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Defining the relationship between arm and leg blood pressure readings: a systematic review and meta-analysis

Arm-leg blood pressure difference

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Conflicts of interest
The authors report no relevant conflicts of interest.

Abstract

Objectives: To define the relationship between arm and leg blood pressure to inform the interpretation of leg blood pressure readings in routine clinical practice where arm readings are not available.
Methods: Systematic review of all existing studies comparing arm and leg blood pressure measurements. A search strategy was designed in MEDLINE and adapted to be run across six further databases. Articles were deemed eligible for inclusion if they measured and reported arm and leg blood pressure taken in the supine position and/or the difference between the two. Mean values for arm-leg blood pressure difference and measures of precision (95% confidence intervals [CI] or standard deviation) were extracted and entered into a random-effects meta-analysis.
Results: A total of 887 articles were screened and 44 were included in the descriptive analyses, including 9,771 patients. In the general population, ankle systolic blood pressure was 17.0 mmHg (95%CI 15.4 to 21.3 mmHg) higher than arm blood pressure in the supine position. For diastolic blood pressure, there was no difference between arm and ankle blood pressure (-0.3 mmHg, 95%CI -1.5 to 1.0 mmHg). In patients with vascular disease, systolic blood pressure was -33.3 mmHg (95%CI -59.1 to -7.6 mmHg) lower in the ankle compared to the arm.
Conclusions: This is the first review to provide empirical data defining the difference between blood pressure in the arm and leg in the general population. Findings suggest a diagnostic threshold of 155/90 mmHg could be used for diagnosing hypertension when only ankle measurements are available in routine practice.

Word count: 250 (250 limit)

Condensed abstract (100 words)
This study systematically reviewed all existing studies comparing arm and leg blood pressure measurements. Mean values for arm-leg blood pressure difference were entered into a random-effects meta-analysis. Based on a total of 44 included studies and 9,771 patients, ankle systolic blood pressure was 17.0 mmHg (95%CI 15.4 to 21.3 mmHg) higher than arm blood pressure in the general population. For diastolic blood pressure, there was no difference. These findings suggest a diagnostic threshold of 155/90 mmHg could be used for diagnosing hypertension when only ankle measurements are available in routine practice.

Key words: Ankle blood pressure, calf blood pressure, arm-leg blood pressure difference, hypertension, diagnostic threshold, meta-regression

Introduction

Blood pressure is normally measured on the upper arm,[1] but occasionally this is not possible for a variety of reasons that prevent placement of the cuff, for example, the presence of fractures, wounds, vascular access devices, morbid obesity, surgical procedures, limb deformities and amputations. Additionally, blood pressure measurement may be inaccurate in the presence of bilateral subclavian artery stenosis, such as that which can occur with Takayasu's arteritis[2] or atherosclerosis.[3] In these circumstances, measurement of blood pressure on the leg may be necessary but currently, there are no clinical guidelines to guide measurement technique or interpretation.

A number of previous studies have compared blood pressure readings made in the leg to those in the upper arm.[4-6] However, these studies have examined different populations using varying measurement techniques, so it is unclear what standard blood pressure difference between upper and lower limbs should be expected. It is also unclear how diagnostic and treatment thresholds should be adjusted when leg blood pressure measurements are relied upon to guide treatment. One previous study has suggested that in the absence of vascular disease, an elevated ankle systolic blood pressure of >175 mmHg should be considered abnormal, based on the risk of cardiovascular disease (CVD).[7] However, it is not clear whether this is equivalent to the 140 mmHg threshold used for brachial blood pressure.[1]

This study aimed to systematically review the literature and summarise existing evidence describing 1) appropriate methods of leg blood pressure measurement and 2) the relationship between arm and leg blood pressure, to provide recommendations on how leg measurements should be interpreted in routine clinical practice.

Methods

Design

Systematic review aiming to capture all existing studies comparing arm and leg blood pressure measurements in the same patients. Mean values for arm-leg blood pressure difference and measures of precision (95% confidence intervals [CI], standard deviation [SD] or 95% limits of agreement) were extracted and entered into a random-effects meta-analysis.

Search strategy

A scoping search was carried out to identify background literature and provide an estimate of the volume of literature on the topic. The search strategy was originally designed in the MEDLINE database (for search terms, see appendix) and was adapted to be run across the following databases: CINAHL (EBSCO), The Cochrane (Wiley) CENTRAL Register of Controlled Trials, EMBASE (Ovid), MEDLINE In Process (Ovid), Science Citation Index – Expanded & Conference Proceedings Citation Index – Science and the ZETOC (Mimas) database.

