Research Article

Blood Pressure during Blood Collection and the Implication for Absolute Cardiovascular Risk Assessment

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Keywords

Phlebotomy · Venepuncture · Medical consultation · Risk factors · Cardiovascular disease

Abstract

Background: Blood collection and blood pressure (BP) measurements are routinely performed during the same consultation to assess absolute cardiovascular disease (CVD) risk. This study aimed to determine the effect of blood collection on BP and subsequent calculation of the absolute CVD risk. **Methods:** Forty-five participants aged 58 ± 9 years (53% male) had systolic BP (SBP) measured using clinical guideline methods (clinic SBP). Then, on a separate visit, BP was measured immediately before, during, and after blood collection. Absolute CVD risk scores were calculated (Framingham equation) using SBP from each measurement condition and compared. **Results:** The prevalence of low ($< 10\%$), moderate ($10\text{--}15\%$), and high ($\geq 15\%$) absolute CVD risks among the participants was 67%, 22%, and 11%, respectively, using clinic SBP. SBP values before and during blood collection were significantly higher compared to values after blood collection (130 ± 18 and 132 ± 19 vs. 126 ± 18 mm Hg; $p = 0.010$ and $p = 0.003$, respectively). However, there were no significant differences between clinic SBP (128 ± 18 mm Hg) and blood collection SBP ($p = 0.99$) or the absolute CVD risk scores (7.3 ± 6.5 ; 7.6 ± 5.9 ; 7.7 ± 6.1 ; and $7.1 \pm 5.7\%$, respectively; $p = 0.995$ for all). The mean intraclass correlation (95% CI) indicated good agreement between absolute CVD risk scores calculated with clinic SBP and each blood collection SBP (0.86 [95% CI $0.74\text{--}0.92$], 0.85 [95% CI $0.71\text{--}0.91$], and 0.87 [95% CI $0.76\text{--}0.93$], respectively; $p < 0.001$, for all). **Conclusion:** Absolute CVD risk calculation is not affected by use of SBP measurements recorded at the time of blood collection. Therefore, it is acceptable to collect blood and measure BP during the same consultation for absolute CVD risk assessment.

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Introduction

Cardiovascular disease (CVD) is the leading cause of death and disability worldwide [1]. The etiology of CVD is attributed to several non-modifiable and modifiable risk factors, such as age, sex, systolic blood pressure (SBP), cholesterol, smoking, and diabetes status. These factors can be entered into risk prediction algorithms to estimate the probability of developing CVD over a defined time [2–4]. Indeed, many clinical guidelines recommend absolute CVD risk assessment to identify high-risk individuals for treatment and management [5–7]. Collection of complete CVD risk factor information may involve both the recording of BP and collection of blood during the same consultation period [8–10]. However, the accuracy of BP is affected by situational anxiety [11–13], and there is some evidence that BP may increase in anticipation of a blood test [14]. Thus, the act of blood collection could elevate SBP to such an extent as to change the estimation of absolute CVD risk and potentially affect clinical decision making. Therefore, the aim of this study was to assess the effect of blood collection on BP and subsequent absolute CVD risk estimation by comparison to BP measured at a separate clinic visit.

Methods

Protocol

The participants attended the Menzies Institute for Medical Research (Hobart, TAS, Australia) and had their BP measured on 2 separate occasions. At the first visit, BP measurements (clinic BP) were taken during an assessment that did not involve blood collection [15]. At the second visit, which occurred within a month of the initial visit, BP measurements were recorded immediately before, during, and after blood collection. The participants were asked to refrain from smoking, caffeine and alcohol consumption, and heavy meals 3 h prior to their assessments. All BP readings were performed according to guidelines with respect to subject positioning (e.g., feet flat on the floor, back supported, and arm supported at heart level) [16]. Cholesterol levels were obtained from blood test reports from accredited pathology services (Diagnostic Services Pty. Ltd. and Royal Hobart Hospital). Additional CVD risk factors and medications were assessed via a self-report questionnaire. Participants on medications maintained their normal treatment schedule during this study. Four separate absolute CVD risk scores were calculated using the SBP recorded in each of the 4 BP measurement conditions (clinic, before, during, and after blood collection). Anxiety and pain levels were measured before and after blood collection, respectively, using an adapted 5-point Likert scale [16]. Standard anthropometric measurements (including height and weight) were recorded at the first clinic visit.

Participants

Sixty-three participants were screened for inclusion. This comprised 42 patients referred by their general practitioner to a specialist academic BP clinic and 21 participants recruited from the general population. In accordance with the Australian absolute CVD risk guidelines, all adults aged 45–74 years were eligible for inclusion in this study [5]. Of the 63 participants recruited, 18 were excluded from final analyses; participants were excluded due to unsuccessful blood collection or venepuncture ($n = 5$), unsuccessful BP measurement ($n = 6$), no available cholesterol results ($n = 4$), or age younger than 45 years ($n = 3$), leaving 45 participants for inclusion in the analyses.

