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Evidence Based Treatment for Unstable Slipped Upper Femoral Epiphysis: systematic review and exploratory patient level analysis.

Introduction

Slipped upper femoral epiphysis (SUFE) is one of the most important paediatric and adolescent hip disorder. Incidence is 1-2:100 000. The cause is poorly understood, it is believed that increased shear forces and weakness of the growth plate (the physis) during adolescence may be contributory factors. The management of SUFE is controversial and is evolving as insight into the condition develops. Infrequency of cases, varying classification and surgical approaches as well as inadequate reporting of outcomes, undermine attempts to formulate evidence-based recommendations for treatment [1-3].

In 1993, Loder [4] introduced the concept of instability of slipped upper femoral epiphysis and demonstrated a strong association between poor outcome and instability. Loder recognised two types of slips: unstable ones where the patient has such severe pain that walking is not possible even with crutches, independent of the duration of the symptoms; and stable slips where the patient can walk with or without crutches. In a series of 55 patients with SUFE, Loder showed that avascular necrosis (FHO) developed in 47% of unstable slips but none of stable hips. This finding has been confirmed by others [1, 5-7].

High risk of FHO in unstable slips has been influential in surgeons' choice of treatments. Some surgeons have adopted a minimal intervention approach such as

pinning in situ or gentle reduction and pinning whereas others advocated an urgent open reduction and stabilisation of slip using various surgical techniques.

In the course of this review a number of treatments options have been identified that are used to treat unstable slips including: epiphysiodesis, pinning in situ (PIS), closed reduction and pinning (CRIF), open reduction and physeal osteotomy (PO), open reduction and internal fixation (ORIF) and Ganz surgical dislocation (SD). Optimal timing of surgery is also uncertain: some surgeons recommend urgent intervention (within 24 hours from presentation) while some surgeons keep patients in traction for 1-2 weeks before surgery.

In the face of these variations in practice, a critical appraisal of published research is timely, both to identify evidence for best practice where this exists and to prioritize questions for future primary research.

Methodology

A systematic review was conducted of studies assessing the outcomes of interventions in unstable slipped upper femoral epiphysis. The work was conducted as part of a Cochrane Review and followed a prospective review protocol [3]. Reporting follows the PRISMA guidelines [8].

Eligibility was determined hierarchically: if randomised controlled trials (RCTs) or controlled clinical trials (CCTs) were inadequately informative inclusion was extended first to controlled observational designs such as controlled before-after studies (CBAs) and interrupted time series (ITS) and second to other uncontrolled design such as case series.

The following were searched: Cochrane Bone, Joint and Muscle Trauma Review Group Specialised Register, the Cochrane Central Register of Controlled Trials (The Cochrane Library, current issue), MEDLINE (1993 to present), EMBASE (1993 to present), CINAHL (1993 to present), and Science Citation Index (ISI Web of Science 1987 to present). Table 1 summarises the search strategy for MEDLINE, which was modified for the other databases. The following web sites were accessed to identify additional unpublished and ongoing studies: Current Controlled Trials (<http://www.controlled-trials.com/>), Centre Watch (www.centerwatch.com), TrialsCentral (<http://www.trialscentral.org/>), the UK Clinical Research Network: Portfolio Database (<http://public.ukcrn.org.uk/search/>), and SUMSearch (<http://sumsearch.org/>). Bibliographies of retrieved trials and other relevant publications, including reviews and meta-analyses, were cross referenced to identify additional studies.

Two reviewers (KT & KS) independently applied the search strategy to identify citations, and reviewed article titles and abstracts independently. Where eligibility was apparent or uncertain, the full article was obtained for further scrutiny. The two reviewers independently assessed each full study report for inclusion and, where necessary, authors were contacted for more information. Disagreement regarding inclusion was resolved by discussion with senior authors (SA & MA).

Data was extracted independently by two authors (KT&KS) using a piloted form. Discrepancies were resolved through discussion. The names of the authors and the institutes were not masked. Data accuracy was double checked by two reviewers (AC & MC).

The primary outcome was the femoral head osteonecrosis (FHO). This usually becomes apparent within a year and is rarely reported after one year. Thus studies were excluded if did not have this minimum one year follow-up. Secondary outcomes were chondrolysis (CL), femoro-acetabular impingement (FAI), osteoarthritis (OA), complications such as infection, nerve palsy or metalwares problems.

