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Inter-arm difference in systolic blood pressure in different ethnic groups and relationship to the "white coat effect": a cross sectional study

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Abstract

Background

Inter-arm differences (IAD) ≥10mmHg in systolic blood pressure (BP) are associated with greater incidence of cardiovascular disease. The effect of ethnicity and the white coat effect (WCE) on significant systolic inter-arm differences (ssIADs) are not well understood.

Methods

Differences in BP by ethnicity for different methods of BP measurement were examined in 770 people (300 White British, 241 South Asian, 229 African-Caribbean). Repeated clinic measurements were obtained simultaneously in the right and left arm using two BP-Tru monitors and comparisons made between the first reading, mean of second and third and mean of second to sixth readings for patients with, and without known hypertension. All patients had ambulatory monitoring (ABPM). WCE was defined as systolic Clinic BP ≥10mmHg higher than daytime ABPM.

Results

No significant differences were seen in the prevalence of ssIAD between ethnicities whichever combinations of BP measurement were used and regardless of hypertensive status. ssIADs fell between the 1st measurement (161, 22%), $2^{nd}/3^{rd}$ (113, 16%) and 2^{nd}-6^{th} (78, 11%) (1st vs $2^{nd}/3^{rd}$ and 2^{nd}-6^{th}, p<0.001). Hypertensives with a WCE were more likely to have ssIADs on 1st, (OR 1.73 (95% CI 1.04-2.86), $2^{nd}/3^{rd}$, (OR 3.05 (1.68-5.53) and 2^{nd}-6^{th} measurements, (OR 2.58 (1.22-5.44). Non-hypertensive participants with a WCE were more likely to have a ssIAD on their first measurement (OR 3.82 (1.77 -8.25) only.

Conclusion

ssIAD prevalence does not vary with ethnicity regardless of hypertensive status but is affected by the number of readings, suggesting the influence of WCE. Multiple readings should be used to confirm ssIADs.

Introduction

Differences in systolic blood pressure (BP) between right and left arms ≥10mmHg independently predict increased risk of cardiovascular events,[1, 2] subclavian stenosis[3] and cardiovascular or all-cause mortality.[2] Measuring BP in both arms is a simple intervention that identifies the higher reading arm, which should be used for future hypertension management, and may identify patients needing investigation, or intensification of cardiovascular risk management.[4] Prevalence of patients with a significant systolic inter-arm difference (ssIAD) varies according to population. A US systematic review, found the prevalence of ssIADs was 7.5% in primary care, 9% for hospital outpatients, and 12.1% for hospital inpatients.[5] A recent study using Framingham data found the prevalence of ssIADs in a community sample, free from cardiovascular disease at baseline, was 9.4%. A UK systematic review considered prevalence of ssIADs in relation to clinical predictors and found 11.2% in hypertensives, 7.4% in people with diabetes and 3.6% in the general population.[6] Characteristics associated with ssIADs are age,[1, 7-9] diabetes,[1] higher systolic BP[1, 6, 8] and increased BMI.[1]

Some ethnic groups are at higher cardiovascular risk.[10-13] South Asians and African-Caribbeans have a higher incidence of diabetes than white Europeans[14] and African-Caribbeans have a greater prevalence of hypertension and stroke.[15, 16] Ethnicity may also affect the prevalence of ssIADs. Countries in the Far East appear to have a lower prevalence of patients with ssIADs than Western populations.[6, 8, 17, 18] To our knowledge there has only been one study so far to look at the effect of ethnicity on the prevalence of ssIADs.[7] It found a higher prevalence of ssIADs ≥15mmHg in African-American and White Americans compared to Hispanic or Chinese Americans.

Method of measurement affects the likelihood of finding a ssIAD; single or sequential BP measurement techniques may overestimate the prevalence.[6, 19 20]

This study, using simultaneous measurements, aimed to evaluate whether prevalence of ssIADs ≥10mmHg varied according to South Asian, African-Caribbean or White British ethnicity, hypertensive status or other participant characteristic and additionally to investigate any association of prevalence with the number of readings, or the presence of a white coat effect (WCE) or white coat hypertension (WCH).