No date limits were applied to the searches, although animal studies, letters, comments and review articles were excluded. Furthermore, it was not possible to assess non-English language articles (due to resource limitations). In addition to searches of electronic databases, reference lists of included studies were checked to identify any further relevant papers. Searches were conducted in August 2016.

Selection criteria

All studies were screened by at least two reviewers (JS, AA, MF or BF) at each stage of screening. Disagreements were resolved with a third reviewer. Articles were selected for data extraction based on the following inclusion criteria:

- Measure arm blood pressure
- Measure leg blood pressure
- Estimate the difference between arm and leg blood pressure and provide a measure of precision for this estimate (95% CIs, SD, 95% limits of agreement)
- Readings taken either simultaneously or sequentially within the same clinic visit
- Cross-sectional, cohort or randomised controlled trial study design
- Describe method of arm and leg blood pressure measurement in sufficient detail that it could be repeated
- Include primary data

Studies were excluded from data extraction if they:

- Examined assessments made in a non-clinical or pharmacy setting
- Studied patients aged <18 years or who were pregnant

Data collection

Data were extracted by four reviewers (JS, AA, BF and LP) who all initially examined 10% of included articles and resolved discrepancies prior to commencing data extraction in the rest of the studies. Data were extracted using a pre-defined data extraction sheet (see online appendix). Data relating to the definition and method of measurement of arm and leg blood pressure, along with mean values for each, mean difference and an estimate of precision were extracted. In addition, any information about the setting and sample population were recorded, including patient demographics, prescribed medication and history of cardiovascular disease events or risk factors.

Assessment of methodological quality

As part of the data extraction, the methodological quality and risk of bias of individual studies was assessed. This quality assessment covered domains of selection bias, detection bias, accuracy of measurement, analysis and confounding using a combination of questions from the QUADAS-2[8] and CASP[9] checklists for assessment of cohort studies. For sensitivity analyses, studies fulfilling the majority of quality domains ($\geq$4 domains) were deemed high quality. Those with unclear reporting or failing to fulfil the majority of quality domains were deemed low or moderate quality.

Outcome measures

The primary outcome of this review was to compare the mean difference between blood pressure measured in the arm and leg in the supine position. Leg blood pressure was defined by readings taken in the ankle, calf or thigh and readings from each location were considered separately. Secondary outcomes were to define this difference in population subgroups (patients with high cardiovascular disease risk or history of vascular disease) and by method of measurement (sequential/simultaneous), arm blood pressure level and age. Further, this review aimed to describe the different approaches to measuring leg blood pressure and arm/leg blood pressure difference in order to inform future clinical guidance on this procedure.

Data synthesis

Descriptive statistics were used to summarise included study characteristics. Blood pressure measurement techniques were described qualitatively. The primary outcome was examined in a random-effects meta-analysis of mean arm-leg blood pressure difference, considering comparisons with ankle, calf and thigh readings separately. Where mean difference was not published, it was estimated from the mean and standard deviation of values in the arm and leg. Analyses focused on measurements taken in the supine position. Where the position of measurement was unclear, it was assumed that readings were taken in the supine position and comparisons were included in the analysis. Heterogeneity was summarised using I-squared statistics.

Data are presented according to measurement technique where feasible. Sub-group analyses were conducted focusing on populations at high risk of cardiovascular disease, those with a history of vascular disease and by measurement device to explore possible sources of heterogeneity. Meta-regression was undertaken to examine the possible association between arm-ankle blood pressure difference and mean arm blood pressure and age.

Sensitivity analyses were conducted using a fixed effects model to examine the assumption of random effect in the primary analysis. Further sensitivity analyses explored:

1) the impact of study quality on the primary outcome (with moderate and low quality studies excluded)
2) excluding studies which did not measure both systolic and diastolic blood pressure in the same patients or those which did not use either auscultation or a validated upper arm device.
3) the difference in arm-ankle blood pressure as a percentage of the arm blood pressure (arm-ankle blood pressure difference divided by arm blood pressure)

Screening was conducted using Covidence (Vertitas Health Innovation Ltd, Melbourne, Australia) and all analyses were undertaken in STATA version 13.1 (MP parallel edition, StataCorp, Texas, USA). Data are presented as proportions of the total study population, means with standard deviation or 95% confidence intervals unless otherwise stated.