Continuous data was recorded as mean, standard deviation (SD) and group size for each trial arm, with the treatment effect being reported as the mean difference (MD) with corresponding 95% confidence interval (95% CI). Dichotomous data was expressed as proportions or risks, with the treatment effect reported as a risk ratio (RR) with 95% CI. Statistical significance was set at $P < 0.05$.

Two authors (SA, KT) independently assessed the risk of bias in included studies. The Newcastle-Ottawa Scale [9] was used to assess the methodological quality of non-randomised studies (NRS) (See table 2). Findings were reported descriptively but not used to adjust meta-analytic findings.

The review was conducted with the intention of doing a trial-based meta-analysis. Suitable studies were not retrieved but instead an exploratory patient-level based meta-analysis of observational data was possible, permitting a tentative comparison of surgical interventions. Simple FHO estimates were reported for interventions, timing of interventions and severity of slip, using descriptive statistics. Generalized logistic regression models were used to estimate odds ratios (ORs) with 95% confidence intervals (CIs), adjusting for available covariates. Potential clustering of treatment effect of subjects was managed hierarchically, fitting studies as a random effect. As the analysis was exploratory and hypothesis generating, adjustment was not made for

multiple testing, and statistical significance $p < 5\%$ was viewed as indicative of an interesting finding.

Results

Description of studies

One hundred and fifty seven citations were identified as potentially relevant studies; of these 110 were subsequently excluded for reasons including duplication, review and commentary. Full publications were obtained for 47 citations. These were assessed and a further 22 citations were excluded (Figure 1), thus twenty five studies were included in the review. No randomised controlled trial was identified. All included studies were retrospective case series or controlled studies. They scored between 2-5 stars (out of 7) for risk of bias. Table 3 summarises the characteristics of the included studies.

A number of treatments options were reported for the study population including epiphysiodesis [10, 11], pinning in situ (PIS) [1, 7, 12-19], closed reduction and pinning (CRIF) [4, 5, 11, 15, 16, 18, 20-25], open reduction and physeal osteotomy (PO)[1, 7, 15, 26] open reduction and internal fixation (ORIF) [23-25, 27] and surgical dislocation (SD) [13, 15, 28-30].

Within one study four cases were treated with hip spica of which three went to develop FHO (75%) [11]. These 4 patients were excluded from the analysis as hip spica as a sole treatment for SUFE has become an obsolete.

Most studies reported more than one treatment. Pinning was the commonest treatment option: pinning in situ (PIS) was defined when authors reported no use of reduction.

Similarly closed reduction and internal fixation (CRIF) was assigned when authors reported that reduction had been used. Reduction was further recorded as intentional or spontaneous, although not all studies were explicit about the occurrence and/or the type of slip reduction. When uncertainty, patients were excluded from the analysis. Similarly patients were excluded when there was uncertainty about other relevant factors such as severity. Table 3 summarises the included studies and indicated patients that were excluded as well as reasons for exclusions. The 25 studies included provided data on 679 hips that underwent various surgical treatments for unstable slips.

Intervention

An overall 142 hips (21%) developed femoral head osteonecrosis (FHO). Table 4 shows a pooled summary of the FHO rates among various interventions. The rate of FHO varied considerably between interventions, varying from a high for pinning (33%) to a low for open reduction and internal fixation group (5%). This variation between interventions was statistically significant (Fisher exact test (5 dof): $P < 0.001$). Four studies [20, 23, 24, 27] included 83 patients with unstable slips were treated with gentle open reduction and fixation: 77.1% of these were treated within 24 hours of the presentation. Four only developed FHO, although the performance of ORIF was heavily determined by one study [27] which provided 64 patients.

Timing of surgery

In 210 (58.7%) of hips treated within 24 hours, 28 developed FHO (13.3%). Of 95 (26.5%) hips that were treated between 24 hours and 72 hours, 38 developed FHO (40.0%). Of 53 (14.8%) hips that were treated after 72 hours, 5 developed FHO

(9.4%). The variation of FHO rate with timing was statistically significant (Fisher exact test $P < 0.001$).

Severity of the slip

Several studies stated that the severity of slip was closely related to the development of FHO. In 57 (23.0%) with mild severity, 4 developed FHO (7.0%). Of 76 (30.6%) with moderate severity, 26 developed FHO (34.2%). Of 115 (46.4%) with severe slip, 29 developed FHO (25.2%). The variation of FHO rate with severity of slip was statistically significant (Fisher exact test $P < 0.001$).

