evidence. The reasons for downgrading were risk of bias and serious imprecision due to low total numbers of events in each arm. A total of three revision surgeries were reported across both arms over two years; as a result, the evidence was downgraded twice for imprecision.

Potential biases in the review process

Our review was based on an extensive electronic literature search and a search for unpublished trials; therefore it is unlikely that relevant trials were missing from this review, provided that they were published as full-text articles or were accessible in trial registries (Egger 2003). Two review authors independently selected studies, extracted data, and assessed ‘risk of bias’ to reduce bias and transcription errors. As a result, we believe potential biases were minimised during the review process.

Limitations

Considerable statistical heterogeneity was observed for pain at day 1 (94%). Through consultation with the *Cochrane Handbook for Systematic Reviews of Interventions*, the review authors believe this was secondary to clinical diversity. Although all studies used the same scale to measure outcomes, participants could have experienced differences including in the amount and type of analgesia, the type of anaesthesia, or the duration of tourniquet use. The amount and type of analgesia were not clearly stated amongst the studies. In addition, pain measurements could have been taken at different times of the day, including before or after physiotherapy; this could explain the clinical heterogeneity. Considerable heterogeneity was also noted for knee function at three months; again this could be explained by clinical heterogeneity, as different tools were used to assess function. Medium-term knee function scores presented in the 'Summary of findings' table showed no heterogeneity (Deeks 2020).

There was also heterogeneity in the following minor outcomes - duration of surgery, length of hospital stay, and blood loss - due to methodological differences in study design and in ways each outcome was measured. For example, intraoperative blood loss was measured through suction drainage or by the change in weight of swabs used during the operation. Both of these methods are surrogate measures of intraoperative blood loss, and heterogeneity could influence the final results. Many studies did not report the criteria used for diagnosis of wound infection; this may have differed across the included studies.

We included studies with small total numbers of participants and studies with small total numbers of events, which can cause problems with precision of estimated treatment effects. However, in the absence of large multi-centre trials or registry data, meta-analysis of data from multiple small trials may be the only way to obtain reliable evidence of an effect for rare but serious outcomes.

The impact of the duration of tourniquet use was not measured, as most studies provided insufficient detail to allow this. However, previous research has demonstrated comparable pain scores and knee function scores between surgery with a tourniquet for the whole procedure versus tourniquet used for part of the procedure (Viashya 2018), but findings show that longer duration of tourniquet use is associated with increased risk of complications.

No published registry data reported outcomes following tourniquet use, and we did not attempt to seek unpublished data from registries, as this was beyond the scope of the review.

Publication bias was formally tested using funnel plots and statistical tests. Statistical evidence of publication bias was noted for intraoperative blood loss and duration of surgery. However, a tourniquet by design restricts intraoperative blood flow and therefore intraoperative blood loss. As a result, there are unlikely to be studies that demonstrate a non-significant result for this outcome. It is likely that even if studies reported non-significant results, this would not affect the overall study findings.

Agreements and disagreements with other studies or reviews

Four previous non-Cochrane reviews have been performed, most of which have focused on blood loss with little focus on risk of pain and complications.

Smith 2010 reviewed 15 studies (nine randomised controlled trials (RCTs) and six observational studies) with 991 participants and found that tourniquet use was associated with significantly greater intraoperative blood loss; however, review authors noted no difference in total blood loss or complications.

Tai 2011 included eight RCTs and three prospective studies with 634 participants. Review authors reported that tourniquet use was associated with significantly reduced intraoperative blood loss and increased risk of thromboembolic events (risk ratio (RR) 1.91, 95% confidence interval (CI) 1.05 to 3.49). There was no significant difference in postoperative blood loss or in total blood loss. Tourniquet use was associated with significantly reduced duration of surgery.

Alcelik 2012 reported on 10 RCTs with 493 participants. Review authors reported that tourniquet use was associated with significantly reduced intraoperative and postoperative blood loss. There was no difference in deep vein thrombosis (DVT) or in pulmonary embolism (PE); however, tourniquet use was associated with significantly greater numbers of complications.

Zhang 2014 performed a meta-analysis of 13 RCTs involving 689 participants. Tourniquet use was associated with significantly reduced intraoperative blood loss (weighted mean difference -198.21 mL, 95% CI -279.82 to -116.60) and reduced duration of surgery (weighted mean difference -4.57 minutes, 95% CI -7.59 to -1.56). However there was no significant difference in total blood loss or in blood transfusion rate. Tourniquets were associated with significantly higher risk of thrombotic events (RR 5.0, 95% CI 1.31 to 19.10) and non-thrombotic complications (RR 2.03, 95% CI 1.12 to 3.67).

Our review is the largest to date (41 RCTs; 2819 participants). Our findings are consistent with those of previous reviews for blood loss and duration of surgery. Previous reviews have alluded to greater risk of complications, which is consistent with our finding that risk of serious adverse events is significantly increased when a tourniquet is used. Previous reviews have not reported on pain, patient-reported function, health-reported quality of life, survival of the implant, length of hospital stay, and implant stability, making our review the most comprehensive review completed to date.

AUTHORS' CONCLUSIONS

Implications for practice

Moderate-certainty evidence shows that tourniquet use was probably associated with an increased risk of serious adverse events, little or no difference in function and higher postoperative pain scores; however, the difference in pain may or not be clinically noticeable. Low-certainty evidence shows that surgery with a tourniquet may have little or no effect on health-related quality of life and global assessment of success. Very low-certainty evidence shows that it is uncertain if tourniquet has an effect on implant survival.

When total knee replacement with the aid of a tourniquet continues to be performed, patients should be informed about the potential risks, in particular, potentially increased pain and risk of developing serious adverse events.

In 2018, 106,000 total knee replacements were performed in the UK (National Joint Registry 2018; Scottish Arthroplasty Project 2019). Based on estimates showing that more than 90% of UK surgeons use a tourniquet (Gibbs 2016; National Joint Registry 2004), along with reports of a number needed to treat for additional harmful outcomes (NNTH) of 48, a change in practice could potentially avoid up to 1987 serious adverse events per year in the UK alone.

Implications for research

Large high-quality multi-centre blinded trials including all types of knee replacement surgery and evaluating cognitive function, health-related quality of life, knee function, and resource use would improve the external validity, quality, and range of outcomes assessed in the existing evidence base. Based on moderate-certainty evidence and previous reviews, the risk of serious adverse events following surgery with a tourniquet is probably higher, which is clinically relevant to patients. Further research is unlikely to change this conclusion and will only improve the confidence limits of the effect estimate. Additional studies of higher quality are required to assess the impact of tourniquet use on implant stability or survival and to assess the quality of cementation and revision risk. This could potentially be the main benefit of tourniquet use, which is currently associated with very low-certainty evidence. Prospective registry data may facilitate improved precision in estimating implant survival.

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REFERENCES

References to studies included in this review

Abdel-Salem 1995 *{published data only}*

Abdel-Salam A, Eyres KS. Effects of tourniquet during total knee arthroplasty; a prospective randomised trial. *Journal of Bone and Joint Surgery (Br)* 1995;**77**(2):250-3.

Aglietti 2000 *{published data only}*

Aglietti P, Baldini A, Vena LM, Abbate R, Fedu S, Falciani M. Effect of tourniquet use on activation of coagulation in total knee replacement. *Clinical Orthopaedics and Related Research* 2000;**371**:169-77.

Alexandersson 2019 *{published data only}*

Alexandersson M, Wang EY, Eriksson S. A small difference in recovery between total knee arthroplasty with and without tourniquet use the first 3 months after surgery: a randomized controlled study. *Knee Surgery, Sports Traumatology, Arthroscopy* 2019;**27**:1035-42. [DOI: DOI: 10.1007/s00167-018-5196-8]

Ayik 2020 *{published data only}*

Ayik O, Demirel M, Birisek F, Ersen A, Balci HI, Sahinkaya T, et al. The effects of tourniquet application in total knee arthroplasty on the recovery of thigh muscle strength and clinical outcomes. Journal of Knee Surgery 2020 February 19. doi: 10.1055/s-0040-1701454. Online ahead of print. [DOI: DOI: 10.1055/s-0040-1701454] [PMID: PMID: 32074652]

Clarke 2001 *{published data only}*

Clarke MT, Longstaff L, Edwards D, Rushton N. Tourniquet-induced wound hypoxia after total knee replacement. *Journal of Bone and Joint Surgery (Br)* 2001;**83-B**(1):40-4.

Dong 2019 *{published data only}***https://doi.org/10.1007/s00540-019-02671-z**

Dong J, Min S, He KH, Peng LH, Cao J, Ran W. Effects of the nontourniquet combined with controlled hypotension technique on pain and long-term prognosis in elderly patients after total knee arthroplasty: a randomized controlled study. *Journal of Anaesthesia* 2019;**33**(5):587-93. [DOI: DOI: 10.1007/s00540-019-02671-z] [PMID: PMID: 31428863]

Ejaz 2014 *{published data only}*

Ejaz A, Laursen AC, Kappel A, Laursen MB, Jakobsen T, Rasmussen S, et al. Faster recovery without the use of a tourniquet in total knee arthroplasty. *Acta Orthopaedica* 2014;**85**(4):422-6.

Ejaz 2015 *{published data only}*

Ejaz A, Laursen A, Jakobsen T, Rasmussen S, Nielsen PT, Laursen MB. Absence of a tourniquet does not affect fixation of cemented TKA: a randomised RSA study of 70 patients. *Journal of Arthroplasty* 2015;**30**(12):2128-32.

Ejaz 2015 b *{published data only}*

* Ejaz A, Laursen AC, Kappel A, Jakobsen T, Nielsen PT, Rasmussen S. Tourniquet induced ischaemia and changes in metabolism during TKA: a randomized study using microdialysis. *BMC Musculoskeletal Disorders* 2015;**16**(326):1-8.

Goel 2019 *{published data only}***http://dx.doi.org/10.2106/JBJS.19.00146**

Goel R, Rondon AJ, Syndor K, Blevins K, O'Malley M, Purtill JJ, Austin MS. Tourniquet use does not affect functional outcomes or pain after total knee arthroplasty: a prospective, double-blinded, randomized controlled trial. *Journal of Bone and Joint Surgery* 2019;**101**:1821-8. [DOI: http://dx.doi.org/10.2106/JBJS.19.00146]

Harston 2015 *{published data only}*

* Harsten A, Bandholm T, Kehlet H, Toksvig-Larsen S. Tourniquet versus no tourniquet on knee-extension strength early after fast-track total knee arthroplasty; a randomized controlled trial. *The Knee* 2015;**22**(2):126-30.

Huang 2017 *{published data only}*

* Huang Z, Xie X, Huang Q, Ma J, Shen B, Kraus VB, Pei F. Intravenous and topical tranexamic acid alone are superior to tourniquet use for primary total knee arthroplasty. *Journal of Bone and Joint Surgery (Am)* 2017;**99-A**(24):2053-61.

Jawhar 2015 *{published data only}*

Jawhar A, Hermanns S, Ponelies N, Obertacke U, Roehl H. Tourniquet-induced ischaemia during total knee arthroplasty results in higher proteolytic activities within vastus medialis cells: a randomized clinical trial. *Knee Surgery, Sports Traumatology and Arthroscopy* 2015;**24**(10):3313-21. [DOI: DOI: 10.1007/s00167-015-3859-2]

Jawhar 2020 *{published data only}***https://doi.org/10.1007/s00167-019-05646-5**

Jawhar A, Skeirek D, Stetzelberger V, Kollowa K, Obertacke U. No effect of tourniquet in primary total knee arthroplasty on muscle strength, functional outcome, patient satisfaction and health status: a randomized clinical trial. *Knee Surgery, Sports Traumatology, Arthroscopy* 2020;**28**(4):1045-54. [DOI: DOI: 10.1007/s00167-019-05646-5] [PMID: PMID: 31372679]

Juelsgaard 2001 *{published data only}*

* Juelsgaard P, Larsen UT, Sorensen JV, Madsen F, Soballe K. Hypotensive epidural anaesthesia in total knee replacement without tourniquet: reduced blood loss and transfusion. *Regional Anaesthesia and Pain Medicine* 2001;**26**(2):105-10.

Kato 2002 *{published data only}*

* Kato N, Nakanishi K, Yoshino S, Ogawa R. Abnormal echogenic findings detected by transesophageal echocardiography and cardiorespiratory impairment during total knee arthroplasty with tourniquet. *Anesthesiology* 2002;**97**(5):1123-8.

Kiss 2005 *{published data only}*

* Kiss H, Raffl M, Neumann D, Hutter J, Dorn U. Epinephrine-augmented hypotensive epidural anesthesia replaced tourniquet use in total knee replacement. *Clinical Orthopaedics and Related Research* 2005;**436**:184-9.

Kumar 2015 *{published data only}*

* Kumar N, Yadav C, Singh S, Kumar A, Vaithlingam A, Yadav S. Evaluation of pain in bilateral total knee replacement with and without tourniquet: a prospective randomised control trial. *Journal of Clinical Orthopaedics and Trauma* 2015;**6**:85-8.

Ledin 2012 *{published data only}*

* Ledin H, Aspenberg P, Good L. Tourniquet use in total knee replacement does not improve fixation, but appears to reduce final range of motion. *Acta Orthopaedica* 2012;**83**(5):499-503.

Li 2008 *{published data only}*

* Li B, Qian Q, Wu H, Zhao H, Lin X, Zhu J, Weng W. The use of a pneumatic tourniquet in total knee arthroplasty: a prospective, randomised study. *Chinese Journal of Surgery* 2008;**46**(14):1054-7.

Li 2009 *{published data only}*

* Li B, Wen Y, Wu H, Qian Q, Lin X, Zhao H. The effect of tourniquet use on hidden blood loss in total knee arthroplasty. *International Orthopaedics (SICOT)* 2009;**33**:1263-8.

Liu 2014 *{published data only}*

Liu D, Graham D, Gillies K, Gillies RM. Effects of tourniquet use on quadriceps function and pain in total knee arthroplasty. *Knee Surgery and Related Research* 2014;**26**(4):207-13.

Liu 2017 *{published data only}*

Liu P, Li D-Q, Zhang Y-K, Lu Q-S, Ma L, Bao X-Z. Influence of tourniquet on wound healing in total knee arthroplasty: a randomized and paired clinical trial. *International Journal of Clinical and Experimental Medicine* 2017;**10**(2):3653-60.

Liu 2017 b *{published data only}*

Liu P-L, Li D-Q, Zhang Y-K, Lu Q-S, Ma L, Bao X-Z, et al. Effects of unilateral tourniquet used in patients undergoing simultaneous bilateral total knee arthroplasty. *Orthopaedic Surgery* 2017;**9**(2):180-5.

Matziolis 2004 *{published data only}*

* Matziolis G, Drahn T, Schroder JH, Krocker D, Tuischer J, Perka C. Endothelin-1 is secreted after total knee arthroplasty regardless of the use of a tourniquet. *Journal of Orthopaedic Research* 2004;**23**:392-6.

Molt 2014 *{published data only}*

* Molt M, Harsten A, Toksvig-Larsen S. The effect of tourniquet use on fixation quality in cemented total knee arthroplasty: a prospective randomized clinical controlled RSA trial. *The Knee* 2014;**21**(2):396-401.

Mori 2016 *{published data only}*

* Mori N, Kimura S, Onodera T, Iwasaki N, Nakagawa I, Masuda T. Use of a pneumatic tourniquet in total knee arthroplasty increases the risk of distal deep vein thrombosis: a prospective, randomised study. *The Knee* 2016;**23**(5):887-9.

Ozkunt 2018 *{published data only}*

Ozkunt O, Sariyilmaz K, Gemalmaz HC, Dikici F. The effect of tourniquet usage on cement penetration in total knee arthroplasty. *Medicine (United States)* 2018;**97**(4):e9668. [DOI: DOI: 10.1097/MD.0000000000009668]

Ozkunt O, Sariyilmaz K, Gemalmaz HC, Dikici F. The effect of tourniquet usage on cement penetration in total knee arthroplasty: a prospective randomized study of 3 methods. *Medicine* 2018;**97**(4):1-5.

Pfitzner 2014 *{published data only}*

Pfitzner T, von Ruth P, Voerkelius N, Mayr H, Perka C, Hube R. Influence of the tourniquet on tibial cement mantle thickness in primary total knee arthroplasty. *Knee Surgery, Sports Traumatology, Arthroscopy* 2016;**24**(1):96-101.

Tai 2012 *{published data only}*

Tai T-W, Chang C-W, Lai K-A, Lin C-J, Ynag C-Y. Effects of tourniquet use on blood loss and soft-tissue damage in total knee arthroplasty. *Journal of Bone and Joint Surgery (Am)* 2012;**94-A**(24):2209-15.

Tetro 2001 *{published data only}*

Tetro AM, Rudan JF. The effects of a pneumatic tourniquet on blood loss in total knee arthroplasty. *Canadian Journal of Surgery* 2001;**44**(1):33-8.

Vandenbussche 2001 *{published data only}*

* Vandenbussche E, Duranthon L-D, Couturier M, Pidhorz L, Augereau B. The effect of tourniquet use in total knee arthroplasty. *International Orthopaedics (SICOT)* 2002;**26**(5):306-9.

Vertullo 2017 *{published data only}*

Vertullo CJ, Nagarajan M. Is cement penetration in TKR reduced by not using a tourniquet during cementation? A single blinded, randomized trial. *Journal of Orthopaedic Surgery* 2017;**25**(1):1-7.

Wakankar 1999 *{published data only}*

* Wakankar HM, Nicholl JE, Koka R, D'Arcy JC. The tourniquet in total knee arthroplasty. *Journal of Bone and Joint Surgery (Br)* 1999;**81-B**(1):30-3.

Wauke 2002 *{published data only}*

Wauke K, Nagashima M, Kato N, Ogawa R, Yoshino S. Comparative study between thromboembolism and total knee arthroplasty with or without tourniquet in rheumatoid arthritis patients. *Archives of Orthopaedic and Trauma Surgery* 2002;**122**(8):442-6.

Wu 2018 *{published data only}*

Wu Y, Lu X, Ma Y, Zeng Y, Xiong H, Bao X, et al. Efficacy and safety of limb position on blood loss and range of motion after total knee arthroplasty without tourniquet: a randomized clinical trial. *International Journal of Surgery* 2018;**60**:182-7. [DOI: https://doi.org/10.1016/j.ijsu.2018.11.008]

Yavarikia 2010 *{published data only}*

Yavarikia A, Amjab GG, Davoudpour K. The influence of tourniquet use and timing of its release on blood loss in total knee arthroplasty. *Pakistan Journal of Biological Sciences* 2010;**13**(5):249-52.

Zhang 2010 *{published data only}*

Zhang F-J, Xiao Y, Liu Y-B, Tian X, Gao Z-Q. Clinical effects of applying a tourniquet in total knee arthroplasty on blood loss. *Chinese Medical Journal* 2010;**123**(21):3031-3.

Zhang 2016 *{published data only}*

Zhang Q, Dong J, Gong K, Li X, Zheng S, Wen T. Effects of tourniquet use on perioperative outcome in total knee arthroplasty. *Chinese Journal of Reparative and Reconstructive Surgery* 2016;**30**(4):421-5.

Zhou 2011 *{published data only}*

Zhou W, Liu D-H, Ma G-T, Gong Y-K, Liu J-S. Relationship between pneumatic tourniquet application in total knee arthroplasty and hypercoagulability. *Journal of Clinical Rehabilitative Tissue Engineering Research* 2011;**15**(9):1541-3.

Zhou 2017 *{published data only}*

Zhou K, Ling T, Wang H, Zhou Z, Shen B, Yang J, et al. Influence of tourniquet use in primary total knee arthroplasty with drainage: a prospective randomised controlled trial. *Journal of Orthopaedic Surgery and Research* 2017;**12**(1):1-6.

References to studies excluded from this review

Ajnin 2020 *{published data only}*

Ajnin S, Fernandes R. Reduced length of stay and faster recovery after total knee arthroplasty without the use of tourniquet. *Journal of Clinical Orthopaedics and Trauma* 2020;**11**(1):129-32. [DOI: DOI: 10.1016/j.jcot.2019.08.016] [PMID: PMID: 32002000]

Bakker 2019 *{published data only}*

Bakker SMK, Kosse NM, Crnic S, Scheffer G-J, Stienstra R. Influence of a tourniquet on opioid consumption after local infiltration of analgesia for total knee arthroplasty. *Turkish Journal of Anaesthesiology and Reanimation* 2019;**47**(2):107-11. [DOI: 10.5152/TJAR.2019.30906] [PMID: 31080951]

Barros 2017 *{published data only}*

Barros MFFH, Ribeiro EJC, Dias RG. Blood level changes in total knee arthroplasty with and without a tourniquet. *Revista Brasileira de Ortoped* 2017;**52**(6):725-30. [DOI: 10.1016/j.rboe.2017.10.001] [PMID: 29234658]

Brin 2015 *{published data only}***10.1016/j.arth.2014.11.022**

Brin YS, Feldman V, Ron Gal I, Markushevitch M, Regev A, Stern A. The sterile elastic exsanguination tourniquet vs. the pneumatic tourniquet for total knee arthroplasty. *Journal of Arthroplasty* 2015;**30**(4):595-9. [DOI: 10.1016/j.arth.2014.11.022] [PMID: 25496927]

Burg 2009 *{published data only}***10.1142/s0218957709002286**

Burg A, Dudkiewicz I, Heller S, Salai M, Velkes S. The effects of using a tourniquet in total knee arthroplasty: a study of 77 patients. *Journal of Musculoskeletal Research* 2009;**12**(3):137-42. [DOI: 10.1142/s0218957709002286]

Dennis 2016 *{published data only}***10.1007/s11999-015-4393-8**

Dennis DA, Kittelson AJ, Yang CC, Miner TM, Kim RH, Stevens-Lapsley JE. Does tourniquet use in TKA affect recovery of lower extremity strength and function? A randomized trial. *Clinical Orthopaedic Related Research* 2016;**474**(1):69-77. [DOI: 10.1007/s11999-015-4393-8] [PMID: 26100254]

Dorr 2014 *{published data only}***10.1007/s11999-014-3551-8**

Dorr LD. Reply to letter to the editor. Tourniquet use during cementation only during total knee arthroplasty: a randomized trial. *Clinical Orthopaedic Related Research* 2014;**472**(5):1660-1. [DOI: 10.1007/s11999-014-3551-8] [PMID: 24658898]

Fakuda 2007 *{published data only}***10.1007/s00402-006-0244-0**

Fukuda A, Hasegawa M, Kato K, Shi D, Sudo A, Uchida A. Effect of tourniquet application on deep vein thrombosis after total knee arthroplasty. *Archives of Orthopaedic and Trauma Surgery* 2007;**127**(8):671-5. [DOI: 10.1007/s00402-006-0244-0] [PMID: 17102960]

Friedrich 1990 *{published data only}*

Friedrich LV, White RL, Brundage DM, Kays MB, Friedman RJ. The effect of tourniquet inflation on cefazolin tissue penetration during total knee arthroplasty. *Pharmacotherapy* 1990;**10**(6):373. [PMID: 2287555]

Harvey 1997 *{published data only}***10.1016/s0883-5403(97)90025-5**

Harvey EJ, Leclerc J, Brooks CE, Burke DL. Effect of tourniquet use on blood loss and incidence of deep vein thrombosis in total knee arthroplasty. *Journal of Arthroplasty* 1997;**12**(3):291. [DOI: 10.1016/s0883-5403(97)90025-5] [PMID: 9113543]

Hasanain 2018 *{published data only}***10.1016/j.arth.2018.02.013**

Hasanain MS, Apostu D, Alrefaee A, Tarabichi S. Comparing the effect of tourniquet vs tourniquet-less in simultaneous bilateral total knee arthroplasties. *Journal of Arthroplasty* 2018;**33**(7):2119-24. [DOI: 10.1016/j.arth.2018.02.013] [PMID: 29510953]

Huang 2015 *{published data only}***10.3928/01477447-20150701-06**

Huang Z, Ma J, Zhu Y, Pei F, Yang J, Zhou Z, et al. Timing of tourniquet release in total knee arthroplasty. *Orthopedics* 2015;**38**(7):445-51. [DOI: 10.3928/01477447-20150701-06]

Husted 2005 *{published data only}***10.1016/j.arth.2004.11.016**

Husted H, Toftgaard Jensen T. Influence of the pneumatic tourniquet on patella tracking in total knee arthroplasty: a prospective randomized study in 100 patients. *Journal of Arthroplasty* 2005;**20**(6):694-7. [DOI: 10.1016/j.arth.2004.11.016] [PMID: 16139703]

Jarolem 1995 *{published data only}*

Jarolem KL, Scott DF, Jaffe WL, Stein KS, Jaffe FF, Atik T. A comparison of blood loss and transfusion requirements in total knee arthroplasty with and without arterial tourniquet. *American Journal of Orthopedics* 1995;**24**(12):906-9. [PMID: 8776080]

Kheir 2018 *{published data only}***10.1016/j.arth.2018.06.038**

Kheir MM, Ziemba-Davis M, Dilley JE, Hood MJ, Meneghini RM Jr. Tourniquetless total knee arthroplasty with modern perioperative protocols decreases pain and opioid consumption

in women. *Journal of Arthroplasty* 2018;**33**(11):3455-9. [DOI: 10.1016/j.arth.2018.06.038] [PMID: 30075878]

Matziolis 2011 *{published data only}***0.1007/s00132-010-1727-9**

Matziolis D, Perka C, Hube R, Matziolis G. Influence of tourniquet ischemia on perioperative blood loss after total knee arthroplasty. *Einfluss der Blutleere auf den Perioperativen Blutverlust nach Knietotalendoprothesenimplantation* 2011;**40**(2):178-82. [DOI: 10.1007/s00132-010-1727-9] [PMID: 21246349]

Mourikis 2009 *{published data only}*

Mourikis A, Tsiridis E, Baltopoulos P, Papaioannou N. Inflammatory responses following tourniquet related ischemia/reperfusion in total knee arthroplasty. *Bone and Joint Journal* 2009;**91-B Suppl I**(77):91.

Mutlu 2015 *{published data only}***10.1016/j.ijsu.2015.04.054**

Mutlu S, Guler O, Mutlu H, Karaman O, Duymus TM, Parmaksizoglu AS. Tourniquet use during total knee arthroplasty does not offer significant benefit: a retrospective cohort study. *International Journal of Surgery* 2015;**18**:123-7. [DOI: 10.1016/j.ijsu.2015.04.054] [PMID: 25917205]

Nicolaiciuc 2019 *{published data only}*

Nicolaiciuc S, Probst P, von Eisenhart-Rothe R, Burgkart R, Hube R. Modern total knee arthroplasty (TKA): with or without a tourniquet? *Surgical Technology International* 2019;**35**:336-40. [PMID: 31282982]

Nicolaiciuc 2019b *{published data only}*

Nicolaiciuc S, Probst P, von Eisenhart-Rothe R, Burgkart R, Hube R. Modern total knee arthroplasty (TKA): with or without a tourniquet? *Surgical Technology International* 2019;**10**(35):336-40. [PMID: PMID: 31282982]

Nielsen 2016 *{published data only}***10.2106/JBJS.15.00810**

Nielsen CS, Jans O, Orsnes T, Foss NB, Troelsen A, Husted H. Combined intra-articular and intravenous tranexamic acid reduces blood loss in total knee arthroplasty: a randomized, double-blind, placebo-controlled trial. *Journal of Bone and Joint Surgery (Am)* 2016;**98**(10):835-41. [DOI: 10.2106/JBJS.15.00810] [PMID: 27194493]

Nishiguchi 2008 *{published data only}*

Nishiguchi M, Takamura N, Kono M, Aoyagi K. Estimation of blood loss in total knee arthroplasty with and without tourniquet. *Acta Medica Nagasakiensia* 2008;**53**(4):105-9.

Padala 2004 *{published data only}***10.1055/s-0030-1247143**

Padala PR, Rouholamin E, Mehta RL. The role of drains and tourniquets in primary total knee replacement: a comparative study of TKR performed with drains and tourniquet versus no drains and adrenaline and saline infiltration. *Journal of Knee Surgery* 2004;**17**(1):24-7. [DOI: 10.1055/s-0030-1247143] [PMID: 14971670]

Schimizu 2016 *{published data only}*

Schimizu M, Kubota R, Nasu M, Usami J, Kataoka H, Nagaoka H, et al. The influence of tourniquet during total knee arthroplasty on perioperative blood loss and postoperative complications. *Japanese Journal of Anesthesiology* 2016;**65**(2):131-5. [PMID: PMID: 27017764]

Schnettler 2017 *{published data only}***10.2106/JBJS.16.00750**

Schnettler T, Papillon N, Rees H. Use of a tourniquet in total knee arthroplasty causes a paradoxical increase in total blood loss. *Journal of Bone and Joint Surgery (Am)* 2017;**99**(16):1331-6. [DOI: 10.2106/JBJS.16.00750] [PMID: 28816892]

Stroh 2011 *{published data only}*

Stroh DA, Johnson AJ, Mont MA, Bonutti PM. Excellent clinical outcomes in total knee arthroplasty performed without a tourniquet. *Surgical Technology International* 2011;**21**:189-93. [PMID: PMID: 22504990]

Zhang 2019 *{published data only}*

Zhang Z, Liang J, Zuo X, Liu R, Dang X, Wang K. Effect of pneumatic tourniquet on perioperative blood loss in total knee arthroplasty. *Chinese Journal of Reparative and Reconstructive Surgery* 2019;**33**(6):681-4.

References to ongoing studies

Duncan 2019 *{published data only}*

Duncan S, Jacobs C. Total Knee Replacement With Tourniquet or Aquamantys. Clinicaltrials.gov 20/08/2019. [https://clinicaltrials.gov/ct2/show/NCT04016285?cond=Tourniquet+AND+Knee&draw=3&rank=11]

Forsmo 2018 *{unpublished data only}*

Husby VS, Winther SB, Forsmo S. The Effects of a Tourniquet in Total Knee Arthroplasty. Clinicaltrials.gov 12/0/2018.

Gill 2018 *{unpublished data only}*

Gill S. A Single-Centre, Parallel-Arm, Double-Blind Randomised Trial Evaluating the Effects of Tourniquet Use in Total Knee Arthroplasty on Intraoperative and Postoperative Outcomes. Australia New Zealand Clinical Trial Registry (https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12618000425291) 2018 March 23.

Kange 2017 *{unpublished data only}*

Kang P, Zhao H. The Efficacy of Oral Tranexamic Acid on Blood Loss in Primary Total Knee Arthroplasty With or Without Tourniquet: A Prospective, Randomized, Controlled Trial. Chinese Clinical Trials Registry (http://www.chictr.org.cn/showproj.aspx?proj=22441) 2017 January 11.

Liebensteiner 2016 *{unpublished data only}*

Liebensteiner M. Effect of Tourniquet on UKA. Clinicaltrials.gov. [CLINICALTRIALS.GOV IDENTIFIER: NCT02465684]

Pei 2016 *{unpublished data only}*

Pei F, Xie X. Tourniquet Versus No Tourniquet on Early Rehabilitation and Cement Mantle After Primary Total Knee Arthroplasty Using a Multimodal Blood Management Protocol: A Randomized Controlled Trial. Chinese Clinical Trials Registry (http://apps.who.int/trialsearch/Trial2.aspx?TrialID=ChiCTR-INR-16009769) 2016 July 11.

Pei 2016 (b) *{published data only}*

Pei F, Huang Z. Is Tourniquet Really Necessary When Multiple Uses of Intravenous and Topical Tranexamic Acid Are Applied in Primary Total Knee Arthroplasty: A Prospective Randomised Controlled Trial. World Health Organization International Clinical Trials Registry Platform Search Portal. (http://www.chictr.org.cn/historyversionpuben.aspx?regno=ChiCTR-INR-16008762) 2016 January 7. [CHINESE CLINICAL TRIALS REGISTRY NUMBER: ChiCTR-INR-16008762]

Shen 2018 *{unpublished data only}*

Shen B, Wu Y. Effect of Postoperative Limb Positions on Blood Loss and Range of Motion in Total Knee Arthroplasty Without Tourniquet: A Randomized Controlled Trial. Chinese Clinical Trials Registry (http://www.chictr.org.cn/showproj.aspx?proj=25406) 2018 February 13.

Singh 2019 *{unpublished data only}*

Singh S, Yadav CS. Randomized Controlled Trial for Comparision of Functional Outcome in Total Knee Replacement With Tourniquet and Without Tourniquet. World Health Organization Trials Portal (http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=6135) 2018 May 31.