Results

Description of included studies

A total of 887 articles were screened after exclusion of duplicates (figure 1). Of the 340 full text articles assessed for eligibility, 44 were included in the final descriptive analyses. Included studies examined a total of 9,771 patients, just under half were female (46%) and the mean age ranged from 30 to 74 years (table 1). Populations were heterogeneous with some including patients with a history of hypertension, diabetes, chronic kidney disease and cardiovascular disease (table 1), conducted in a variety of settings (eTable 1, online appendix).

The methodological quality of included studies was mixed (table 2). Most studies avoided inappropriate exclusions and measured the outcome variables appropriately. However, the method of participant selection was rarely described and it was difficult to judge whether the intended population had been captured in the majority of studies.

There was no consistent method or standardised approach for measuring the arm-leg blood pressure difference. Studies compared blood pressure measured over the brachial artery to readings taken on the ankle, calf, foot or thigh, using a variety of measurement techniques and devices (eTable 3). These included standard auscultatory and oscillometric sphygmomanometers, Doppler probes and mercury strain-gauge plethysmography. Most studies (n=35/44) clearly stated that readings were taken with patients in the supine position and simultaneous readings were more common than sequential readings (18 studies vs. 16 studies [10 studies did not state the order of readings]; eTables 2 and 3, online appendix).

Primary outcome

Ankle-arm difference in a supine position

In the general population, ankle systolic blood pressure was 17.0 mmHg (95% CI 15.4 to 21.3 mmHg) higher than arm blood pressure, and this difference was consistent whether blood pressure was measured simultaneously (18.3 mmHg, 95% CI 17.1 to 19.5 mmHg) or sequentially (16.1 mmHg, 95% CI 13.4 to 19.0 mmHg; figure 2). Overall heterogeneity was significant (I^2=95.1%; p<0.001) and was not reduced in subgroups examining simultaneous or sequential measurements. For diastolic blood pressure, there was no difference between arm and ankle blood pressure (-0.3 mmHg, 95% CI -1.5 to 1.0 mmHg; figure 3). Once again this was unaffected by whether readings were taken simultaneously (-1.2 mmHg, 95% CI -2.8 to 0.3 mmHg) or sequentially (1.9 mmHg, 95% CI -3.9 to 7.7 mmHg), and there was significant heterogeneity across studies (I^2=93.6%; p<0.001).

Calf/thigh-arm differences in supine position

Average calf systolic blood pressure was higher than arm blood pressure, but the mean difference was not as large as arm-ankle differences (10.1 mmHg, 95% CI 4.5 to 15.6 mmHg; I^2=94.8; p<0.001; eFigure 1, online appendix). There was no difference between arm and calf diastolic blood pressure (0.2 mmHg, 95% CI -1.5 to 1.8 mmHg; I^2=99.1; p<0.001). There were not enough studies in similar populations to provide pooled estimates of the arm-thigh blood pressure difference.

Secondary outcomes

In patients with a history of cardiovascular disease, ankle systolic blood pressure was lower than arm blood pressure (-33.3 mmHg, 95% CI -59.1 to -7.6 mmHg; figure 4), although there was significant variation depending on the disease type (I^2=99.1%; p<0.001). Focusing on patients with high risk of cardiovascular disease did not affect the point estimates for arm-ankle systolic or diastolic blood pressure difference, compared to the general population, or reduce the overall heterogeneity observed (eFigure 2, online appendix). Sub-group analyses by measurement device used for ankle measurements did not reduce the observed heterogeneity within groups (eFigure 3, online appendix). No association was observed between arm-ankle blood pressure difference and mean arm blood pressure or age (figure 5).

Sensitivity analyses

Sensitivity analyses were undertaken examining arm-ankle blood pressure difference in the general population assuming fixed effects and found similar findings to the primary analyses (eFigures 4 and 5, online appendix). Exclusion of studies deemed to be of moderate or low quality had no impact on the point estimates for arm-ankle blood pressure difference, but did reduce the observed heterogeneity between studies making simultaneous comparisons, albeit remaining significant (I^2=77.4%; p=0.001; eFigures 6 and 7). Exclusion of studies which did not measure both systolic and diastolic pressures in the same patients had no impact on the main study findings (eFigure 8). Exclusion of studies which did not use auscultation or a validated upper arm device did not affect the point estimates for arm-ankle blood pressure difference, but it did reduce the observed heterogeneity (I^2=38.4%; p=0.150 [systolic comparison] eFigure 9; I^2=42.7%; p=0.175 [diastolic comparison] eFigure 10). Examining the difference in arm-ankle blood pressure as a percentage of the arm blood pressure gave similar findings to the primary analysis, with systolic blood pressure in the ankle being 12.9% (95% CI 11.5% to 14.3%) higher than in the arm (eFigure 11).