Regression analysis

In simple analyses, type of intervention, timing of surgery and severity of slip all significantly influenced FHO rate. A cohort of 130 hips provided data on the types of intervention, timing of intervention, severity of the slip as well as FHO. This cohort of hips was analysed further to explore the importance of these factors.

In general linear model with FHO as the dependent variable, and intervention, severity and timing as explanatory factors, only intervention and timing were independently significant predictors of FHO ($P = 0.001$ and < 0.001) respectively.

Subgroups analysis

Open reduction and internal fixation is found to be associated with the lowest FHO rate. Further analysing this group of patients showed that more FHO with increased severity (0% in mild slip, 4 % in moderate slip and 12 % in severe slip) and this did not reach a statistical significant (Fisher exact test $P = 0.38$).

There was only one FHO in 64 hips (2%) who had ORIF within 24 hours in comparison to 3 among 19 hips (16%) in those treated after 24 hours. This was statistically significant (Fisher exact test $P=0.04$).

Surgeons usually consider corrective osteotomy when the slip is moderate or severe. Subgroups analysis of moderate and severe slips showed that FHO rates were 10% with epiphysiodesis, 55% in PIS, 46% in CRIF, 8% in ORIF, 30% in PO and 8% in surgical dislocation. Timing of surgery remains an important prognostic factor in predicting FHO in these subgroups of slips. The FHO rates were 6%, 52% and 7% when the interventions were performed within 24 hours, between 24-72 hours and after 72 hours respectively.

Discussion

Slipped upper femoral epiphysis is an important paediatric orthopaedic problem that is still controversial with regard to aetiology, pathology, management and outcomes. In 1993, Loder [4] introduced the concept of “slip instability” which was fundamental in better understanding of certain aspects of the condition. Two different types of SUFE became apparent; unstable slips where the patient cannot ambulate even with crutches and stable slips where the patient can walk. Loder showed that FHO developed in 47% of unstable slips but none of stable hips. This finding has been replicated by others [1, 5-7].

These two types of SUFE present differently and progress differently; hence treatments are likely to be different. For this reason, we approached them as two separate conditions. The review was conducted with the intention of doing a trial-based meta-analysis. However suitable studies were not retrieved but instead an

exploratory patient-level based meta-analysis of observational data was possible. A similar work is being carried out for stable SUFE and will be reported separately.

Twenty five studies met our inclusion criteria included 679 hips that underwent various surgical treatments for unstable slips. These are epiphysiodesis [10, 11], pinning in situ (PIS) [1, 7, 12-19], closed reduction and pinning (CRIF) [4, 5, 11, 15, 16, 18, 20-25], open reduction and physeal osteotomy (PO) [1, 7, 15, 26] open reduction and internal fixation (ORIF) [23-25, 27] and surgical dislocation (SD) [13, 15, 28-30].

An overall 142 hips (21%) developed femoral head osteonecrosis (FHO). The rate of FHO varied considerably between interventions. It was high (33%) in pinning and low (5%) in open reduction and internal fixation group. This variation between interventions was statistically significant (Fisher exact test (5 dof): $P < 0.001$). Four studies [20, 23, 24, 27] included 84 patients with unstable slips that were treated with open reduction and fixation. Sixty eight percent were treated within 24 hours of the presentation. Four only developed FHO. As most data was provided by a single study [27], excluding the data of the study did not change the fact that FHO rate was significantly lower in the ORIF group (5%, Fisher exact test: $P = 0.008$).

Several studies showed a direct relationship between severity, instability and FHO. Severe slip is likely to be unstable and likely to develop FHO. Individual patient data on types of intervention, timing of surgery, severity of the slip and FHO were available for 130 hips. In general linear model with FHO as the dependent variable, and intervention, severity and timing as explanatory factors, only intervention and timing were independently significant predictors of FHO ($P = 0.001$ and < 0.001) respectively. Interestingly a similar trend was found in the open reduction and internal

fixation group where there are more FHO with increasing severity (0% in mild slip, 4% in moderate slip and 12% in severe slip (not statistically significant)) and delaying surgery more than 24 hours (2% vs. 16%) (statistically significant)).