Methods

Blood pressure monitoring in different ethnic groups (BP-ETH), was a primary care based observational study conducted between June 2010 and December 2012. The detailed methods have been published previously[21] and are outlined below.

Population

Participants were aged 40–74 years, purposefully recruited from three ethnic groups: white British, South Asian and African-Caribbean (WB, SA, and AC). Ethnicity was self-defined using standard UK criteria.[22] Respondents attended three research clinics at their own practice. Twenty-eight practices were recruited from the Primary-Care-Research-Network, Central England, United Kingdom, chosen to represent the required range of ethnicities. Around 40 participants were recruited from each practice, both with (HT) and without hypertension (NHT), as defined by a clinical code in the patient's record. People unable to consent, belonging to a different ethnic group or whose general practitioner felt they were unable to take part were excluded.

Procedure

Following at least five minutes rest, sitting BP measurements were taken by a research nurse using two BPTru monitors (BpTru Medical Devices BPM-200), set to take six readings at one minute intervals and used simultaneously on both arms.[23] The research nurse remained in the room with the patient whilst the readings were being taken. One BPTru monitor was used consistently for the right arm and the second used for the left. This is considered to be the most accurate way of establishing an IAD.[6, 19 20]

Participants were fitted with an ambulatory monitor (Spacelabs 90217-1Q)[24] on either the first or second clinic visit.

Ambulatory (ABPM) readings were recorded at half hourly intervals during the day and hourly overnight for a total of 24 hours. Participants' non-dominant arm was used unless systolic BP was ≥20mmHg between the right and left arm on the first reading, which included 32 patients. In the case of these patients the arm with the higher reading was used.

Analysis

Significant systolic inter-arm difference (ssIAD) for the first measurement was defined as an absolute difference ≥10mmHg between the right and left arm.[3] SSIADs were further defined using absolute ssIADs of the 1st reading alone, mean of the 2nd/3rd and mean of the 2nd to 6th readings.

There is no accepted definition of the WCE or WCH therefore different analyses were undertaken based on the literature[25, 26] using the following systolic BP definitions:

1. White coat effect (1st BP measurement):
    a. (1st clinic measurement–mean daytime ABPM) ≥10mmHg
2. White coat effect (mean of 2nd/3rd BP measurements)
    b. (Mean of 2nd/3rd clinic measurement–mean daytime ABPM) ≥10mmHg
3. White coat effect (2nd-6th BP measurement)
    c. (Mean of 2nd-6th clinic measurement– mean daytime ABPM) ≥10mmHg

Trends between the ethnic groups for prevalence of ssIADs were tested using the Extended Mantel-Haenszel chi squared test for linear trend.[27]

Univariable analyses were conducted between ssIADs and baseline characteristics stratified by diagnosed hypertension (HT) and not known to be hypertensive (NHT) patients. Chi squared test was used when comparing binary/categorical variables. The two sample t-test was used when comparing the mean difference between two groups. Non parametric tests were used for skewed variables such as BMI.[27]

A multivariate logistic regression model was also used where we adjusted for the following variables: Ethnicity, Diabetes, Age, Gender, CHD, log(BMI), medication, smoking and deprivation score.

Differences in the proportion of patients with an absolute ssIAD, dependent on the number of measurements, were investigated using a Cochran Q test.[27] All BP comparisons were for measurements in the same arm.

The same analysis was conducted checking for any differences in the prevalence of the WCE across different combinations of measurements. Post hoc analyses were conducted using the McNemar test.[27] Association between ssIADs and the corresponding WCE was examined by the use of logistic regression models adjusted for baseline characteristics.

Sensitivity analyses were carried out to check the effect on WCE when using differences between clinic systolic BP and systolic ABPM of 5 and 15mmHg.

Ethics and Research Governance Approval

Ethical Approval for the BP-ETH study was gained from the Black Country Research Ethics Committee, West Midlands, United Kingdom (Ref 09/H1202//114).

Results

Baseline Demographic Data

770 people participated in BP-ETH of whom 300 were WB, 229 were AC and 241 were SA. (Table 1a – appendix). There were no significant differences in baseline characteristics between WB, AC and SA groups, or between HT and NHT participants, although more HT participants (481) were recruited than NHT (289).