Discussion

Summary of findings

This is the first systematic review to examine studies comparing blood pressure measured in the arm to measurements taken in the leg and provides average differences to guide interpretation in routine clinical practice. In a general population measured in a supine position, readings taken in the ankle were found to be between 16-18 mmHg higher than those taken in the arm, and this was unaffected by whether measurements were taken simultaneously or sequentially. These data suggest clinicians should consider adding 15 mmHg to the systolic treatment threshold for hypertension (giving a threshold of 155/90mmhg) when using ankle measurements rather than readings taken in the arm.

Strengths and limitations

This large systematic review followed a pre-specified protocol (see online appendix) and utilised a comprehensive search of seven relevant databases to capture all potential studies examining the difference between arm and leg blood pressure. Pre-defined inclusion/exclusion criteria were applied to each article identified in the search and a total of 44 relevant articles were included in the final review. Unfortunately, it was not possible to locate further potentially eligible articles, despite visiting the British Library to locate them. Other articles had to be excluded because they were written in non-English language and there were insufficient resources to translate them for screening. Despite this, the consistent direction and magnitude of differences observed in a large number of included articles suggest that even if some of these papers had provided relevant data, the overall findings of the study would have likely remained the same.

It was possible to pool data for meta-analysis in the present study, however there was significant heterogeneity across studies so caution should be exercised when interpreting the results. Subgroup and sensitivity analyses by cardiovascular disease history, cardiovascular disease risk, measurement method/device and methodological quality did not sufficiently explain the observed variation, although exclusion of studies not using auscultation or a validated upper arm device did reduce some the observed heterogeneity, suggesting this may have been a contributing factor. Although age has previously been shown to affect the magnitude of arm-ankle blood pressure difference,[5] meta-regression by age revealed no such association in the present data. Other factors contributing towards the observed heterogeneity might include the blood pressure device and model used, number of readings taken and the observer making the measurement (e.g. doctor, nurse, researcher), all of which were likely to have varied across the included studies.

Since this study examined only aggregate data, it was not possible to study arm-leg blood pressure difference at different blood pressure levels for individual patients. However, meta-regression by mean arm blood pressure, and sensitivity analyses of the arm-ankle difference as a percentage of the arm blood pressure suggested no relationship exists. Whilst the aim of this study was to define the average arm-leg blood pressure difference for occasions where measurement in the arm is not possible, we cannot rule out the possibility that such a difference would be greater in the absence of limbs, due to the effects of changing resistance and altered reflection points.

Comparison with previous literature

Whilst there are many previous studies which have measured arm and leg blood pressure in the same patient, most focus on estimating ankle-brachial index for detection of underlying vascular disease.[10-14] Few studies have set out to measure the arm-leg blood pressure difference in the general population to aid interpretation of leg measurements in clinical practice. One study by Gong *et al.,*[5] showed in 948 patients that blood pressure was 17.4 mmHg (95% CI 16.7 to 18.1 mmHg) higher when measured in the ankle than when measured in the arm, findings which are consistent with the present review.

Implications for clinical practice

Current clinical guidelines pay little attention to measurement of blood pressure in the leg and there is no guidance on the most appropriate method of measurement.[1] The present study found no agreed measurement protocol for estimating leg blood pressure across studies. Generally, older studies used Doppler probes and strain-gauge plethysmography techniques.[15-19] Newer studies using validated oscillometric sphygmomanometers found similar arm-leg blood pressure differences to those using other devices[4, 5, 10], although the statistical heterogeneity across studies was reduced. When measuring arm-leg blood pressure differences, for example in the assessment of peripheral vascular disease, the present data suggest similar differences can be observed using sequential versus simultaneous methods. This approach is likely to be more clinically acceptable when assessing patients, particularly where resources limit the use of blood pressure monitors capable of connecting to two cuffs. Previous studies suggest that like the arms, an inter-ankle difference may be associated with an increased risk of mortality and so using readings from the leg which provides the higher value may be important.[20]