The timing of surgery to stabilise SUFE is controversial. Given the rarity of the condition (incidence 2/100 000), most studies that looked at the timing of surgery and outcome are suboptimum. Lowndes et al [31] in a meta-analysis of 5 studies (130 unstable SUFEs ; 56 were treated within 24 hours and 74 were treated after 24 hours of symptoms onset. They found that the odds for developing FHO if treatment occurs within 24 hours were half than those of developing FHO if treatment occurs beyond this point. Although the difference was large, it was not statistically significant ($P=0.44$) and may be a chance finding. Peterson et al [11] showed early stabilisation within 24 hours was associated with less FHO (3/42=7%) in comparison with those stabilised after 24 hours (10/49=20%). Kalogrianitis et al. [7] showed that FHO developed in 50% (8/16) of the unstable SUFE in their series. All but one were treated between 24 and 72 hours after symptom onset. They recommended immediate stabilisation of unstable slips presenting within 24 hour. If this is not possible, then delaying the operation until at least a week has elapsed. In contradiction, Loder [32] noted more FHO in patients treated within 48 hours (7/8 versus 7/21).

Our findings supported Kalogrianitis's findings; in 210 hips with unstable slips that underwent surgery within 24 hours, 28 (13.3%) developed FHO in comparison to 38 (40%) and 5 (9.4)% for those who had their operation between 24-72 hours and those who had their operation after 72 hours respectively. This was statistically significant (Fisher exact test $P<0.001$).

Surgical dislocation has been promoted to treat severe SUFE with a low FHO [33-37] however pooled data from 5 studies (SD) [13, 15, 28-30] showed a high rate of FHO

(25%). This rate was comparable to closed reduction and internal fixation. When mild slips were excluded, the rate of FHO in the surgical dislocation group was 8%. This was comparable to the open reduction and internal fixation group.

Loder's work has been a stepping stone in the understanding of the disease process of SUFE however researchers around the world expressed that "non-weight bearing status" is too simplistic to explain the huge differences between the two types. They believe that slip instability is more complex than "weight bearing status" and believe that slip instability has not yet been satisfactorily defined.

Kallio [38, 39] stated that a stable slip should imply an adherent physis during weight-bearing, active leg movements, or gentle joint manipulation. Physeal instability implies that the displaced epiphysis can move in relation to the metaphysis. In a study of 55 SUFEs, he found that physeal instability is better indicated by joint effusion and inability to bear weight. A slip is very unlikely to be unstable in a child who is able to bear weight and has no joint effusion on an ultrasound test.

Ziebarth [40] found that clinical stability of SUFE as defined by Loder does not correlate with intra-operative stability. They retrospectively reviewed 82 patients with SUFE treated by open surgery. They defined intra-operative instability as disrupted physis with visible and demonstrable mobility between metaphysis and epiphysis. They found the stable/unstable classification of Loder had relatively high specificity (76%) but low sensitivity (39%) for predicting intra-operative physeal stability. The low sensitivity highlights the fact that clinical symptoms alone are insufficient to determine physeal stability.

Parsch et al [27] definition of instability is, in part, different from the definition established by Loder. They categorise slips as unstable in the presence of the intra-articular effusion in addition to the acute event of a fall or a stumble followed by acute hip pain and the radiographic presence of a slip. In contrast to this, if there is no effusion detected by ultrasound, the slip is most certainly stable and cannot (and should not) be moved by a reduction maneuver. This uncertainty about the definition of instability should be considered when interpreting our findings.

To the best of our knowledge, this is the largest systematic review of the interventions to treat unstable slip. The review confirms the common belief that instability is an important risk factor for FHO. It also suggests two important facts: open reduction and internal fixation seems to be associated with less FHO in comparison to other interventions. Surgical dislocation using Ganz flip osteotomy has similar rate of FHO in moderate and severe slips only. Intervention should ideally be done within 24 hours of the presentation and if this is not possible delaying the operation to more than 72 hours may be associated with less FHO. A well designed randomised controlled trial is required to answer the above questions with more certainty.