Vasquez 2019 *{unpublished data only}*

Vazquez AC, Valencia JL. After Surgery Acute Renal Failure Incidence in Total Knee Arthroplasty With and Without Tourniquet. Clinicaltrials.gov (https://clinicaltrials.gov/ct2/show/NCT03795805?term=After+Surgery+Acute+Renal+Failure+Incidence+in+Total+Knee+Arthroplasty+With+and+Without+Tourniquet&draw=2&rank=1) 2019 January 8. [CLINICALTRIALS.GOV IDENTIFIER: NCT03795805]

Wall 2016 *{unpublished data only}*

Wall P. Safety and Feasibility Evaluation of Tourniquets for Total Knee Replacement Study. ISRCTN Registry (http://www.isrctn.com/ISRCTN20873088) 2016 February 17.

Wang 2016 *{unpublished data only}*

Wang G, Zhu Q. Tourniquet Versus No Tourniquet on Rehabilitation After Fast-Track Total Knee Arthroplasty. Chinese Clinical Trials Registry (http://apps.who.int/trialsearch/Trial2.aspx?TrialID=ChiCTR-IIR-16008794) 2016 July 6.

Additional references

Alcelik 2012

Alcelik I, Pollock RD, Sukeik M, Bettany-Saltikov J, Armstrong PM, Fismer P. A comparison of outcomes with and without a tourniquet in total knee arthroplasty: a systematic review and meta-analysis of randomized controlled trials. *Journal of Arthroplasty* 2012;**27**(3):331-40.

Bellamy 1997

Bellamy N, Kirwan J, Boers M, Brooks P, Strand V, Tugwell P, et al. Recommendations for a core set of outcome measures for future phase III clinical trials in knee, hip, and hand osteoarthritis. Consensus development at OMERACT III. *Journal of Rheumatology* 1997;**24**(4):799-802. [PMID: 9101522]

Benjamin 2016

Benjamin S, Warwick D. Venous thromboembolism after total knee replacement or total hip replacement: what can be learnt from root-cause analysis? *Annals of the Royal College of Surgeons England* 2016;**98**(8):538-42. [DOI: doi: 10.1308/rcsann.2016.0202]

Berman 1998

Berman AT, Parmet JL, Harding SP, Israelite CL, Chandrasekaran K, Horrow JC, et al. Emboli observed with use of transesophageal echocardiography immediately after tourniquet release during total knee arthroplasty with cement. *Journal of Bone and Joint Surgery (Am)* 1998;**80**(3):389-96.

Cates 2008 [Computer program]

Visual Rx. Version 3. Dr Christopher Cates EBM website. www.nntonline.net, 2008.

Chean Lee 2017

Chean Lee W, Kwan YH, Chong HC, Yeo SJ. The minimal clinically important difference for Knee Society Clinical Rating System after total knee arthroplasty for primary osteoarthritis. *Knee Surgery, Sports Traumatology, Arthroscopy* 2017;**25**(11):3354-9. [DOI: https://doi.org/10.1007/s00167-016-4208-9]

Chiu 2012

Chiu FY, Hung SH, Chuang TY, Chiang SC. The impact of exsanguination by Esmarch bandage on venous hemodynamic changes in total knee arthroplasty - a prospective randomized study of 38 knees. *Knee* 2012;**19**(3):213-7. [DOI: DOI: 10.1016/j.knee.2011.03.005]

Clement 2014

Clement ND, Macdonal D, Simpson AHRW. The minimal clinically important difference in Oxford Knee score and Short Form 12 score after total knee arthroplasty. *Knee Surgery, Sports Traumatology, Arthroscopy* 2014;**22**(8):1933-9. [DOI: https://doi.org/10.1007/s00167-013-2776-5]

Deeks 2020

Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 10. Analysing data and undertaking meta-analyses. In: Cochrane Handbook for Systematic Reviews of Interventions. Version 6.1. The Cochrane Collabroation, 2020.

Deo 2011

Deo H, West G, Butcher C, Lewis P. The prevalence of cognitive dysfunction after conventional and computer-assisted total knee replacement. *Knee* 2011;**18**(2):117-20.

Dworkin 2008

Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *Journal of Pain* 2008;**9**(2):105-21.

Egger 1997

Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *British Medical Journal* 1997;**315**:629-34.

Egger 2003

Egger M, Juni P, Bartlett C, Holenstein F, Stern J. How important are comprehensive literature searches and the assessment of trial quality in systematic reviews? Empirical study. *Health Technology Assessment* 2003;**7**(1):1-76.

Gibbs 2016

Gibbs V, Price A, Wall PDH, SAFE-TKR Study Group. Surgical tourniquet use in total knee replacement surgery: a survery of BASK members. *Knee* 2016;**23**(4):III-IV.

GRADEpro 2015 [Computer program]

McMaster University (developed by Evidence Prime, Inc) GRADEpro Guideline Development Tool. McMaster University (developed by Evidence Prime, Inc), 2015. [Available from www.gradepro.org]

Grewal 1992

Grewal R, Rimmer MG, Freeman MA. Early migration of prostheses related to long-term survivorship. Comparison of tibial components in knee replacement. *Journal of Bone and Joint Surgery (Br)* 1992;**74**(2):239-42.

Gross 1983

Gross JB. Estimating allowable blood loss: corrected for dilution. *Anesthesiology* 1983;**58**(3):277-80. [DOI: DOI: 10.1097/00000542-198303000-00016] [PMID: PMID: 6829965]

Gurung 2015

Gurung T, Ellard DR, Mistry D, Patel S, Underwood M. Identifying potential moderators for response to treatment in low back pain: a systematic review. *Physiotherapy* 2015;**101**(3):243-51. [DOI: 10.1016/j.physio.2015.01.006] [PMID: PMID: 25769189]

Harbord 2009

Harbord RM, Harris RJ, Sterne JAC. Updated tests for small-study effects in meta–analyses. *The STATA Journal* 2007;**9**:197-210.

Higgins 2020a

Higgins JPT, Savović J, Page MJ, Elbers RG, Sterne JAC. Chapter 8: Assessing risk of bias in a randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.1 (updated September 2020). Cochrane, 2020. Available from www.training.cochrane.org/handbook.

Higgins 2020b

Higgins JPT, Li T, Deeks JJ (editors). Chapter 6: Choosing effect measures and computing estimates of effect. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.1 (updated September 2020). Cochrane, 2020. Available from www.training.cochrane.org/handbook.

Huh 2012

Huh IY, Kim DY, Lee JH, Shin SJ, Cho YW, Park SE. Relation between preoperative autonomic function and blood pressure change after tourniquet deflation during total knee replacement arthroplasty. *Korean Journal of Anesthesiology* 2012;**62**(2):154-60.

Juhl 2012

Juhl C, Lund H, Roos EM, Zhang W, Christensen R. A hierarchy of patient-reported outcomes for meta-analysis of knee osteoarthritis trials: empirical evidence from a survey of high impact journals. *Arthritis* 2012;**2012**:136245. [PMID: 22792458]

Karjalainen 2019

Karjalainen TV, Jain NB, Page CM, Lähdeoja TA, Johnston RV, Salamh P, et al. Subacromial decompression surgery for rotator cuff disease. *Cochrane Database of Systematic Reviews* 2019;**12**:Art. No.: CD005619. [DOI: 10.1002/14651858.CD005619.pub3]

Kelly 2001

Kelly AM. The minimum clinically significant difference in visual analogue scale pain score does not differ with severity of pain. *Emergency Medicine Journal* 2001;**18**(3):205-7.

Kumar 2016

Kumar K, Railton C, Tawfic C. Tourniquet application during anesthesia: "what do we need to know?". *Journal of Anaesthesiology and Clinical Pharmacology* 2016;**32**(4):424-30. [DOI: DOI: 10.4103/0970-9185.168174]

National Joint Registry 2004

National Joint Registry. 1st Annual Report. www.njrcentre.org.uk/njrcentre/Portals/0/Documents/England/Reports/NJR_AR_1.pdf 2004 (accessed 8 November 2017).

National Joint Registry 2018

National Joint Registry. 16th Annual Report 2019. National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. (https://reports.njrcentre.org.uk/Portals/0/PDFdownloads/NJR%2016th%20Annual%20Report%202019.pdf) 2019.

Page 2020

Page MJ, Higgins JPT, Sterne JAC. Chapter 13: Assessing risk of bias due to missing results in a synthesis. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.1 (updated September 2020). Cochrane, 2020. Available from www.training.cochrane.org/handbook.

Parmet 1998

Parmet JL, Horrow JC, Berman AT, Miller F, Pharo G, Collins L. The incidence of large venous emboli during total knee arthroplasty without pneumatic tourniquet use. *Anesthesia and Analgesia* 1998;**87**(2):439-44.

Pfitzner 2016

Pfitzner T, von Ruth P, Voerkelius N, Mayr H, Perka C, Hube R. Influence of the tourniquet on tibial cement mantle thickness in primary total knee arthroplasty. *Knee Surgery, Sports Traumatology, Arthroscopy* 2016;**24**(1):96-101.

RevMan 2014 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Schunemann 2020a

Schünemann HJ, Higgins JPT, Vist GE, Glasziou P, Akl EA, Skoetz N, Guyatt GH. Chapter 14: Completing 'Summary of findings' tables and grading the certainty of the evidence. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.1 (updated September 2020). Cochrane, 2020. Available from www.training.cochrane.org/handbook.

Schunemann 2020b

Schünemann HJ, Vist GE, Higgins JPT, Santesso N, Deeks JJ, Glasziou P, Akl EA, Guyatt GH. Chapter 15: Interpreting results and drawing conclusions. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.1 (updated September 2020). Cochrane, 2020. Available from www.training.cochrane.org/handbook.

Schwarzer 2007

Schwarzer G. meta: an R package for meta-analysis. R News;**7**(3):40-5. [https://cran.r-project.org/doc/Rnews/Rnews_2007-3.pdf]

Scottish Arthroplasty Project 2019

Scottish Arthroplasty Project. Scottish Arthroplasty Project Annual Report 2019. (https://spark.adobe.com/page/TLheJCYhNm8ON/) 2019.

Skou 2016

Skou ST, Roos EM, Laursen MB. A randomized, controlled trial of total knee replacement. *New England Journal of Medicine* 2016;**374**(7):692.

Smith 2010

Smith TO, Hing CB. Is a tourniquet beneficial in total knee replacement surgery? A meta-analysis and systematic review. *Knee* 2010;**17**(2):141-7.

Sterne 2016

Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;**355**:e4919.

Sulek 1999

Sulek CA, Davies LK, Enneking FK, Gearen PA, Lobato EB, et al. Cerebral microembolism diagnosed by transcranial Doppler during total knee arthroplasty: correlation with transesophageal echocardiography. *Anesthesiology* 1999;**91**(3):672-6.

Tai 2011

Tai TW, Lin CJ, Jou IM, Chang CW, Lai KA, Yang CY. Tourniquet use in total knee arthroplasty: a meta-analysis. *Knee Surgery, Sports Traumatology, Arthroscopy* 2011;**19**(7):1121-30.

The Swedish Knee Arthroplasty Register 2012

The Swedish Knee Arthroplasty Register: Annual Report 2012. Department of Orthopedics Skåne University Hospital, Lund. Available at http://www.myknee.se.

Viashya 2018

Vaishya R, Agarwal AK, Vijay V, Tiwari MK. Short term outcomes of long duration versus short duration tourniquet in primary total knee arthroplasty: a randomized controlled trial. *Journal of Clinical Orthopaedics and Trauma* 2018;**9**(1):46-50. [DOI: 10.1016/j.jcot.2017.11.016] [PMID: 29628683]

Wall 2017

Wall PDH, Parsons NR, Parsons H, Achten J, Balasubramanian S, Thompson P, et al. A pragmatic randomised controlled trial comparing the efficacy of a femoral nerve block and periarticular infiltration for early pain relief following total knee arthroplasty. *Bone & Joint Journal* 2017;**99-B**(7):904-11.

Zhang 2014

Zhang W, Li N, Chen S, Tan Y, Al-Aidaros M, Chen L. The effects of a tourniquet used in total knee arthroplasty: a meta-analysis. *Journal of Orthopaedic Surgery and Research* 2014;**9**(1):13.

References to other published versions of this review

Ahmed 2017

Ahmed I, Chawla A, Underwood M, Price AJ, Metcalfe A, Hutchinson C, et al. Tourniquet use for knee replacement surgery. *Cochrane Database of Systematic Reviews* 2017, Issue 11. Art. No: CD012874. [DOI: 10.1002/14651858.CD012874]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abdel-Salem 1995

Study characteristics	
Methods	Two groups: surgery with a tourniquet; surgery without a tourniquet Follow-up: 2 years Study design: single-centre randomised controlled trial

Abdel-Salem 1995 *(Continued)*

Participants	80 participants in total Male:Female: 17:23; 15:25 Age, years (range): 72 (65 to 80); 74 (64 to 82) Inclusion criteria: non-diabetic patients who had no previous knee surgery; normal neurovascular supply to the leg (proved by Doppler) Duration of illness: unspecified
Interventions	Group A (n = 50): total knee replacement surgery performed with a tourniquet Group B (n = 50): total knee replacement surgery performed without a tourniquet All operations were performed under general anaesthesia by one surgeon. For all patients, cefuroxime 1.5 g was given intravenously at the time of induction of anaesthesia and two further doses of 750 mg were given postoperatively. Anticoagulant prophylaxis was with Fragmin, started 2 hours preoperatively and continued postoperatively until the patient was fully mobile. A pneumatic tourniquet was placed around the thigh in both groups but was inflated only for patients in group A. The limb was first exsanguinated by elevation for 2 minutes, and the tourniquet was inflated to twice the systolic blood pressure (in group A)
Outcomes	1. Hospital for Special Surgery knee score: knee-related score assessing pain, stability (measured as total varus-valgus arc, extension), motion (measured as total passive arc), quadriceps strength (measured as 10% of normal for age and gender), and subtractions for contractures or fixed varus/valgus. Score ranges from 0 to 100. The higher the score, the better the outcome 2. Postoperative pain on a linear analogue scale between 0 and 10. A score of 10 is the highest pain score; therefore the lower the score, the better the outcome 3. Analgesia consumption: measures as the total amount of opiate injected, measured in milligrams delivered to the patient. A higher score indicates a worse outcome. This was measured over the first 24 hours postoperatively 4. Duration of surgery: measured in minutes 5. Overall blood loss: measured in millilitres on day 1 postoperatively. The higher the score, the worse the outcome 6. Range of knee movement at 5 days, 10 days, and 6 weeks. Measured as time to straight leg raised, measured in days, with higher scores indicating worse outcomes, Knee extension and flexion measured in degrees with higher scores indicating better outcomes. These scores were measured at days 5 and 10, at week 6, and 1 year postoperatively
Identification	Contact information: A Abdel-Salem, Consultant orthopaedic surgeon, George Elliot Hospital NHS Trust, Nuneaton, CV10 7DJ
Notes	Country: UK Language: English Study author contacted: no contact details given Trial registry record or protocol available: none found Funding source/declaration of interest: none reported Adverse events: In group A: 5 patients had wound infection; 3 patients had confirmed venous thrombosis In group B: no adverse events were reported

Risk of bias

Abdel-Salem 1995 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Card system
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	HSS, pain, analgesia consumption Not stated if patients were blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition; no CONSORT diagram
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement; no protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Aglietti 2000

Study characteristics	
Methods	Two groups: surgery with a tourniquet; surgery without a tourniquet Follow-up: up to 24 hours post surgery Study design: single-centre randomised controlled trial
Participants	20 participants in total Male:Female: 3:10; 4:6 Age, years (SD): 70(8); 68 (4.5) BMI, years (SD): 27.9; 27.3 Inclusion criteria: patients undergoing total knee replacement surgery for osteoarthritis Exclusion criteria: disturbances of coagulation, history of deep vein thrombosis, previous surgery of the knee, neoplastic disease, inflammatory disease, had received anticoagulant therapy or drugs that affected the haemostatic system during the last 2 weeks Duration of illness: unspecified
Interventions	Group I (n = 10): total knee replacement surgery performed with a tourniquet

Aglietti 2000 *(Continued)*

	Group II (n = 10): total knee replacement surgery performed without a tourniquet Anaesthetic techniques were standardised. All patients received subarachnoid spinal anaesthesia by injection of 4 mL of 0.5% bupivacaine at the L2-L3 interspace approximately 1 hour before surgery and were sedated with midazolam and fentanyl intravenously. Ringer's lactate solution was infused as needed to maintain haernodynamic stability. Patients did not receive blood transfusions during the observation period. Autologous blood was transfused postoperatively as needed after the study was completed. Unilateral primary cemented total knee replacements (M.B.K. prosthesis, Zimmer, Warsaw, IN, USA) were performed on all patients by the same surgeon at approximately the same time of the morning. Patients were assigned randomly to either Group I or Group II. Group I comprised 10 patients who underwent total knee replacement with a tourniquet inflated at the root of the limb. Group II consisted of 10 patients who underwent total knee replacement without the tourniquet. Before the surgical incision was begun in patients in Group I, the limb was exsanguinated with an elastic bandage and the tourniquet inflated at the pressure of 0.8 bar
Outcomes	1. Duration of surgery: measured in minutes 2. Intraoperative blood loss: measured in millilitres. The higher the score, the worse the outcome 3. Postoperative blood loss: measured in millilitres. The higher the score, the worse the outcome 4. Overall blood loss: measured in millilitres. The higher the score, the worse the outcome 5. Intravenous fluid usage: measured in millilitres. The higher the score, the worse the outcome 6. Prothrombin time, activated partial thromboplastin time, and fibrinogen level: venous blood samples were drawn after 4 mL of blood was discarded to clear the venous line and to prevent haemodilution. Samples were collected via a 3-way stopcock from a 14-gauge antecubital vein cannula at the following 4 times: 1 hour before anaesthesia (Sample Tl); after bone cuts (Sample T2); 2 minutes after tourniquet deflation (Group I) or after cementing the prosthesis (Group 11) (Sample T3); and 1 hour after the end of the operation (Sample T4). Samples were collected in citrated tubes (9:1 volume to volume), immediately placed in ice, and centrifuged at 2000 g for 10 minutes at 4° C. Plasma samples were stored immediately at -70°C until assay
Identification	Contact information: P Aglietti, MD, Second Orthopaedic Clinic, Largo P. Palagi 1, 50139, Florence, Italy
Notes	Country: Italy Language: English Study author contacted: yes, however, received no reply Trial registry record or protocol available: none found Funding source/declaration of interest: none reported Adverse events: none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement

Aglietti 2000 *(Continued)*

Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: none
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Alexandersson 2019

Study characteristics	
Methods	Two groups: surgery with a tourniquet; surgery without a tourniquet Follow-up: 3 months Study design: single-centre randomised controlled trial
Participants	81 participants in total Male:Female: 18:20; 22:21 Age, years (SD): 68 (7.4); 69.7 (6.4) BMI (SD): 28.6 (3.4); 27.9 (3.5) Inclusion criteria: patients between 50 and 80 years of age undergoing total knee replacement surgery for treatment of primary osteoarthritis Exclusion criteria: revision surgery, valgus deformity > 30°, 1-stage bilateral procedures, rheumatoid arthritis, BMI > 35 Duration of illness: unspecified
Interventions	Group A (n = 38): total knee replacement surgery performed with a tourniquet Group B (n = 41): total knee replacement surgery performed without a tourniquet One group underwent surgery with a tourniquet (34 in., single bladder, dual port, Zimmer) around the thigh that applied pressure of 300 mmHg; the other group underwent surgery without a tourniquet. No femoral nerve block was used. A standard medial parapatellar incision was used The cemented NexGen CR- or PS-Flex fixed bearing knee (Zimmer) prosthesis was used without patellar resurfacing. Infiltration with 150 mL of ropivacaine-supplemented ketorolac and adrenaline was applied during surgery. If a tourniquet was used, it was released after the bandages were applied. Tranexamic acid (1 g) was given intravenously, 10 minutes before surgery in the non-tourniquet group, and 10 minutes before tourniquet release in the tourniquet group. 2 g of cloxacillin was administered intravenously just before and twice after surgery. Low-molecular-weight heparin (Fragmin, 5000 IE subcutaneously) was used for the first 14 postoperative days. Postoperative pain management included oxy-

Alexandersson 2019 *(Continued)*

	codone 5 to 10 mg (controlled-release oral formulation) twice a day, paracetamol 1 g 4 times a day, and oxycodone 5 mg when needed
Outcomes	Primary outcome Active range of motion (AROM) in the knee is measured before surgery, at day 3, and at 3-month control with a goniometer, with the patient lying supine Secondary outcomes: 1. Timed up and go (TUG) is carried out before surgery, at day 3, and at 3-month control. TUG is a functional test in which the time taken for the patient to get up from a chair, walk 3 metres, turn, and sit down again is measured 2. Visual analogue scale (VAS) is used for pain assessment. The patient answers the question, "How painful is your leg?" according to a 0 to 10 scale. This is done before surgery, 24 hours after surgery, 72 hours after surgery (± 2 hrs), and at 3-month control. The question is asked before training while the patient is at rest, and any additional analgesia given is noted 3. Swelling is assessed by measuring the circumference 10 cm proximal to the superior border of the patella, at the superior border of the patella, and 10 cm distal to the superior border of the patella with the patient lying supine. This is done before surgery, at day 3, and at 3-month control 4. Quadriceps function is tested by asking the patient to perform a straight leg raise while lying supine with the other leg in flexion with the foot on the base of support. The result is noted as able to/not able to perform the action. This is carried out before surgery, at day 3, and at 3-month control 5. Gait speed is assessed using the 10-metre walk test. Patients are asked to walk as quickly and safely as possible for 14 metres, of which the middle 10 metres are timed 6. Patients are asked to fill in the Oxford 12-Item Knee Score, which is a well-validated outcome questionnaire designed for use with knee arthroplasty patients
Identification	Contact information: Staffan Eriksson, Centre for Clinical Research Sormland, Uppsala University, Kungsgatan 1, 531 88 Eskilstuna, Sweden, Staffankarldavid.eriksson@dll.se
Notes	Country: Sweden Language: English Study author contacted: no Trial registry record or protocol available: clinical trial number ISRCTN85166072 Funding source/declaration of interest: none reported Adverse events: In non-tourniquet group: 1 patient had a urinary tract infection In tourniquet group: 2 patients had a wound infection

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Low risk	Computer-generated random numbers table
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants blinded; surgeons not blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or

Alexandersson 2019 *(Continued)*

		quality of cementation. It is unlikely that a surgeon would alter his or her performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: TUG, VAS, and OKS Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: swelling, quadriceps function, and gait speed Outcome assessors were blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources of bias identified

Ayik 2020

Study characteristics	
Methods	Two groups: surgery with a tourniquet; surgery without a tourniquet Follow-up: 3 months Study design: single-centre randomised controlled trial
Participants	70 participants randomised Mean age in tourniquet group: 65.39% 7.25; mean age in control group: 4.90% 6.58 Male:Female: 14:18; 14:19 Mean BMI in tourniquet group: 31.38 ± 4.72; mean BMI in control group: 30.31 ±.10 Inclusion criteria: patients undergoing total knee replacement surgery with a diagnosis of osteoarthritis (stage 3 to 5 on Ahlback rating), BMI < 35, and ASA score of I or II Exclusion criteria: ASA > III, BMI > 40, diagnosis of secondary gonarthrosis, preoperative range of motion < 90 degrees in affected knee, concomitant neuromuscular or orthopaedic disorders that can affect recovery of the lower limb, concomitant rheumatological disorder, concomitant peripheral vascular disease, diabetes mellitus, history of previous knee surgery, use of anticoagulant medication, and unwillingness to participate in the study Duration of illness unspecified
Interventions	Intervention: In Group A, exsanguination was accomplished by wrapping the limb with an elastic bandage approximately 10 cm wide, starting at the toes and continuing to just distal to the tourniquet. Next, cuff pressure was inflated to 100 mmHg above systolic blood pressure In Group B, a tourniquet was applied; however, it was not inflated All TKAs were performed by the same surgeon (O.A.), who specialised in hip and knee replacement according to a standard protocol, which included spinal anaesthesia, an appropriate perioperative antibiotic regimen for infection prophylaxis, thrombosis prophylaxis, postoperative pain management, and rehabilitation. Low-molecular-weight heparin was started 12 hours before spinal anaesthesia for thrombosis prophylaxis and was concluded when patients were completely mobile. The surgical course involved a midline skin incision made via a standard medial parapatellar approach. All patients in both groups received the GENESIS II cemented, posterior cruciate ligament-retaining, fixed-bearing total knee endoprosthesis with ultra-high-molecular-weight polyethylene (Smith & Nephew Orthope-

Ayik 2020 *(Continued)*

	dics, Inc., Memphis, TN, USA). An intramedullary guide was utilised for the femur and an external guide for the tibia. The patella was not replaced in any case, and only marginal osteophytes were removed. Dressings were applied after wound closure, and the cuff was rapidly deflated in Group A
Outcomes	1. Isokinetic muscle strength of knee extensors (quadriceps) and flexors (hamstrings) was measured in Newton meters (Nm) by a CYBEX 350 isokinetic dynamometer (- HUMAC/CYBEX 2009, Stoughton, MA, USA). In both groups, peak torque and total work were evaluated preoperatively and at 1 and 3 months postoperatively 2. Knee Society score measured at 1 and 3 months postoperatively 3. Pain measured on a visual analogue score at 1 and 3 months postoperatively 4. Knee range of motion measured at 1 and 3 months postoperatively
Identification	Contact information: Mehmet Demirel, MD, Department of Orthopaedics and Traumatology, Istanbul University, Istanbul School of Medicine, Istanbul, Turkey, dr88.mehmet.demirel@gmail.com
Notes	Country: Turkey Language: English Study author contacted: no Trial registry record or protocol available: study was approved by the local ethics committee (1127-Istanbul University) Funding source/declaration of interest: no source of funding reported or identified Adverse events: no adverse events reported in groups Number in each group 35:35

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomised
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients blinded; surgeons not blinded
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Participants were blinded; therefore low risk of bias Self-reported outcomes: KSS, pain
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors are blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing outcome data balanced in numbers across intervention groups with similar reasons for missing data across groups
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources identified

Clarke 2001

Study characteristics	
Methods	Three groups: surgery without a tourniquet; surgery with a tourniquet at low pressure (225 mmHg); surgery with a tourniquet at high pressure (350 mmHg) Follow-up: 7 days Study design: single-centre randomised controlled trial
Participants	31 participants in total Male:Female: not reported Age, years (SD): not reported BMI (SD): not reported 31 participants Inclusion criteria: patients undergoing total knee replacement surgery Exclusion criteria: patients with non-osteoarthritic disease, previous open knee surgery, systemic or local hypoxia, receiving anticoagulant or antiplatelet agents or steroid, with significant varus or valgus deformity or preoperative lateral release Duration of illness: unspecified
Interventions	Group A: surgery without a tourniquet (n = 10) Group B: surgery with a tourniquet at low pressure (225 mmHg) (n = 10) Group C: surgery with a tourniquet at high pressure (350 mmHg) (n = 11) A standard protocol was followed utilising a tourniquet 11.5 cm wide, with an effective pressurising width of 9 cm (DePuy UK Ltd, Leeds, UK), with exsanguination in extension via a Rhys-Davies device where appropriate. All patients had general (non-halothane) anaesthesia, a midline skin incision, a medial parapatellar approach, insertion of a cemented Insall-Burnstein II TKR (Zimmer, Warsaw, IN, USA), and skin closure using continuous Vicryl (Ethicon Ltd, Somerville, NJ, USA) over a single drain. All were mobilised on the second postoperative day. No patient received thromboembolic prophylaxis or used a continuous passive motion machine
Outcomes	1. Blood transfusion use: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 2. Wound hypoxia: measurement of tissue oxygenation was performed with transcutaneous oxygen pressure electrodes (Radiometer Ltd, Crawley, UK) placed on the skin. Electrodes were placed on each wound flap with a reference electrode sited in the infraclavicular region to determine intrapatient and interpatient differences in systemic oxygen delivery both before and after operation. Electrodes were attached to 2 Radiometer TCM3 TINA units (Radiometer Ltd). Measurements were taken before operation and on each day after surgery for 1 week or until discharge from hospital 3. Return to preoperative levels of oxygenation 4. Subjective assessment of wound healing: assessed by 2 observers for haematoma, infection, skin necrosis, dehiscence, or contusion
Identification	Contact information: Mr M.T. Clarke, Box 37, Orthopaedic Surgery, Addenbrookes Hospital, Cambridge, CB2 2QQ
Notes	Country: UK Language: English Study author contacted: yes, no reply from author.