Prevalence of Inter-arm Differences by Ethnicity and Hypertensive Status

BP measurements in the right and left arms were available for 750 of the 770 participants who were grouped into HT and NHT and then sub-divided into participants with a ssIAD or not. There was no systematic difference in the systolic BP of the right arm vs that of the left (Table 2a – appendix) therefore the following ssIADs are expressed as an absolute difference.

The overall prevalence of ssIADs for HT participants was 61/469 (13.0%) and 26/281 (9.3%) for NHT participants (Table 1). Overall prevalence of ssIADs in the HT was group was higher but this difference was not found to be significant, (Table 1). Association between ssIAD and ethnic group was not significant for the HT or NHT group (Table 1). There were no significant differences in the prevalence of ssIAD by ethnicity in the HT and NHT groups whichever combination of measurements was used (1st, mean of 2nd/3rd or mean of 2nd–6th). Therefore only the sIAD using the mean of the 2nd–6th measurement is presented here as prevalence dropped the more measurements were used and this mean represented the nadir. A multivariate logistic regression model was used where we adjusted for Diabetes, Age, Gender, CHD, log(BMI), deprivation score and mean blood pressure. Ethnicity remained non -significant in both HT and NHT patients (Table 3).

Characteristics of Participants with and without an Inter-arm Difference

Table 2 shows characteristics of participants with and without a ssIAD by hypertensive status. As the prevalence of ssIADs was not significantly associated with ethnicity, the three ethnic groups are combined for analysis of the remaining characteristics. Significantly higher mean BP was associated with a ssIAD for both HT (140.1mmHg [ssIAD] vs 131.6mmHg [no ssIAD], p<0.001) and NHT groups (132.0 [ssIAD] vs 124.7 [no ssIAD], p=0.031) (Table 2). The multivariate analysis also showed a significantly higher BP was associated with a ssIAD in both the HT and NHT groups (Table 3). Significantly higher daytime ABPM was associated with a ssIAD in the HT but not the NHT group.

As BMI was a skewed variable this is reported as a median value with an interquartile range using the non-parametric test Wilcoxon rank sum for the p value (Table 2). Participants with a ssIAD had a significantly higher BMI in the HT group, (31.0 vs 28.7, p = 0.025), however this significance disappeared in the multivariate analysis (Table 3). Similarly in the NHT group, where ssIAD was actually associated with a lower BMI (27.3 vs 29.4, p = 0.025) (Table 2), the BMI no longer remained significant in the multivariate analysis (Table 3). Multivariate analysis showed that NHT participants with a ssIAD were significantly more likely to smoke, which may have affected the univariate analysis of BMI.

Difference in age between HT participants with a ssIAD and HT participants without a ssIAD was of borderline significance (58.4 vs 60.8, p = 0.053). This effect was not seen in the NHT group and the effect was no longer significant when other variables were accounted for in the multivariate analysis (Table 3). There were no other significant differences between participants with and without ssIAD (Table 2).

Changes in Inter-arm Blood Pressure Differences between the 1st Reading, 2nd and 3rd Reading and 2 – 6th Reading

449/469 HT participants had all six BP readings available on both arms. The number of participants with a ssIAD fell as more pairs of readings were included in the calculation of mean BP (table 3a - Appendix): 101 (22%) for the 1st measurement, 69 (15%) for the mean of the 2nd/3rd measurements, and 54 (12%) for the mean of the 2nd–6th measurements. Post-hoc analysis revealed a significant difference (p<0.001) between the number of participants with a ssIAD on the 1st pair of readings versus the number with a ssIAD on the mean of the 2nd/3rd and the 2nd–6th pairs of readings, with a smaller non-significant difference between the latter two measurement methods (Table 3a - Appendix). NHT (271/281) patients showed a similar pattern (Table 3a – Appendix).

This effect was mirrored by the decline in the prevalence of a WCE; numbers of HT participants with a WCE on the 1st measurement was 128 (35%), 89 (25%) for the mean of the 2nd/3rd and 66 (18%) for 2nd–6th BP readings (1st vs 2nd/3rd P <0.001; 1st vs 2nd–6th reading P<0.001) (Table 4a - Appendix). This decline was also seen in the NHT participants (Table 4a – Appendix).