Table 1 Search strategies

- 1 Epiphyses, Slipped/
- 2 (slipped adj3 upper adj3 femoral adj3 epiphysis).tw.
- 3 Femur Head/ab, pa, su [Abnormalities, Pathology, Surgery]
- 4 exp Femur Neck/ab, pa, su [Abnormalities, Pathology, Surgery]
- 5 SUFE.tw.
- 6 (slipped adj3 epiphyses).tw.
- 7 exp Slipped Capital Femoral Epiphyses/
- 8 SCFE.mp. or SCUFE.tw. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
- 9 or/1-8
- 10 randomized controlled trial.pt.
- 11 controlled clinical trial.pt.
- 12 randomized.ab.
- 13 placebo.ab.
- 14 drug therapy.fs.
- 15 randomly.ab.
- 16 trial.ab.
- 17 groups.ab.
- 18 or/10-17
- 19 exp animals/ not humans.sh.
- 20 18 not 19
- 21 9 and 20

Table 2 Risk of Bias Assessment Tool for Cohort Studies

Domain	Items	Maximum Number of stars	Notes
Selection	1) Representativeness of the exposed cohort	1	Maximum possible stars is 4
	2) Selection of the non exposed cohort	1	
	3) Ascertainment of exposure	1	
	4) Demonstration that outcome of interest was not present at start of study	1	
Comparability	Comparability of cohorts on the basis of the design or analysis	2	Maximum possible stars is 2
Outcome	1) Assessment of outcome	1	Maximum possible stars is 3
	2) Was follow-up long enough for outcomes to occur	1	
	3) Adequacy of follow up of cohorts	1	

Figure 1 flow chart of study selection process

Table 3 characteristics of the included studies

Study	Hips	Intervention	Time	R	Type of reduction	FHO	Others	Notes
Alshryda [1]	22	7 PIS	> 48 h	Y	Spontaneous	2		Severity (2:2:3)
		15 PO	> 48 h	Y	Intentional	5	2 loss of fixation Hip dislocation	Severity (0:1:14)
Alves [5]	12	6 CRIF	24.3 h (± 7.9 h)	Y	Intentional	2		Severity (1:3:1)
		6 SD	22.2 h (± 7.9 h).	Y	Intentional	4		Severity (2:2:?)
Aronson [20]	15	6 CRIF	<24 h	Y	Intentional	2		All patients went on traction.
		9 ORIF	<24 h	Y	Intentional	0		All patients went on traction. Authors described a new controlled open reduction and stabilisation using 2 screws
Biring [26]	25	PO	NR	Y	Intentional	3	4 Chondrolysis	25 Acute SUFEs (2 stable)
Chen [21]	30	25 CRIF	21 <24 h 7 24h -72h 1 >72h	Y	Spontaneous	4	1 slip progression 1 Chondrolysis	Severity (13:9:8) 16 percutaneous capsulotomy , 5 open capsulotomy
		5 ORIF	4 < 24 h 1 at 72h		Intentional	0		
Fallath [22]	14	CRIF	28 hours (range 3.5–72 hr).	Y	2 Spontaneous, 9 Intentional 2 PIS	3		10 single screw, 3 Knowles pin, 1 two screws 7 acute and 7 acute-on-chronic All FHO in the CR group; fixed with a single screw and duration of symptoms (72, 19 and 36h)
Gordon [23]	16	12 CRIF	7 <24 h 3 <72 h 2 > a week	Y	Intentional	2		Severity (2:4:6) 1 FHO within 24h and another 168 h
		4 ORIF	<24 h		Intentional	0		Severity (0:4:0) All patients had capsulotomy and 2 screws
Kalogrianitis	16	14 PIS	5 < 24 h	Y	Spontaneous	8		5 < 24 h (1 FHO)

Study	Hips	Intervention	Time	R	Type of reduction	FHO	Others	Notes
[7]		2PO	7 >24<72 h 3 > 8 days					7 >24<72 h (7 FHO) 3 > 8 days (no FHO) No FHO in PO Severity (2:6:8) 10 acute and 6 acute-on-chronic 6 FHO are type III and 2 type II
Kennedy [24]	27	20 pinning: 1 Spontaneous 14 CRIF 3 PIS 2 ORIF	Traction ranged from <24 hours to 6 days	Y	1 Spontaneous 17 Intentional 3 PIS	3		19 two screws and 7 single screw, 1 FHO in a mild and the second is in a severe one. Both had traction of <24h and closed reduction. Third FHO was in ORIF group
		6 PO 1 Epi		Y	7 Intentional	1		1 FHO had a failed PIS which was treated with OR and osteotomy. It was moderate slip.
Lim [18]	24	13 PIS	Traction for 6 days (range 1- 15days)	N	PIS	1		All acute or acute on chronic 2 of the 24 hips were stable but not clear which group Severity (16:7:1)
		11 CRIF		Y	Intentional	1		
Loder [4]	30	26 CRIF	4±3.8 d		4 PIS 26 Intentional	14		17 acute or 13 acute on chronic Severity (2:9:19) FHO group from presentation to operation was (2±1.8 d) and for non FHO groups (6+3.8d) (P=0.0004). FHO (4/5 hips) that were operated within 24h and (10/25) were operated after 24h. FHO (7/8 hips) that were operated within 48h and (7/22) were operated after 48h.
Madan [29]	17	17 SD	Traction 11 days	Y	Intentional	4		9 acute, 8 acute-on-chronic All severe
Palocaren [17]	27	PIS	16<24 h 3<48h	N	2 Spontaneous 25 PIS	6		16<24 h (4 FHO) 3<48h (1 FHO)