Clarke 2001 *(Continued)*

Trial registry record or protocol available: none reported

Funding source/declaration of interest: funded by grants from the Wishbone Trust and from the research and development fund of West Suffolk Hospital

Adverse events: none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes**:** none
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors are blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Dong 2019

Study characteristics

Methods	2 groups: surgery performed with a tourniquet inflated; surgery performed without a tourniquet inflated Follow-up: 1 year Study design: single-centre randomised controlled trial
Participants	129 participants randomised Mean age in tourniquet group 68.2 ± 17.1; mean age in non-tourniquet group 69.5 ± 15.9 Male:Female: 20:38; 23:41 Mean weight in tourniquet group 67.7 ± 17.6; mean weight in non-tourniquet group 65.9 ± 15.9 Inclusion criteria: patients who were 60 to 85 years old, undergoing unilateral total knee replacement surgery, NYHA classification I to III, ASA physical status I and II

Dong 2019 *(Continued)*

	Exclusion criteria: severe cardiovascular or cerebrovascular disease, illiteracy, mental illness, cognitive impairment, refusal to participate in the study Duration of illness: unspecified
Interventions	Patients in both groups were anaesthetised by general anaesthesia. General anaesthesia induction drugs included midazolam 0.5 mg/kg, propofol 1.5 mg/kg, sulfentanyl 0.5 μg/kg, and rocuronium 0.8 mg/kg by intravenous bolus injection. Intermittent injection of rocuronium 10 mg per 40 to 60 minutes, continuous intravenous infusion of remifentanil 0.1 to 0.3 μg/kg/min, and propofol 2 to 4 mg/kg/h; continuous inhalation of sevoflurane was used for anaesthesia maintenance. All patients underwent TKA via a standardised technique and process Patients in group T underwent surgery with a tourniquet inflated to 100 mmHg above systolic blood pressure; patients in group H underwent surgery without a tourniquet The orthopaedic surgeon injected 20 mL of a 'cocktail mixture' into the posterior capsular ligament, peripheral capsular ligament, and ligamentum patellae before the artificial prosthesis was embedded to relieve pain and inflammation. The formula for the 'cocktail' is as follows: ropivacaine 100 mg, tranexamic acid 3 g, adrenaline 3 drops, methylprednisolone 40 mg, in a total volume of 20 mL with the addition of normal saline
Outcomes	1. Pain assessed via a numerical rating scale from 0 (no pain) to 10 (worst pain imaginable). Collected on days 1, 2, 3, and 7 and 1 year after the operation 2. Active range of motion measured in degrees; collected on days 1, 2, 3, and 7 and 1 year after the operation 3. Intraoperative blood loss 4. Total blood loss 5. Circumferences of the lower and middle thighs of patients were measured before the operation and on day 1, day 2, and day 3 after the operation, to judge swelling of the operative side thigh 6. A Montreal Cognitive Assessment Scale (MoCA) with a total score of 30 points was used to analyse the cognitive function of patients on day 1, day 2, day 3, and day 7 after the operation. MoCA value < 26 points was considered to show cognitive impairment 7. Serum creatinine 8. Glomerular filtration rate collected on days 1, 2, and 3 postoperatively 9. C-reactive protein collected on days 1, 2, 3, and 7 postoperatively
Identification	Contact information: Jun Dong, dongjun441@163.com, Department of Anesthesiology, The First Affiliated Hospital of Chongqing Medical University, No. 1 Youyi Road, Yuzhong District, Chongqing, China
Notes	Country: China Language: English Study author contacted: no Trial registry record or protocol available: protocol was approved by the ethics committee of the First Affiliated Hospital of Chongqing Medical University (2012-2-21) and was registered at ClinicalTrials.com (NCT02576015) Funding source/declaration of interest: no source of funding reported or identified Adverse events: no adverse events reported in groups Number in each group: 66:63

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement

Dong 2019 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Insufficient information to permit judgement Self-reported outcomes: pain, Montreal Cognitive Assessment Scale
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Insufficient information to permit judgement Assessor-reported outcomes: range of motion, blood loss, thigh swelling, serum creatinine, GFR, CRP
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources identified

Ejaz 2014

Study characteristics	
Methods	Two groups: surgery with a tourniquet; surgery without a tourniquet Follow-up: 12 months Study design: single-centre randomised controlled trial
Participants	64 participants in total Male:Female: 18:15; 17:14 Age, years (SD): 68 (8.4); 68 (7.8) BMI (SD): 25 (2.0); 25 (2.5) Inclusion criteria: patients aged 50-85 undergoing an elective unilateral total knee replacement because of arthritis Exclusion criteria: rheumatoid arthritis, peripheral vascular disease, diabetes, prior knee surgery, use of anticoagulant medication, BMI > 35 Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 33) Group B: surgery performed without a tourniquet (n = 31) All procedures were standardised with regard to preoperative tranexamic acid, spinal anaesthesia, postoperative pain treatment, and rehabilitation regimen. Before surgery, tranexamic acid (1 g) was administered orally, and cefuroxime (1.5 g) was administered intravenously immediately before skin incision. In addition, tranexamic acid (0.5 g) was given 3 hours after surgery, and cefuroxime (750 mg) was given 6 and 12 hours postoperatively. Thrombosis prophylaxis was achieved with the use of rivaroxaban (10 mg/d) throughout the hospital stay. Both groups had an appropriately sized thigh

Ejaz 2014 *(Continued)*

	tourniquet applied, but it was inflated only in the Tq group; in the non-Tq group, it was placed on the thigh but was not inflated, thereby serving as a safety device in case of uncontrollable bleeding. In the Tq group, limb exsanguination was done by elevation for 2 minutes, and the cuff was inflated to 250 mmHg
Outcomes	1. Knee Outcome and Osteoarthritis Severity score (KOOS) at 12 months: validated knee-specific patient-reported outcome measure consisting of 42 items in 5 subsets (pain, symptoms, activities of daily living, sports/recreation, quality of life); score ranges from 0 to 100; zero indicates extreme knee problems, and 100 represents no knee problems 2. Pain score on days 1 and 3 postoperatively. Assessed as a visual analogue scale between 0 and 10; zero indicates no pain, and 10 indicates extreme pain 3. Analgesia consumption was expressed as a mean morphine equivalent during hospitalisation; consumption was standardised with 10 mg of morphine used as reference analgesic dose 4. Duration of surgery: measured in minutes 5. Intraoperative blood loss: measured in millilitres. The higher the score, the worse the outcome 6. Blood transfusion rate: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 7. Deep vein thrombosis
Identification	Contact information: Ashir Ejaz, Department of Orthopaedic Surgery, Aslborg University Hospital, Aalborg, Denmark, Asej@m.dk No source of funding identified
Notes	Country: Denmark Language: English Study author contacted: yes, no reply from author Trial registry record or protocol available: clinical trials number NCT1209035 Funding source/declaration of interest: none reported Adverse events: In the tourniquet group: 2 patients had confirmed DVT, and 2 patients required further operations on the index knee In the non-tourniquet group: 1 patient had confirmed DVT

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomised
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients blinded; surgeons not blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery

Ejaz 2014 *(Continued)*

Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: KOOS, pain, analgesia consumption, DVT Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing outcome data balanced in numbers across interventions
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources of bias identified

Ejaz 2015

Study characteristics	
Methods	Two groups: surgery with a tourniquet; surgery without a tourniquet Follow-up: 5 hours Study design: single-centre randomised controlled trial
Participants	62 participants in total Male:Female: 16:15; 17:14 Age, years (SD): 68.3 (8.4); 68.2 (7.8) BMI (SD): 25.1(2.0); 25.2 (2.5) Inclusion criteria: patients aged 50 to 85 undergoing elective unilateral cemented total knee replacement because of arthritis Exclusion criteria: rheumatoid arthritis, peripheral vascular disease, diabetes, prior knee surgery, use of anticoagulant medication, BMI > 35 Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 31) Group B: surgery performed without a tourniquet (n = 31) All procedures were standardised with regard to preoperative tranexamic acid, spinal anaesthesia, postoperative pain treatment, and rehabilitation regimen. Before surgery, tranexamic acid (1 g) was administered orally and cefuroxime (1.5 g) was administered intravenously immediately before skin incision. In addition, tranexamic acid (0.5 g) was given 3 hours after surgery, and cefuroxime (750 mg) was given 6 and 12 hours postoperatively. Thrombosis prophylaxis was achieved with the use of rivaroxaban (10 mg/d) throughout the hospital stay. Both groups had an appropriately sized thigh tourniquet applied, but it was inflated only in the Tq group. In the non-Tq group, it was placed on the thigh but was not inflated, thereby serving as a safety device in case of uncontrollable bleeding. In the Tq group, limb exsanguination was done by elevation for 2 minutes and the cuff was inflated to 250 mmHg

Ejaz 2015 *(Continued)*

Outcomes	1. Change in pyruvate, glucose, lactate, and glycerol concentrations. Samples were taken from the dialysate fluid. Microdialysis catheters were inserted into the gastrocnemius muscle at the time of surgery. Samples were collected every 20 minutes postoperatively until 5 hours 2. Duration of surgery: measured in minutes
Identification	Contact information: Ashir Ejaz, Department of Orthopaedic Surgery, Aslborg University Hospital, Aalborg, Denmark, Asej@m.dk No source of funding identified
Notes	Country: Denmark Language: English Study author contacted: yes, no reply from author Trial registry record or protocol available: clinical trials number NCT1209035 Funding source/declaration of interest: none reported Adverse events: none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomised
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants blinded; surgeons not blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: none
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing outcome data balanced in numbers across intervention groups with similar reasons for missing data
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources of bias identified

Ejaz 2015 b

Study characteristics	
Methods	Two groups: surgery with a tourniquet; surgery without a tourniquet Follow-up: 24 months Study design: single-centre randomised controlled trial
Participants	57 participants in total Male:Female: 13:16; 15:13 Age, years (SD): 68.3 (8.0); 68.2 (7.8) BMI (SD): 25.1 (2.0); 25.2 (2.5) Inclusion criteria: patients aged 50 to 85 undergoing elective unilateral total knee replacement because of arthritis Exclusion criteria: rheumatoid arthritis, peripheral vascular disease, diabetes, prior knee surgery, use of anticoagulant medication, BMI > 35 Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 29) Group B: surgery performed without a tourniquet (n = 28) All procedures were standardised with regard to preoperative tranexamic acid, spinal anaesthesia, postoperative pain treatment, and rehabilitation regimen. Before surgery, tranexamic acid (1 g) was administered orally, and cefuroxime (1.5 g) was administered intravenously immediately before skin incision. In addition, tranexamic acid (0.5 g) was given 3 hours after surgery, and cefuroxime (750 mg) was given 6 and 12 hours postoperatively. Thrombosis prophylaxis was achieved with the use of rivaroxaban (10 mg/d) throughout the hospital stay. Both groups had an appropriately sized thigh tourniquet applied, but it was inflated only in the Tq group. In the non-Tq group, it was placed on the thigh but was not inflated, thereby serving as a safety device in case of uncontrollable bleeding. In the Tq group, limb exsanguination was done by elevation for 2 minutes and the cuff was inflated to 250 mmHg
Outcomes	1. Radiosterometric analysis (maximum total point motion) at 8 weeks, 6 months, 12 months, and 24 months. MTPM represents the vector length of a marker in the rigid body that has the longest translational motion, not considering direction, and always has a positive value. Translations along the axes were given as x-translation (medial–lateral movement), y-translation (superior/lift-off and inferior/subsidence movement), and z-translation (anterior and posterior movements). Rotations around the axes were expressed as x-rotation, y-rotation, and z-rotation, which represent anterior-posterior tilt, internal-external rotation, and varus–valgus tilt, respectively
Identification	Contact information: Ashir Ejaz, Department of Orthopaedic Surgery, Aslborg University Hospital, Aalborg, Denmark, Asej@m.dk No source of funding identified
Notes	Country: Denmark Language: English Study author contacted: yes, no reply from author. Trial registry record or protocol available: clinical trials number NCT1209035 Funding source/declaration of interest: none reported

Ejaz 2015 b *(Continued)*

Adverse events: none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomised
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants blinded; surgeons not blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: none
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Assessor-reported outcomes: RSA analysis Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing outcome data balanced in numbers across intervention groups with similar reasons for missing data
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources of bias identified

Goel 2019

Study characteristics

Methods	2 groups: surgery with a tourniquet; surgery performed without a tourniquet Follow-up: 8 months Study design: randomised controlled trial performed at an academic university hospital and a private orthopaedic hospital
Participants	200 participants randomised Mean age in the tourniquet group 66 (7); mean age in the non-tourniquet group 65.5 (7.8) Male:Female ratio: 50:50; 48:52 Mean BMI in the tourniquet group 30.9 (4.6); mean BMI in the non-tourniquet group 31.3 (4.5) Inclusion criteria: all unilateral primary knee arthroplasties performed by investigators participating in this study will be eligible for inclusion and diagnosis of osteoarthritis Exclusion criteria: revision surgery, bilateral knee surgery, age < 18 or > 80, BMI > 40, baseline lower extremity strength < 5/5, vascular calcifications, history of chronic narcotic use defined as more than 5 mg of oxycodone q4 hours, functionally limiting spine disease, other functionally limiting lower extremity disorder (i.e. symptomatic ipsilateral hip disease), patients who cannot perform baseline functional

Goel 2019 *(Continued)*

	tests, allergy/contraindication to protocol medications, post-traumatic arthritis, Inflammatory arthritis, pregnancy, prisoners and patients receiving care as part of a workers' compensation injury Duration of illness: unspecified
Interventions	In the tourniquet group, surgery was performed with a tourniquet inflated at 225 mmHg or 300 mmHg depending on surgeon preference. In the non-tourniquet group, surgery was performed without a tourniquet All total knee replacements were done with the patient under sedation and spinal anaesthesia utilising bupivacaine without an opioid. All patients received an adductor canal block, and a pneumatic tourniquet was applied to all patients. Patients received 1 g of intravenous tranexamic acid 30 minutes before the incision when it was deemed appropriate by the anaesthesiologist. A standard midline incision and a medial parapatellar approach were utilised for all surgical procedures. For patients randomised to tourniquet inflation, the tourniquet was inflated at the start of the procedure and was deflated after application of sterile dressings. Either the DePuy Synthes P.F.C. SIGMA or the Zimmer Biomet Persona implant system was used. The tourniquet system used was the Stryker Color Cuff Dual Port inflated to either 300 or 225 mmHg, depending on surgeon preference
Outcomes	1. Duration of surgery 2. Overall blood loss 3. Surgeon-rated difficulty in visualisation 4. Pain measured on a visual analogue scale at 4 to 6 weeks and at 6 to 8 months 5. Stair climb test measured at 4 to 6 weeks and at 6 to 8 months 6. Time to up and go test measured at 4 to 6 weeks and at 6 to 8 months 7. KOOS score measured at 4 to 6 weeks and at 6 to 8 months 8. SF-12 measured at 4 to 6 weeks and at 6 to 8 months 9. Wound complications 10. Deep vein thrombosis
Identification	Contact information: Rahul Goel, Department of Orthopaedic Surgery, Emory University, Atlanta, Georgia, USA ORCID ID for R Goel: 0000-0002-0515-0361
Notes	Country: USA Language: English Study author contacted: no Trial registry record or protocol available: study was registered at ClinicalTrials.gov (NCT02907047) Funding source/declaration of interest: no source of funding reported or identified Adverse events: 1 person in the tourniquet group had a wound complication requiring antibiotics 1 patient in each group had postoperative wound blistering 1 patient in the non-tourniquet group developed symptomatic DVT Number in each group 100;100

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number generator
Allocation concealment (selection bias)	Low risk	Envelopes with allocation opened before incision

Goel 2019 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients blinded; surgeons not blinded
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: pain, satisfaction, SF-12, KOOS Patients blinded
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Outcome assessors blinded Assessor-reported scores: blood loss, duration of surgery, range of motion, stair climb test, time to up and go
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing outcome data balanced in numbers across intervention groups with similar reasons for missing data across groups
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources identified

Harston 2015

Study characteristics	
Methods	Two groups: surgery with a tourniquet; surgery without a tourniquet Follow-up: 48 hours Study design: single-centre randomised controlled trial
Participants	64 participants in total Male:Female: 17:15; 18:14 Age, years (SD): 68 (8.0); 66 (8) BMI (SD): 27.4; 28.4 Inclusion criteria: ASA I to III, able to understand given information, 45 to 85 years of age Exclusion criteria: previous major knee surgery to the same knee, preoperative inability to flex the knee > 90 degrees, rheumatoid arthritis, allergy to any of the drugs used in the study Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 32) Group B: surgery performed without a tourniquet (n = 32) As premedication, all patients received oral celecoxib 400 mg and acetaminophen 1 g; thereafter 12-hourly (celecoxib 200 mg) and 6-hourly (acetaminophen 1 g). No subjects received an indwelling urinary catheter, and no drains were used. A low-volume fluid regimen was used with 2000 mL of Ringer's solution during the first 24 hours. All subjects were given 1 g of tranexamic acid i.v. Oxycodone 5 mg i.v. was used as postoperative rescue pain medication. No femoral nerve blocks were used. All patients were anaesthetized using intrathecal administration of hyperbaric bupivacaine 0.5%, 3 mL. An infusion

Harston 2015 *(Continued)*

	of propofol 10 mg mL−1 was given to induce light sedation during surgery. All patients breathed spontaneously with supplemental oxygen 2 L min−1
Outcomes	1. Knee extension strength: measured from pre-surgery to 48 hours after surgery in the operated leg. Knee extension strength was measured isometrically at 60° knee flexion using an isokinetic dynamometer (Biodex) and was expressed as Newtons per kilo body mass 2. Pain: assessed as a visual analogue scale between 0 and 10; zero indicates no pain, and 10 indicates extreme pain 3. Swelling: not reported how this was collected. 4. Nausea: not reported how this was collected. 5. Duration of surgery: measured in minutes
Identification	A. Harsten, Department of Anaesthesiology, Hassleholm Hospital, Box 351, 281 25 Hassleholm, Sweden, telephone +46451298848, andreas.harston@skane.se
Notes	Country: Sweden Language: English Study author contacted: author not contacted Trial registry record or protocol available: clinical trials number NCT01808859 Funding source/declaration of interest: study was supported by institutional grants Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Patients and surgeons not blinded
Blinding of outcome assessment - self-reported outcomes (detection bias)	High risk	Self-reported outcomes: pain and nausea Patients not blinded; therefore high risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: knee extension strength, swelling, duration of surgery Outcome assessors blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources of bias identified

Huang 2017

Study characteristics	
Methods	Three groups: surgery with a tourniquet as well as multiple doses of intravenous tranexamic acid (TXA); surgery with no tourniquet and multiple doses of TXA; surgery with a tourniquet and no TXA Follow-up: 6 months Study design: single-centre randomised controlled trial
Participants	150 participants in total Male:Female: 18:32; 16:34 Age, years (SD): 66.2 (8.3); 65.1 (6.8) BMI (SD): 25.1 (1.5); 24.4 (1.5) Inclusion criteria: patients older than 18 scheduled for primary total knee arthroplasty for end stage-osteoarthritis Exclusion criteria: revision procedures, bilateral procedures, previous knee surgery, flexion deformity > 30 degrees, anaemia, contraindication for TXA, ASA grade IV, coagulation disorder Duration of illness: unspecified
Interventions	Group A: surgery with a tourniquet and multiple doses of TXA (n = 50) Group B: surgery without a tourniquet and multiple doses of TXA (n = 50) Group C: surgery with a tourniquet and no TXA (n = 50) A surgeon-selected cemented posterior-stabilised prosthetic design was used. Vacuum wound drainage was used for every patient and was removed the next morning. An intraoperative periarticular injection of ropivacaine and postoperative oral diclofenac sodium (Voltaren; 50 mg twice daily) were administered for pain. On the day of the surgery and 3 times daily thereafter until hospital discharge, all patients were evaluated by a physical therapist and began walking with partial weight-bearing and wearing a knee brace to protect the surgical site
Outcomes	1. HSS score at 6 months: knee-related score assessing pain, stability (measured as total varus-valgus arc, extension), motion (measured as total passive arc), quadriceps strength (measured as 10% of normal for age and gender), and subtractions for contractures or fixed varus/valgus. Score ranges from 0 to 100. The higher the score, the better the outcome 2. Duration of surgery: measured in minutes 3. Intraoperative blood loss: measured in millilitres 4. Total blood loss: measured in millilitres 5. Transfusion rate: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 6. Length of hospital stay: measured in number of days 7. Patient satisfaction: all patients completed a satisfaction questionnaire regarding outcomes of surgery, which asked them to rate their satisfaction on a 7-point scale ranging from very dissatisfied to extremely satisfied 8. Deep vein thrombosis 9. Pulmonary embolism 10. Swelling ratio: the swelling ratio was defined as the knee circumference of the operatively treated limb divided by the circumference of the contralateral limb, with the knee circumference encompassing the upper and lower poles of the patella

Huang 2017 *(Continued)*

Identification	Contact information: ZeYu Huang, MD, PhD, Department of Orthopaedic Surgery, West China Hospital, West China Medical School, Sichuan University, Cheng Du, Sichuan Province, People's Republic of China
Notes	Country: China Language: English Study author contacted: no Trial registry record or protocol available: registered on Chinese clinical trials registry ChiCTR-INR-16009762 Funding source/declaration of interest: none reported Adverse events: Group A: 1 patient had a superficial wound infection Group B: no adverse events were reported Group C: 3 patients developed a superficial wound infection and 3 patients reported blistering We reported groups A and B in our analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants blinded; surgeons blinded only until the morning of the operation However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: HSS score, patient satisfaction, DVT, PE Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: duration of surgery, intraoperative blood loss, total blood loss, transfusion rate, length of hospital stay, swelling Outcome assessors blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources of bias identified

Jawhar 2015

Study characteristics	
Methods	Two groups: surgery with a tourniquet; surgery without a tourniquet Follow-up: 60 minutes postoperatively Study design: single-centre randomised controlled trial
Participants	34 participants in total Male:Female: 8:15; 8:15 Age, years (SD): 70.6 (7); 70.6 (6) BMI (SD): 32.1 (5); 33.8 (5) Inclusion criteria: 55 to 85 years of age, osteoarthritis of the knee joint (degree III or IV), physical status (ASA I or II), BMI < 45, able to provide written informed consent Exclusion criteria: < 55 or > 85 years of age, osteoarthritis of the knee joint (degree I or II), ASA physical status III or IV, BMI > 45, unable to provide written consent, malignant disease, rheumatoid disease, infectious disease, coagulation disorder, history of deep vein thrombosis or pulmonary embolism, peripheral arterial disease, immune deficiency, medication (glucocorticoid, aspirin, heparin, cumarin, warfarin), neurological dysfunction, liver insufficiency, coronary heart disease, immobility Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 17) Group B: surgery performed without a tourniquet (n = 17) After accomplishment of the anaesthesia, a pneumatic tourniquet was applied at the proximal third of the thigh. Thereafter, a standard sterilisation procedure was performed. The tourniquet was inflated (380 mmHg) immediately before the skin incision. The standard medial parapatellar approach was performed in all cases. For each of these groups, 2 biopsies were taken from the vastus medialis. The first muscle biopsy was obtained immediately after surgery was performed; this was followed by the second muscle biopsy exactly 60 minutes later (before tourniquet deflation). Biopsy volume was set to be 5 × 5 × 5 mm (125 mm^3) with distance between biopsies > 10 mm. Muscle extracts were frozen in liquid nitrogen until further analyses
Outcomes	Primary outcome: Measurement of intracellular proteolytic activity: the total ubiquitination, as a result of total ubiquitin-protein ligase activity (tUbPL), was determined as biotinylated ubiquitin incorporation into the sum of the cytosolic proteins. The ubiquitination was expressed in katal, which is defined as 1 mol biotinylated ubiquitin incorporated into cytosolic proteins per second Secondary outcomes: 1. Blood loss (1 week postoperative): measured in millimetres 2. Complication (within 6 months of operation date) 3. WOMAC score (6 months postoperatively): consists of 24 items divided into 3 subscales (pain, stiffness, and physical function). Total score is 96, with 0 indicating no problems with the knee and 98 representing extreme problems with the knee 4. Prosthesis position on radiograph (1 week postoperatively): not stated in protocol how this was to be measured 5. Nerve function analysis: not stated in protocol how this was to be measured

Jawhar 2015 *(Continued)*

Identification	Contact information: Ahmed Jawhar, Department of Orthopaedics and Trauma Surgery, University Medical Centre Mannheim of University Heidelberg, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany, Jawhar_ahmed@yahoo.de No conflicts of interest
Notes	Country: Germany Language: English Study author contacted: yes, no reply from author Trial registry record or protocol available: clinical trials ID NCT02475603 Funding source/declaration of interest: no sources of funding stated Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients were blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No missing outcome data
Selective reporting (reporting bias)	High risk	Outcomes in registration/protocol not reported
Other bias	Low risk	No other sources of bias identified

Jawhar 2020

Study characteristics

Methods	2 groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 6 months

Jawhar 2020 *(Continued)*

	Study design: single-centre randomised controlled trial
Participants	99 participants included in this study Mean age in the tourniquet group 69.3 (7.4); mean age in the non-tourniquet group 68.3 (7.3) Mean BMI in the tourniquet group 31.9 (6); mean BMI in the non-tourniquet group 31.4 (5.5) Male:Female ratio: 17:33; 19:30 Inclusion criteria: 50 to 85 years of age; Osteoarthritis Kellgren and Lawrence score III or IV; ASA score I, II, III; BMI < 45 kg/m^2; able to provide written consent Exclusion criteria: < 50 years or > 85 years of age, Osteoarthritis Kellgren and Lawrence score I or II, ASA IV, BMI > 45 kg/m^2, unable to provide written consent, other implant designs, unicondylar knee arthroplasty, malignant disease, rheumatoid disease, infectious disease, coronary heart disease, neurological dysfunction, immobility - not able to walk , liver insufficiency, coagulation disorder, glucocorticoids, aspirin, heparin, coumadin, warfarin, history of DVT or pulmonary embolism Duration of illness: unspecified
Interventions	All TKAs were performed at the Department of Orthopaedics and Trauma Surgery according to institutional standard operating procedure. Medial parapatellar approach and femur first surgical technique were performed to implant a cemented prosthesis design (SmartSet Bone cement, DePuy Synthes, Warsaw, IN, USA) (PFC® SIGMA®). After introduction of anaesthesia, a pneumatic tourniquet (Balbina™, Ulrich Medical, Ulm, Germany) was placed on the proximal thigh and was inflated only in the tourniquet group to 360 mmHg, immediately before skin incision. The tourniquet was released on completion of wound closure and after application of an elastic–compressive bandage. In the non-tourniquet group, the same surgery was performed without a tourniquet
Outcomes	1. Oxford Knee Score collected at 6 weeks and 6 months 2. WOMAC score collected at 6 weeks and 6 months 3. Mancuso score collected at 6 weeks and 6 months 4. EQ-5D (VAS and Index) collected at 6 weeks and 6 months 5. Hospital Anxiety and Depression score collected at 6 weeks and 6 months 6. Muscle strength (muscle peak force (Newton), workload (Joule), total workload (Joule), power (Watt)) collected at 6 weeks and 6 months 7. Complications such as postoperative haematoma, DVT/PE, surgical site infection, and vascular/nerve injury
Identification	Ahmed Jawhar, ahmed.jawhar@umm.de, Department of Orthopaedics and Trauma Surgery, University Medical Center Mannheim of University Heidelberg, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany
Notes	Country: Germany Language: English Study author contacted: no Trial registry record or protocol available: the protocol was registered at clinicaltrials.gov (ClinicalTrials.gov NCT02475603). The Institutional Ethics Committee approved the protocol (file reference 2012-334 N-MA/University Medical Center Mannheim of University Heidelberg) Funding source/declaration of interest: no source of funding reported or identified Adverse events: In the tourniquet group, 1 deep vein thrombosis occurred, 1 patient underwent revision surgery due to surgical site infection, 2 patients underwent revision surgery due to haematoma in the tourniquet groups In the non-tourniquet group, 1 patient had revision surgery due to surgical site infection, 2 patients had delayed wound healing, 1 patient with delayed wound healing needed revision surgery Number in each group 50:49
Risk of bias	

Jawhar 2020 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing outcome data balanced in numbers across intervention groups with similar reasons for missing data across groups
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources identified

Juelsgaard 2001

Study characteristics	
Methods	Two groups: surgery with a tourniquet; surgery without a tourniquet Follow-up: 2 days Study design: single-centre randomised controlled trial
Participants	30 participants in total Male:Female: 7:9; 4:10 Age, years (range): 69 (52 to 89); 64 (46 to 86) BMI (SD): not reported Inclusion criteria: patients undergoing primary cemented TKR Exclusion criteria: patients younger than 18 years, recent (< 6 months) myocardial infarction, unstable angina, severe aortic or mitral valve stenosis, previous stroke, unmedicated hypertension, treatment with beta-antagonist or anticoagulant Duration of illness: unspecified
Interventions	Group A: surgery performed with epidural anaesthesia without a tourniquet (n = 14)

Juelsgaard 2001 *(Continued)*

	Group B: surgery performed with spinal anaesthesia and a tourniquet (n = 16) In all cases, the leg planned for operation was exsanguinated with an Esmarch bandage before the tourniquet was inflated around the upper femur; tourniquet inflation pressure was maintained at 350 to 400 mmHg during the operation. At the end of surgery, the surgeon deflated the tourniquet to enable establishment of haemostasis; during surgery, sedation was adjusted to a level where communication was possible. Oxygen was delivered at 3L/min on a nasal catheter. All patients had urine output monitored via a urinary bladder catheter
Outcomes	1. Mean arterial pressure: measured intraoperatively calculated as (cardiac output multiplied by systemic vascular resistance) added to central venous pressure 2. Intraoperative blood loss: measured in millilitres through volume in the suction apparatus and weighing of towels 3. Postoperative blood loss: measured in millilitres through volume in postoperative drains 4. Total blood loss: measured in millilitres 5. Intravenous fluid usage: measured in millilitres as the amount of colloid or crystalloid administered in the first 24 hours 6. Blood transfusion rate: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 7. Blood hematocrit, creatinine, APTT, and platelet level at 1, 3, and 7 days postoperatively 8. Postoperative arterial pH and base excess
Identification	Contact information: Palle Juelsgaard, MD, Tokkerbakken 20, DK-8240, Risskov, Denmark, juelsgaard@dadlnet.dk No source of funding stated
Notes	Country: Denmark Language: English Study author contacted: not contacted Trial registry record or protocol available: none stated or identified Funding source/declaration of interest: no sources of funding stated Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants blinded; insufficient information on whether surgeons were blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery

Juelsgaard 2001 *(Continued)*

Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: none
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	High risk	Had potential source of bias related to specific study design (different methods of anaesthesia)

Kato 2002

Study characteristics	
Methods	Two groups: surgery with a tourniquet; surgery without a tourniquet Follow-up: no follow-up beyond operation Study design: single-centre randomised controlled trial
Participants	46 participants in total Male:Female: 2:20; 2:23 Age, years (SD): 65 (10); 63 (8) BMI (SD): not reported Inclusion criteria: patients due to undergo primary total knee replacement surgery Exclusion criteria: none stated Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 22) Group B: surgery performed without a tourniquet (n = 24) Anaesthesia was induced with intravenous propofol (1.5 mg/kg) and fentanyl citrate (0.1 mg). Tracheal intubation was facilitated with vecuronium bromide (0.1 mg/kg); anaesthesia was maintained with 66% nitrous oxide in 33% oxygen and sevoflurane. During the operation, all patients were ventilated with a tidal volume of 10 mL/kg and had a respiratory rate of 10 breaths/min. In the tourniquet group, the involved limb was exsanguinated by elevation and an Esmarch bandage, after which a pneumatic thigh tourniquet was applied to the limb and was inflated to pressure of 350 mmHg. No tourniquet was applied to the legs of control patients. The same surgeon performed all procedures; a similar surgical technique was used in each patient
Outcomes	1. Number of embolic events: measured via ultrasound. To identify the residue, it was Sudan-stained to detect fat and Giemsa-stained to detect thrombus and bone marrow. Echogenic materials were

Kato 2002 *(Continued)*

	graded as follows: Grade 0 no emboli, Grade 1 few fine emboli, Grade 2 a cascade of fine emboli or embolic masses < 5 mm, Grade 3 fine emboli mixed with large embolic masses > 5 mm 2. Duration of surgery: measured in minutes 3. Pulmonary embolism 4. Mean arterial pressure: measured intraoperatively, calculated as (cardiac output multiplied by systemic vascular resistance) added to central venous pressure 5. Blood loss: measured in millilitres 6. Tranfusion volume: measured as total volume of blood transfused to all patients in millilitres
Identification	Contact information: Dr. Kato, Department of Anesthesia, Chiba Hokusoh Hospital, Nippon Medical School, 1715 Kamakari, Inba-mura, Inba-gun, Chiba 270-1694, Japan, n-kato@mva.biglobe.ne.jp No sources of funding mentioned for this study
Notes	Country: Japan Language: English Study author contacted: yes, no reply from the author Trial registry record or protocol available: none stated or identified Funding source/declaration of interest: no sources of funding stated Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgment
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients were blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors are blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Kiss 2005

Study characteristics	
Methods	Two groups: surgery with epinephrine-augmented hypotensive anaesthesia without use of a tourniquet; normotensive epidural anaesthesia with a tourniquet Follow-up: 6 days Study design: single-centre randomised controlled trial
Participants	100 participants in total Male:Female: 13:36; 10:41 Age, years (SD): 74.7 (7.4); 72.6 (7.1) BMI (SD): 28.5 (3.3); 28.8 (3.9) Inclusion criteria: patients listed for total knee replacement surgery, ASA grade I and II Exclusion criteria: patients with history of myocardial infarction with angina, severe aortic or mitral valve stenosis, untreated hypertension, renal disease, preoperative bleeding disorders Duration of illness: unspecified
Interventions	Group A: surgery performed with epinephrine-augmented hypotensive epidural anaesthesia and no tourniquet group (n = 49) Group B: surgery performed with normotensive epidural anaesthesia with tourniquet group (n = 51) All patients were given oral premedication of 7.5 mg midazolam. Arterial blood pressure was monitored by inserting a 20-gauge cannula into the radial artery. In all patients, a central venous catheter was placed into the right internal jugular vein to measure central venous pressure. The catheter also was used to administer the epinephrine infusion to the group of patients who received EAHEA (Group A) In Group A, patients received 100 to 200 mL Ringer's solution (Fresenius Kabi Austria GmbH, Graz, Austria) before the epidural dose as a fluid preload. Epidural anaesthesia was done at the Th12-L1 and L1-L2 interspace by a paramedian approach with ropivacaine 1% (20 to 30 mL) and fentanyl (50 micrograms) In Group B, patients received 500 mL Ringer's solution (Fresenius Kabi Austria GmbH) before the epidural dose as fluid preload. Epidural anaesthesia was administered at the L3-L4 and L4-L5 interspaces through a paramedian approach with ropivacaine 1% (15 mL) and fentanyl (50 micrograms)
Outcomes	1. Change in haemoglobin: haemoglobin measured in grams/dL was taken via blood sample at 6 hours and days 1 to 6 postoperatively 2. Blood transfusion rate: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 3. Duration of surgery: measured in minutes
Identification	Contact information: Martin Raffl, MD, Clinic for Anesthesiology and Intensive Care, Paracelsus Medical Private School, Salzburg, Muellner Hauptstrasse 48, A-5020, Salzburg, Austria Phone 0043-662-4482-2701; Fax 0043-662-4482-2703; m.raffl@salk.a
Notes	Country: Austria Language: English Study author contacted: yes, no reply from the author Trial registry record or protocol available: none stated or identified

Kiss 2005 *(Continued)*

	Funding source/declaration of interest: no sources of funding stated Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgment
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: none
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: change in haemoglobin, blood transfusion rate, duration of surgery Outcome assessors blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	High risk	Had potential source of bias related to specific study design

Kumar 2015

Study characteristics

Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 6 weeks Study design: single-centre randomised controlled trial
Participants	30 participants in total Male:Female: 9:21 Age, years (range): 58 (45 to 69) BMI (SD): not reported Inclusion criteria: patients undergoing bilateral total knee replacement Exclusion criteria: patients with severe cardiac comorbidities or neurological problems