Association of the White Coat Effect and Inter-arm Blood Pressure Difference

The relationship between the WCE and ssIAD was investigated using a logistic regression model and adjusted for baseline characteristics. Resulting odds ratios show that in the HT group there was a significant association between the WCE and ssIAD for the 1st measurement, 2nd/3rd and 2nd–6th measurement (Table 4).

In the NHT group the OR was significant for the association between WCH and ssIAD for the first reading (4.06, 95% CI, 1.83, 9.00) (Table 4) but no significant differences were found in the association of WCH and ssIAD between the mean of the 2nd/3rd and the 2nd–6th readings (Table 4).

Sensitivity analyses using definitions of a 5mmHg and 15mmHg difference between clinic systolic BP and the systolic mean daytime ABPM showed a similar pattern of results (Tables 5a and 6a – Appendix).

Discussion

Summary

In this community-based study, ethnicity had no significant impact on the prevalence of ssIAD. The HT group had a greater prevalence of ssIADs overall but the difference between the HT and the NHT groups was not significant. However the prevalence of ssIADs significantly increased with increasing BP regardless of hypertensive status. NHT Participants with a ssIAD were more likely to be a smoker but there did not appear to be the same association for BMI and age. There was no systematic difference in systolic BP between the right and the left arm, which was in keeping with the results of a recent meta-analysis.[28]

Calculating ssIAD with increasing numbers of repeated measurements significantly reduced the prevalence of a ssIAD and this appeared to be associated with the WCE, especially for HT participants. For NHT participants the association between a ssIAD and WCH was present on the first measurement but not thereafter.

Strengths and Limitations

The main strength of this study was that it was large, community-based and recruited approximately equal numbers of patients from each of three ethnic groups. It included patients with a diagnosis of hypertension, those with no known diagnosis and did not exclude patients with co-morbidities. Measurements were taken in a Primary Care setting, which is where most office BP is taken and provides the most generalisable comparison of the WCE.[29] The study used six BP measurements, allowing for analysis of ssIADs over several consecutive readings, and measurements were taken simultaneously with a validated monitor which is widely acknowledged as the most accurate way to measure IAD.[19, 30 31] The number of patients with ssIADs was relatively small which affected power to assess associations and differences between groups. Only systolic blood pressure was assessed therefore any associated or independent effects on interarm difference between diastolic BP are unknown.

The current study did not include Far Eastern ethnicities such as Chinese, who may have significantly lower incidence of ssIADs than Western groups.[6] Despite the range of ethnicities, there was only one area of the UK studied, which does not take into account potential effects different environments may have.

The population here came from more deprived areas in comparison with the rest of the UK. Whilst we do not know what association deprivation would have with the prevalence of ssIADs, hypertension is more prevalent in deprived settings so a concomitant trend to increased prevalence of ssIADs with deprivation might be predicted.[32]

In this study the definition of a clinically significant systolic IAD was defined as ≥10mmHg. Current European hypertension guidelines suggest a ssIAD >10mmHg between arms carries an increase in cardiovascular risk[33] and although the UK guidelines suggest a difference in systolic BP ≥20mmHg is indicative of vascular disease, they only specify a ssIAD <10mmHg as normal.[4] Although a ssIAD ≥10mmHg may show less specificity for peripheral artery disease than that of 15mmHg, it is more sensitive[34] and, in addition, it is in keeping with the definition used in many current studies.[1, 3, 5, 35]

Using this definition meant that our work could be compared to the current literature more easily and was clinically relevant.

As there is no accepted definition of the WCE or WCH, a pragmatic definition for the study was developed using an arbitrary level of the clinic-ambulatory difference (≥10mmHg).[4] Differences between clinic and ambulatory BP are potentially subject to bias, principally from variation in the clinic BP due to operator error, hypertensive status and activities and environment of the patient.[36] However, given the controlled nature of the research measurements, such errors would be expected to be minimised in this study.