Study	Hips	Intervention	Time	R	Type of reduction	FHO	Others	Notes
			3<72 5>120h					3<72 (1 FHO) 5>120h
Parsch [27]	64	64 ORIF	49<24h 15>24h	Y	Intentional	3	4 metalware problems	Severity (20:24:20) FHO1 (moderate slip, within 24h), FHO2 (severe slip, > 24h) FHO3 (severe slip, > 24h)
Peterson [11]	91	91 CR: 41 CRIF 4 spica 46 Epi	42<24 h 12 >24<48 h 7 >48<72 h 30>72 h	Y	Intentional	13		42<24 h (3 FHO) 12 >24<48 h (3 FHO) 7 >48<72 h (4 FHO) 30>72 h (3 FHO) 41 CRIF (4 FHO) 4 spica (3 FHO) 31 Epi + spica (2 FHO) 15 Epi + IF (4 FHO) Severity (5:67:19)
Phillips [25]	14	12 CRIF 2 PO	<24	Y	Intentional	0		Severity (0:3:11)
Ramachandran [19]	22	PIS	NR	N	PIS	12		
Rao [10]	18	Epi	NR 4> 2w traction		Intentional	1	1 Chondrolysis	Severity (6:7:5) FHO in moderate
Rhoad [16]	10	Pinning	NR	R	8 Spontaneous 2 PIS	5	1 Chondrolysis (and FHO in same patients) in PIS group	2 PIS (1 FHO)
Sankar [15]	70	16 PIS	40<24h	N	16 PIS	3		40<24h (10 FHO)
		38 CRIF	12<24>48h	Y	38 Spontaneous	10		12<24>48h (2 FHO)
		8 PO	18>48	Y	Intentional	1		18>48 (2 FHO)
		8 SD		Y	Intentional	0		
Sankar [28]	27	SD	20<24h	R	Intentional	7	4 metalware problems	20<24h (4 FHO)

Study	Hips	Intervention	Time	R	Type of reduction	FHO	Others	Notes
			4<48h 3>72 h 35.9 hours (Range, 6 to 184 h).					4<48h (2FHO) 3>72 h (1FHO)
Seller [14]	33	MPF	<48h	Y	Intentional	2	1 Chondrolysis 8 outgrow fixation 4 subtrochanteric osteotomy	1 FHO in mild and another in severe
Souder [13]	14	7 PIS	NR	N	7 PIS	3		
		7 SD	NR	Y	Intentional	2		
Tokmakova [12]	36	Pinning	NR		21 Intentional 15 Unclear (Excluded)	21		Severity (8:20:8) 1 FHO in mild slip 14 FHO in moderate slips 6 FHO in severe slip All FHO patients had reduction 8 in acute slips and 13 in chronic slip
Ziebarth [30]	12	SD	NR	Y	Intentional	0	0 Chondrolysis	Severity (3:3:4:2)

R= reduction
FHO=femoral head osteonecrosis
h=hour
PIS= pinning in situ, CRIF=closed reduction and internal fixation, PO=physeal osteotomy, SD=surgical dislocation (Ganz), MPF=multiple pins fixation, Epi=epiphysiodesis
NR=not reported
Severity (mild, moderate, severe)

Table 4 Pooled summary of studies of unstable slips treatments

Interventions	Hips	FHO (%)	95% CI
Epiphysiodesis	64	6 (9%)	- 5% to 19.2%
Pinning in situ	115	38 (33%)	26% to 40%
Closed reduction and pinning	269	71 (26%)	22% to 31%
open reduction and internal fixation	84	4 (5%)	-4% to 13%
open reduction and physeal osteotomy	59	10 (17%)	7% to 27%
surgical dislocation	70	13 (18%)	9% to 28%
Total	661*	142 (21%)	