Kumar 2015 *(Continued)*

	Duration of illness: unspecified
Interventions	30 patients undergoing bilateral knee replacement surgery Group A: surgery performed with a tourniquet (n = 30) Group B: surgery performed without a tourniquet (n = 30) All surgeries were performed by the same surgical team with standard technique. Epidural anaesthesia was used in all patients given with epidural morphine 50 mg/kg along with 0.1% bupivacaine in 10 mL normal saline. Along with that, IV diclofenac sodium was used twice daily for 5 days postoperatively and then was shifted to oral formulation accordingly. Both knees were prepared at the same time, and a single set of instruments were used. One knee was operated first and then the other by senior author [CSY]. All patients received perioperative antibiotics (amoxicillin-clavulanic acid 1.2 grams intravenously). The thigh that will receive the tourniquet pressure will be randomised according to a coin toss just before the start of surgery. The tourniquet cuff used was 85 cm long and 8.5 cm wide One soft roll pad was applied between the skin and the cuff In thigh 1, tourniquet used side was inflated to systolic blood pressure plus 100 mmHg and was released after the first quadriceps stitch. Haemostasis was achieved before closure. The wound was closed after wound irrigation, then elastic bandages were applied. In thigh 2, the tourniquet was wrapped around the thigh but was not inflated during surgery
Outcomes	1. Pain score at days 1, 2, 3, weeks 2 and 6 postoperatively: assessed on a visual analogue scale between 0 and 10; zero indicates no pain, and 10 indicates extreme pain
Identification	Corresponding author: c/o Bipin Kumar, Sector-4/D, Quarter No. 1038, Bokarosteel City, Jharkhand, India, knishikant@ymail.com (N. Kumar)
Notes	Country: India Language: English Study author contacted: no Trial registry record or protocol available: none stated or identified Funding source/declaration of interest: no sources of funding stated Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Coin toss
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Self-reported outcome: pain Not stated if patients were blinded; therefore unclear risk of bias

Kumar 2015 *(Continued)*

Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: none
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Ledin 2012

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 2 years Study design: single centre randomised controlled trial
Participants	50 participants in total Male:Female: 10:15; 9:14 Age, years (SD): 70 (8); 71 (6) BMI (SD): 29 (4.8); 28 (4.8) Inclusion criteria: patients on the waiting list for elective primary total knee surgery due to arthritis, ASA I or II Exclusion criteria: Inability to give informed consent, rheumatic arthritis, malignancy, coagulation disorder or medical treatment influencing coagulation, liver disease, severe heart disease, bilateral operation Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 25) Group B: surgery performed without a tourniquet (n = 25) All operations were done under spinal anaesthesia. The Nexgen CR all-poly tibia knee prosthesis (Zimmer) was inserted after pulsed lavage and was cemented with Palacos R + G (Heraeus Medical Nordic, Sollentuna, Sweden) (40 g Palacos and 0.5 g gentamicin). 2 g cloxacillin was given intravenously just before and 3 times after the operation Low–molecular-weight heparin (Innohep, 4500 IE subcutaneously) was used for the first 14 postoperative days
Outcomes	1. Maximum total point motion at 6 months, 12 months, and 24 months: MTPM represents vector length of a marker in the rigid body that has the longest translational motion, not considering direction, and always has a positive value. Translations along the axes were given as x-translation (medial–lateral movement), y-translation (superior/lift-off and inferior/subsidence movement), and z-translation (anterior and posterior movements). Rotations around the axes were expressed as x-rotation, y-rotation, and z-rotation, which represent anterior-posterior tilt, internal-external rotation, and varus–valgus tilt, respectively

Ledin 2012 *(Continued)*

2. Pain: assessed as a visual analogue scale between 0 and 10; zero indicates no pain, and 10 indicates extreme pain
3. Blood loss: measured during surgery by weighing the surgical sponges and by subtracting the amount of irrigation fluid used from the content of the suction drain. Postoperative overt bleeding volume (in the drains) was estimated by measuring the haemoglobin content of the drains in relation to the blood haemoglobin concentration. Total blood loss was estimated by the haemoglobin dilution method based on blood volume
4. Range of motion: ROM was measured before surgery and after 3 days, 4 days, 6 weeks, 3 months, 6 months, 1 year, and 2 years. These measurements were performed by a physiotherapist who did not know whether a tourniquet had been used

Identification	Contact information: Department of Orthopedics, Aleris Specialist Care Motala; Department of Orthopedics, Linköping University Hospital, Linköping; Department of Orthopedics, Oskarshamn Hospital, Oskarshamn, Sweden, hakan.ledin@lio.se
Notes	Country: Sweden Language: English Study author contacted: no Trial registry record or protocol available: none stated or identified Funding source/declaration of interest: the study was funded by Swedish Research Council (VR-2009-6725) Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomised
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients blinded; surgeons not blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcome: pain Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: MTPM, blood loss, range of motion Outcome assessors blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data

Ledin 2012 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Li 2008

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 7 days Study design: single-centre randomised controlled trial
Participants	60 participants in total Male:Female: 9:21; 10:20 Age, years (SD): 71 (7); 70 (7) BMI (SD): 24 (5); 24 (5) Inclusion criteria: patients with initial unilateral TKA osteoarthritis (OA), rheumatoid arthritis (RA) Exclusion criteria: patients with diabetes, haemorrhagic haematological disease, haemoglobin (Hb) < 100 g/L, peripheral neurovascular disease, malignant tumour, history of vascular embolism, history of infection in the affected lower limb Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 30) Group B: surgery performed without a tourniquet (n = 30) All surgical prostheses were replaced with posterior cruciate ligament instead of a cemented artificial knee joint (GENES II, Smith & Nephew, Andover, MA, USA). Surgery was performed by the same group of physicians using the midvastus route. 3 g of haemostatic powder was sprayed on the surface of the joint cavity and soft tissue before the incision was sutured. Tourniquet pressure in the tourniquet group was the patient's own arterial systolic pressure + 100 mmHg (1 mmHg = 0.133 kPa); the wound was closed, and the tourniquet was loosened with standard dressing. Operation of the non-haemostatic group was the same as above, but the anaesthetist reduced basal blood pressure by 30 to 40 mmHg during the period from osteotomy to the bone cement-covered bone bed to reduce bleeding and found that the active bleeding point was electrocoagulated in time. All patients had no drainage in the incision [6]. Low-molecular-weight heparin calcium and plantar pump were routinely used postoperatively for anti-deep vein thrombosis. The wound dressing was replaced when it was oozing out or when the dressing of the incision was slightly tight to prevent distal blood flow. The knee joint was not passively exercised after CPM, and the affected limb was lifted higher than the heart plane
Outcomes	1. Hb and haematocrit (HCT) values: all patients were treated with blood tests 24 hours after surgery; patients with haemoglobin values < 90 g/L were treated with blood transfusion. The number of transfused patients in the 2 groups was recorded 2. Surgical time: record operating time from cutting the skin to suturing the skin measured in minutes 3. Intraoperative blood loss (IBL): calculation of intraoperative blood loss includes liquid in the aspirator bottle minus flushing fluid used in the procedure, plus net weight of the gauze pad 4. Postoperative wound blood loss (PWBL): postoperative blood loss is mainly the increase in net weight after the dressing is weighted; the amount of wound exudation is obtained and converted into volume. Exudate in the dressing has a certain volatilisation before the dressing change, so there is a cer-

Li 2008 *(Continued)*

	tain error between the calculated amount of exudation and the actual amount. To minimise errors caused by volatilisation, we have increased the thickness of the dressing and increased the frequency of dressing changes 5. Total measured blood loss (TMBL): IBL + PWBL 6. Periarticular circumference and contusion: the circumference of the knee was measured on the 3rd and 14th days after surgery, and the increase in rate compared with preoperative rate was calculated. The maximum extent of soft tissue plaque around the joint was measured, and the percentage of surface area of the plaque was calculated by the palm method 7. Pain: patients were routinely given analgesia after surgery, intramuscular injection of morphine 10 mg within 6 hours after surgery, oral celecoxib 200 mg twice daily. If the patient feels unbearable pain after the operation, the morphine 10 mg intramuscular injection is given at any time on the premise of ensuring safety of the anaesthetic. Postoperative anaesthetic use was compared between the 2 groups. The patient's femoral pain was recorded and pain scores were obtained on 6th, 24th, 48th, and 7th postoperative days on a 10-degree scale. The number of patients with straight leg elevations at 24 hours and 7 days after operation was observed and recorded. The maximum angle of spontaneous flexion of the knee joints at 1, 3, and 7 days after surgery was recorded 8. Adverse events included deep vein thrombosis
Identification	Contact information: 200003 Shanghai, Changzheng Hospital, Second Military Medical University, Department of Orthopedics Corresponding author: Qian Qi Rong, qianqr @ 163. corn No funding mentioned for this study
Notes	Country: China Language: Chinese Study author contacted: yes, no reply from study author Trial registry record or protocol available: none stated or identified Funding source/declaration of interest: none stated or identified Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients blinded; surgeons not blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: pain, adverse events Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor re-	Low risk	Assessor-reported outcomes: change in haemoglobin and haematocrit, duration of surgery, blood loss, periarticular circumference

Li 2008 *(Continued)*

ported outcomes (detection bias)		Outcome assessors blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Li 2009

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 14 days Study design: single-centre randomised controlled trial
Participants	80 participants in total Male:Female: 11:29; 13:27 Age, years (SD): 71 (6); 70 (7) BMI (SD): 27.3 (6.3); 26.8 (5.1) Inclusion criteria: patients with primary osteoarthritis or rheumatoid arthritis undergoing primary total knee replacement Exclusion criteria: bilateral total knee replacement either simultaneously or staged at less than 3-month intervals, diabetes, haemostatic defect, history of peripheral vascular disease, presence of malignant tumour, preoperative level of Hb < 10 g/L, previous thromboembolism Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 40) Group B: surgery performed without a tourniquet (n = 40) All procedures were performed by 4 similar staff surgeons. The implant used was the type of posterior cruciate ligament substituting total knee prosthetic components (Genesis II, Smith & Nephew, Memphis, TN, USA). In group A, the tourniquet was inflated to 100 mmHg above systolic blood pressure after the leg was elevated and exsanguinated, and deflation was performed after the wound was closed and the compressive dressing applied. The tourniquet was not used in group B, and active bleeding points were promptly sealed with electrical coagulation. A uniform perioperative regimen was used in all cases. Antibiotic treatment with second-generation cephalosporin was infused intravenously (1 dose preoperatively and for the next 2 days). The quantity of saline transfused intravenously within 24 hours postoperatively was 2500 to 3000 mL
Outcomes	1. Postoperative range of motion: measured in degrees of active knee flexion. Assessed at days 1, 3, and 7 2. Number of people conducting self-leg raise: measured at days 1, 3, and 7 3. Circumference length of the knee: on postoperative days 3 and 14, the circumference length of the knee was measured through the superior patellar pole, and the increased rate compared with the preoperative result was calculated

Li 2009 *(Continued)*

	4. Duration of surgery 5. Intraoperative blood loss: assessed by adding the volume in suction bottles after reduction of wound irrigation fluid and the net blood weight of sponges used during the procedure 6. Postoperative blood loss: soaked dressings were weighed and converted to volume. Due to evaporation from soaked dressings before changing, there was an error between calculated volume and actual volume. So we increased the thickness of the dressings and the frequency of changing 7. Total blood loss: measurement of overall blood loss in millimetres
Identification	Contact details: B Li: H Wu; Q Qian; X Lin; H Zhao, Department of Orthopaedic Surgery, Arthritis Institute, Changzheng Hospital, Second Military Medical University, Shanghai 200003, People's Republic of China, surgeon_li@126.com
Notes	Country: China Language: English Study author contacted: yes, no reply from study author Trial registry record or protocol available: none stated or identified Funding source/declaration of interest: none stated or identified Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number list was used
Allocation concealment (selection bias)	High risk	Open random allocation schedule
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients blinded; surgeons not blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: number of people conducting straight leg raise Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: range of motion, circumference of knee, duration of surgery, intraoperative blood loss, postoperative blood loss, total blood loss Outcome assessors blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified

Li 2009 *(Continued)*

Other bias	Low risk	No other sources of bias identified

Liu 2014

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 12 months Study design: single-centre randomised controlled trial
Participants	20 participants in total Male:Female: 7:3; 9:1 Age, years (SD): 67; 70 BMI (SD): 25.6; 27.1 Inclusion criteria: patients undergoing total knee replacement for osteoarthritis Exclusion criteria: patients with symptomatic peripheral vascular disease or contraindication to tourniquet use Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 10) Group B: surgery performed without a tourniquet (n = 10) All patients underwent TKA by the senior surgeon (Liu) through a standardised technique and prosthesis. All patients received a general anaesthetic without regional blocks or local anaesthesia, in an effort to minimise confounding variables that may influence pain scores. A medial parapatellar approach was used with eversion of the patella. An intra-articular drain on low suction was inserted before wound closure and was removed day 1 postoperatively. All patients received patient-controlled analgesia with morphine sulphate for the first 24 hours. Patients were mobilised day 1 postoperatively and were discharged home when mobilising safely. The same standardised physiotherapy protocol was undertaken in all patients postoperatively. Active and passive range of motion was encouraged without the use of continuous passive motion
Outcomes	1. Pain: a score from 1 to 10 was recorded 4 times daily up to discharge and was averaged for each day. Pain scores were recorded at 600, 1200, 1800, and 2200 with the patient at rest for 5 consecutive days. These times coincided with the timing of routine panadol administration by the nurses 2. Blood transfusion rate: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 3. Thigh and knee swelling: thigh and knee swelling was recorded with use of a tape measure at the midpoint of the patella and 10 cm above the superior pole of the patella 4. Length of hospital stay: measured in days 5. Range of motion: measured as range of flexion 6. Oxford Knee Score: 12-item patient-reported outcome measure used to report outcomes following knee replacement. Scores range from 0 to 60. 0 indicates extreme knee problems, and 60 indicates a normal knee. Not stated when OKS was collected 7. Quadriceps function: measured during active knee extension against gravity using surface EMG. Surface EMG data were recorded (Pocket EMG; BTS S.p.A., Milano, Italy) for each participant on the day of surgery preoperatively, and at 6 weeks and 6 and 12 months postoperatively. The vastus medialis, rectus femoris, and vastus lateralis muscles for both treated and control knees were recorded. Sur-

Liu 2014 *(Continued)*

face EMG electrodes (3M Red Dot; 3M Australia, Sydney, Australia) were placed on the skin surface of the muscle

8. Cement penetration: measured on the femur and tibia as the depth in centimetres the cement penetrates

Identification	Contact details: David Liu, FRACS Gold Coast Centre for Bone and Joint Surgery, John Flynn Private Hospital, Suite 8A, Fred McKay House, 42 Inland Dr, Tugun Queensland 4224, Australia Tel: +61-7-5598-0205, fax: +61-7-5598-0205, dliu01@bigpond.com Smith & Nephew Australia provided financial support
Notes	Country: Australia Language: English Study author contacted: yes, no reply from study author Trial registry record or protocol available: none stated or identified Funding source/declaration of interest: Smith & Nephew Australia provided financial support Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients blinded; insufficient information on whether surgeons were blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: pain, OKS Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Outcome assessors blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Liu 2017

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 12 months Study design: single-centre randomised controlled trial
Participants	56 participants in total Male:Female: 16:36 Age, years (SD): 67 (8) BMI (SD): 28.1 (5.5) Inclusion criteria: bilateral severe osteoarthritis with pain, accompanied with or without significant deformity, failure of conservative treatment Exclusion criteria: recent or current knee sepsis, extensor mechanism discontinuity or severe dysfunction, age > 70 years, coagulation disorder or treatment with drugs known to influence coagulation, diabetes, renal or liver disease, severe cardiovascular problems, lung disease, neurological disorders, cancer Duration of illness: unspecified
Interventions	Patients undergoing bilateral knee replacement surgery Group A: surgery performed with a tourniquet (n = 56) Group B: surgery performed without a tourniquet (n = 56) The tourniquet was applied on a layer of cotton wool padding applied over the thigh. Both right and left thighs were prepared with a tourniquet before surgery; only the limb of the TG side was elevated and exsanguinated with a rubber limb Eschmarch's bandage. The tourniquet was then inflated to pressure of 125 mmHg above systolic blood pressure (SBP) just before the incision. Longitudinal incisions were made at the midline with the knee positioned in 90 degrees flexion, from 4 cm proximal to the upper end of the patella up to the tibial tuberosity. The tourniquet was inflated for less than 120 minutes until wound closure was done and compressive dressing was applied. For NG knees, SBP was maintained at a level of approximately 100 mmHg at the time of cementation with antihypertensive drugs. Posterior stabilised knee prostheses (26 GENESIS II, Smith & Nephew, Memphis, TN, USA; 26 Vanguard, Biomet, Warsaw, IN, USA) were used in the surgery. Periarticular injection of ropivacaine (200 mg), adrenaline hydrochloride (0.1 mg), and morphine (5 mg) was administered just before skin closure Intravenous patient-controlled analgesia (PCA) with morphine was started postoperatively. All patients received rivaroxaban (10 mg once a day) from the first postoperative day, for 2 weeks, as prophylaxis against thromboembolic complications
Outcomes	1. Duration of surgery: length of every knee procedure from skin incision to wound closure 2. Pain score: pain scores were measured on a visual analogue scale (VAS) of 0 to 10 preoperatively and on postoperative days 1, 3, 5, 7, 14, and 30 3. Range of motion: ROM was measured with a standard handheld goniometer preoperatively and on postoperative days 7, 14, 30, and 90. Its centre of rotation was placed in line with the centre of the knee, the fixed arm of the goniometer aligned with the greater trochanter, and the mobile arm aligned with the lateral malleolus 4. Time to straight leg raise: the time in days to achieve the first straight leg raise of each leg was recorded 5. Swelling: this was assessed from the change in suprapatellar girth (cm). With the knee fully extended, suprapatellar girth was measured with a standard tape measure at the superior margin of the patella preoperatively and on postoperative days 3, 7, 14, and 30

Liu 2017 *(Continued)*

6. Wound healing: postoperatively, the surgical wound was examined for wound length, ooze, soakage, erythema, skin blister, and ecchymosis
7. Deep vein thrombosis: in case of any suspicion of DVT on clinical grounds, a duplex sonography was performed for confirmation of VTE
8. Knee Society Score: knee scoring system developed to evaluate patients post total knee replacement surgery. Consists of a knee score and a functional score. Score ranges from 0 to 100; a score < 60 indicates poor knee function, and a score of 80 to 100 indicates excellent knee function

Identification	Contact details: Pei-lai Liu, PhD, Department of Orthopaedics, Qilu Hospital, Shandong University, 107 Wenhua West Road, Jinan, China 250012 Tel: 0086-531-82166542; fax: 0086-531-86927544; gklpl@163.com No source of funding for this study identified
Notes	Country: China Language: English Study author contacted: no Trial registry record or protocol available: none stated or identified Funding source/declaration of interest: no source of funding identified for this study Adverse events: In the tourniquet group: 4 knees had symptomatic DVT In the non-tourniquet group: 4 knees had symptomatic DVT

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Surgeon not blinded - always performed the non-tourniquet side first; not stated if patients blinded
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: duration of surgery, range of motion, swelling, wound healing Outcome assessors blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement

Liu 2017 *(Continued)*

		No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Liu 2017 b

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 12 months Study design: single-centre randomised controlled trial
Participants	26 participants in total Male:Female: 8:18 Age, years (SD): 65.8 (9.2) BMI (SD): 28.2 (5.6) Inclusion criteria: patients undergoing bilateral total knee replacement surgery Exclusion criteria: history of coagulation disorder or medications likely to influence coagulation; diabetes; renal or liver disease; severe cardiovascular problems and lung disease; nerve disorder; cancer; skin disease; history of a previous surgical procedure of the knee other than arthroscopy; apparent keloid constitution Duration of illness: unspecified
Interventions	Patients undergoing bilateral knee replacement surgery Group A: surgery performed with a tourniquet (n = 26) Group B: surgery performed without a tourniquet (n = 26) As per the surgeon's usual practice, TKA with or without tourniquet placement was first completed on the left knee, then was performed on the right side after closure. All surgeries were performed under general anaesthesia by the same team of surgeons. A layer of cotton wool padding was applied over both thighs, above which the tourniquet was applied. The tourniquet size was 105 cm × 7 cm. Further, the lower limb on the side assigned to the TP group was elevated, and a rubber limb exsanguinator was inflated to pressure of 125 mmHg above systolic blood pressure immediately before the incision was made. Intravenous morphine for patient-controlled analgesia (PCA) was started postoperatively. All patients received rivaroxaban (10 mg 2 times daily) for 2 weeks from the first day of the operation as prophylaxis against thromboembolic complications
Outcomes	1. Duration of surgery: was recorded from when the incision was made until it was closed. Measured in minutes 2. Wound healing: measured as oozing that was classified as severe if the gauze was completely soaked or more than 10 layers of the gauze dressing were soaked with blood or serous fluid. Oozing was classified as non-severe if fewer than 10 layers of sterile absorbent gauze were stained by serous fluid or blood. All wounds were evaluated on postoperative day 2 3. Mean change in suprapatellar girth: measured in terms of change in suprapatellar girth (postoperative girth - preoperative girth, cm). Measurement was made at the superior margin of the patella with the knee at extension as far as possible by using a standard tape; differences between preoperative measurements and measurements obtained on postoperative days 3, 7, 14, and 30 were calculated 4. Range of motion: measured with a standard handheld goniometer preoperatively and on postoperative days 7, 14, 30, and 90. The centre of rotation was set in line with the centre of the knee, while

Liu 2017 b *(Continued)*

	the fixed arm was aligned with the greater trochanter and the mobile arm was aligned with the lateral malleolus 5. Wound length: measured in centimetres with the knee in extension as far as possible on postoperative day 2 while the dressing was changed after the drain was pulled out 6. Revision rate: indicating the number of patients in each group requiring revision surgery up to 1 year postoperatively 7. MSS score: was used for an objective evaluation of the aesthetic appearance of the scar at the end of postoperative year 1. MSS encompasses several factors, including colour, appearance, contour, distortion, and texture of the scar. All these parameters are graded on a scale of 1 to 4 points, except the last one, which is rated as 1 for matte and 2 for shiny appearance. In addition, the overall appearance of the incision scar was evaluated via a visual analogue scale (VAS), with a score of 0 indicating an excellent outcome and 10 indicating the worst possible outcome
Identification	Contact details: Pei-lai Liu, PhD, Department of Orthopaedics, Qilu Hospital, Shandong University, 107 Wenhua West Road, Jinan, China 250012 Tel: 0086-531-82166542; fax: 0086-531-86927544; gklpl@163.com
Notes	Country: China Language: English Study author contacted: yes, no reply from study author Trial registry record or protocol available: none stated or identified Funding source/declaration of interest: no source of funding identified for this study Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: none
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: duration of surgery, wound healing, mean change in suprapatellar girth, range of motion, wound length, revision rate, MSS score Outcome assessors blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement

Liu 2017 b *(Continued)*

		No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Matziolis 2004

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 48 hours Study design: single-centre randomised controlled trial
Participants	20 participants in total Male:Female: 2:8; 3:7 Age, years (range): 72.4 (64 to 83); 76.6 (65 to 84) BMI (range): 28.3 (19.3 to 35.5); 29.5 (24 to 43.8) Inclusion criteria: patients listed for primary total knee replacement surgery Exclusion criteria: diabetes mellitus, presence of peripheral arterial occlusive disease (pAOD) or cardiopulmonary diseases ruled out by clinical examination and if necessary duplex ultrasound, medical history of thrombosis or embolism and renal insufficiency (creatinine mmol/L). Patients with severe varus or valgus deformity > 15" or flexion contracture > 20" were excluded from the study to minimise bias due to different soft tissue trauma by preparation and postoperative tension of the skin Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 10) Group B: surgery performed without a tourniquet (n = 10) In all cases, a cemented PFC Sigma total knee replacement (DePuy, Warsaw, IN, USA) without resurfacing of the patella was implanted by the same surgeon (GM) through a midline incision and a medial parapatellar approach
Outcomes	1. Postoperative endothelin-1 measurement: blood was taken preoperatively (2 mL in EDTA tube). 10 further determinations were made at time points 5, 15, and 30 minutes, and 1, 2, 3, 4, 6, 24, and 48 hours after the end of surgery or opening of the tourniquet. Blood samples were centrifuged for l0 minutes at 40°F and 2000 G within a half-hour of sampling and were frozen at -4°F until determination 2. Blood transfusion rate: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 3. Duration of surgery: measured in minutes 4. Change in haemoglobin: change in haemoglobin concentration between preoperative reading and first postoperative day reading 5. Change in C-reactive protein (CRP): change in blood CRP reading between preoperative reading and first postoperative day reading 6. Range of motion: number of degrees of knee flexion achieved preoperatively and on the day of discharge 7. Revision rate 8. Nerve injury
Identification	Contact information: G Matziolis, Centre for Musculoskeletal Surgery, Charite University Hospital, Schumannsir, 20-21, 10117, Berlin, Germany, georg.matziolis@charite.de

Matziolis 2004 *(Continued)*

Notes	Country: Germany Language: English Study author contacted: yes, no reply from study author Trial registry record or protocol available: none stated or identified Funding source/declaration of interest: no financial affiliation has been paid by third parties others than the Center for Musculoskeletal Surgery of the Charite University Hospital Adverse events: In the tourniquet group: 1 patient had a wound healing disorder that required revision surgery In the non-tourniquet group: 1 patient had nerve injury

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	High risk	Open random allocation schedule
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants blinded; insufficient information to specify if surgeons were blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcome: nerve injury Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources identified

Molt 2014

Study characteristics

Molt 2014 *(Continued)*

Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 2 years Study design: single-centre randomised controlled trial
Participants	60 participants in total Male:Female: 16:14; 16:14 Age, years (SD): 70 (7); 67 (9) BMI (SD): 28 (3); 28 (3) Inclusion criteria: patients suffering exclusively from OA, stages II to V; patients requiring knee prosthesis suitable for the use of a triathlon knee system; patients understanding the conditions of the study and willing and able to comply with scheduled postoperative clinical and radiographic evaluations and prescribed rehabilitation; patients who signed the Ethics Committee approved informed consent form before surgery Exclusion criteria: previous major knee arthroplasty; significant disabling problems from the muscular-skeletal system other than the knees; obese patients with obesity severe enough to affect their ability to perform activities of daily living (BMI > 35); patients with active or suspected infection; patients with active malignancy; patients with severe osteoporosis, Paget's disease, renal osteodystrophy; patients immunologically suppressed or receiving steroids in excess of physiological dose requirements; patients with a neuromuscular or neurosensory deficit that would limit their ability to assess performance of the device or that interferes with the patient's ability to limit weight-bearing or places an extreme load on the implant during the healing period; pregnancy; systemic or metabolic disorders leading to progressive bone deterioration; concurrent illness such as sickle cell anaemia, SLE, or renal disease requiring dialysis Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 30) Group B: surgery performed without a tourniquet (n = 30) Each patient was given preoperative antibiotics and tranexamic acid. Surgeries were performed via a midline incision with a parapatellar medial entrance to the joint using appropriate guide instruments according to the surgical technique supplied to the knee system. In both groups, the bony surfaces were prepared in the same manner, were cleansed by saline pulse lavage, and were kept clean of blood by saline-prepared medical pads. At the time of surgery, 8 tantalum markers (0.8 mm diameter; RSA Biomedical, Umeå, Sweden) were inserted into the proximal tibial metaphysis and 5 markers were inserted into the polyethylene tibial insert. The tourniquet was applied during dressing and was inflated to 300 mmHg just before the start of surgery and was not deflated until the leg was sutured and dressed. The group operated on without the use of a tourniquet was operated on with the same surgical and cementing technique. The cement used was Refobacin® Bone Cement R (Biomet Inc., Warsaw, IN, USA). No patellar components were used in either group. Postoperatively, low-molecular-weight heparin was used for thromboembolic prophylaxis. Early full weight-bearing and mobilisation were similar for both groups
Outcomes	1. Duration of surgery 2. Length of hospital admission 3. Radiostereometric analysis: the RSA investigation was done within 2 to 3 days postoperatively after full weight-bearing, then at 3 months, 1 year, and 2 years postoperatively. RSA was performed with the patient in a supine position, with the knee of interest inside a calibration cage (Cage 10, RSA Biomedical, Umeå, Sweden). 3D tibial component migration was measured with UmRSA software (v6.0, RSA Biomedical, Umeå, Sweden). The precision of the RSA system according to the double exams was 0.12 mm, 0.21 mm, and 0.14 mm for x-, y-, and z-translations, and 0.12°, 0.11°, and 0.09° for x-, y-, and z-rotations

Molt 2014 *(Continued)*

4. Maximum total point motion: positive directions for translations along the orthogonal axes were transverse (medial to lateral), longitudinal (caudal to cranial), and sagittal (posterior to anterior). Positive directions for rotations about the coordinate axes were anterior tilt (transverse axis), internal rotation (longitudinal axis), and varus (sagittal axis). An increase in MTPM > 0.2 mm between first and second year follow-up was considered as continuous migration
5. Mortality
6. Deep vein thrombosis
7. Stroke
8. Blood transfusion rate: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome

Identification	Contact information: Mats Molt, Department of Orthopaedics Hässleholm-Kristianstad Ystad, Hässleholm, Sjukhusorganisation, Box 351, S-281, 25 Hässleholm, Sweden Tel.: +46 451298707, mats.molt@skane.se (M. Molt)
Notes	Country: Sweden Language: English Study author contacted: no Trial registry record or protocol available: clinical trial ID: NCT01604382 Funding source/declaration of interest: no funding for this study Adverse events: In the tourniquet group: 2 patients required re-operation; 1 patient reported instability in the index knee at 2 years' follow-up In the non-tourniquet group: 1 patient died due to postoperative septicaemia; 1 patient had a stroke; 1 patient had DVT

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients were blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias)	Low risk	No missing outcome data

Molt 2014 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources of bias identified

Mori 2016

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 7 days Study design: single-centre randomised controlled trial
Participants	103 participants in total Male:Female: 6:45; 9:43 Age, years (SD): 72.8 (7.3); 74.6 (7.6) BMI (SD): 27.7 (3.4); 29.2 (3.9) Inclusion criteria: patients undergoing total knee replacement surgery Exclusion criteria: patients showing preoperative DVT, coagulation disorder, abnormal coagulation test values, or receiving anticoagulants; patients who received anticoagulant therapy postoperatively according to the judgement of the physician Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 51) Group B: surgery performed without a tourniquet (n = 52) All operations were conducted by a single surgeon (S.K.). All patients received spinal and epidural anaesthesia in conjunction with general anaesthesia, and the tube for the epidural continuation was removed on the second postoperative day. Exposure of the knee was through a midline skin incision (approximately 8 to 10 cm) and a mid-vastus approach. All patients had a Scorpio non-restrictive geometry posterior-stabilised system (Stryker Howmedica Osteonics, Allendale, NJ, USA) cemented arthroplasty. An extramedullary guide was used for the tibia, and an intramedullary osteotomy guide was used for the distal cut of the femur. The patella was resurfaced in all patients In patients of group T, a pneumatic thigh tourniquet was applied, was inflated to pressure of 250 mmHg, then was deflated after skin closure. Elastic stockings were worn postoperatively by all patients. All patients were managed with a foot pump (Kendall SCD 700, Covidien, MA, USA) on both legs to prevent DVT. Walking was permitted from the day after surgery. Two days after the operation, the drain was removed
Outcomes	1. Duration of surgery: measured in minutes 2. Overall blood loss: the amount of intraoperative and postoperative blood loss was measured in all cases based on suction volume and weight of the sponges 3. Deep vein thrombosis: bilateral ultrasonography of the lower extremities (iU22 Vision 2006, Philips, Seattle, WA, USA) was performed by highly skilled physicians. Ultrasonography was scheduled preoperatively and 7 days postoperatively. A thrombus located in anterior tibial vein (ATV), peroneal vein (PeV), soleal vein (SoV), posterior tibial vein (PTV), and very small tertiary vessels was defined as distal DVT. A thrombus located in femoral vein (FV), deep femoral vein (DFV), great saphenous vein (GSV),

Mori 2016 *(Continued)*

	small saphenous vein (SSV), and popliteal vein (PV) was defined as proximal DVT. Total DVT included distal DVT and/or proximal DVT 4. Pulmonary embolism
Identification	Contact information: Noriaki Mori, Department of Orthopaedic Surgery, Wajo Eniwa Hospital, Koganechuo 2-1-1, Eniwa City 061-1449, Japan Tel.: +81 123 33 2333; fax: +81 123 335108; noriakki@hotmail.co.jp (N.Mori)
Notes	Country: Japan Language: English Study author contacted: yes, no reply from author Trial registry record or protocol available: none reported or identified Funding source/declaration of interest: no funding for this study Adverse events: no additional adverse events reported in the 2 groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Ozkunt 2018