Comparison with Existing Literature

The prevalence of ssIADs in the HT and NHT groups was 13.0% and 9.3% respectively. In the NHT group this appeared to be high for a general population.[6]

A recent systematic review, analysing prevalence of ssIADs from 16 studies, found a prevalence of 3.6%. However the population group included two studies of Far Eastern origin which had a much lower prevalence than studies of Western origin and therefore reduced the pooled prevalence.[6] There was a higher prevalence in a hypertensive population (11.2%) and when studies causing statistical heterogeneity were removed, the prevalence of ssIADs in a Western, hypertensive population was 13.3%, almost identical to the prevalence found here.[6] Similar to the current study, the multi-ethnic study of atherosclerosis (MESA) also reported no significant differences in ssIADs between African-American and white non-Hispanic groups.[7] However there was a significantly lower prevalence of ssIADs in Hispanic and Chinese Americans suggesting that Hispanic and Far Eastern ethnicities may be less predisposed to ssIADs than Western populations.

A higher BMI has been previously reported [1, 7, 8] as being associated with a ssIAD and is likely to relate to patients with ssIADs having a higher cardiovascular risk.[1] However another study[9] found that age was the only significant predictor for ssIADs. Neither age nor BMI was found to have a significant association here with a ssIAD in the HT or NHT group. However BMI was higher in the HT group so this may have been compounded by the fact that the number of patients with a ssIAD was small. The NHT group had a significant association between smoking and ssIAD, which is in keeping with the link between ssIADs and a greater cardiovascular risk. However the link between smoking and ssIADs is varied with some studies showing some association[7] but others showing no significance.[1] The number of participants in this study who smoked was very small and is likely to affect the significance of any associations here.

Results here are in agreement with that found in the Framingham Heart Study, a study in a Japanese population and a recent large meta-analysis of 16 IAD studies showing that those patients with a ≥10mmHg difference between arms had significantly higher systolic BP compared to those without.[1, 6, 8] This is likely to be an effect of the absolute IAD increasing as absolute BP increases and may in part explain why patients with a ssIAD appear to be at higher risk of a cardiovascular event.[1]

Systolic BP decreased over the six clinic measurements, and the prevalence of ssIAD followed the same pattern. This pattern has been seen in other studies[35, 37, 38] and a study by Martin et al suggested that the effect may be associated with the WCE,[30] although they used sequential measurements to estimate IAD which can overestimate its prevalence.[19]

A significant association was found here between WCH and ssIAD on the first reading for participants in the NHT group and between the WCE and ssIADs for all BP measurements used in the HT patients.

For HT patients, the strongest association between the WCE and ssIAD was using the mean of 2nd/3rd readings which may be explained by HT participants having a stronger, more persistent WCE than those with no diagnosis. There is closer agreement between clinic and ambulatory BP when a patient's BP is closer to normal levels.[33, 36, 38-40] This suggests that the increase in prevalence of ssIADs in response to higher BP levels may be linked to the WCE.

Implications for Practice

There appears to be little difference in the prevalence of ssIADs between SA and AC cohorts compared to a WB population. However those with higher mean clinic BP were more likely to have a ssIAD regardless of hypertensive status. European guidelines recommend simultaneous measurement to exclude clinical ssIADs.[33] A much greater effect was seen in terms of the number of measurements used, hence, health professionals should not rely on single BP measurements to identify ssIADs.

This study and others[19] have shown that the prevalence of a ssIAD continues to fall when greater numbers of pairs of readings are taken into account. Therefore, if a ssIAD is detected on the first measurement, we propose that BP should be taken simultaneously at least three times in both arms with the mean IAD calculated for the 2nd and 3rd readings in order to more accurately estimate a "true" IAD.

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Conflicts

RM Has received BP monitoring equipment from Omron and Lloyds Pharmacies. The other authors declare no conflict of interest.

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Legend for Tables

Table 1 – Incidence of ssIADs by hypertensive status and ethnic group

Table 2 – Showing demographic and health differences between those patients with an interarm BP difference and those without for the HT and NHT groups, * Index of multiple deprivation 2007, #BMI reported as a median value with (Inter Quartile Range)

Table 3 – ORs for ssIADs when the white coat effect is present in HT and NHT groups. Logistic regression model was used and adjusted for practice, sex and high-risk group.

Table 4 – ORs for ssIADs when the white coat effect is present in HT and NHT groups. Logistic regression model was used and adjusted for gender, ethnicity, logarithm of BMI, age, CHD, daytime ABPM, Diabetes, Smoking, Medication and IMD.