*18 excluded from analysis (see table 3 for reasons)

References

1. Alshryda, S., et al., *Severe slipped upper femoral epiphysis; fish osteotomy versus pinning-in-situ: an eleven year perspective*. Surgeon, 2013. **12**(5): p. 244-8.
2. Alshryda, S. and J. Wright, *Acute Slipped Capital Femoral Epiphysis: The Importance of Physcal Stability*, in *Classic Papers in Orthopaedics, 2014*. 2014, Springer London. p. 547-548.
3. Mason, S.A.K.T.J.A.-S.J.B.A.A.R.M.J., *Interventions for treating slipped upper femoral epiphysis (SUFE)*. Cochrane Database of Systematic Reviews 2013, Issue 2. Art. No.: CD010397. DOI: 10.1002/14651858.CD010397., 2013.
4. Loder, R.T., et al., *Acute slipped capital femoral epiphysis: the importance of physcal stability*. J Bone Joint Surg Am, 1993. **75**(8): p. 1134-40.
5. Alves, C., et al., *Open reduction and internal fixation of unstable slipped capital femoral epiphysis by means of surgical dislocation does not decrease the rate of avascular necrosis: a preliminary study*. J Child Orthop, 2013. **6**(4): p. 277-83.
6. Aronsson, D.D. and R.T. Loder, *Treatment of the unstable (acute) slipped capital femoral epiphysis*. Clin Orthop Relat Res, 1996(322): p. 99-110.
7. Kalogrianitis, S., et al., *Does unstable slipped capital femoral epiphysis require urgent stabilization?* J Pediatr Orthop B, 2007. **16**(1): p. 6-9.
8. Moher, D., et al., *Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement*. BMJ, 2009. **339**: p. b2535.
9. Wells GA, S.B., O'Connell D, Peterson J, Welch V, Losos M, Tugwell P, *The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses*. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm (accessed 11 Novmber 2012). 2008.
10. Rao, S.B., et al., *Open bone peg epiphysiodesis for slipped capital femoral epiphysis*. J Pediatr Orthop, 1996. **16**(1): p. 37-48.
11. Peterson, M.D., et al., *Acute slipped capital femoral epiphysis: the value and safety of urgent manipulative reduction*. J Pediatr Orthop, 1997. **17**(5): p. 648-54.
12. Tokmakova, K.P., R.P. Stanton, and D.E. Mason, *Factors influencing the development of osteonecrosis in patients treated for slipped capital femoral epiphysis*. J Bone Joint Surg Am, 2003. **85-A**(5): p. 798-801.
13. Souder, C.D., J.D. Bomar, and D.R. Wenger, *The role of capital realignment versus in situ stabilization for the treatment of slipped capital femoral epiphysis*. J Pediatr Orthop, 2014. **34**(8): p. 791-8.
14. Seller, K., et al., *Clinical outcome after transfixation of the epiphysis with Kirschner wires in unstable slipped capital femoral epiphysis*. Int Orthop, 2006. **30**(5): p. 342-7.
15. Sankar, W.N., et al., *The unstable slipped capital femoral epiphysis: risk factors for osteonecrosis*. J Pediatr Orthop, 2010. **30**(6): p. 544-8.
16. Rhoad, R.C., et al., *Pretreatment bone scan in SCFE: a predictor of ischemia and avascular necrosis*. J Pediatr Orthop, 1999. **19**(2): p. 164-8.
17. Palocaren, T., et al., *Outcome of in situ pinning in patients with unstable slipped capital femoral epiphysis: assessment of risk factors associated with avascular necrosis*. J Pediatr Orthop, 2009. **30**(1): p. 31-6.
18. Lim, Y.J., et al., *Management outcome and the role of manipulation in slipped capital femoral epiphysis*. J Orthop Surg (Hong Kong), 2007. **15**(3): p. 334-8.
19. Ramachandran, M., et al., *Intravenous bisphosphonate therapy for traumatic osteonecrosis of the femoral head in adolescents*. J Bone Joint Surg Am, 2007. **89**(8): p. 1727-34.