Study characteristics	
Methods	Three groups: surgery performed with a tourniquet for the entire procedure; surgery performed with a tourniquet for cementing only; surgery performed without a tourniquet Follow-up: 6 weeks Study design: single-centre randomised controlled trial
Participants	69 participants in total Male:Female: not stated Age, years (range): 65.05 (52 to 81) BMI (SD): not stated Inclusion criteria: patients diagnosed with arthritis refractory to conservative treatment and identified as TKA candidates Exclusion criteria: secondary arthritis, extreme deformity, previous cardiovascular disease Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet for the entire procedure (n = 24) Group B: surgery performed with a tourniquet for cementing only (n = 20) Group C: surgery performed without a tourniquet (n = 25) Posterior cruciate retaining Genesis II (Smith & Nephew, Memphis, TN, USA) cemented knee system and OrCem 3 low-viscosity polymethylmethacrylate (PMMA) bone cement (European Medical Contract Manufacturing, Nijmegen, Netherlands) were used in all patients. All patients were operated under general anaesthesia with propofol and desfluran
Outcomes	1. Blood transfusion rate: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 2. Pain: measured as a VAS score between 0 and 10 at 6 weeks 3. Knee Society score: knee scoring system developed to evaluate patients post total knee replacement surgery. Consists of a knee score and a functional score. Score ranges from 0 to 100; a score < 60 indicates poor knee function, and a score of 80 to 100 indicates excellent knee function 4. Cement penetration depth: measured as the depth in centimetres the cement penetrated the femur and tibia at the 6-week radiograph
Identification	Contact information: Okan Ozkunt, Department of Orthopedics and Traumatology, Acibadem University Atakent Hospital, Halkali/Kucukcekmece, Istanbul, 34303, Turkey, drdeto@gmail.com
Notes	Country: Turkey Language: English Study author contacted: yes, no reply from author Trial registry record or protocol available: none reported or identified Funding source/declaration of interest: no funding for this study Adverse events: no additional adverse events reported in the 2 groups
Risk of bias	

Ozkunt 2018 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Pfitzner 2014

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 4 days Study design: single-centre randomised controlled trial
Participants	90 participants in total Male:Female: 21:24; 11:34 Age, years (range): 69 (47 to 85); 70.5 (50 to 90) BMI (range): 27.8 (18.5 to 38.1); 26 (18.5 to 33.9) Inclusion criteria: patients with primary end-stage osteoarthritis receiving unilateral total knee arthroplasty (TKA) Exclusion criteria: patients receiving any anticoagulation before surgery (e.g. acetylsalicylic acid, phenprocoumon, warfarin, clopidogrel, dabigatran, rivaroxaban, low-molecular-weight heparin) with the diagnosis of liver dysfunction/coagulation dysfunction or a history of peripheral arterial obstructive disease or thromboembolic events

Pfitzner 2014 *(Continued)*

	Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 45) Group B: surgery performed without a tourniquet (n = 45) All patients received a cemented, posterior-stabilised primary TKA (Nexgen LPS Flex, Zimmer, Warsaw, IN, USA) with a fixed bearing design without patellar resurfacing. A total of 40 g of bone cement (Palacos R®, Heraeus, Hanau, Germany) was used with a fourth-generation cementing technique including pulsatile lavage, vacuum mixture, double-cementing technique, and cement gun pressurisation. Every patient received the same standardised postoperative pain medication protocol
Outcomes	1. Pain: measured as a VAS score between 0 and 10 on the second and fourth postoperative days. Pain was measured at rest and on mobilisation 2. Overall blood loss: to determine overall blood loss, peripheral blood was taken preoperatively and on the first postoperative day. Total blood loss was calculated using the method of Bourke and Smith to take both obvious and hidden blood losses into account 3. Cement mantle thickness: measured as the depth in centimetres the cement penetrated the femur and tibia at the day 4 radiograph
Identification	Contact information: T Pfitzner, P von Roth, C Perka, Orthopaedic Department, Center for Musculoskeletal Surgery, Charité – Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany, Tilman.pfitzner@charite.d
Notes	Country: Germany Language: English Study author contacted: yes, no reply from author Trial registry record or protocol available: none reported or identified Funding source/declaration of interest: no funding for this study Adverse events: no additional adverse events reported in the 2 groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients were blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias

Pfitzner 2014 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Tai 2012

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 4 days Study design: single-centre randomised controlled trial
Participants	72 participants in total Male:Female: 9:27; 8:28 Age, years (SD): 72.1 (6.9); 71.5 (6.8) BMI (SD): 28.6 (4.5); 27.9 (4.2) Inclusion criteria: patients undergoing total knee replacement surgery for osteoarthritis Exclusion criteria: rheumatoid arthritis, coagulopathy, uncontrolled hypertension, peripheral vascular disease Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 36) Group B: surgery performed without a tourniquet (n = 36) All patients underwent primary total knee arthroplasty with minimally invasive techniques and cemented prostheses (Genesis II Total Knee System, Smith & Nephew, Memphis, TN, USA; or U2 Knee System, United Orthopedic, Taipei, Taiwan). All operations were performed through the medial parapatellar approach by experienced knee surgeons. An intramedullary guide was used for both tibial and femoral cuts. No drainage system was used postoperatively for any patient In the tourniquet group, the tourniquet was inflated to systolic blood pressure plus 100 mmHg and was released after the joint capsule had been closed. A 40-mL local anaesthetic mixture (2% lidocaine with epinephrine, bupivacaine, and gentamicin) was injected into the joint space for pain control and as a temporary tamponade. The wound was closed after wound irrigation and haemostasis and then was wrapped with elastic bandages. In the non-tourniquet group, the tourniquet was wrapped around the thigh but was not inflated during surgery
Outcomes	1. Intraoperative blood loss: measured by weighing sponges and measuring suction volume 2. Blood transfusion rate: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 3. Overall blood loss: calculated by multiplying estimated blood loss by the decrease in haematocrit 4. Change in haemoglobin: repeated blood tests were performed daily from days 1 to 4. The haemoglobin concentration in the blood was recorded each day

Tai 2012 *(Continued)*

	5. Change in haematocrit: repeated blood tests were performed daily from days 1 to 4. The haematocrit concentration in the blood was recorded on each day 6. Serum creatine phosphokinase, myoglobin, lactate dehydrogenase, C-reactive protein: blood tests were performed daily from days 1 to 4 postoperatively. Concentrations of these enzymes was re-scored at each time point 7. Pain: measured on a VAS score between 0 and 10 on days 1 and 4 postoperatively 8. Duration of surgery: measured in minutes
Identification	Contact information: Ta-Wei Tai, Department of Orthopaedics, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan No funding for this study
Notes	Country: Taiwan Language: English Study author contacted: yes, no reply from author Trial registry record or protocol available: none reported or identified Funding source/declaration of interest: no funding for this study Adverse events: no additional adverse events reported in the 2 groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients blinded; surgeons not blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcome: pain Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: intraoperative blood loss; overall blood loss; blood transfusion rate; change in haemoglobin; change in haematocrit, serum creatinine phosphokinase, myoglobin, lactate dehydrogenase, CRP, duration of surgery Outcome assessors blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement

Tai 2012 *(Continued)*

		No protocol reported or identified
Other bias	Low risk	No sources of bias identified

Tetro 2001

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 10 days Study design: single-centre randomised controlled trial
Participants	63 participants in total Male:Female: 15:18; 11:19 Age, years (SD): 69.8 (6.7); 69.8 (9.0) BMI (SD): 28.6 (4.5); 27.9 (4.2) Inclusion criteria: patients undergoing total knee replacement for osteoarthritis or rheumatoid arthritis Exclusion criteria: bilateral TKA required simultaneously or staged at less than 3-month intervals; history of bleeding diathesis; revision TKA; history of musculoskeletal infection of the affected limb; history of peripheral vascular disease Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 33) Group B: surgery performed without a tourniquet (n = 30) Groups were similar with respect to operative procedure. Lateral release was performed in 22 patients in the tourniquet group and in 20 in the non-tourniquet group (Table 1). One synovectomy was performed in each group. All patients received a primary cemented total knee replacement with a cemented polyethylene patellar replacement. In the tourniquet group, the leg was elevated and exsanguinated (without use of an Esmarch bandage) before tourniquet inflation. The tourniquet was set at 125 to 150 mmHg above systolic blood pressure, up to a maximum value of 300 mmHg. The tourniquet was deflated after the bone cement had set, and only then was electrocautery used for haemostasis. In the non-tourniquet group, electrocautery was used as necessary throughout the procedure
Outcomes	1. Intraoperative blood loss: recorded by the anaesthetist by method estimation (i.e. suction drainage - irrigation volume (soaked sponges were considered equivalent to 80 mL of blood)) 2. Blood transfusion rate: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 3. Duration of surgery: measured in minutes 4. Deep vein thrombosis 5. Infection 6. Haemaglobin level: blood haemoglobin was collected on postoperative days 1, 2, 3, 5, and 7 7. Postoperative blood loss: recorded in terms of suction volume at 36 hours after the operation 8. Overall blood loss: measures by the sum of intraoperative blood loss and postoperative drainage volume
Identification	Contact information: Dr John F Rudan, Department of Surgery, Queen's University, Kingston ON K7L 3N6

Tetro 2001 *(Continued)*

	Fax 613 549-2529, cmg@post.queensu.ca
Notes	Country: Kingston Language: English Study author contacted: yes, no reply from author Trial registry record or protocol available: none reported or identified Funding source/declaration of interest: no funding for this study Adverse events: In the tourniquet group: 4 wound infections In the non-tourniquet group: 1 wound infection, 1 gastrointestinal haemorrhage

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients 'blindly' randomised; surgeons not blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: DVT, infection Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	High risk	Assessor-reported outcomes:**i**ntraoperative blood loss, blood transfusion rate, duration of surgery, haemoglobin level, postoperative blood loss, overall blood loss Outcome assessors were not blinded; therefore high risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of blinding identified

Vandenbussche 2001

Study characteristics

Vandenbussche 2001 *(Continued)*

Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 3 months Study design: single-centre randomised controlled trial
Participants	80 participants in total Male:Female: 9:31; 16:24 Age, years (range): 73.65 (52 to 110); 80.25 (50 to 110) BMI (SD): not reported Inclusion criteria: patients undergoing primary total knee replacement surgery for osteoarthritis Exclusion criteria: patients with diabetes, haemostasis defect, rheumatoid arthritis, previous thromboembolism, abnormal vascular supply to the leg, previous open knee surgery, bilateral TKA Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 40) Group B: surgery performed without a tourniquet (n = 40) All operations were performed under general anaesthesia by a single surgeon or by house staff using a standardised technique. Cefamandol 1500 mg was given intravenously at induction of anaesthesia, and 4 further doses of 750 mg were given postoperatively. Standard anticoagulant prophylaxis using enoxaparin was started the evening before surgery and continued until the patient was fully mobile. In group A, the limb was first exsanguinated by elevation for 2 minutes, then the tourniquet was inflated to 350 mmHg. If the duration of tourniquet use exceeded 90 minutes, the tourniquet was released intraoperatively and haemostasis was completed. After 10 minutes of release, a new exsanguination was instituted. The tourniquet was not released until after the wound was closed and the compressive dressing was applied
Outcomes	1. Duration of surgery: measured in minutes 2. Change in haemoglobin: blood concentrations recorded preoperatively and on first and tenth days postoperatively 3. Change in haematocrit: blood concentrations recorded preoperatively and on first and tenth days postoperatively 4. Overall blood loss: was calculated as the sum of compensated and non-compensated blood loss. Blood concentrations were recorded preoperatively and on first and tenth days postoperatively 5. Thigh pain: study authors did not include data on pain scores in the final report. They stated that pain scores were significantly lower in the control group when compared to the tourniquet group 6. Wound complications 7. Implant loosening: radiographic analysis was conducted at 3 months to look for lucency - a sign of loosening 8. Time to achieve straight leg raise 9. Range of knee flexion: measured in degrees at days 5 and 10 and at 3 months
Identification	Contact information: E Vandenbussche, L-D Duranthon, B Augereau, Department of Orthopaedic Surgery, Hôpital Européen Georges Pompidou, 20 Rue Louis Blanc, 75908 Paris Cedex 15, France, eric.vdb@egp.ap-hop-paris.fr
Notes	Country: France Language: English Study author contacted: yes, no reply from author Trial registry record or protocol available: none reported or identified

Vandenbussche 2001 *(Continued)*

	Funding source/declaration of interest: no funding for this study Adverse events: In the tourniquet group: 1 patient had DVT In the non-tourniquet group: 2 patients had DVT

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients blinded; surgeons not blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: pain, complications, time to achieve straight leg raise Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: duration of surgery, change in haemoglobin, change in haematocrit, overall blood loss, implant loosening, range of knee flexion Outcome assessors were blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Vertullo 2017

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 2 days Study design: single-centre randomised controlled trial
Participants	40 participants in total Male:Female: 10:10; 11:9

Vertullo 2017 *(Continued)*

	Age, years (SD): 67.85 (6.91); 65.65 (8.54) BMI (SD): 30.43 (5.07); 31 (5.31) Inclusion criteria: Patients with end stage knee osteoarthritis who have failed non-operative management and are being listed for a primary total knee replacement. Exclusion criteria: history of peripheral vascular disease that precluded tourniquet use or required a semi-constrained prosthesis due to ligament instability necessitating a fixed bearing tibial component with tibial stem Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 20) Group B: surgery performed without a tourniquet (n = 20) In both groups, the knee replacement procedure was commenced with a tourniquet applied but without inflation. The patient's blood pressure was maintained hypotensive if no contraindications were applied, else normotensive. Proximal tibial osteotomy was undertaken via a computerised navigation system, with all resections at 90 to the tibial long axis, removing a planned 10-mm resection of the lateral tibial plateau. After bone resection and preparation were undertaken, patients were randomised to group A or B. In group A, the leg was elevated for 1 minutes, then the tourniquet was inflated to 300 mmHg for the duration of the cementing procedure. In group B, the tourniquet was not inflated
Outcomes	1. Cement penetration depth: distance in millimetres the cement penetrated the femur and the tibia on the postoperative radiograph. This was assessed on day 2
Identification	Contact information: Christopher John Vertullo, Orthopaedic Surgery & Sports Medicine Centre, 8-10 Carrara Street, Benowa, QLD, Australia, chris.vertullo@icloud.com
Notes	Country: France Language: English Study author contacted: no Trial registry record or protocol available: none reported or identified Funding source/declaration of interest: no funding for this study Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: none

Vertullo 2017 *(Continued)*

Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: cement penetration depth Outcome assessors were blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Wakankar 1999

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 4 months Study design: single-centre randomised controlled trial
Participants	77 participants in total Male:Female: 11:26; 14:26 Age, years (range): 72.5 (57 to 85); 71.8 (43 to 91) BMI (SD): not reported Inclusion criteria: patients undergoing primary total knee arthroplasty Exclusion criteria: patients with diabetes, rheumatoid arthritis, previous thromboembolism, active malignancy, those having 1-stage bilateral surgery Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 37) Group B: surgery performed without a tourniquet (n = 40) All patients had identical anaesthesia, which included premedication with temazepam and general anaesthesia with fentanyl. No patient had spinal or epidural anaesthesia Postoperatively, all had 'patient-controlled analgesia' (PCA) with an infusion of morphine sulphate. All patients received intravenous cefuroxime (1.5 g) after induction of anaesthesia and twice postoperatively. Those in group A had TKA under a tourniquet after the leg had been exsanguinated. Tourniquet pressure was twice the systolic blood pressure. Patients in group B did not have a tourniquet applied to the leg. Low-dose warfarin was given to maintain the international normalised ratio between 1.3 and 2.0, and was continued until discharge from the hospital. Mobilisation began on removal of the drains, 48 hours after the operation
Outcomes	1. Pain: assessed as a visual analogue scale between 0 and 10; zero indicates no pain, and 10 indicates extreme pain. Measured on week 1, on week 6, and at 4 months. Study authors did not report raw data, instead reporting a change in pain score 2. Change in knee flexion: measured in degrees. The number of degrees the knee can flex at week 1, week 6, and 4 months

Wakankar 1999 *(Continued)*

	3. Change in swelling of the thigh, knee, and calf: the circumference of the limb at the level of the superior pole of the patella and at points 10 cm above and below. Measured at week 1, week 6, and 4 months 4. Deep vein thrombosis 5. Adverse events
Identification	Contact information: JC D'Arcy, FRCS, Consultant Orthopaedic Surgeon, Department of Orthopaedics, Eastbourne District General Hospital, King's Drive, Eastbourne, East Sussex BN21 2UD, UK
Notes	Country: UK Language: English Study author contacted: no Trial registry record or protocol available: none reported or identified Funding source/declaration of interest: no funding for this study Adverse events: In the tourniquet group: 6 patients required manipulation under anaesthesia, 1 patient had wound leakage, 1 patient died from unrelated causes In the non-tourniquet group: 5 patients required manipulation under anaesthesia, 2 patients died from unrelated causes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Wauke 2002

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 4 weeks Study design: single-centre randomised controlled trial
Participants	37 participants in total Male:Female: not reported Age, years (SD): 63.2 (8.7); 61.4 (7.4) BMI (SD): not reported Inclusion criteria: patients undergoing primary total knee replacement surgery Duration of illness: unspecified
Interventions	All patients under general anaesthesia using sevoflurane and propofol. Endotracheal intubation and mechanical ventilation were employed to maintain a constant end-tidal CO_2 level. The fractional inspired O_2 concentration (33%) did not change during the operation. In the with tourniquet group, a tourniquet was applied at approximately 100 mmHg above systolic blood pressure. The operations were performed with autologous blood transfusion and used a postoperative blood conservation system. Blood losses in the 2 groups were measured and compared. Heparin at 5000 U/d was postoperatively administered to all patients for 3 weeks
Outcomes	1. Overall blood loss: measured in millilitres 2. Postoperative blood loss: measured in millilitres using a postoperative drainage catheter 3. Deep vein thrombosis 4. Pulmonary embolism 5. Number of embolic events: measured via ultrasound. To identify the residue, it was Sudan-stained to detect fat, and it was Giemsa-stained to detect thrombus and bone marrow. Echogenic materials were graded as follows: Grade 0 no emboli, Grade 1 few fine emboli, Grade 2 a cascade of fine emboli or embolic masses < 5 mm, Grade 3 fine emboli mixed with large embolic masses > 5 mm
Identification	Contact information: N Kato, R Ogawa, Department of Anesthesiology, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo, Japan
Notes	Country: Japan Language: English Study author contacted: no Trial registry record or protocol available: none reported or identified Funding source/declaration of interest: no funding for this study reported Adverse events: In the tourniquet group: 1 patient had PE and 2 patients had DVT In the non-tourniquet group: 0 patients had PE or DVT

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Wauke 2002 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients were blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Wu 2018

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 6 months Study design: single-centre randomised controlled trial
Participants	100 participants in total Male:Female: 22:28; 19:31 Age, years (SD): 67.58 (4.61); 68.06 (3.16) BMI (SD): 24.10 (2.16); 23.87 (2.13) Inclusion criteria: patients undergoing primary total knee replacement surgery for osteoarthritis Exclusion criteria: patients < 18 years or > 85 years of age, rheumatoid arthritis, allergy to TXA, history of thrombosis, coagulation dysfunction, uncontrolled hypertension, infection, body mass index (BMI) > 35 Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 50) Group B: surgery performed without a tourniquet (n = 50)

Wu 2018 *(Continued)*

	All patients were treated intravenously with 15 mg/kg TXA 10 minutes before skin incision; an additional 1 g TXA was used after 3 hours. All patients were treated by a senior orthopaedic surgeon under general anaesthesia. Drainage tubes were used in all patients and were removed 24 hours postoperatively if blood loss was < 300 mL. Otherwise, they continued to be used until the quantity was < 50 mL
Outcomes	1. Total blood loss: in millilitres estimated using the formula of Gross et al 2. Intraoperative blood loss: measured in millilitres. The higher the score, the worse the outcome 3. Hidden blood loss: measured in millilitres. The higher the score, the worse the outcome 4. Drainage volume: measured in millilitres. The higher the score, the worse the outcome 5. Transfusion requirements: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 6. Maximum Hb drop: defined as the difference between preoperative Hb level and lowest postoperative Hb level received during hospital stay and the lowest Hb level before any blood transfusion 7. Knee circumference: the circumference of the limb at the level of the superior pole of the patella and at points 10 cm above and below. Measured on postoperative days 1, 3, and 5, and at 6 months 8. Pain: measured on a visual analogue score between 0 and 10 9. ROM: number of degrees of knee flexion. Measured on postoperative days 1, 3, and 5, and at 1 and 6 months 10. Postoperative hospital stay 11. Deep vein thrombosis (DVT) and/or pulmonary embolism (PE) events 12. Wound-related complications as second outcomes
Identification	Contact information: Yuangang Wu, Department of Orthopaedics, West China Hospital, Sichuan University, 37 # Guoxue Road, Chengdu, 610041, People's Republic of China, wuuiangang23@163.com
Notes	Country: China Language: English Study author contacted: no Trial registry record or protocol available: researchregistry4423 Funding source/declaration of interest: study was funded by the Science and Technology Department of Sichuan Province (2017FZ0056 and No. 2018HH0141), and also by the Health Department of Sichuan Province (N0. 18ZD016) Adverse events: no adverse events reported between the 2 groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants blinded; surgeons not blinded However surgeons would be able to influence/alter their performance only for intraoperative outcomes such as intraoperative blood loss, operative time, or quality of cementation. It is unlikely that surgeons would alter their performance to influence these outcomes for fear of damaging the overall quality and safety of the surgery

Wu 2018 *(Continued)*

Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: pain, DVT, wound-related complications Patients blinded; therefore low risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	High risk	Assessor-reported outcomes: total blood loss, intraoperative blood loss, hidden blood loss, drainage volume, transfusion requirements, maximum Hb drop, knee circumference, range of motion, length of stay Outcome assessors not blinded; therefore high risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources of bias identified

Yavarikia 2010

Study characteristics	
Methods	Three groups: surgery performed with a tourniquet inflated until wound closure; surgery performed with a tourniquet inflated until components were inserted; surgery performed without a tourniquet Follow-up: day 1 Study design: single-centre randomised controlled trial
Participants	84 participants in total Male:Female: 6:16; 9:24; 7:22 Age, years (range): 68 (54 to 72); 64 (54 to 73); 66 (51 to 74) BMI (SD): not reported Inclusion criteria: patients with a diagnosis of severe primary osteoarthritis, insertion of bicompartmental prosthesis, absence of any known coagulation disorder Exclusion criteria: Patients undergoing a unicondylar knee replacement or a revision knee replacement. Presence of a known coagulation disorder or a patient who is routinely taking anticoagulant medication. Duration of illness: unspecified
Interventions	Group 1: surgery performed without a tourniquet (n = 29) Group 2: surgery performed with a tourniquet inflated until components inserted (n = 33) Group 3: surgery performed with a tourniquet inflated until wound closure (n = 22) For all patients, suction drainage was used routinely and was removed after 24 hours. Low-molecular-weight heparin was administered to all patients, and no monitoring for INR was performed. Antibiotic prophylaxis was started just before the tourniquet was inflated with 1 g cefazolin, then was continued 3 times daily for 48 hours

Yavarikia 2010 *(Continued)*

Outcomes	1. Change in haemoglobin: difference between preoperative haemoglobin and day 1 postoperative haemoglobin 2. Change in haematocrit: difference between preoperative haematocrit and day 1 postoperative haematocrit 3. Overall blood loss: measured in miilimetres 4. Blood transfusion rate: defined as number of units delivered to the patient. The higher the number of units, the worse the outcome 5. Duration of surgery: measured in minutes
Identification	Contact information: Alireza Yavarika, Department of Orthopaedics, Ward of Orthopaedics, Besat Hospital, Hamadan University of Medical Sciences, Hamadan, Iran, tel +959144122542
Notes	Country: Iran Language: English Study author contacted: yes, no reply from study author Trial registry record or protocol available: none reported or identified Funding source/ declaration of interest: no source of funding reported or identified Adverse events: no adverse events reported between the 2 groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Low risk	Self-reported outcomes: none
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Zhang 2010

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: not reported Study design: single-centre randomised controlled trial
Participants	60 participants in total Male:Female: 8:22; 11:19 Age, years (SD): 72 (6); 71 (6) BMI (SD): 25 (4); 26 (4) Inclusion criteria: patients undergoing primary total knee replacement surgery for osteoarthritis or rheumatoid arthritis Exclusion criteria: patients with diabetes, haemorrhagic disease, Hb < 100 g/L, peripheral neurovascular disease, malignant tumour, history of vascular thrombosis, history of infection in the lower limb Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 30) Group B: surgery performed without a tourniquet (n = 30) Tourniquet pressure in the tourniquet group was based on the patient's arterial systolic pressure + 100 mmHg (1 mmHg = 0.133 kPa). The wound was closed and dressed with standard wound dressings and compression before the tourniquet was loosening. Procedures applied in the control group were identical, but between osteotomy and bone cement insertion, the anaesthesiologist controlled blood pressure at 30 to 40 mmHg to reduce bleeding. Intraoperative active bleeding was coagulated electrically. Conventional low-molecular-weight heparin and a foot pump were used postoperatively to prevent deep vein thrombosis (DVT)
Outcomes	1. Change in haemoglobin: difference between preoperative haemoglobin and postoperative haemoglobin 2. Change in haematocrit: difference between preoperative haematocrit and postoperative haematocrit 3. Intraoperative blood loss: was calculated as volume of liquid in the suction bottle plus increase in gauze weight minus volume of irrigation fluid used during surgery 4. Postoperative blood loss: was principally recorded as volume of visible wound drainage fluid, including volume of blood transfused 6 hours after surgery 5. Overall blood loss: preoperative patient blood volume (PBV) × (preoperative HCT – postoperative HCT) 6. Adverse events
Identification	Contact information: Dr ZHANG Fu-jiang, Department of Orthopaedics, Tianjin Hospital, Tianjin 300211, China No funding for this study
Notes	Country: China Language: English Study author contacted: no Trial registry record or protocol available: none reported or identified Funding source/declaration of interest: no source of funding reported or identified

Zhang 2010 *(Continued)*

	Adverse events: no adverse events reported between the 2 groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table
Allocation concealment (selection bias)	High risk	Open random allocation schedule
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients were blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Zhang 2016

Study characteristics

Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: 22 months Study design: single-centre randomised controlled trial
Participants	166 participants in total Male:Female: 12:72; 13:69 Age, years (range): 63.2 (46 to 80); 65.2 (46 to 83) BMI: 28.1; 28.8 Inclusion criteria: unilateral primary total knee arthroplasty for knee osteoarthritis; volunteers to participate in the study

Zhang 2016 *(Continued)*

	Exclusion criteria: severe medical disease, peripheral vascular disease or deep venous thrombosis of the lower extremities, abnormal coagulation function, severe internal and external valgus deformity of the knee joint Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 84) Group B: surgery performed without a tourniquet (n = 82) Surgery was performed under general anaesthesia (34 cases) or sciatic nerve combined with femoral nerve block anaesthesia (50 cases) in the tourniquet group. Surgery under general anaesthesia (29 cases) or sciatic nerve was combined with femoral nerve block anaesthesia (53 cases) in the non-tourniquet group. Regular intravenous infusion of antibiotics (cefuroxime or ceftriaxone or vancomycin) from 30 mmn to 48 hours after surgery. Intraoperative routine infusion, ambulation, 2 U autologous blood or suspended red blood cells, fresh frozen plasma, blood transfusion treatment was given when the patient developed anaemia symptoms and Hb was lower than 80 g/L. Oral rivaroxaban 5 mg/d was given to prevent thrombosis within 28 days after surgery; was combined with non-steroidal and opioid drugs to relieve pain. Drainage tube was removed on the first day after surgery and lower limb function training was started
Outcomes	1. Pain: measured on a visual analogue scale between 0 and 10. VAS scores were used to evaluate knee pain before and 3, 5, 14, and 28 days after surgery 2. Duration of surgery: measured in minutes 3. Intraoperative blood loss: measured in millilitres 4. Deep vein thrombosis 5. Hospital for Special Surgery knee score: knee-related score assessing pain, stability (measured as total varus-valgus arc, extension), motion (measured as total passive arc), quadriceps strength (measured as 10% of normal for age and gender), and subtraction for contracture or fixed varus/valgus. Score ranges from 0 to 100. The higher the score, the better the outcome
Identification	Contact information: DONG Jiyuan, dongjiyuan81301@l63.com, Department of Orthopaedics, PLA General Hospital, Beijing, 100853
Notes	Country: China Language: English Study author contacted: yes, no reply from the author Trial registry record or protocol available: none reported or identified Funding source/declaration of interest: no source of funding reported or identified Adverse events: In the tourniquet group: 9 patients had DVT In the non-tourniquet group: 2 patients had DVT

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement

Zhang 2016 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients were blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Zhou 2011

Study characteristics	
Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet Follow-up: not reported Study design: single-centre randomised controlled trial
Participants	39 participants in total Male:Female: 7:13; 5:14 Age, years (SD): 63.12 (6.79); 61.89 (7.93) BMI: not reported Inclusion criteria: patients undergoing total knee replacement surgery, able to provide informed consent and adhere to the study protocol Exclusion criteria: patients with a history of deep venous thrombosis of the lower extremities Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 20) Group B: surgery performed without a tourniquet (n = 19)
Outcomes	1. Change in D-dimer, fibrinogen, plasma viscosity, and antithrombin III: measured in blood concentration before surgery and 5 minutes after surgery 2. Change in haematocrit: measured in blood concentration before surgery and 5 minutes after surgery 3. Pain score: study authors did not mention specific values in the final report. They stated that pain scores were significantly lower in the control group

Zhou 2011 *(Continued)*

Identification	Contact information: Zhou Wei, Master attending physician, Department of Orthopaedics, First People's Hospital of Pingdingshan, Pingdingshan 467000, Henan Province, China, zhouwei666999@sina.com No funding for this study
Notes	Country: China Language: English Study author contacted: yes, no reply from the author Trial registry record or protocol available: none reported or identified Funding source/declaration of interest: no source of funding reported or identified Adverse events: no adverse events reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computerised random number generator
Allocation concealment (selection bias)	Low risk	Sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients were blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Low risk	Assessor-reported outcomes: change in haematocrit, D-dimer, fibrinogen, plasma viscosity, antithrombin III Outcome assessors were blinded; therefore low risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement No protocol reported or identified
Other bias	Low risk	No other sources of bias identified

Zhou 2017

Study characteristics

Methods	Two groups: surgery performed with a tourniquet; surgery performed without a tourniquet

Zhou 2017 *(Continued)*

	Follow-up: 6 months Study design: single-centre randomised controlled trial
Participants	140 participants in total Male:Female: 13:59; 7:61 Age, years (SD): 66.8 (8.6); 69.1 (7.6) BMI: 25.7 (3.4); 26.1 (4.1) Inclusion criteria: patients with end-stage osteoarthritis or rheumatoid arthritis scheduled for unilateral total knee arthroplasty Exclusion criteria: patients with prior surgery involving the femur or tibia, prior lower extremity fracture, coagulopathy, uncontrolled hypertension Duration of illness: unspecified
Interventions	Group A: surgery performed with a tourniquet (n = 72) Group B: surgery performed without a tourniquet (n = 68) All operations were performed by the same surgeon using a Sigma fixed or rotating plant posterior-stabilised total knee prosthesis (PFC, Johnson & Johnson/DePuy, Warsaw, IN, USA). All patients with controlled hypotension received a general anaesthetic. Each patient received the same perioperative treatment strategies: tranexamic acid (TXA), pain control, rehabilitation. TXA was given at initiation of surgery and just before closure
Outcomes	1. Intraoperative blood loss: measured by weighing sponges in addition to fluid in suction tubing 2. Postoperative blood loss: amount of fluid in postoperative drainage tubing 3. Blood transfusion rate: defined as the number of units delivered to the patient. The higher the number of units, the worse the outcome 4. Pain: measured on a VAS between 0 and 10. Measured on days 1, 3, and 5 and at weeks 3 and 12 5. HSS score: knee related score assessing pain, stability (measured as total varus-valgus arc, extension), motion (measured as total passive arc), quadriceps strength (measured as 10% of normal for age and gender), subtractions for contractures or fixed varus/valgus. Score ranges from 0 to 100. The higher the score, the better the outcome. Measured at 3 and 6 months 6. Length of hospital stay: measured in days 7. Number of DVTs 8. Knee ROM: number of degrees of knee flexion. Measured on postoperative days 1, 3, and 5, at week 3, and at months 3 and 6 9. Calf swelling
Identification	Contact information: correspondence: Zhouzongke2016@163.com, Department of Orthopaedics, West China Hospital of Sichuan University, Chengdu 610041, China
Notes	Country: China Language: English Study author contacted: no Trial registry record or protocol available: this study was funded by Health Industry Special Scientific Research Projects of China - the safety and effectiveness evaluation of arthroplasty (grant number 201302007) Funding source/declaration of interest: Chinese clinical trials registry number ChicTR-IOR-16007851 Adverse events:

Zhou 2017 *(Continued)*

	In the tourniquet group: 5 patients developed infection and 2 had DVT In the non-tourniquet group: 3 patients developed infection

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment - self-reported outcomes (detection bias)	Unclear risk	Not stated if patients were blinded; therefore unclear risk of bias
Blinding of outcome assessment - assessor reported outcomes (detection bias)	Unclear risk	Not stated if outcome assessors were blinded; therefore unclear risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcome measures reported
Other bias	Low risk	No other sources of bias

APTT: activated partial thromboplastin time.
ASA: American Society of Anesthesiologists.
BMI: body mass index.
CRP: C-reactive protein.
DVT: deep venous thrombosis.
EDTA: ethylene diamine tetra-acetic acid.
EQ-5D: EuroQoL Group Quality of Life Questionnaire based on five dimensions.
GFR: glomerular filtration rate.
HSS: Hospital for Special Surgery.
NYHA: New York Heart Association.
OA: osteoarthritis.
PE: pulmonary embolism.
RA: rheumatic arthritis.
ROM: range of motion.
RSA: radiostereometric analysis.
SD: standard deviation.
SF-12: 12-Item Short Form Survey.
TKA: total knee arthroplasty.
TXA: tranexamic acid.
VAS: visual analogue scale.
WOMAC: Western Ontario McMaster Arthritis Index.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ajnin 2020	Non-randomised study with fewer than 1000 participants
Bakker 2019	Non-randomised study with fewer than 1000 participants
Barros 2017	Non-randomised study with fewer than 1000 participants
Brin 2015	Wrong comparator
Burg 2009	Non-randomised study with fewer than 1000 participants
Dennis 2016	Wrong comparator
Dorr 2014	Commentary piece
Fakuda 2007	Non-randomised study with fewer than 1000 participants
Friedrich 1990	Wrong comparator
Harvey 1997	Wrong study design
Hasanain 2018	Non-randomised study with fewer than 1000 participants
Huang 2015	Wrong study design
Husted 2005	Wrong comparator
Jarolem 1995	Non-randomised study with fewer than 1000 participants
Kheir 2018	Non-randomised study with fewer than 1000 participants
Matziolis 2011	Non-randomised study with fewer than 1000 participants
Mourikis 2009	Supplementary piece
Mutlu 2015	Non-randomised study with fewer than 1000 participants
Nicolaiciuc 2019	Non-randomised study with fewer than 1000 participants
Nicolaiciuc 2019b	Wrong study design
Nielsen 2016	Wrong comparator
Nishiguchi 2008	Non-randomised study with fewer than 1000 participants
Padala 2004	Wrong comparator
Schimizu 2016	Non-randomised study with fewer than 1000 participants
Schnettler 2017	Non-randomised study with fewer than 1000 participants
Stroh 2011	Non-randomised study with fewer than 1000 participants

Study	Reason for exclusion
Zhang 2019	Non-randomised study with fewer than 1000 participants

Characteristics of ongoing studies *[ordered by study ID]*

Duncan 2019

Study name	Total Knee Replacement With Tourniquet or Aquamantys
Methods	Double-blind randomised controlled trial
Participants	Participants aged 18 to 100 Inclusion criteria: primary total knee arthroplasty Exclusion criteria: repeat knee replacement (revision arthroplasty), bilateral knee replacements on the same day, partial knee replacements, health or social limitations that do not allow the participant to be discharged to home on the same day or on the day after surgery
Interventions	Control: surgery performed with tourniquet inflated to control bleeding Intervention: the Aquamantys bipolar sealer is a device used during surgery to help reduce bleeding in the joint. The system uses radiofrequency energy and sterile saline (salt water) to close small blood vessels in the knee to help reduce bleeding
Outcomes	Primary outcome: Isometric quadriceps strength [Time Frame: 2 weeks] Secondary outcomes: 1. Pain (VAS) [Time Frame: preoperative, 2 weeks, 6 weeks, 12 weeks] 2. Knee Injury Osteoarthritis Outcome Score, Joint Replacement (KOOS, JR) patient-reported outcome score 3. Emotional health (VR-12 MCS). The Veterans Rand-12 Mental Component Score will be used to quantify the impact of participants' emotional health on their daily activities. The VR-12 consists of 12 questions and is scored from 0 to 100, with lower scores indicating that emotional health has a more dramatic impact on the participant's daily life 4. Knee function questionnaire [Time Frame: preoperative, 2 weeks, 6 weeks, 12 weeks] 5. Sit to stand test [Time Frame: 6 weeks, 12 weeks] 6. Opioid use [Time Frame: preoperative, 2 weeks, 6 weeks, 12 weeks] 7. Isometric quadriceps strength [Time Frame: 6 weeks, 12 weeks]
Starting date	15/08/2019
Contact information	Stephen Duncan University of Kentucky Lexington, Kentucky, USA 40536 859-323-5533; stdunc2@uky.edu
Notes	ClinicalTrials.gov Identifier NCT04016285

Forsmo 2018

Study name	The Effects of a Tourniquet in Total Knee Arthroplasty
Methods	Triple-blinded randomised controlled trial
Participants	Participants aged 18 and older Inclusion criteria: knee osteoarthrosis qualifying for total knee arthroplasty Exclusion criteria: coagulation disease, rheumatoid arthritis, peripheral vascular disease, malignant disease, pregnancy, ongoing infection, not able to understand written and oral information in Norwegian
Interventions	No use of tourniquet during surgery vs use of tourniquet during surgery where cuff will be inflated to 300 mmHg
Outcomes	Primary outcome measures: 1. Mmax [Time Frame: (1) change from preoperative (baseline) to day 2 postoperative, (2) change from preoperative to 8 weeks postoperative, (3) change from preoperative to 1 year postoperative]. EMG recordings are made using 10 mm electrodes (Ag-AgCl) attached in a bipolar configuration over the vastus lateralis and rectus femoris 2. Nerve growth factor (NGF) [Time Frame: change from during surgery to 8 weeks postoperative]. Analysis from muscle biopsies harvested from the m vastus lateralis 3. Forgotten joint score [Time Frame: (1) change from preoperative (baseline) to day 2 postoperative, (2) change from preoperative to 8 weeks postoperative, (3) change from preoperative to 1 year postoperative]. The stair climbing test measures the time (in seconds) to ascend, turn around, and descend a regular stairway of 11 steps. Patients are asked to perform the test as quickly as possible Secondary outcome measures: 1. Maximal leg strength [Time Frame: (1) change from preoperative (baseline) to day 2 postoperative, (2) change from preoperative to 8 weeks postoperative, (3) change from preoperative to 1 year postoperative]. 1 RM leg strength is measured using a leg press ergometer with the participant in a supine position (Steens Physical, Ring Mekanikk, Moelv, Norway) 2. Maximal knee extension strength [Time Frame: (1) change from preoperative (baseline) to day 2 postoperative, (2) change from preoperative to 8 weeks postoperative, (3) change from preoperative to 1 year postoperative]. 1 RM knee extension is measured using knee extension equipment (Body-Solid, Forest Park, IL, USA) with the participant in a seated position 3. Rate of force development, voluntary activation, and muscle contractility [Time Frame: (1) change from preoperative (baseline) to day 2 postoperative, (2) change from preoperative to 8 weeks postoperative, (3) change from preoperative to 1 year postoperative] 4. Daily physical activity [Time Frame: change from day 3 to day 10 postoperative to 1 year postoperative (1 week measurement)]. Body-worn activity monitor 5. EuroQual 5D-L [Time Frame: preoperative, 8 weeks, 1 year postoperative]. Patient-reported outcome measure 6. Numerical Rating Scale (NRS) [Time Frame: preoperative, from day 1 postoperative to 4 weeks postoperative, 8 weeks, and 1 year postoperative]. Evaluating pain. the scale range from 0 (no pain) to 10 (worst pain imaginable). Patients are asked to write down NRS values both at rest and during activity each day for the first 4 weeks postoperatively in a home log 7. Haemoglobin values [Time Frame: preoperative, day 1 postoperative], g/dL 8. Volume of bleeding [Time Frame: during surgery and day 1 postoperative]. Total volume of bleeding during surgery and in the drain 9. Length of hospital stay [Time Frame: from day of surgery until 10 days postoperative]. Number of days 10. Knee circumference [Time Frame: preoperative and day 1 postoperative]. The circumference of the knee is measured 1 cm proximal to the patellar base 11. Knee joint range of motion [Time Frame: preoperative; 1 day, 8 weeks, 1 year postoperative]. Maximal flexion and extension

Forsmo 2018 *(Continued)*

	12. Forgotten joint score [Time Frame: preoperative; 8 weeks, 1 year postoperative]. Patient-reported outcome measure 13. Gene expression analyses. RT-PCR for expression levels for VEGF, NGF, SP, CGRP, IL-6, IL-1, TNF-alpha, Bad, Bax, Bid, Bim, Fas, Fas-ligand, Bcl-2, Mcl, and FLIP. Results will be normalised to GAPDH expression levels [Time Frame: preoperative and 8 weeks postoperative]. Analysis from muscle biopsies harvested from the vastus lateralis (muscle) 14. Neuronal markers, PGP, GAP-43 [Time Frame: during surgery and 8 weeks postoperative]. Analysis from muscle biopsies harvested from the vastus lateralis (muscle) 15. Neuromediators, SP, CGRP, glutamate [Time Frame: during surgery and 8 weeks postoperative]. Analysis from muscle biopsies harvested from the vastus lateralis (muscle) 16. Pain receptors, glutamate receptors [Time Frame: during surgery and 8 weeks postoperative]. Analysis from muscle biopsies harvested from the vastus lateralis (muscle)
Starting date	12/09/2018
Contact information	Vigdis Schnell Husby, PhD, +4773412312, vigdis.schnell.husby@ntnu.no; Siri Bjorgen Winther, PhD, +4772573669, siri.bjorgen@ntnu.no
Notes	Sponsors and Collaborators Norwegian University of Science and Technology, Zimmer Biomet, University of British Columbia, Karolinska University Hospital, St Olav's Hospital, University Hospital in Trondheim, Kristiansund Hospital NCT03666598

Gill 2018

Study name	A Single-Centre, Parallel-Arm, Double-Blind Randomised Trial Evaluating the Effects of Tourniquet Use in Total Knee Arthroplasty on Intraoperative and Postoperative Outcomes
Methods	Randomised controlled trial
Participants	90 participants with osteoarthritis Inclusion criteria: undergoing primary total knee replacement for primary osteoarthritis; > 18 years of age; willing, able, and mentally competent to provide informed consent Exclusion criteria: undergoing bilateral total knee replacement, neurological deficit affecting operated knee, rheumatoid arthritis, preoperative knee flexion < 60 (degree of flexion required for strength testing), varus/valgus deformity > 15, opioid tolerant (current use of oxycontin, opioid patches, or tramadol; > 4 tabs panadeine forte per day), sulphonamide allergy (to allow parecoxib/celecoxib use), intolerant/allergic to oxycodone, poorly controlled diabetes (HbA1C > 8) (impact on choice of dexamethasone as antiemetic), cognitively impaired (mini-mental state examination < 25/30), eGFR < 60 mL/min/1.73m^2 (to allow parecoxib/celecoxib use)
Interventions	Surgery with a tourniquet vs surgery without a tourniquet
Outcomes	Primary outcome: Isometric quadriceps strength will be measured in Newtons Secondary outcomes: 1. Analgesic requirements will be determined from patients; hospital medication charts and average morphine equivalent daily dose calculated (mg) 2. Cement mantle quality according to the Knee Society total knee arthroplasty roentgenographic evaluation and scoring system 3. Complications during inpatient stay as recorded in patients' hospital medical record (deep vein thrombosis, pulmonary embolus) 4. EQ-5D-5L (quality of life)

Gill 2018 *(Continued)*

	5. Hospital length of stay according to patients' hospital medical records 6. Intraoperative blood loss (mL) will be estimated visually by the treating surgeon 7. Isometric quadriceps strength will be measured in Newtons 8. Knee pain will be assessed using a 0 to 10 Likert scale (0 = no pain, 10 = extreme pain) 9. Operation and anaesthetic time as recorded in patients' hospital medical records 10. Oxford Knee Score (OKS) (self-reported pain and physical function) 11. Patient satisfaction assessed with a 0 to 10 visual analogue scale 12. Revision surgery as recorded in patients' hospital medical records 13. Surgeon satisfaction with intraoperative visual field, assessed using a 1 to 10 Likert scale (1 = completely unsatisfied, 10 = completely satisfied) 14. Tourniquet inflation time as recorded in patients' hospital medical records 15. Transfusions given (units) as recorded in patients' hospital medical records 16. WOMAC (self-reported pain and physical function)
Starting date	1/10/2014
Contact information	Name: Dr Stephen Gill Address: Barwon Centre for Orthopaedic Research and Education, St John of God Hospital, Myers Street, Geelong, Victoria, Australia 3220 Telephone: +61 3 52150902 Email: stephen.gill2@deakin.edu.au Study registered with the Australian New Zealand Clinical Trials Registry: ACTRN12618000425291
Notes	Funded by Barwon Health

Kange 2017

Study name	The Efficacy of Oral Tranexamic Acid on Blood Loss in Primary Total Knee Arthroplasty With or Without Tourniquet: A Prospective, Randomized, Controlled Trial
Methods	Randomised controlled trial
Participants	60 participants in total: 30 with a tourniquet vs 30 without a tourniquet Inclusion criteria: patients with osteoarthritis of the knee Exclusion criteria: patients with bilateral arthroplasty, allergy to TXA, history of renal failure, kidney transplant, history of an arterial thromboembolic event such as myocardial infarction or stroke in past years, history of hypercoagulation, haemophilia, deep vein thrombosis, pulmonary embolism
Interventions	Surgery with a tourniquet vs surgery without a tourniquet
Outcomes	1. Blood loss 2. Range of motion 3. Pain 4. Swelling
Starting date	25/10/2017
Contact information	Name: Kang Pengde Address: 37 Guoxuexiang, Chengdu, China Telephone: +86 18980601953 Email: kangpd@163.com Affiliation: West China Hospital, Sichuan University

Kange 2017 *(Continued)*

Notes	Funded by the National Health and Family Planning Commission of China

Liebensteiner 2016

Study name	Effect of Tourniquet on UKA
Methods	Triple-blinded randomised controlled trial
Participants	30 participants Inclusion criteria: waiting list for unicondylar knee arthroplasty Exclusion criteria: failed upper tibial osteotomy, insufficiency of collateral or anterior cruciate ligaments, fixed varus or valgus deformity (not passively correctable) above 15°, flexion deformity > 15°, rheumatoid arthritis, intake of medicinal anticoagulation before surgery, liver dysfunction/coagulation dysfunction, peripheral arterial occlusive disease
Interventions	UKA surgery with tourniquet vs UKA surgery without tourniquet
Outcomes	Primary outcome measure: Cement mantle thickness [Time Frame: 1 week]
Starting date	08/06/2015
Contact information	Michael Liebensteiner, +4351250480547, Michael.liebensteiner@i-med.ac.at
Notes	Not yet recruiting ID: NCT02465684

Pei 2016

Study name	Tourniquet Versus No Tourniquet on Early Rehabilitation and Cement Mantle After Primary Total Knee Arthroplasty Using a Multimodal Blood Management Protocol: A Randomized Controlled Trial
Methods	Randomised controlled trial
Participants	60 participants in total Inclusion criteria: patients aged 18 years and older, scheduled for primary TKA because of end-stage osteoarthritis Exclusion criteria: revisions, bilateral procedures, previous knee surgery history, flexion deformity 30°, varus/valgus deformity 30°, anaemia (< 120 g/L for female, < 130 g/L for male), contraindications for use of TXA, coagulation disorder
Interventions	Surgery with a tourniquet vs surgery without a tourniquet
Outcomes	1. Total blood loss 2. Bone cement mantle interface 3. Pain score 4. Swelling

Pei 2016 *(Continued)*

	5. Change in Hb 6. CRP 7. IL-6 8. Transfusion rate 9. Patient satisfaction
Starting date	07/11/2016
Contact information	Name: Fuxing Pei Address: 37 Guoxuexiang, Chengdu, China 610041 Telephone: +86 13541242147 Email: peifuxing1952@163.com Affiliation: West China Hospital, Sichuan University
Notes	Funded by China National Health and Family Planning Commission

Pei 2016 (b)

Study name	Is Tourniquet Really Necessary When Multiple Uses of Intravenous and Topical Tranexamic Acid Are Applied in Primary Total Knee Arthroplasty? A Prospective Randomised Controlled Trial
Methods	Randomised controlled trial
Participants	150 participants Inclusion criteria: aged 18 years and older, scheduled for primary TKA because of end-stage osteoarthritis Exclusion criteria: revisions, bilateral procedures, previous knee surgery history, flexion deformity 30°, varus/valgus deformity 30°, anaemia (< 120 g/L for female, < 130 g/L for male), contraindications for use of TXA, coagulation disorder Age minimum: 18 Age maximum: 80 Gender: both
Interventions	Group A: tourniquet + 20 mg/kg IV TXA administered 5 to 10 minutes before skin incision and 10 mg/kg TXA administered 3, 6, 12, and 24 hours later Group B: 20 mg/kg IV TXA administered 5 to 10 minutes before skin incision and 10 mg/kg TXA administered 3, 6, 12, and 24 hours later Group C: only tourniquet used during surgery
Outcomes	Primary outcomes: 1. Hidden blood loss 2. Maximum Hb change 3. CRP 4. IL-6 Secondary outcomes:

Pei 2016 (b) *(Continued)*

	1. Lower limb swelling ratio 2. VAS pain score 3. Length of hospital stay 4. Transfusion rate 5. Patient satisfaction 6. Complications
Starting date	01/07/2016
Contact information	Fuxing Pei37 Guoxuexiang, Chengdu, China 610041, +8613551068719, peifuxing1951@163.com, West China Hospital, Sichuan University
Notes	Currently recruiting ID: ChiCTR-INR-16008762

Shen 2018

Study name	Effects of Postoperative Limb Positions on Blood Loss and Range of Motion in Total Knee Arthroplasty Without Tourniquet: A Randomized Controlled Trial
Methods	Randomised controlled trial
Participants	100 participants with osteoarthritis undergoing total knee replacement surgery Inclusion criteria: with total knee replacement Exclusion criteria: infection, anaemia, thrombosis
Interventions	Surgery with a tourniquet vs surgery without a tourniquet
Outcomes	1. Blood loss 2. Range of motion
Starting date	13/02/2018
Contact information	Name: Bin Shen Address: 37 Guo Xue Xiang, Chengdu, Sichuan, China Telephone: +86 18980601390 Email: wuyuangang23@163.com, shenbin_1971@163.com Affiliation: West China Hospital, Sichuan University Registration: ChiCTR1800014896
Notes	No source of funding

Singh 2019

Study name	Randomized Controlled Trial for Comparision of Functional Outcome in Total Knee Replacement With Tourniquet and Without Tourniquet

Singh 2019 *(Continued)*

Methods	Randomised controlled trial
Participants	60 participants diagnosed with osteoarthritis undergoing primary total knee replacement surgery Inclusion criteria: diagnosed with osteoarthritis, scheduled for unilateral cemented TKA, either sex, < 80 years of age Exclusion criteria: severe obesity, previous operation in concerning knee, lack of informed consent, severe cardiovascular condition, receiving general anaesthesia during surgery
Interventions	Surgery with a tourniquet vs surgery without a tourniquet
Outcomes	1. Postoperative limb pain 2. Blood loss 3. Range of motion 4. Deep vein thrombosis 5. Radiolucency at bone cement interface
Starting date	01/04/2013
Contact information	Name: Swapnil Singh Address: Office of Dept of Orthopaedics, 5th floor teaching block, AIIMS New Delhi, Room 88, Hostel 7; AIIMS boys hostel; AIIMS New Delhi, 110029 South Delhi, India Telephone: 9868397115 Email: csyadavortho@gmail.com Affiliation: AIIMS, New Delhi
Notes	Funded by Orthopedics Unit 2, AIIMS New Delhi 110029

Vasquez 2019

Study name	After Surgery Acute Renal Failure Incidence in Total Knee Arthroplasty With and Without Tourniquet
Methods	Double-blinded randomised controlled trial
Participants	100 participants Inclusion criteria: knee arthrosis, requiring surgical treatment with total knee arthroplasty Exclusion criteria: not acceptable to be in study, no signed consent form, not having blood sample for creatinine measure
Interventions	Total knee arthroplasty and use of tourniquet limb cuff at 270 mmHg vs total knee arthroplasty with intra-articular lidocaine
Outcomes	Primary outcome measures: 1. Creatinine before surgery [Time Frame: creatinine before surgery]. Blood creatinine measured in mg/dL before surgery 2. Creatinine after surgery 1 [Time Frame: creatinine after surgery 1 at 24 hours]. Blood creatinine measured in mg/dL at 24 hours 3. Creatinine after surgery 2 [Time Frame: creatinine after surgery 2 at 48 hours]. Blood creatinine measured in mg/dL at 48 hours

Vasquez 2019 *(Continued)*

Starting date	08/01/2019
Contact information	Avelino Colin Vazquez, MD Instituto Mexicano del Seguro Social
Notes	ID: NCT03795805

Wall 2016

Study name	Safety and Feasibility Evaluation of Tourniquets for Total Knee Replacement Study
Methods	Randomised controlled trial
Participants	50 participants undergoing total knee replacement surgery Inclusion criteria: aged 18 years and over, undergoing primary unilateral knee replacement, able to give written informed consent and to participate fully in trial interventions and follow-up procedures Exclusion criteria: patients for whom magnetic resonance (MR) imaging is contraindicated due to non-compliant heart pacemaker or defibrillator, non-compliant metallic foreign body (e.g. in one or both eyes, aneurysm clips in the brain), claustrophobia (e.g. difficulty in an elevator or telephone box); not suitable for a thigh tourniquet (e.g. significant peripheral vascular disease); previous participation in the SAFE-TKR trial
Interventions	Surgery with a tourniquet vs surgery without a tourniquet
Outcomes	Primary outcome: 1. Total volume of acute brain lesions detected on magnetic resonance (MR) brain imaging per patient, day 1 or 2 postoperatively Secondary outcomes: 1. Montreal Cognitive Assessment (MoCA) preoperatively; on days 1, 2, and 7 postoperatively; and at 6 and 12 months postoperatively 2. Oxford Cognitive Screen (OCS) preoperatively and on days 1, 2, and 7 postoperatively 3. Mini-mental state examination (MMSE) scores preoperatively and on days 1, 2, and 7 postoperatively 4. Knee pain measured using the Oxford Knee Score postoperatively at baseline, at 1 week, and at 6 and 12 months 5. Thigh pain measured using the visual analogue scale (VAS) for acute thigh pain at baseline, day 1, day 2, and 1 week 6. Knee pain measured using the EQ-5D-5L at baseline, at 1 week, at 6 and 12 months 7. Number of symptomatic VTE events measured by questionnaire up to 12 months postoperatively 8. Surgical complication rate measured by questionnaire up to 12 months postoperatively 9. Number of intra/postoperative blood transfusions measured by patient notes up until discharge 10. Revision rate of TKR prosthesis measured by questionnaire or patient notes at 12 months 11. All-cause mortality rates measured by patient notes or by next of kin at 12 months 12. Change in haemoglobin concentration between preoperative haemoglobin and postoperative haemoglobin
Starting date	17/02/2016
Contact information	Peter Wall University of Warwick

Wall 2016 *(Continued)*

	Clinical Sciences Research Institute Clinical Sciences Building Clifford Bridge Road Coventry CV2 2DX United Kingdom p.d.h.wall@warwick.ac.uk
Notes	Funded by National Institute of Health Research ID: ISRCTN20873088

Wang 2016

Study name	Tourniquet Versus No Tourniquet on Rehabilitation After Fast-Track Total Knee Arthroplasty
Methods	Randomised controlled trial
Participants	60 participants (30 in each group) Inclusion criteria: adult patients who plan to undergo primary TKA on simultaneous bilateral knee joints with diagnosis of osteoarthritis but not of rheumatoid arthritis Exclusion criteria: aged > 50 or < 80 years; body mass index (BMI) > 35 kg/m^2; rheumatoid arthritis; current long-term anticoagulation therapy; abnormal coagulation function; local or systemic infection; severe deformity of the knee > 20° varus or ectropion, > 30° flexion contracture; previous open knee surgery; disease of the blood system, cerebral infarction, cerebral haemorrhage, active malignancy; peripheral vascular or nerve disease; preoperative anaemia (haemoglobin value < 100 g/L); surgery not by project surgeon; patient refusal to participate in the study; psychiatric illness
Interventions	Surgery with a tourniquet vs surgery without a tourniquet
Outcomes	1. Quadriceps strength 2. Pain score 3. Postoperative knee flexion 4. Postoperative knee swelling 5. Intraoperative bleeding 6. Patient satisfaction
Starting date	01/10/2015
Contact information	Name: Gang Wang Address: 127 West Changle Road, Xi'an, Shaanxi, China Telephone: +86 13810347690 Email: 564325747@qq.com Affiliation: Department of Orthopaedics, Xijing Hospital, Fourth Military Medical University
Notes	Funded by the Boosting Academic Program of Xijing Hospital

BMI: body mass index.
CGRP: calcitonin gene-related peptide.
eGFR: estimated glomerular filtration rate.
EQ-5D-5L: EuroQoL Group Quality of Life Questionnaire based on five-level scale.

IL: interleukin.
NGF: nerve growth factor.
NRS: numerical rating scale.
RT-PCR: reverse transcriptase polymerase chain reaction.
TKA: total knee arthroplasty.
TNF: tumour necrosis factor.
UKA: unicompartmental knee arthroplasty.
VEGF: vascular endothelial growth factor.
VTE: venous thromboembolism.

DATA AND ANALYSES

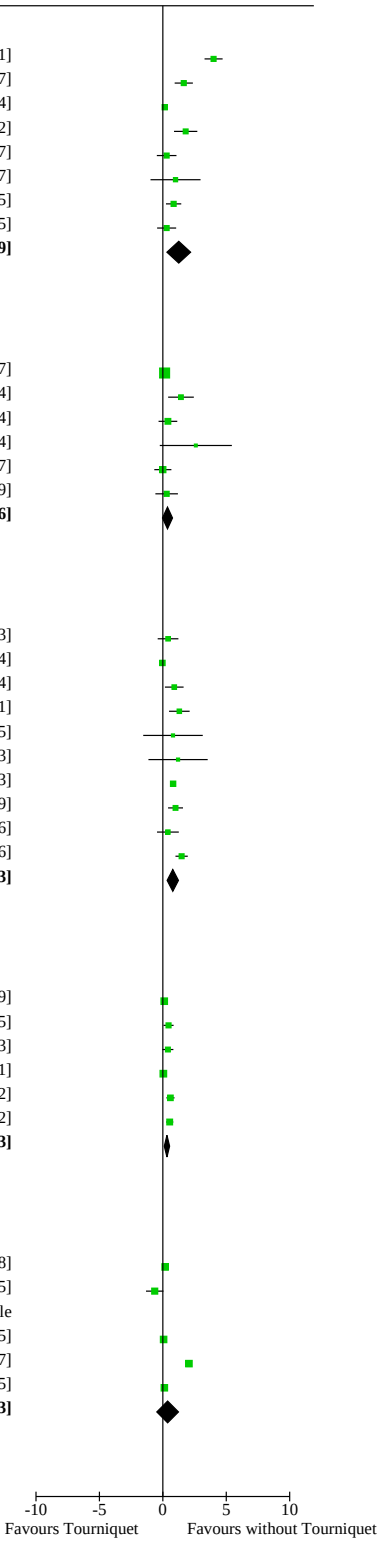
Comparison 1. Surgery with a tourniquet vs surgery without a tourniquet

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Pain at different postoperative days (visual analogue scale 0 to 10, lower is better)	14		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1.1 Pain: day 1	8	577	Mean Difference (IV, Random, 95% CI)	1.25 [0.32, 2.19]
1.1.2 Pain: day 2	6	394	Mean Difference (IV, Random, 95% CI)	0.37 [-0.03, 0.76]
1.1.3 Pain: day 3	10	807	Mean Difference (IV, Random, 95% CI)	0.78 [0.34, 1.23]
1.1.4 Pain: week 2	6	562	Mean Difference (IV, Random, 95% CI)	0.32 [0.12, 0.53]
1.1.5 Pain: week 6	6	637	Mean Difference (IV, Random, 95% CI)	0.38 [-0.48, 1.23]
1.2 Function: patient-reported knee function at 3 months (scale 0 to 100, higher is better)	4	425	Std. Mean Difference (IV, Random, 95% CI)	-0.64 [-1.52, 0.25]
1.3 Function: patient-reported knee function at 12 months (scale 0 to 100, higher is better)	5	611	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.22, 0.10]
1.4 Global assessment of success: participant-reported satisfaction at 3 months (based on number of participants, higher is better)	1	100	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.92, 1.14]
1.5 Global assessment of success: participant-reported satisfaction at 6 months (based on number of participants, higher is better)	1	100	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.91, 1.10]
1.6 Health-related quality of life: SF-12 mental component at 6 weeks (0 to 100, higher is better)	1	199	Mean Difference (IV, Random, 95% CI)	2.58 [-0.09, 5.25]
1.7 Health-related quality of life: SF-12 mental component at 6 months (0 to 100, higher is better)	1	199	Mean Difference (IV, Random, 95% CI)	1.53 [-0.85, 3.91]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.8 Serious adverse events	21	1799	Risk Ratio (M-H, Random, 95% CI)	1.73 [1.10, 2.73]
1.9 Serious adverse event: venous thromboembolic event (VTE)	17	1575	Risk Ratio (M-H, Random, 95% CI)	1.95 [0.99, 3.82]
1.10 Serious adverse event: deep vein thrombosis (DVT)	17	1602	Risk Ratio (M-H, Random, 95% CI)	2.05 [1.35, 3.13]
1.10.1 Symptomatic DVT	16	1499	Risk Ratio (M-H, Random, 95% CI)	1.83 [0.92, 3.65]
1.10.2 Asymptomatic DVT	1	103	Risk Ratio (M-H, Random, 95% CI)	2.20 [1.29, 3.74]
1.11 Serious adverse event: pulmonary embolism (PE)	5	416	Risk Ratio (M-H, Random, 95% CI)	4.51 [0.49, 41.81]
1.12 Serious adverse event: infection	9	846	Risk Ratio (M-H, Random, 95% CI)	2.72 [1.15, 6.42]
1.13 Serious adverse event: re-operation	3	157	Risk Ratio (M-H, Random, 95% CI)	1.63 [0.61, 4.34]
1.14 Survival of the implant: risk of revision up to 2 years	3	214	Risk Ratio (M-H, Random, 95% CI)	1.44 [0.23, 8.92]
1.15 Blood loss: postoperative transfusion risk (lower is better)	18	1286	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.86, 1.67]
1.16 Blood loss: intraoperative (mL, lower is better)	15	1187	Mean Difference (IV, Random, 95% CI)	-147.05 [-190.97, -103.12]
1.17 Blood loss: postoperative (mL, lower is better)	12	776	Mean Difference (IV, Random, 95% CI)	57.72 [13.58, 101.87]
1.18 Blood loss: overall blood loss (mL, lower is better)	18	1500	Mean Difference (IV, Random, 95% CI)	8.61 [-83.76, 100.97]
1.19 Blood loss: change in haemoglobin (g/dL, lower is better)	9	713	Mean Difference (IV, Random, 95% CI)	-0.14 [-0.48, 0.19]
1.20 Economic: length of hospital stay (days, lower is better)	12	995	Mean Difference (IV, Random, 95% CI)	0.34 [0.03, 0.64]
1.21 Economic: duration of surgery (minutes, lower is better)	27	2070	Mean Difference (IV, Random, 95% CI)	-3.70 [-5.53, -1.87]
1.22 Implant stability: maximum total point motion at 8 weeks (mm, lower is better)	2	130	Mean Difference (IV, Random, 95% CI)	-0.06 [-0.13, 0.01]
1.23 Implant stability: maximum total point motion at 1 year (mm, lower is better)	2	130	Mean Difference (IV, Random, 95% CI)	0.05 [-0.09, 0.18]
1.24 Implant stability: maximum total point motion at 2 years (mm, lower is better)	2	130	Mean Difference (IV, Random, 95% CI)	0.06 [-0.08, 0.19]

Analysis 1.1. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 1: Pain at different postoperative days (visual analogue scale 0 to 10, lower is better)