The present study found the mean difference between leg and arm blood pressure when measured in a supine position to be 17/0 mmHg (ankle) and 10/0 mmHg (calf). Using the traditional 140/90 mmHg threshold for hypertension,[21] these differences translate into a diagnostic threshold of 155/90 mmHg for ankle blood pressure and 150/90 mmHg for calf blood pressure. This is in contrast to the 175 mmHg threshold previously suggested by Hietanen *et al.*,[7] which was based on risk of subsequent cardiovascular morbidity and mortality. Since there are no trials of treatment based on leg blood pressure, it is logical to use thresholds which are equivalent to those used for the arm readings, which are underpinned by a large body of evidence.[22] The slightly more conservative difference of 15 mmHg recommended here would ensure maximum sensitivity albeit with reduced specificity for true hypertension. The lack of difference in diastolic arm-leg blood pressure appears to support the concept of pressure amplification: systolic pressure increases with greater distance toward the periphery, but there is little change in diastolic pressure. This may suggest caution is warranted in using oscillometric monitors optimised for analysing brachial pressure as the relationship between mean and systolic pressure may differ in the lower limb.

It should be noted that all blood pressure readings examined in this study were taken in the supine position, whereas in previous blood pressure lowering trials (which have established diagnostic thresholds), readings are usually taken in the sitting position.[22] It is unclear what impact this would have on the proposed thresholds, since some studies suggest arm blood pressures measured in the sitting position are higher than readings taken in the supine position,[23, 24] whereas others suggest no difference[24] or higher readings in the supine position.[25, 26] Our sensitivity analyses suggest that blood pressure measured in the ankle (in the supine position) was, on average, 12.9% higher than that in the arm (in the supine position); this would equate to an equivalent diagnostic threshold based on sitting readings of 158/90 mmHg, assuming the relative differences are the same in both positions. Given this debate, we recommend that physicians use the proposed threshold with caution, particularly when initiating new treatment in patients who are found to be close to the diagnostic threshold. In addition, given that ankle and calf blood pressures are likely to be significantly lower in patients with vascular occlusive diseases, it may be advisable that further investigation is considered in patients with apparently low ankle systolic blood pressure readings, despite the presence of cardiovascular risk factors such as diabetes, renal disease or cardiovascular disease.

For the assessment of leg blood pressure alone (when no arm blood pressure measurement is possible) the results from this review suggest that ankle blood pressure measured in a supine position using the dorsalis pedis artery may be the most clinically appropriate leg measurement given the paucity of data in the arm/calf and arm/thigh comparisons. In addition, ankle measurements are less likely to cause discomfort than calf or thigh measurements and the cuff will be easier to fit, particularly in obese patients. Data from the primary studies included in this review did not consistently report the number of repeat readings taken in the ankle, with only 11/30 studies reporting this information at all (eTable 3). The vast majority of studies comparing arm-ankle blood pressure took measurements in the ankle with the patient in the supine position, with a 5-10 minute rest period prior to measurement.

Given the lack of detailed reporting on leg blood pressure measurement methods, it is not possible to make further specific recommendations regarding measurement protocols. No oscillometric BP monitors have specifically been validated for leg measurements and the use of ambulatory readings for diagnosis will not be possible in patients who need to have leg blood pressure measurements. The use of auscultation may present practical difficulties with placement of the stethoscope and use of Doppler “return to flow” will only give a systolic reading. Further work should aim to determine the optimal leg blood pressure measurement protocol to aid the clinical utility of this paper’s findings.

Conclusions

This review is the first to provide empirical data for defining the difference between blood pressure in the arm with blood pressure measured in the ankle or calf. It suggests that in the general population, clinicians should expect systolic readings which are at least 15 mmHg higher than those taken in the arm in the supine position. A diagnostic threshold of 155/90 mmHg could therefore be used for diagnosing hypertension when relying on ankle measurements alone.