20. Aronson, J. and E.A. Tursky, *The torsional basis for slipped capital femoral epiphysis*. Clin Orthop Relat Res, 1996(322): p. 37-42.
21. Chen, R.C., et al., *Urgent reduction, fixation, and arthrotomy for unstable slipped capital femoral epiphysis*. J Pediatr Orthop, 2009. **29**(7): p. 687-94.
22. Fallath, S. and M. Letts, *Slipped capital femoral epiphysis: an analysis of treatment outcome according to physeal stability*. Can J Surg, 2004. **47**(4): p. 284-9.
23. Gordon, J.E., et al., *Early reduction, arthrotomy, and cannulated screw fixation in unstable slipped capital femoral epiphysis treatment*. J Pediatr Orthop, 2002. **22**(3): p. 352-8.
24. Kennedy, J.G., et al., *Osteonecrosis of the femoral head associated with slipped capital femoral epiphysis*. J Pediatr Orthop, 2001. **21**(2): p. 189-93.
25. Phillips, S.A., W.E. Griffiths, and N.M. Clarke, *The timing of reduction and stabilisation of the acute, unstable, slipped upper femoral epiphysis*. J Bone Joint Surg Br, 2001. **83**(7): p. 1046-9.
26. Biring, G.S., A. Hashemi-Nejad, and A. Catterall, *Outcomes of subcapital cuneiform osteotomy for the treatment of severe slipped capital femoral epiphysis after skeletal maturity*. J Bone Joint Surg Br, 2006. **88**(10): p. 1379-84.
27. Parsch, K., S. Weller, and D. Parsch, *Open reduction and smooth Kirschner wire fixation for unstable slipped capital femoral epiphysis*. J Pediatr Orthop, 2009. **29**(1): p. 1-8.
28. Sankar, W.N., et al., *The modified Dunn procedure for unstable slipped capital femoral epiphysis: a multicenter perspective*. J Bone Joint Surg Am, 2013. **95**(7): p. 585-91.
29. Madan, S.S., et al., *The treatment of severe slipped capital femoral epiphysis via the Ganz surgical dislocation and anatomical reduction: a prospective study*. Bone Joint J, 2013. **95-B**(3): p. 424-9.
30. Ziebarth, K., et al., *Capital realignment for moderate and severe SCFE using a modified Dunn procedure*. Clin Orthop Relat Res, 2009. **467**(3): p. 704-16.
31. Lowndes, S.K., A.; Emery, D.; Sim, J.; Maffulli, N., *Management of unstable slipped upper femoral epiphysis: a meta-analysis*. Br Med Bull, 2009. **90**: p. 133-46.
32. Loder, R.T.R., B. S.; Shapiro, P. S.; Reznick, L. R.; Aronson, D. D., *Acute slipped capital femoral epiphysis: the importance of physeal stability*. J Bone Joint Surg Am, 1993. **75**(8): p. 1134-40.
33. Ganz, R., et al., *Surgical dislocation of the adult hip a technique with full access to the femoral head and acetabulum without the risk of avascular necrosis*. J Bone Joint Surg Br, 2001. **83**(8): p. 1119-24.
34. Gautier, E., et al., *Anatomy of the medial femoral circumflex artery and its surgical implications*. J Bone Joint Surg Br, 2000. **82**(5): p. 679-83.
35. Leunig, M., et al., *Slipped capital femoral epiphysis: early mechanical damage to the acetabular cartilage by a prominent femoral metaphysis*. Acta Orthop Scand, 2000. **71**(4): p. 370-5.
36. Leunig, M., T. Slongo, and R. Ganz, *Subcapital realignment in slipped capital femoral epiphysis: surgical hip dislocation and trimming of the stable trochanter to protect the perfusion of the epiphysis*. Instr Course Lect, 2008. **57**: p. 499-507.
37. Leunig, M., et al., *Subcapital correction osteotomy in slipped capital femoral epiphysis by means of surgical hip dislocation*. Oper Orthop Traumatol, 2007. **19**(4): p. 389-410.
38. Kallio, P.E., et al., *Slipped capital femoral epiphysis. Incidence and clinical assessment of physeal instability*. J Bone Joint Surg Br, 1995. **77**(5): p. 752-5.
39. Kallio, P.E., et al., *Classification in slipped capital femoral epiphysis. Sonographic assessment of stability and remodeling*. Clin Orthop Relat Res, 1993(294): p. 196-203.

40. Ziebarth, K., et al., *Clinical stability of slipped capital femoral epiphysis does not correlate with intraoperative stability*. Clin Orthop Relat Res, 2012. **470**(8): p. 2274-9.