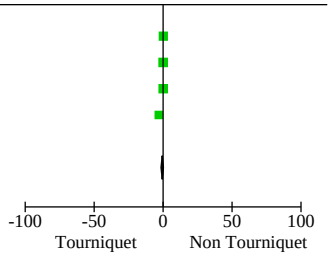
Study or Subgroup	Tourniquet Mean	SD	Total	without tourniquet Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Pain: day 1								
Abdel-Salem 1995	8	1.92	40	4	1.261775	40	13.0%	4.00 [3.29 , 4.71]
Alexandersson 2019	4.44	1.92	38	2.79	1.261775	43	13.0%	1.65 [0.93 , 2.37]
Dong 2019	2.58	0.56	64	2.43	0.53	58	14.0%	0.15 [-0.04 , 0.34]
Kumar 2015	5.75	1.45	15	3.95	1.09	15	12.4%	1.80 [0.88 , 2.72]
Li 2008	7.7	1.8	30	7.4	1.2	30	12.8%	0.30 [-0.47 , 1.07]
Liu 2014	6	2.51	10	5	1.9571	10	8.6%	1.00 [-0.97 , 2.97]
Liu 2017	6.17	1.92	56	5.32	1.261775	56	13.3%	0.85 [0.25 , 1.45]
Tai 2012	5.9	1.92	36	5.6	1.261775	36	12.9%	0.30 [-0.45 , 1.05]
Subtotal (95% CI)			**289**			**288**	**100.0%**	**1.25 [0.32 , 2.19]**
Heterogeneity: Tau² = 1.61; Chi² = 124.75, df = 7 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 2.64 (P = 0.008)								
1.1.2 Pain: day 2								
Dong 2019	2.69	0.147	64	2.55	0.5	58	38.5%	0.14 [0.01 , 0.27]
Kumar 2015	4.4	1.75	15	2.97	0.97	15	11.1%	1.43 [0.42 , 2.44]
Li 2008	6.5	1.6	30	6.1	1.3	30	16.8%	0.40 [-0.34 , 1.14]
Liu 2014	6.6	3.63	10	4	2.8	10	1.8%	2.60 [-0.24 , 5.44]
Pfitzner 2014	3	1.5	45	3	1.75	45	18.6%	0.00 [-0.67 , 0.67]
Tai 2012	4.9	2.12	36	4.6	1.7	36	13.3%	0.30 [-0.59 , 1.19]
Subtotal (95% CI)			**200**			**194**	**100.0%**	**0.37 [-0.03 , 0.76]**
Heterogeneity: Tau² = 0.10; Chi² = 9.65, df = 5 (P = 0.09); I² = 48%								
Test for overall effect: Z = 1.82 (P = 0.07)								
1.1.3 Pain: day 3								
Alexandersson 2019	2.85	2.06	38	2.44	1.63	43	10.0%	0.41 [-0.41 , 1.23]
Dong 2019	2.14	0.4	64	2.17	0.52	58	14.7%	-0.03 [-0.20 , 0.14]
Ejaz 2014	5.5	1.6	33	4.6	1.4	31	10.7%	0.90 [0.16 , 1.64]
Kumar 2015	3.35	1.42	15	2.05	0.75	15	10.0%	1.30 [0.49 , 2.11]
Ledin 2012	4.9	5.09	25	4.1	3.15	25	2.9%	0.80 [-1.55 , 3.15]
Liu 2014	4.8	2.52	10	3.6	2.8	10	2.9%	1.20 [-1.13 , 3.53]
Liu 2017	5.73	0.6	56	4.92	0.57	56	14.5%	0.81 [0.59 , 1.03]
Pfitzner 2014	3	1.75	45	2	1	45	11.9%	1.00 [0.41 , 1.59]
Tai 2012	4.5	2.06	36	4.1	1.63	36	9.6%	0.40 [-0.46 , 1.26]
Zhang 2016	5.32	1.45	84	3.84	1.72	82	12.8%	1.48 [1.00 , 1.96]
Subtotal (95% CI)			**406**			**401**	**100.0%**	**0.78 [0.34 , 1.23]**
Heterogeneity: Tau² = 0.34; Chi² = 69.48, df = 9 (P < 0.00001); I² = 87%								
Test for overall effect: Z = 3.46 (P = 0.0005)								
1.1.4 Pain: week 2								
Dong 2019	1.58	0.53	64	1.47	0.5	58	20.9%	0.11 [-0.07 , 0.29]
Kumar 2015	1.7	0.65	15	1.25	0.44	15	13.1%	0.45 [0.05 , 0.85]
Li 2008	3.6	0.9	30	3.2	0.8	30	12.1%	0.40 [-0.03 , 0.83]
Liu 2017	1.18	0.45	56	1.14	0.47	56	21.3%	0.04 [-0.13 , 0.21]
Tai 2012	4.1	0.715	36	3.5	0.675	36	15.6%	0.60 [0.28 , 0.92]
Zhang 2016	2.44	0.86	84	1.9	0.99	82	17.1%	0.54 [0.26 , 0.82]
Subtotal (95% CI)			**285**			**277**	**100.0%**	**0.32 [0.12 , 0.53]**
Heterogeneity: Tau² = 0.05; Chi² = 17.93, df = 5 (P = 0.003); I² = 72%								
Test for overall effect: Z = 3.05 (P = 0.002)								
1.1.5 Pain: week 6								
Alexandersson 2019	0.47	0.495	38	0.29	0.398	43	20.5%	0.18 [-0.02 , 0.38]
Goel 2019	3.25	2.19	100	3.89	2.72	99	18.2%	-0.64 [-1.33 , 0.05]
Kumar 2015	1.1	0.3	15	0	0	15		Not estimable
Liu 2017	0.45	0.53	56	0.39	0.51	56	20.5%	0.06 [-0.13 , 0.25]
Ozkunt 2018	3.58	0.37	24	1.52	0.38	25	20.4%	2.06 [1.85 , 2.27]
Zhang 2016	1.74	0.78	84	1.62	0.7	82	20.4%	0.12 [-0.11 , 0.35]
Subtotal (95% CI)			**317**			**320**	**100.0%**	**0.38 [-0.48 , 1.23]**
Heterogeneity: Tau² = 0.92; Chi² = 262.50, df = 4 (P < 0.00001); I² = 98%								
Test for overall effect: Z = 0.87 (P = 0.39)								
Test for subgroup differences: Chi² = 6.54, df = 4 (P = 0.16), I² = 38.8%								



Analysis 1.2. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 2: Function: patient-reported knee function at 3 months (scale 0 to 100, higher is better)

Study or Subgroup	Tourniquet Mean	SD	Total	without tourniquet Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ayik 2020	79	19	32	76	20	33	25.3%	0.15 [-0.34 , 0.64]
Goel 2019	69.15	19.45	100	69.06	14.18	99	26.7%	0.01 [-0.27 , 0.28]
Liu 2017	90.3	4.2	56	90.2	3.9	56	26.2%	0.02 [-0.35 , 0.39]
Ozkunt 2018	63	5.68	24	82	6.21	25	21.8%	-3.14 [-4.00 , -2.28]
Total (95% CI)			**212**			**213**	**100.0%**	**-0.64 [-1.52 , 0.25]**

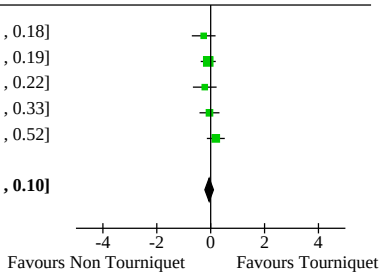
Heterogeneity: Tau² = 0.75; Chi² = 50.26, df = 3 (P < 0.00001); I² = 94%
Test for overall effect: Z = 1.41 (P = 0.16)
Test for subgroup differences: Not applicable



Analysis 1.3. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 3: Function: patient-reported knee function at 12 months (scale 0 to 100, higher is better)

Study or Subgroup	Tourniquet Mean	SD	Total	Without tourniquet Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Abdel-Salem 1995	90	3.85	40	91	3.78	40	13.0%	-0.26 [-0.70 , 0.18]
Goel 2019	83.43	19.19	100	85.04	16.21	99	32.7%	-0.09 [-0.37 , 0.19]
Huang 2017	90	4.75	40	91	4.25	40	13.1%	-0.22 [-0.66 , 0.22]
Liu 2017	93.2	2.3	56	93.3	2.2	56	18.4%	-0.04 [-0.41 , 0.33]
Zhou 2017	90.7	4.5	72	89.8	4.9	68	22.9%	0.19 [-0.14 , 0.52]
Total (95% CI)			**308**			**303**	**100.0%**	**-0.06 [-0.22 , 0.10]**

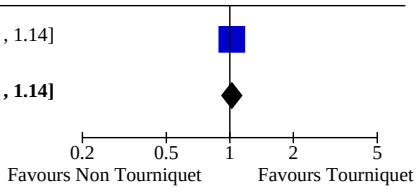
Heterogeneity: Tau² = 0.00; Chi² = 3.53, df = 4 (P = 0.47); I² = 0%
Test for overall effect: Z = 0.70 (P = 0.49)
Test for subgroup differences: Not applicable



Analysis 1.4. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 4: Global assessment of success: participant-reported satisfaction at 3 months (based on number of participants, higher is better)

Study or Subgroup	Tourniquet Events	Total	without tourniquet Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Huang 2017	47	50	46	50	100.0%	1.02 [0.92 , 1.14]
Total (95% CI)		**50**		**50**	**100.0%**	**1.02 [0.92 , 1.14]**
Total events:	47		46			

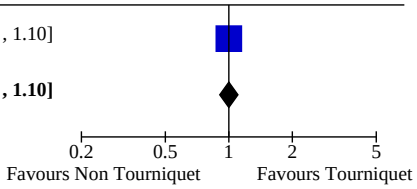
Heterogeneity: Not applicable
Test for overall effect: Z = 0.39 (P = 0.70)
Test for subgroup differences: Not applicable



Analysis 1.5. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 5: Global assessment of success: participant-reported satisfaction at 6 months (based on number of participants, higher is better)

Study or Subgroup	Tourniquet Events	Tourniquet Total	without tourniquet Events	without tourniquet Total	Weight	Risk Ratio M-H, Random, 95% CI
Huang 2017	47	50	47	50	100.0%	1.00 [0.91 , 1.10]
Total (95% CI)		**50**		**50**	**100.0%**	**1.00 [0.91 , 1.10]**
Total events:	47		47			

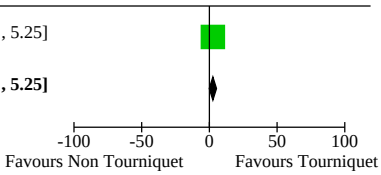
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)
Test for subgroup differences: Not applicable



Analysis 1.6. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 6: Health-related quality of life: SF-12 mental component at 6 weeks (0 to 100, higher is better)

Study or Subgroup	Tourniquet Mean	Tourniquet SD	Tourniquet Total	without tourniquet Mean	without tourniquet SD	without tourniquet Total	Weight	Mean Difference IV, Random, 95% CI
Goel 2019	54.33	9.31	100	51.75	9.9	99	100.0%	2.58 [-0.09 , 5.25]
Total (95% CI)			**100**			**99**	**100.0%**	**2.58 [-0.09 , 5.25]**

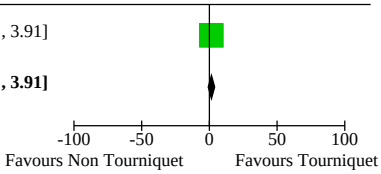
Heterogeneity: Not applicable
Test for overall effect: Z = 1.89 (P = 0.06)
Test for subgroup differences: Not applicable



Analysis 1.7. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 7: Health-related quality of life: SF-12 mental component at 6 months (0 to 100, higher is better)

Study or Subgroup	Tourniquet Mean	Tourniquet SD	Tourniquet Total	Without tourniquet Mean	Without tourniquet SD	Without tourniquet Total	Weight	Mean Difference IV, Random, 95% CI
Goel 2019	56.17	7.72	100	54.64	9.33	99	100.0%	1.53 [-0.85 , 3.91]
Total (95% CI)			**100**			**99**	**100.0%**	**1.53 [-0.85 , 3.91]**

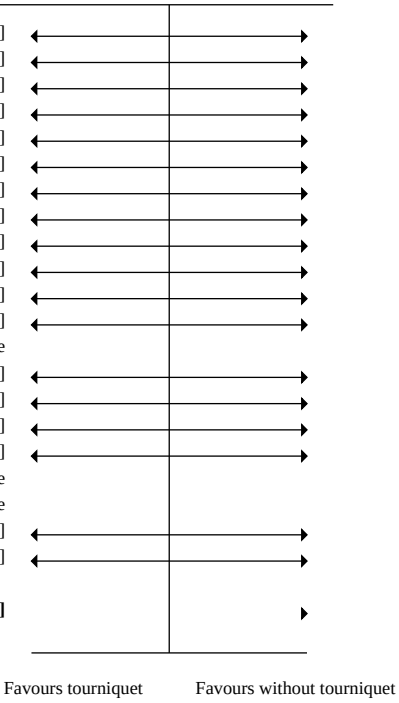
Heterogeneity: Not applicable
Test for overall effect: Z = 1.26 (P = 0.21)
Test for subgroup differences: Not applicable



Analysis 1.8. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 8: Serious adverse events

Study or Subgroup	Tourniquet Events	Tourniquet Total	Without tourniquet Events	Without tourniquet Total	Weight	Risk Ratio M-H, Random, 95% CI
Abdel-Salem 1995	5	40	0	40	2.5%	11.00 [0.63 , 192.56]
Alexandersson 2019	2	38	0	43	2.3%	5.64 [0.28 , 113.94]
Ejaz 2015 b	2	33	1	31	3.8%	1.88 [0.18 , 19.70]
Goel 2019	3	100	3	99	8.4%	0.99 [0.20 , 4.79]
Huang 2017	1	50	0	50	2.1%	3.00 [0.13 , 71.92]
Jawhar 2020	3	50	2	49	6.8%	1.47 [0.26 , 8.42]
Kato 2002	1	22	0	24	2.1%	3.26 [0.14 , 76.10]
Li 2008	2	30	0	30	2.3%	5.00 [0.25 , 99.95]
Liu 2017	1	26	0	26	2.1%	3.00 [0.13 , 70.42]
Liu 2017 b	4	56	4	56	11.6%	1.00 [0.26 , 3.80]
Matziolis 2004	1	10	0	10	2.2%	3.00 [0.14 , 65.90]
Molt 2014	0	30	2	30	2.3%	0.20 [0.01 , 4.00]
Mori 2016	0	51	0	52		Not estimable
Tetro 2001	4	33	1	30	4.6%	3.64 [0.43 , 30.75]
Vandenbussche 2001	1	40	2	40	3.7%	0.50 [0.05 , 5.30]
Wakankar 1999	7	37	6	40	21.0%	1.26 [0.47 , 3.41]
Wauke 2002	2	19	0	18	2.4%	4.75 [0.24 , 92.65]
Wu 2018	0	50	0	50		Not estimable
Zhang 2010	0	30	0	30		Not estimable
Zhang 2016	9	84	2	82	9.2%	4.39 [0.98 , 19.72]
Zhou 2011	5	72	3	68	10.7%	1.57 [0.39 , 6.34]
Total (95% CI)		**901**		**898**	**100.0%**	**1.73 [1.10 , 2.73]**
Total events:	53		26			

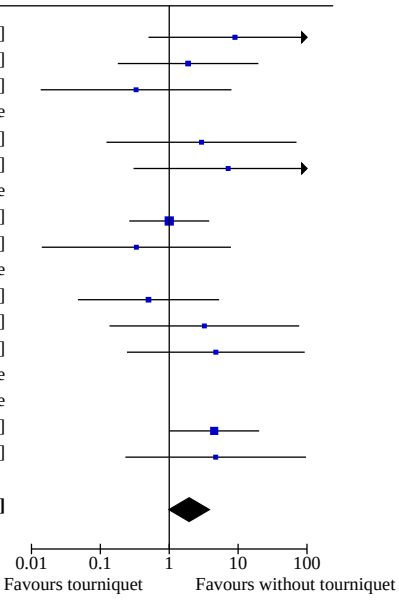
Heterogeneity: Tau² = 0.00; Chi² = 10.35, df = 17 (P = 0.89); I² = 0%
Test for overall effect: Z = 2.35 (P = 0.02)
Test for subgroup differences: Not applicable



Analysis 1.9. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 9: Serious adverse event: venous thromboembolic event (VTE)

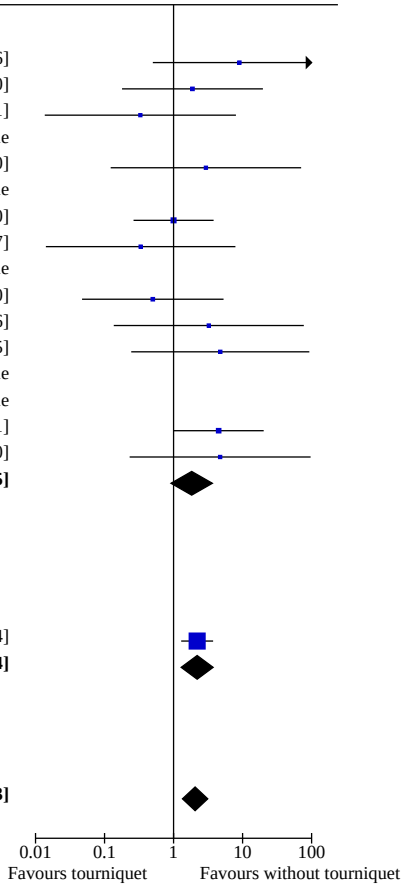
Study or Subgroup	Tourniquet Events	Tourniquet Total	Without tourniquet Events	Without tourniquet Total	Weight	Risk Ratio M-H, Random, 95% CI
Abdel-Salem 1995	4	40	0	40	5.4%	9.00 [0.50 , 161.86]
Ejaz 2015 b	2	33	1	31	8.2%	1.88 [0.18 , 19.70]
Goel 2019	0	100	1	99	4.5%	0.33 [0.01 , 8.01]
Huang 2017	0	50	0	50		Not estimable
Jawhar 2020	1	50	0	49	4.5%	2.94 [0.12 , 70.50]
Kato 2002	1	22	0	54	4.5%	7.17 [0.30 , 169.67]
Li 2008	0	30	0	30		Not estimable
Liu 2017 b	4	56	4	56	25.4%	1.00 [0.26 , 3.80]
Molt 2014	0	30	1	30	4.5%	0.33 [0.01 , 7.87]
Tetro 2001	0	33	0	30		Not estimable
Vandenbussche 2001	1	40	2	40	8.1%	0.50 [0.05 , 5.30]
Wakankar 1999	1	37	0	40	4.5%	3.24 [0.14 , 77.06]
Wauke 2002	2	19	0	18	5.1%	4.75 [0.24 , 92.65]
Wu 2018	0	50	0	50		Not estimable
Zhang 2010	0	30	0	30		Not estimable
Zhang 2016	9	84	2	84	20.1%	4.50 [1.00 , 20.21]
Zhou 2011	2	72	0	68	5.0%	4.73 [0.23 , 96.70]
Total (95% CI)		**776**		**799**	**100.0%**	**1.95 [0.99 , 3.82]**
Total events:	27		11			

Heterogeneity: Tau² = 0.00; Chi² = 8.45, df = 11 (P = 0.67); I² = 0%
Test for overall effect: Z = 1.94 (P = 0.05)
Test for subgroup differences: Not applicable



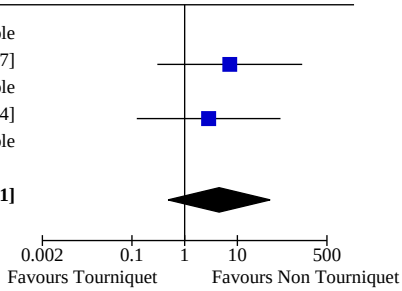
Analysis 1.10. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 10: Serious adverse event: deep vein thrombosis (DVT)

Study or Subgroup	Tourniquet Events	Tourniquet Total	without tourniquet Events	without tourniquet Total	Weight	Risk Ratio M-H, Random, 95% CI
1.10.1 Symptomatic DVT						
Abdel-Salem 1995	4	40	0	40	2.1%	9.00 [0.50 , 161.86]
Ejaz 2015 b	2	33	1	31	3.2%	1.88 [0.18 , 19.70]
Goel 2019	0	100	1	99	1.7%	0.33 [0.01 , 8.01]
Huang 2017	0	50	0	50		Not estimable
Jawhar 2020	1	50	0	49	1.8%	2.94 [0.12 , 70.50]
Li 2008	0	30	0	30		Not estimable
Liu 2017 b	4	56	4	56	10.0%	1.00 [0.26 , 3.80]
Molt 2014	0	30	1	30	1.8%	0.33 [0.01 , 7.87]
Tetro 2001	0	33	0	30		Not estimable
Vandenbussche 2001	1	40	2	40	3.2%	0.50 [0.05 , 5.30]
Wakankar 1999	1	37	0	40	1.8%	3.24 [0.14 , 77.06]
Wauke 2002	2	19	0	18	2.0%	4.75 [0.24 , 92.65]
Wu 2018	0	50	0	50		Not estimable
Zhang 2010	0	30	0	30		Not estimable
Zhang 2016	9	84	2	84	7.9%	4.50 [1.00 , 20.21]
Zhou 2011	2	72	0	68	1.9%	4.73 [0.23 , 96.70]
Subtotal (95% CI)		**754**		**745**	**37.4%**	**1.83 [0.92 , 3.65]**
Total events:	26		11			
Heterogeneity: Tau² = 0.00; Chi² = 7.78, df = 10 (P = 0.65); I² = 0%						
Test for overall effect: Z = 1.72 (P = 0.09)						
1.10.2 Asymptomatic DVT						
Mori 2016	28	51	13	52	62.6%	2.20 [1.29 , 3.74]
Subtotal (95% CI)		**51**		**52**	**62.6%**	**2.20 [1.29 , 3.74]**
Total events:	28		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.90 (P = 0.004)						
Total (95% CI)		**805**		**797**	**100.0%**	**2.05 [1.35 , 3.13]**
Total events:	54		24			
Heterogeneity: Tau² = 0.00; Chi² = 7.88, df = 11 (P = 0.72); I² = 0%						
Test for overall effect: Z = 3.34 (P = 0.0008)						
Test for subgroup differences: Chi² = 0.17, df = 1 (P = 0.68), I² = 0%						



Analysis 1.11. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 11: Serious adverse event: pulmonary embolism (PE)

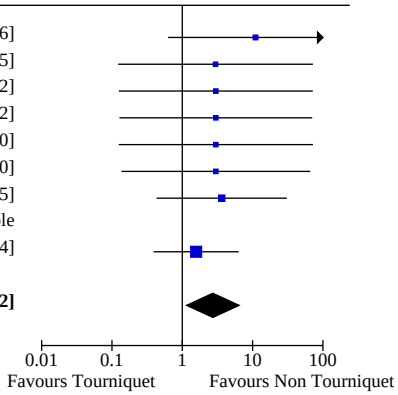
Study or Subgroup	Tourniquet Events	Tourniquet Total	Without tourniquet Events	Without tourniquet Total	Weight	Risk Ratio M-H, Random, 95% CI
Huang 2017	0	50	0	50		Not estimable
Kato 2002	1	22	0	54	49.6%	7.17 [0.30 , 169.67]
Mori 2016	0	51	0	52		Not estimable
Wauke 2002	1	19	0	18	50.4%	2.85 [0.12 , 65.74]
Wu 2018	0	50	0	50		Not estimable
Total (95% CI)		**192**		**224**	**100.0%**	**4.51 [0.49 , 41.81]**
Total events:	2		0			
Heterogeneity: Tau² = 0.00; Chi² = 0.17, df = 1 (P = 0.68); I² = 0%						
Test for overall effect: Z = 1.32 (P = 0.19)						
Test for subgroup differences: Not applicable						



Analysis 1.12. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 12: Serious adverse event: infection

Study or Subgroup	Tourniquet Events	Tourniquet Total	Without tourniquet Events	Without tourniquet Total	Weight	Risk Ratio M-H, Random, 95% CI
Abdel-Salem 1995	5	40	0	40	9.0%	11.00 [0.63 , 192.56]
Goel 2019	1	100	0	99	7.2%	2.97 [0.12 , 72.05]
Huang 2017	1	50	0	50	7.3%	3.00 [0.13 , 71.92]
Liu 2017	1	26	0	26	7.4%	3.00 [0.13 , 70.42]
Liu 2017 b	1	56	0	56	7.3%	3.00 [0.12 , 72.10]
Matziolis 2004	1	10	0	10	7.7%	3.00 [0.14 , 65.90]
Tetro 2001	4	33	1	30	16.1%	3.64 [0.43 , 30.75]
Vandenbussche 2001	0	40	0	40		Not estimable
Zhou 2011	5	72	3	68	38.0%	1.57 [0.39 , 6.34]
Total (95% CI)		**427**		**419**	**100.0%**	**2.72 [1.15 , 6.42]**
Total events:	19		4			

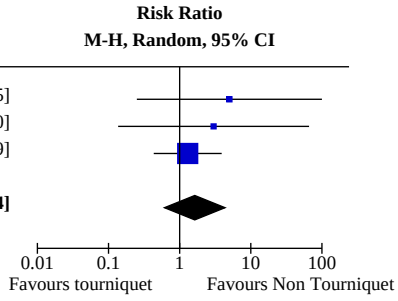
Heterogeneity: Tau² = 0.00; Chi² = 1.66, df = 7 (P = 0.98); I² = 0%
Test for overall effect: Z = 2.29 (P = 0.02)
Test for subgroup differences: Not applicable



Analysis 1.13. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 13: Serious adverse event: re-operation

Study or Subgroup	Tourniquet Events	Tourniquet Total	Without tourniquet Events	Without tourniquet Total	Weight	Risk Ratio M-H, Random, 95% CI
Li 2008	2	30	0	30	10.7%	5.00 [0.25 , 99.95]
Matziolis 2004	1	10	0	10	10.0%	3.00 [0.14 , 65.90]
Wakankar 1999	6	37	5	40	79.3%	1.30 [0.43 , 3.89]
Total (95% CI)		**77**		**80**	**100.0%**	**1.63 [0.61 , 4.34]**
Total events:	9		5			

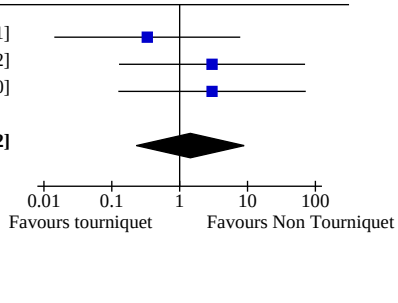
Heterogeneity: Tau² = 0.00; Chi² = 0.88, df = 2 (P = 0.64); I² = 0%
Test for overall effect: Z = 0.98 (P = 0.33)
Test for subgroup differences: Not applicable



Analysis 1.14. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 14: Survival of the implant: risk of revision up to 2 years

Study or Subgroup	Tourniquet Events	Tourniquet Total	Without tourniquet Events	Without tourniquet Total	Weight	Risk Ratio M-H, Random, 95% CI
Ledin 2012	0	25	1	25	33.5%	0.33 [0.01 , 7.81]
Liu 2017	1	26	0	26	33.5%	3.00 [0.13 , 70.42]
Liu 2017 b	1	56	0	56	33.0%	3.00 [0.12 , 72.10]
Total (95% CI)		**107**		**107**	**100.0%**	**1.44 [0.23 , 8.92]**
Total events:	2		1			

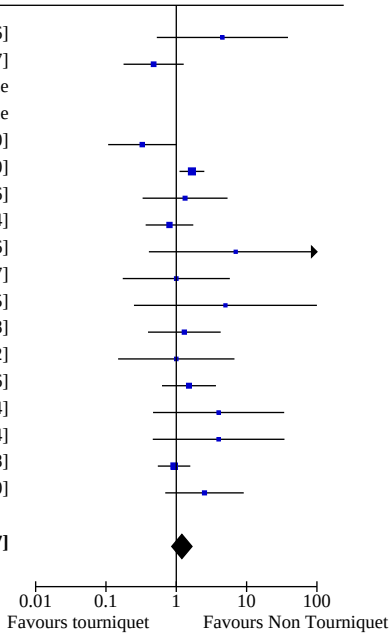
Heterogeneity: Tau² = 0.00; Chi² = 1.24, df = 2 (P = 0.54); I² = 0%
Test for overall effect: Z = 0.39 (P = 0.70)
Test for subgroup differences: Not applicable



Analysis 1.15. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 15: Blood loss: postoperative transfusion risk (lower is better)

Study or Subgroup	Tourniquet Events	Tourniquet Total	Without tourniquet Events	Without tourniquet Total	Weight	Risk Ratio M-H, Random, 95% CI
Alexandersson 2019	4	38	1	43	2.2%	4.53 [0.53 , 38.76]
Clarke 2001	5	21	5	10	7.9%	0.48 [0.18 , 1.27]
Ejaz 2015 b	0	33	0	31		Not estimable
Huang 2017	0	50	0	50		Not estimable
Juelsgaard 2001	3	16	8	14	6.6%	0.33 [0.11 , 1.00]
Kiss 2005	33	51	19	49	19.0%	1.67 [1.11 , 2.50]
Ledin 2012	4	25	3	25	4.7%	1.33 [0.33 , 5.36]
Li 2008	8	30	10	30	10.7%	0.80 [0.37 , 1.74]
Liu 2014	3	10	0	10	1.3%	7.00 [0.41 , 120.16]
Matziolis 2004	2	10	2	10	3.1%	1.00 [0.17 , 5.77]
Molt 2014	2	30	0	30	1.2%	5.00 [0.25 , 99.95]
Ozkunt 2018	5	24	4	25	6.0%	1.30 [0.40 , 4.28]
Tai 2012	2	36	2	36	2.7%	1.00 [0.15 , 6.72]
Tetro 2001	10	33	6	30	9.2%	1.52 [0.63 , 3.66]
Vandenbussche 2001	4	40	1	40	2.2%	4.00 [0.47 , 34.24]
Wu 2018	4	50	1	50	2.2%	4.00 [0.46 , 34.54]
Zhang 2016	20	84	21	82	15.8%	0.93 [0.55 , 1.58]
Zhou 2011	8	72	3	68	5.3%	2.52 [0.70 , 9.10]
Total (95% CI)		**653**		**633**	**100.0%**	**1.20 [0.86 , 1.67]**
Total events:	117		86			

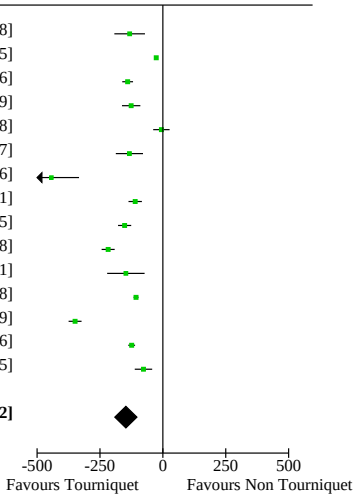
Heterogeneity: Tau² = 0.11; Chi² = 20.98, df = 15 (P = 0.14); I² = 29%
Test for overall effect: Z = 1.08 (P = 0.28)
Test for subgroup differences: Not applicable



Analysis 1.16. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 16: Blood loss: intraoperative (mL, lower is better)

Study or Subgroup	Tourniquet Mean	Tourniquet SD	Tourniquet Total	without tourniquet Mean	without tourniquet SD	without tourniquet Total	Weight	Mean Difference IV, Random, 95% CI
Aglietti 2000	350	12	10	482	97.4	10	6.3%	-132.00 [-192.82 , -71.18]
Dong 2019	56	12.53	58	82.34	17.62	64	7.1%	-26.34 [-31.73 , -20.95]
Ejaz 2015 b	140	32.7	33	280	52	31	7.0%	-140.00 [-161.44 , -118.56]
Harston 2015	56	55.92	32	182	89.3	32	6.8%	-126.00 [-162.51 , -89.49]
Huang 2017	144.8	80.1	50	150.6	86	50	6.8%	-5.80 [-38.38 , 26.78]
Juelsgaard 2001	13	27	16	146	100	14	6.4%	-133.00 [-187.03 , -78.97]
Kato 2002	67	120	22	510	244	24	4.9%	-443.00 [-552.74 , -333.26]
Li 2008	333	65	30	443	36	30	6.9%	-110.00 [-136.59 , -83.41]
Li 2009	317	72	40	469	44	40	6.9%	-152.00 [-178.15 , -125.85]
Tai 2012	25.6	30.9	36	243.1	73.1	36	6.9%	-217.50 [-243.42 , -191.58]
Tetro 2001	148	81	33	295	193	30	5.9%	-147.00 [-221.39 , -72.61]
Wu 2018	159.06	11.31	50	265.74	32.75	50	7.1%	-106.68 [-116.28 , -97.08]
Zhang 2010	207	56	30	556	45	30	6.9%	-349.00 [-374.71 , -323.29]
Zhang 2016	112	45	84	236	44	82	7.1%	-124.00 [-137.54 , -110.46]
Zhou 2011	138.6	93.9	72	215.7	113.7	68	6.8%	-77.10 [-111.75 , -42.45]
Total (95% CI)		**596**				**591**	**100.0%**	**-147.05 [-190.97 , -103.12]**