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Tables

Table 1. Participant characteristics in included studies

Author/Year (sub-population)	**Total pop. (n)**	**Gender (n, % female)**	**Age (years, mean ± sd)**	**Hypertensive (n, %)**	**Anithypertensive medication (n, %)**	**History of CVD (n, %)**	**Diabetes (n, %)**	**CKD (n, %)**	**BMI (kg/m^2, mean ± sd)**	**ABI (mean)**
Allison 1973 (SVD)**[27]**	78	-	55 ± 14	-	-	-	-	-	-	0.81
Allison 1973 (VOD)**[27]**	22	-	54 ± 19	-	-	22 (100%)	-	-	-	0.73
Arveschoug 2008 (Middle aged patients)**[28]**	14	12 (86%)	51	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-	1.22
Arveschoug 2008 (Elderly patients)**[28]**	31	25 (81%)	71	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-	1.17
Atsma 2005**[29]**	320	320 (100%)	66 ± 6	110 (34%)	-	3 (1%)	23 (7%)	-	-	-
Banner 1991**[30]**	6	-	-	-	-	-	-	-	-	1.21
Barani 2005**[31]**	198	99 (50%)	74 ± 10	-	-	198 (100)	100 (51%)	-	25.1 ± 4.7	0.30
Bell 1973**[15]**	30	0 (0%)	(13-55)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-
Bollinger 1976 (AOD - Intra-arterial readings)**[32]**	13	3 (23%)	58 ± 15	-	-	-	-	-	-	0.67
Bollinger 1976 (AOD - Indirect readings)**[32]**	11	3 (27%)	60 ± 14	-	-	-	-	-	-	0.67
Bollinger 1976 (Healthy - Intra-arterial readings)**[32]**	13	0 (0%)	39 ± 11	-	-	-	-	-	-	1.15
Bollinger 1976 (Healthy - Indirect readings) **[32]**	3	0 (0%)	27 ± 4	-	-	-	-	-	-	1.15
Cao 2014**[4]**	414	214 (52%)	61 ± 13	414 (100%)	414 (100%)	-	-	-	-	1.11
Engvall 1989**[16]**	19	9 (47%)	34	0 (0%)	-	0 (0%)	-	-	-	1.18
Engvall 1995**[17]**	22	9 (41%)	33	22 (100%)	-	-	-	-	-	-
Freitas 2014 (Normotensives)**[10]**	50	47 (94%)	41 ± 2	0 (0%)	-	-	0 (0%)	-	28.1 ± 0.76	1.15
Freitas 2014 (Hypertensives)**[10]**	50	37 (74%)	58 ± 2	50 (100%)	-	-	0 (0%)	-	31.7 ± 1.1	1.12
Freitas 2014 (White coat hypertensives)**[10]**	35	30 (86%)	54 ± 3	35 (100%)	-	-	0 (0%)	-	30.6 ± 1.2	1.13
Gardner 1998**[11]**	50	3 (6%)	69 ± 7	29 (58%)	-	50 (100%)	11 (22%)	-	27.6 ± 4.3	0.67
Gemignani 2012a**[33]**	197	117 (59%)	52 ± 1	75 (38%)	-	-	28 (14%)	-	26.4 ± 0.3	-
Gemignani 2012b**[34]**	130	77 (59%)	34 ± 1	-	0 (0%)	-	-	-	24.8 ± 0.4	-
Goldstein 2014**[35]**	201	63 (31%)	34	-	-	0 (0%)	0 (0%)	-	25.6	1.11
Goldthorp 1986**[36]**	30	-	(23-76)	-	-	-	-	-	-	-
Gong 2015**[5]**	948	-	48 ± 19	0 (0%)	-	0 (0%)	0 (0%)	-	22.9 ± 3.5	1.15
Grenon 2009**[37]**	12	4 (33%)	26 ± 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	22.3	1.17
Instebo 2004 (Arm-leg difference <1 mmHg)**[38]**	13	6 (46%)	26 ± 7	0 (0%)	-	-	-	-	22.4	-
Instebo 2004 (Arm-leg difference 1-20 mmHg)**[38]**	12	5 (42%)	24 ± 9	12 (100%)	-	-	-	-	22.9	-
Instebo 2004 (Arm-leg difference >20 mmHg)**[38]**	16	5 (31%)	24 ± 7	16 (100%)	-	-	-	-	24	-
Koay 1985**[39]**	15	5 (33%)	45	-	-	-	-	-	-	1.11
Lee 1996**[18]**	110	1 (1%)	69	-	-	30 (27%)	53 (48%)	-	-	0.92
Lee 2011**[40]**	60	25 (42%)	43 (20-78)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-	1.14
Maldonado 2008**[12]**	224	0 (0%)	17.1 ± 5.6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	22.3 ± 13.8	1.18
Malhotra 2002**[41]**	41	18 (44%)	52 ± 14	19 (46%)	-	-	-	-	25.1	1.72
Martins 2010**[13]**	75	36 (48%)	60 ± 10.2	75 (100%)	>50 (>50%)	-	20 (27%)	0 (0%)	29.8 ± 4.9	1.20
Moore 2008**[6]**	100	65 (65%)	(20 – 64)	0 (0%)	0 (0%)	0 (0%)	-	-	-	-
Oguanobi 2012 (Sickle cell anaemia patients)**[42]**	62	31 (50%)	28.3 ± 5.6	-	-	-	-	-	20.5 ± 2.7	0.88
Oguanobi 2012 (Healthy controls)**[42]**	62	31 (50%)	28.4 ± 5.9	-	-	-	-	-	23.9 ± 3.2	1.03

Okada 2013**[43]**	314	121 (39%)	66.2 ± 8.5	-	183 (58%)	-	314 (100%)	-	23.6 ± 3.7	1.11
Pan 2007**[44]**	946	481 (51%)	44.9	274 (29%)	61 (6.5%)	-	-	-	22.1	-
Quong 2016**[45]**	73	31 (42%)	24.3 ± 2.0	-	-	-	-	-	21.9	1.09
Rahiala 2001**[46]**	20	20 (100%)	18.8 ± 0.9	-	-	-	-	-	-	1.10
Richart 2009**[47]**	105	55 (52%)	56.5	26 (25%)	-	-	-	-	26.2	1.13
Sahli 2004**[48]**	437	199 (46%)	54	87 (20%)	-	-	300 (69%)	-	25.5	-
Sareen 2012**[49]**	250	-	-	-	-	-	-	-	-	-
Sheng 2013**[20]**	3,133	1,750 (56%)	69	-	1,215 (39%)	-	285 (9%)	-	23.6	-
Siggaard-Andersen 1972**[19]**	34	4 (12%)	55	-	-	-	-	-	-	-
Su 2007**[50]**	38	8 (21%)	58.7 ± 14	27 (71%)	-	-	-	-	-	-
Swan 2003 (Coarctation patients)**[51]**	45	17 (38%)	29.8 ± 11.0	8 (18%)	8 (18)	45 (100%)	-	-	30.3 ± 14.8	-
Swan 2003 (Controls)**[51]**	33	13 (39%)	30.6	0 (0%)	0 (0%)	0 (0%)	-	-	31.6 ± 12.6	-
Thulesius 1978 (Controls)**[52]**	18	-	52	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-	-
Thulesius 1978 (Patients with minor PAI)**[52]**	14	-	60	-	-	14 (100%)	-	-	-	-
Thulesius 1978 (Patients with severe PAI)**[52]**	58	-	60	-	-	14 (100%)	-	-	-	-
Vriend 2005**[53]**	73	30 (41%)	29.8	33 (45%)	9 (12%)	33 (45%)	-	-	23.4 ± 3.3	-
Weatherley 2006**[14]**	119	70 (59%)	55.0 ± 5.7	43 (36)	-	-	13 (11%)	-	27.0 ± 4.78	-
Wilkes 2004**[54]**	45	23 (51%)	55	0 (0%)	0 (0%)	-	-	-	27.3	1.18
Williamson 1921**[55]**	15	1 (7%)	43.0 ± 10.6	-	-	15 (100%)	-	-	-	-
Yeragani 2007 (Controls)**[56]**	22	7 (32%)	47 ± 15	0 (0%)	0 (0%)	0 (0%)	-	-	24	1.06
Yeragani 2007 (Participants with anxiety)**[56]**	26	7 (27%)	44 ± 13	0 (0%)	0 (0%)	0 (0%)	-	-	26	1.07
Yeragani 2007 (Patients with CVD)**[56]**	72	19 (26%)	59 ± 13	21 (29%)	7 (10%)	72 (100%)	-	-	27	1.07

CVD=cardiovascular disease; CKD=chronic kidney disease; BMI=body mass index; ABI=Ankle-brachial index; SVD=small vessel disease; VOD=vascular occlusive disease; AOD=arterial occlusive disease; PAI=peripheral arterial insufficiency