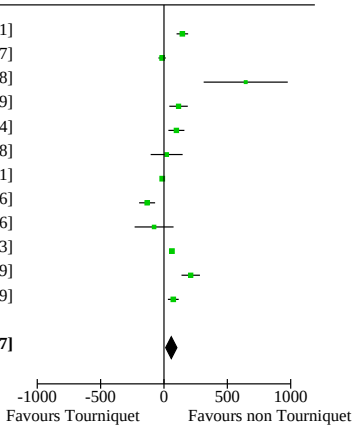
Heterogeneity: Tau² = 7058.44; Chi² = 1112.19, df = 14 (P < 0.00001); I² = 99%
Test for overall effect: Z = 6.56 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.17. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 17: Blood loss: postoperative (mL, lower is better)

Study or Subgroup	Tourniquet Mean	SD	Total	without tourniquet Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Aglietti 2000	290	54	10	145	50	10	10.0%	145.00 [99.39 , 190.61]
Huang 2017	168.5	72.5	50	183.2	74.8	50	10.6%	-14.70 [-43.57 , 14.17]
Juelsgaard 2001	1461	612	16	816	271	14	1.5%	645.00 [313.22 , 976.78]
Li 2008	253	162.92	30	138	121.82	30	8.5%	115.00 [42.21 , 187.79]
Li 2009	237	162.92	40	139	121.82	40	9.1%	98.00 [34.96 , 161.04]
Liu 2014	457.1	162.92	10	436	121.82	10	5.8%	21.10 [-104.98 , 147.18]
Ozkunt 2018	245	24.6	24	258.76	32.4	25	11.0%	-13.76 [-29.83 , 2.31]
Vandenbussche 2001	528.5	162.92	40	661.6	121.82	40	9.1%	-133.10 [-196.14 , -70.06]
Wauke 2002	346.5	191.4	19	424.6	275.3	18	4.7%	-78.10 [-231.66 , 75.46]
Wu 2018	231.8	41.71	50	169.18	32.23	50	11.0%	62.62 [48.01 , 77.23]
Zhang 2010	487	162.92	30	276	121.82	30	8.5%	211.00 [138.21 , 283.79]
Zhou 2011	253.7	144.2	72	180.2	111	68	10.1%	73.50 [31.01 , 115.99]
Total (95% CI)			**391**			**385**	**100.0%**	**57.72 [13.58 , 101.87]**

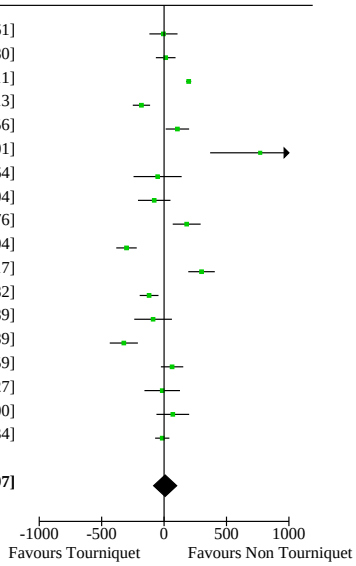
Heterogeneity: Tau² = 4555.20; Chi² = 159.17, df = 11 (P < 0.00001); I² = 93%
Test for overall effect: Z = 2.56 (P = 0.01)
Test for subgroup differences: Not applicable



Analysis 1.18. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 18: Blood loss: overall blood loss (mL, lower is better)

Study or Subgroup	Tourniquet Mean	SD	Total	without tourniquet Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Abdel-Salem 1995	800	276.87	40	805	235.365	40	5.7%	-5.00 [-117.61 , 107.61]
Aglietti 2000	640	120	10	627	42	10	5.9%	13.00 [-65.80 , 91.80]
Dong 2019	455.45	69.47	64	258.34	40.85	58	6.2%	197.11 [177.11 , 217.11]
Goel 2019	966.64	260.91	100	1148.02	237.03	99	6.0%	-181.38 [-250.63 , -112.13]
Huang 2017	734.5	274.2	50	627.7	198.1	50	5.8%	106.80 [13.04 , 200.56]
Juelsgaard 2001	1826	765	16	1056	272	14	2.9%	770.00 [368.99 , 1171.01]
Ledin 2012	1184	346	25	1236	349	25	4.9%	-52.00 [-244.64 , 140.64]
Li 2008	545	276.87	30	624	235.365	30	5.5%	-79.00 [-209.04 , 51.04]
Li 2009	1298	285	40	1117	221	40	5.7%	181.00 [69.24 , 292.76]
Mori 2016	470	219	51	771	205	52	5.9%	-301.00 [-382.96 , -219.04]
Pfitzner 2014	900	276.87	45	600	235.365	45	5.7%	300.00 [193.83 , 406.17]
Tai 2012	303	119	36	423	197	36	6.0%	-120.00 [-195.18 , -44.82]
Tetro 2001	654	324	33	742	287	30	5.3%	-88.00 [-238.89 , 62.89]
Vandenbussche 2001	1234.9	276.87	40	1557.4	235.365	40	5.7%	-322.50 [-435.11 , -209.89]
Wu 2018	1103.95	201.93	50	1039.86	251.98	50	5.9%	64.09 [-25.41 , 153.59]
Yavarikia 2010	795	266	22	810	244	29	5.4%	-15.00 [-157.27 , 127.27]
Zhang 2010	1360	237	30	1290	279	30	5.5%	70.00 [-61.00 , 201.00]
Zhou 2011	374.5	165.3	72	389.2	178.3	68	6.1%	-14.70 [-71.74 , 42.34]
Total (95% CI)			**754**			**746**	**100.0%**	**8.61 [-83.76 , 100.97]**

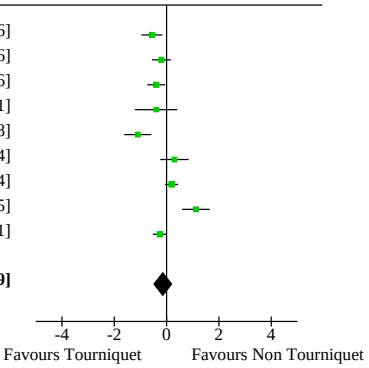
Heterogeneity: Tau² = 35816.17; Chi² = 401.67, df = 17 (P < 0.00001); I² = 96%
Test for overall effect: Z = 0.18 (P = 0.86)
Test for subgroup differences: Not applicable



Analysis 1.19. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 19: Blood loss: change in haemoglobin (g/dL, lower is better)

Study or Subgroup	Tourniquet Mean	SD	Total	without tourniquet Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Alexandersson 2019	2.08	0.8656	38	2.64	0.9792	43	11.6%	-0.56 [-0.96 , -0.16]
Kiss 2005	2.2	0.8656	51	2.4	0.9792	49	12.0%	-0.20 [-0.56 , 0.16]
Li 2008	4.7	0.87	30	5.1	0.39	30	12.1%	-0.40 [-0.74 , -0.06]
Matziolis 2004	2.5	0.8656	10	2.9	0.9792	10	7.7%	-0.40 [-1.21 , 0.41]
Tai 2012	2.6	0.9	36	3.7	1.3	36	10.5%	-1.10 [-1.62 , -0.58]
Tetro 2001	4.1	1.2	33	3.8	1	30	10.2%	0.30 [-0.24 , 0.84]
Wu 2018	3.46	0.6	50	3.27	0.67	50	12.9%	0.19 [-0.06 , 0.44]
Yavarikia 2010	2.37	0.932	22	1.25	0.9792	29	10.3%	1.12 [0.59 , 1.65]
Zhang 2016	3.317	0.758	84	3.573	0.996	82	12.7%	-0.26 [-0.53 , 0.01]
Total (95% CI)			**354**			**359**	**100.0%**	**-0.14 [-0.48 , 0.19]**

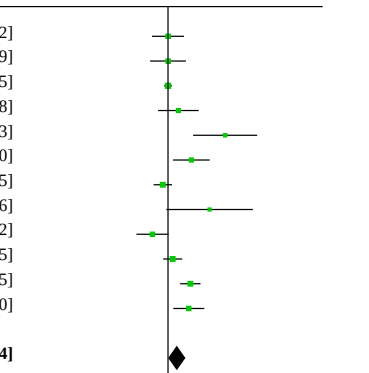
Heterogeneity: Tau² = 0.21; Chi² = 52.03, df = 8 (P < 0.00001); I² = 85%
Test for overall effect: Z = 0.85 (P = 0.40)
Test for subgroup differences: Not applicable



Analysis 1.20. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 20: Economic: length of hospital stay (days, lower is better)

Study or Subgroup	Tourniquet Mean	SD	Total	without tourniquet Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Abdel-Salem 1995	12	1.6243	40	12	1.1486	40	8.5%	0.00 [-0.62 , 0.62]
Harston 2015	2	1.6243	32	2	1.1486	32	7.8%	0.00 [-0.69 , 0.69]
Huang 2017	5.12	0.38	50	5.12	0.4	50	12.6%	0.00 [-0.15 , 0.15]
Ledin 2012	4.9	1.6243	25	4.5	1.1486	25	7.0%	0.40 [-0.38 , 1.18]
Liu 2014	7.5	1.6243	10	5.3	1.1486	10	4.1%	2.20 [0.97 , 3.43]
Molt 2014	4.5	1.8	30	3.6	0.8	30	7.6%	0.90 [0.20 , 1.60]
Tai 2012	3.5	0.6	36	3.7	0.9	36	11.1%	-0.20 [-0.55 , 0.15]
Tetro 2001	8.5	4.3	33	6.9	2.2	30	2.6%	1.60 [-0.06 , 3.26]
Vandenbussche 2001	11.2	1.6243	40	11.8	1.1486	40	8.5%	-0.60 [-1.22 , 0.02]
Wu 2018	5.36	1.01	50	5.18	0.85	50	10.9%	0.18 [-0.19 , 0.55]
Zhang 2016	5.63	1.38	84	4.77	1.19	82	10.7%	0.86 [0.47 , 1.25]
Zhou 2011	7.1	1.9	72	6.3	1.7	68	8.6%	0.80 [0.20 , 1.40]
Total (95% CI)			**502**			**493**	**100.0%**	**0.34 [0.03 , 0.64]**

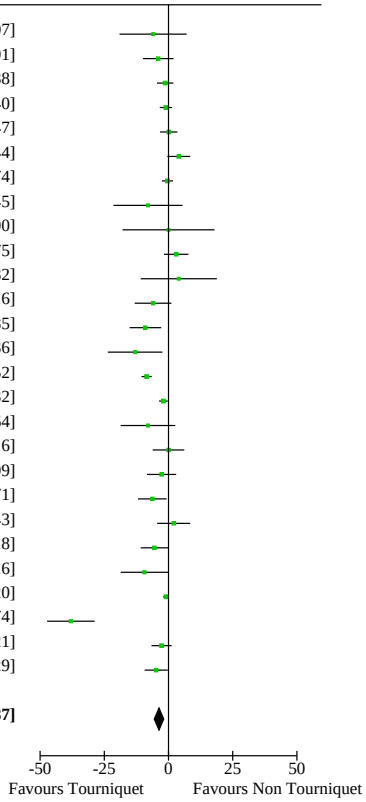
Heterogeneity: Tau² = 0.18; Chi² = 48.94, df = 11 (P < 0.00001); I² = 78%
Test for overall effect: Z = 2.19 (P = 0.03)
Test for subgroup differences: Not applicable



Analysis 1.21. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 21: Economic: duration of surgery (minutes, lower is better)

Study or Subgroup	Tourniquet Mean	SD	Total	without tourniquet Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Aglietti 2000	90	18	10	96	11	10	1.5%	-6.00 [-19.07 , 7.07]
Ayik 2020	68	13.1	32	72	11.1	33	3.7%	-4.00 [-9.91 , 1.91]
Dong 2019	71.6	9.48	58	72.9	8.35	64	5.1%	-1.30 [-4.48 , 1.88]
Ejaz 2015 b	70	5.3	33	71	4.5	31	5.5%	-1.00 [-3.40 , 1.40]
Goel 2019	71.6	13.1	100	71.5	11.1	99	5.1%	0.10 [-3.27 , 3.47]
Harston 2015	43	10	32	39	8	32	4.5%	4.00 [-0.44 , 8.44]
Huang 2017	51.8	4.6	50	52.2	6.2	50	5.6%	-0.40 [-2.54 , 1.74]
Jawhar 2015	79	20	17	87	20	17	1.4%	-8.00 [-21.45 , 5.45]
Kato 2002	111	41	22	111	13	24	0.9%	0.00 [-17.90 , 17.90]
Kiss 2005	94.8	13.1	51	91.8	11.1	49	4.3%	3.00 [-1.75 , 7.75]
Ledin 2012	85	30	25	81	23	25	1.2%	4.00 [-10.82 , 18.82]
Li 2008	77	16	30	83	12	30	3.2%	-6.00 [-13.16 , 1.16]
Li 2009	73	13	40	82	15	40	3.6%	-9.00 [-15.15 , -2.85]
Liu 2014	83	13.1	10	96	11.1	10	2.0%	-13.00 [-23.64 , -2.36]
Liu 2017	81.2	3.1	26	89.7	4.1	26	5.7%	-8.50 [-10.48 , -6.52]
Liu 2017 b	80	4	56	82	5	56	5.8%	-2.00 [-3.68 , -0.32]
Matziolis 2004	85	13.1	10	93	11.1	10	2.0%	-8.00 [-18.64 , 2.64]
Molt 2014	58	10	30	58	14	30	3.6%	0.00 [-6.16 , 6.16]
Mori 2016	63.6	11.4	51	66.3	17.5	52	3.8%	-2.70 [-8.39 , 2.99]
Tai 2012	72	8.4	36	78.3	14.9	36	3.9%	-6.30 [-11.89 , -0.71]
Tetro 2001	83	13	33	81	13	30	3.5%	2.00 [-4.43 , 8.43]
Vandenbussche 2001	151	13.1	40	156.5	11.1	40	4.0%	-5.50 [-10.82 , -0.18]
Wauke 2002	75.1	15.7	19	84.5	12.9	18	2.4%	-9.40 [-18.64 , -0.16]
Wu 2018	67.22	3.12	50	68.16	2.67	50	6.0%	-0.94 [-2.08 , 0.20]
Yavarikia 2010	77	18	22	115	12	19	2.4%	-38.00 [-47.26 , -28.74]
Zhang 2016	81.69	14.07	84	84.4	11.61	82	4.8%	-2.71 [-6.63 , 1.21]
Zhou 2011	77.2	14.5	72	82	12.7	68	4.5%	-4.80 [-9.31 , -0.29]
Total (95% CI)			**1039**			**1031**	**100.0%**	**-3.70 [-5.53 , -1.87]**

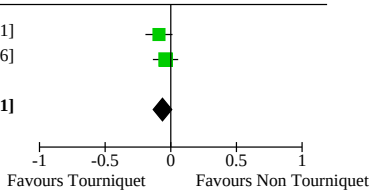
Heterogeneity: Tau² = 14.38; Chi² = 141.31, df = 26 (P < 0.00001); I² = 82%
Test for overall effect: Z = 3.95 (P < 0.0001)
Test for subgroup differences: Not applicable



Analysis 1.22. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 22: Implant stability: maximum total point motion at 8 weeks (mm, lower is better)

Study or Subgroup	Tourniquet Mean	SD	Total	without tourniquet Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ejaz 2014	0.44	0.22	35	0.53	0.22	35	46.6%	-0.09 [-0.19 , 0.01]
Molt 2014	0.37	0.2	30	0.41	0.18	30	53.4%	-0.04 [-0.14 , 0.06]
Total (95% CI)			**65**			**65**	**100.0%**	**-0.06 [-0.13 , 0.01]**

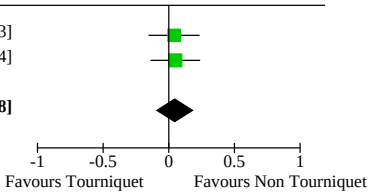
Heterogeneity: Tau² = 0.00; Chi² = 0.48, df = 1 (P = 0.49); I² = 0%
Test for overall effect: Z = 1.76 (P = 0.08)
Test for subgroup differences: Not applicable



Analysis 1.23. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 23: Implant stability: maximum total point motion at 1 year (mm, lower is better)

	Tourniquet			without tourniquet				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Ejaz 2014	0.57	0.4	35	0.53	0.43	35	48.5%	0.04 [-0.15 , 0.23]	
Molt 2014	0.58	0.47	30	0.53	0.24	30	51.5%	0.05 [-0.14 , 0.24]	
Total (95% CI)			**65**			**65**	**100.0%**	**0.05 [-0.09 , 0.18]**	

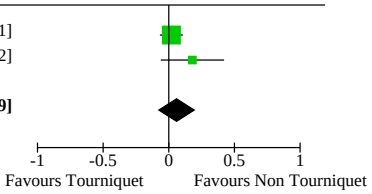
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.94); I² = 0%
Test for overall effect: Z = 0.65 (P = 0.51)
Test for subgroup differences: Not applicable



Analysis 1.24. Comparison 1: Surgery with a tourniquet vs surgery without a tourniquet, Outcome 24: Implant stability: maximum total point motion at 2 years (mm, lower is better)

	Tourniquet			without tourniquet				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Ejaz 2014	0.47	0.16	35	0.45	0.21	35	75.6%	0.02 [-0.07 , 0.11]	
Molt 2014	0.71	0.64	30	0.53	0.21	30	24.4%	0.18 [-0.06 , 0.42]	
Total (95% CI)			**65**			**65**	**100.0%**	**0.06 [-0.08 , 0.19]**	

Heterogeneity: Tau² = 0.00; Chi² = 1.50, df = 1 (P = 0.22); I² = 33%
Test for overall effect: Z = 0.86 (P = 0.39)
Test for subgroup differences: Not applicable



ADDITIONAL TABLES

Table 1. Baseline characteristics

Author	Number of participants	Number in tourniquet group	Number in control group	Mean age in tourniquet group (SD)	Mean age in control group (SD)	Proportion of males in tourniquet group, %	Proportion of males in control group, %	BMI in tourniquet group (SD)	BMI in control group (SD)
Abdel-Salem 1995	80	40	40	73	73				
Aglietti 2000	20	10	10	70 (8)	68 (4.5)	30	40	27.9	27.3
Alexandersson 2018	81	38	43	68 (7.4)	69.7 (6.4)	47	51	28.6 (3.4)	27.9 (3.5)
Ayik 2020	65	32	33	65.39 (7.25)	64.90 (6.58)	44	42	31.38 (4.72)	30.3 (7.1)
Clarke 2001	31	21	10						
Dong 2019	122	58	64	68.2 (17.1)	69.5 (15.9)	34	35		
Ejaz 2014	64	33	31	68 (8.4)	68 (7.4)	55	55	25 (2)	25 (2.5)
Ejaz 2015	62	31	31	68 (6.3)	68.2 (7.2)	52	55	25.1 (2)	25.2 (2.5)
Ejaz 2015 b	57	29	28	68.3 (8.4)	68.2 (7.8)	45	54	25.1 (2)	25.2 (2.5)
Goel 2019	199	100	99	66.0 (7.0)	65.5 (7.8)	50	48	30.9 (4.6)	31.3 (4.5)
Harston 2015	64	32	32	68 (8)	66 (8)			27.4	28.4
Huang 2017	100	50	50	66.2 (8.3)	65.1 (8.1)	36	32	25.1 (1.5)	24.2 (1.5)
Jawhar 2015	34	17	17	70.6 (6)	70.6 (6)	53	53	32.1 (5)	33.8 (5)
Jawhar 2019	99	50	49	69.3 (7.4)	68.3 ± 7.8	34	39	31.9 (6)	31.4 (5.5)
Juelsgaard 2001	30	16	14	69	64	44	29		
Kato 2002	46	22	24	65	63				
Kiss 2015	100	51	49	72.6 (7.1)	74.7 (7.4)	20	27	28.8 (3.9)	28.5 (3.3)
Kumar 2015	30	30	30	58	58	30	30		

Table 1. Baseline characteristics *(Continued)*

Ledin 2012	50	25	25	70 (8)	71 (6)	67	39	29 (4.8)	28 (4.8)
Li 2008	60	30	30	71 (7)	70 (7)			24 (5)	24 (5)
Li 2009	80	40	40	71 (6)	70 (7)	28	33	27.3 (6.3)	26.8 (5.1)
Liu 2014	20	10	10	67	60	70	90	25.5	28.7
Liu 2017	52	52	52	67 (8)	67 (8)			28.1 (5.5)	28.1 (5.5)
Liu 2017 b	26	26	26	65.8 (9.2)	65.8 (9.2)	35	35	28.2 (5.6)	28.2 (5.6)
Matziolis 2015	20	10	10	72.4	76.6	80	70	28.3	29.5
Molt 2014	60	30	30	70 (7)	67 (9)	53	53	28 (3)	28 (3)
Mori 2016	103	51	52	72.8 (7.3)	74.6 (7.6)	12	17	27.7 (3.4)	29.2 (3.9)
Ozkunt 018	49	24	25	65.05	65.05				
Pfitzner 2014	90	45	45	69.3	70.5	47	24	27.8	26
Tai 2012	72	36	36	72.1 (6.9)	71.5 (6.8)			28.6 (4.5)	27.9 (4.2)
Tetro 2001	63	33	30	69.8 (6.7)	69.8 (9)	45	37		
Vandenbussche 2001	80	40	40	72.5	68.5	22.5	40		
Vertullo 2017	40	20	20	67.85 (6.91)	65.65 (8.54)	50	55	30.43 (5.07)	31 (5.31)
Wakankar 1999	77	37	40	72.5	71.8	30	35		
Wauke 2002	37	19	18	63.2 (8.7)	61.4 (7.4)				
Wu 2018	100	50	50	68.06 (3.16)	67.58 (4.61)	38	44	23.87 (2.13)	24.10 (2.16)
Yavarikia 2010	51	22	29	68	66	27	24		
Zhang 2010	60	30	30	72 (6)	71 (6)	27	37	25 (4)	26 (4)
Zhang 2016	166	84	82	84	82				

Table 1. Baseline characteristics *(Continued)*

Zhou 2011	39	20	19	63.12 (6.79)	61.89 (7.93)	35	26		
Zhou 2017	140	72	68	72	68	18	10	26.1 (4.1)	25.7 (3.4)

Table 2. Statistical tests for publication bias

Outcome	Bias estimate (standard error)	P value
Pain	3.875 (2.168)	0.097
Intraoperative blood loss	-8.732 (2.596)	0.005
Overall blood loss	5.585 (3.968)	0.178
Postoperative blood loss	-0.049 (3.420)	0.989
Transfusion rate	0.47 (0.63)	0.468
Length of stay	0.219 (2.182)	0.922
Duration of surgery	-2.947 (1.113)	0.014
Serious adverse events	0.567 (0.552)	0.318

APPENDICES

Appendix 1. CENTRAL search strategy

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <February 2020>
1 arthroplasty, replacement, knee/ (2397)
2 knee Prosthesis/ (695)
3 Tkr.ti,ab. (611)
4 exp knee/ (757)
5 Knee.ti,ab. (26815)
6 4 or 5 (26892)
7 exp arthroplasty/ (4793)
8 joint prosthesis/ (152)
9 (arthroplast$ or prosthe$ or replac$).ti,ab. (44454)
10 or/7-9 (45239)
11 6 and 10 (8683)
12 or/1-3,11 (8836)
13 exp tourniquet/ (502)
14 Tourniquet.ti,ab. (1777)
15 Esmarch.ti,ab. (39)
16 Lofquist.ti,ab. (1)
17 Cuff.ti,ab. (4665)
18 or/13-17 (6389)
19 12 and 18 (539)

Appendix 2. MEDLINE search strategy for RCTs

Database: Ovid MEDLINE(R) ALL <1946 to March 26, 2020>
1 arthroplasty, replacement, knee/ (23209)
2 knee Prosthesis/ (11497)
3 Tkr.ti,ab. (1965)
4 exp knee/ (14079)
5 Knee.ti,ab. (136670)
6 4 or 5 (141363)
7 exp arthroplasty/ (67501)
8 joint prosthesis/ (10183)
9 (arthroplast$ or prosthe$ or replac$).ti,ab. (553274)

10 or/7-9 (570385)
11 6 and 10 (43440)
12 or/1-3,11 (47102)
13 exp tourniquet/ (3806)
14 Tourniquet.ti,ab. (5763)
15 Esmarch.ti,ab. (143)
16 Lofquist.ti,ab. (5)
17 Cuff.ti,ab. (26604)
18 or/13-17 (33350)
19 12 and 18 (945)
20 randomized controlled trial.pt. (502716)
21 controlled clinical trial.pt. (93585)
22 randomized.ab. (474264)
23 placebo.ab. (206347)
24 clinical trials as topic.sh. (190551)
25 randomly.ab. (329990)
26 trial.ti. (215554)
27 or/20-26 (1277741)
28 exp animals/ not humans.sh. (4683296)
29 27 not 28 (1175436)
30 19 and 29 (340)

Appendix 3. Embase search strategy for RCTs

Database: Embase <1974 to 2020 March 27>
1 knee arthroplasty/ (15292)
2 knee prosthesis/ (8310)
3 total knee replacement/ (20943)
4 (knee adj3 (arthroplast$ or replac$ or prosthe$)).ti,ab. (41589)
5 or/1-4 (50915)
6 exp tourniquet/ (6272)
7 tourniquet$.ti,ab. (7325)
8 Esmarch.ti,ab. (157)
9 Lofquist.ti,ab. (8)
10 Cuff.ti,ab. (36952)
11 or/6-10 (45707)
12 5 and 11 (1189)
13 random$.tw. (1517280)
14 factorial$.tw. (37582)
15 crossover$.tw. (74987)
16 cross over.tw. (31934)
17 cross-over.tw. (31934)
18 placebo$.tw. (305092)
19 (doubl$ adj blind$).tw. (207633)
20 (singl$ adj blind$).tw. (24601)
21 assign$.tw. (389504)
22 allocat$.tw. (150203)
23 volunteer$.tw. (254706)
24 crossover procedure/ (62618)
25 double blind procedure/ (170919)
26 randomized controlled trial/ (596807)
27 single blind procedure/ (38387)
28 or/13-27 (2300219)
29 12 and 28 (411)

Appendix 4. Clinicaltrials.gov

Search performed 28th March 2020

Search terms:

Tourniquet AND Knee (42)

Appendix 5. WHO ICTRP

Search performed 7th August 2019

Search terms:

Tourniquet AND Knee (108)

Appendix 6. MEDLINE search strategy for observational studies

Database: Ovid MEDLINE(R) ALL <1946 to March 26, 2020>
1 arthroplasty, replacement, knee/ (23209)
2 knee Prosthesis/ (11497)
3 Tkr.ti,ab. (1965)
4 exp knee/ (14079)
5 Knee.ti,ab. (136670)
6 4 or 5 (141363)
7 exp arthroplasty/ (67501)
8 joint prosthesis/ (10183)
9 (arthroplast$ or prosthe$ or replac$).ti,ab. (553274)
10 or/7-9 (570385)
11 6 and 10 (43440)
12 or/1-3,11 (47102)
13 exp tourniquet/ (3806)
14 Tourniquet.ti,ab. (5763)
15 Esmarch.ti,ab. (143)
16 Lofquist.ti,ab. (5)
17 Cuff.ti,ab. (26604)
18 or/13-17 (33350)
19 12 and 18 (945)
20 exp animals/ not humans.sh. (4683296)
21 Cohort studies/ or comparative study/ or follow-up studies/ or prospective studies/ or risk factors/ or cohort.mp. or compared.mp. or groups.mp. or multivariate.mp. (7434644)
22 21 not 20 (6243355)
23 19 and 22 (656)

Appendix 7. Embase search strategy for observational studies

Database: Embase <1974 to 2020 March 27>
1 knee arthroplasty/ (15292)
2 knee prosthesis/ (8310)
3 total knee replacement/ (20943)
4 (knee adj3 (arthroplast$ or replac$ or prosthe$)).ti,ab. (41589)
5 or/1-4 (50915)
6 exp tourniquet/ (6272)
7 tourniquet$.ti,ab. (7325)
8 Esmarch.ti,ab. (157)
9 Lofquist.ti,ab. (8)
10 Cuff.ti,ab. (36952)
11 or/6-10 (45707)
12 5 and 11 (1189)
13 Clinical article/ or controlled study/ or major clinical study/ or prospective study/ or cohort.mp. or compared.mp. or groups.mp. or multivariate.mp. (14008642)
14 exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/ (27151487)
15 human/ or normal human/ or human cell/ (20781357)
16 14 and 15 (20718818)
17 14 not 16 (6432669)
18 (12 and 13) not 17 (879)

HISTORY

Protocol first published: Issue 11, 2017
Review first published: Issue 12, 2020

CONTRIBUTIONS OF AUTHORS

All authors were involved in the writing and approval of the final review.

IA, AC, and PW performed the search, screened articles, and extracted data.

IA, PW, and HP performed the data analysis.

IA, AC, and PW wrote the first draft of the review.

PW is the guarantor for the review.

All authors were involved in interpreting the results and approving the final review; all authors had access to the data and took responsibility for the accuracy of data analysis.

DECLARATIONS OF INTEREST

IA declares funding from NIHR.

AC has no conflicts of interest.

MU is chief investigator or co-investigator on multiple previous and current research grants from the UK National Institute for Health Research, Arthritis Research UK, and is a co-investigator on grants funded by the Australian NHMRC. He is an NIHR Senior Investigator. He has received travel expenses for speaking at conferences from the professional organisations hosting the conferences. He is a director and shareholder of Clinvivo Ltd, which provides electronic data collection for health services research. He is part of an academic partnership with Serco Ltd, funded by the European Social Fund, related to return to work initiatives. He is a co-investigator on two NIHR-funded studies, receiving additional support from Stryker Ltd. He has accepted honoraria for teaching/lecturing from Consortium for Advanced Research Training in Africa (CARTA). He was until 2020 an editor of the NIHR journal series and was a member of the NIHR Journal Editors Group, for which he received a fee.

AP is a Consultant Orthopaedic Surgeon who routinely undertakes independent TKR surgery and currently routinely performs TKR surgery with a tourniquet unless patients express a preference or there are contraindications to using a tourniquet. AP undertakes Consultancy work for Zimmer Biomet, but this is unrelated to the subject of this review.

AM leads two randomised trials (START:REACTS and RACER), in which HP and MU are co-investigators, which are funded by the National Institute for Health Research (NIHR), in the UK. For both studies, Stryker (USA) is providing devices or costs for delivery of treatment to participating hospitals, although Stryker is not otherwise funding the studies and has no other financial relationship. Contracts are in place to ensure the full independence of the trial team with regard to study design and delivery, analysis, and reporting of results, aligning to the NIHR standard agreement. There is no direct relationship between these studies and the topic of the review. AM is a Consultant Orthopaedic Surgeon who routinely undertakes independent TKR surgery and currently routinely performs TKR surgery with a tourniquet unless patients express a preference or there are contraindications to using a tourniquet.

CH has no conflicts of interest.

JW declares funding from NIHR.

KS has no conflicts of interest.

HP declares funding from NIHR and funding in kind from Stryker.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We aimed to assess non-randomised studies using the ROBINS-I tool; however, given that we identified no non-randomised studies that met our inclusion criteria, we did not use this tool.

We did not perform subgroup analysis as we did not identify any studies that reported surgery other than primary total knee replacement. In addition, all studies used pneumatic tourniquets for the procedure.

All studies reporting outcomes and pain used a tourniquet from initial incision through to wound closure. Only one study reporting serious adverse events used a different tourniquet technique (Tetro 2001). In this study, the tourniquet was released after cementation. We did not include formal sensitivity analysis in the final report, as removing this study did not significantly affect the results (RR 2.07, 95% CI 1.27 to 3.38).

We planned to group outcomes based on short term (up to 3 months), medium term (> 3 to 12 months), and longer term (> 12 months). However, after consultation with patients and surgeons, the consensus was that earlier time points were more appropriate for pain, as this is when the intervention was likely to have the greatest effect. Therefore the primary endpoint for pain was day 1 postoperatively (and in our report, SoF and pain scores were also reported for day 2, day 3, two weeks, and six weeks.