Table 2. Methodological quality of included studies

Author	Patient selection			Outcome measurement	Analysis	Confounding	Overall quality rating*
	Was selection of patients appropriate?	Did the study avoid inappropriate exclusions?	Was the study sample representative of the intended population?	Is the outcome variable measured appropriately?	Was the arm-leg BP difference the primary focus of the study?	Were all important confounding factors identified?	
Allison 1973**[27]**	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Low
Arveschoug 2008**[28]**	Unclear	Yes	Yes	Yes	Yes	Yes	High
Atsma 2005**[29]**	Unclear	Yes	Unclear	Yes	Yes	Yes	High
Banner 1991**[30]**	Unclear	Unclear	Unclear	Yes	No	Unclear	Low
Barani 2005**[31]**	Yes	Yes	Yes	Unclear	No	Yes	High
Bell 1973**[15]**	Unclear	No	No	Yes	Yes	Unclear	Low
Bollinger 1976**[32]**	Unclear	Yes	Unclear	Yes	No	Yes	Moderate
Cao 2014**[4]**	Yes	No	Yes	Yes	Yes	Unclear	High
Engvall 1989**[16]**	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Low
Engvall 1995**[17]**	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Low
Freitas 2014**[10]**	No	Yes	Unclear	Yes	No	Yes	Moderate
Gardner 1998**[11]**	Unclear	Yes	Unclear	Yes	No	Yes	Moderate
Gemignani 2012a**[33]**	Unclear	Yes	Unclear	Yes	No	Yes	Moderate
Gemignani 2012b**[34]**	Unclear	Yes	Unclear	Yes	Yes	Yes	High
Goldstein 2014**[35]**	Unclear	Yes	Unclear	Yes	Yes	Yes	High
Goldthorp 1986**[36]**	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Low
Gong 2015**[5]**	Unclear	Yes	Unclear	Yes	Yes	Unclear	Moderate
Grenon 2009**[37]**	Unclear	Yes	Unclear	Yes	Yes	Yes	High
Instebo 2004**[38]**	Unclear	Yes	Unclear	Yes	No	No	Low
Koay 1985**[39]**	Yes	Yes	Unclear	Yes	Yes	Yes	High
Lee 1996**[18]**	Yes	Unclear	Yes	Yes	No	Unclear	Moderate
Lee 2011**[40]**	Unclear	Yes	Unclear	Yes	No	Yes	Moderate
Maldonado 2008**[12]**	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Low
Malhotra 2002**[41]**	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Low
Martins 2010**[13]**	Yes	Yes	Yes	Yes	No	Yes	High
Moore 2008**[6]**	Unclear	Yes	Unclear	Yes	Yes	Yes	High
Oguanobi 2012**[42]**	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Low
Okada 2013**[43]**	Yes	Yes	Unclear	Yes	Yes	Unclear	High
Pan 2007**[44]**	Yes	Yes	Unclear	Yes	Yes	Unclear	High
Quong 2016**[45]**	Unclear	Yes	Unclear	Yes	Yes	Unclear	Moderate
Rahiala 2001**[46]**	Unclear	unclear	Unclear	Yes	Yes	Unclear	Low
Richart 2009**[47]**	Yes	Unclear	Unclear	Yes	Yes	Unclear	Moderate

Sahli 2004**[48]**	Unclear	Yes	Unclear	Yes	Yes	Yes	High
Sareen 2012**[49]**	Unclear	Yes	Unclear	Yes	Yes	Yes	High
Sheng 2013**[20]**	Yes	Yes	Unclear	Yes	Yes	Yes	High
Siggaard-Andersen 1972**[19]**	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Low
Su 2007**[50]**	Yes	Yes	Unclear	Unclear	Yes	Yes	High
Swan 2003**[51]**	Yes	Yes	No	Unclear	Yes	Unclear	Moderate
Thulesius 1978**[52]**	Unclear	Unclear	Unclear	Unclear	Yes	No	Low
Vriend 2005**[53]**	Yes	Unclear	Yes	Unclear	Yes	Yes	High
Weatherley 2006**[14]**	No	Unclear	Yes	Yes	Yes	Unclear	Moderate
Wilkes 2004**[54]**	Yes	No	No	Yes	Yes	Yes	High
Williamson 1921**[55]**	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Low
Yeragani 2007**[56]**	Yes	Yes	Unclear	Unclear	No	Yes	Moderate

*High quality = 4 or more quality domains present; Moderate = 3 quality domains present; low=2 or less quality domains present

Figure legends

Figure 1. Selection of studies
BP=blood pressure; SD=standard deviation; CI=confidence intervals; RCT=randomised controlled trial

Figure 2. Arm-ankle systolic blood pressure difference in the general population (n=24 studies)
Mean sBP difference given in mmHg. sBP=systolic blood pressure; CI=confidence intervals; ED=emergency department; CVD=cardiovascular disease; BP=blood pressure.

Figure 3. Arm-ankle diastolic blood pressure difference in the general population (n=16 studies)
Mean dBP difference given in mmHg. dBP=diastolic blood pressure; CI=confidence intervals; ED=emergency department; CVD=cardiovascular disease; BP=blood pressure.

Figure 4. Arm-ankle blood pressure difference in patients with a history of cardiovascular disease (n=7 studies)
Mean BP difference given in mmHg. BP=blood pressure; CI=confidence intervals

Figure 5. Meta-regression of arm-ankle blood pressure difference in the general population by mean arm blood pressure and age
BP=blood pressure; Moore et al., (2008) excluded due to lack of data on mean arm blood pressure and age; Banner et al., (1991) excluded due to lack of data on age.