Clinic BP

Clinic BP was recorded as the average of 2 readings after 10 min of seated rest with 1 min between measurements, as per guidelines [15]. Validated oscillometric devices were used for all measures (either IEM Mobil-O-Graph [17] [$n = 42$] or OMRON HEM-907 [18] [$n = 21$] monitors) [15].

Blood Collection BP

A trained phlebotomist identified the preferred arm for venepuncture at the antecubital fossa and a BP cuff was placed on the opposite arm. Three BP measurements were taken both immediately before and after blood collection, and 1 BP measurement was obtained during blood collection starting from the time blood

Table 1. Demographic and clinical characteristics of the study participants

Variable	Value
Age, years	58±9
Males	24 (53)
Height, cm	170±11
Weight, kg	84±18
BMI, kg/m ²	29.1±5.9
Current smokers	10 (22)
Type 2 diabetes	10 (22)
Total cholesterol, mmol/L	5.3±1.1
High-density lipoprotein cholesterol, mmol/L	1.8±1.9
Clinic SBP, mm Hg	128±18
Clinic DBP, mm Hg	74±15
Clinic absolute CVD risk, %	7±6
Low	30 (67)
Moderate	10 (22)
High	5 (11)
Medications	
Antihypertensive	25 (56)
Statin	12 (27)
Both	9 (19)
Amount of blood drawn, mL	24±7

The total number of patients is 45. Data are expressed as means ± SD or numbers (%).

flow began from the vein. The average of the second and third before- and after-blood collection measurements was used for analyses. The same BP device was used for all blood collection BP measurements (IEM Mobil-O-Graph). Participants were not informed of their BP values until the conclusion of the protocol.

Blood Biochemistry

For participants recruited from the BP clinic, lipid profiles were obtained from previous blood test results by accredited pathology services on referral by their general practitioner. Those participants who did not have recent cholesterol results had a sample of blood drawn for analysis at the Royal Hobart Hospital pathology laboratory.

Assessment of Additional CVD Risk Factors

A self-report health questionnaire was administered by research staff at the initial assessment to confirm age, sex, smoking status, diabetes status, and medications including antihypertensive and statin therapy. Diabetes status was defined as a previous diagnosis from a medical professional and smoking status was defined as current smoker within the last 12 months.

Absolute CVD Risk Assessment

Absolute CVD risk scores were calculated using the adjusted 5-year Framingham risk equation according to National Vascular Disease Prevention Alliance guidelines [5]. Age, SBP, total cholesterol, and high-density lipoprotein cholesterol were entered as continuous variables and sex, diabetes status, and smoking status were entered as dichotomous variables to produce a risk score for each participant. Low, moderate, and high absolute CVD risks were defined as <10, 10–15, and >15%, respectively, as per guidelines [5].

Anxiety and Pain during Blood Collection

Anxiety was assessed prior to blood collection using a 5-point Likert scale. Participants were shown a scale from 1 (not anxious at all) to 5 (very anxious) and asked to self-select their level of anxiety. Pain was assessed after blood collection, once the needle had been removed, using a 5-point Likert scale ranging from 1 (no pain at all) to 5 (severe pain).

Table 2. Differences between clinic BP and BP measured before, during, and after blood collection

BP variable	Mean ± SD	Mean difference from clinic BP (95% CI)	p value ¹	ICC (95% CI)	p value
Clinic SBP, mm Hg	128±18	REF		REF	<0.001
Before-blood collection SBP, mm Hg	130±18	3 (–7 to 12)	0.999	0.39 (–1.12 to 0.66)	0.055
During-blood collection SBP, mm Hg	132±19	4 (–6 to 14)	0.999	0.36 (–0.16 to 0.65)	0.071
After-blood collection SBP, mm Hg	126±18	–2 (–11 to 7)	0.999	0.42 (–0.07 to 0.68)	0.040
Clinic DBP, mm Hg	74±15	REF		REF	<0.001
Before-blood collection DBP, mm Hg	83±12	9 (3 to 16)	0.002	0.42 (–0.02 to 0.67)	0.015
During-blood collection DBP, mm Hg	85±12	11 (5 to 17)	<0.001	0.41 (–0.05 to 0.68)	0.009
After-blood collection DBP, mm Hg	80±12	7 (1 to 13)	0.022	0.52 (0.14 to 0.73)	0.004

The total number of patients is 45. REF, reference measure used for comparison. ¹ Comparison with clinic BP values by ANOVA.

Statistical Analysis

All data were analyzed using SPSS for Windows software version 24 (SPSS, Chicago, IL, USA). Repeated measures analysis of variance (ANOVA) was used to compare clinic and blood collection BP measures and subsequent absolute CVD risk scores with adjustment for gender, antihypertensive medication, and BP device. Intraclass correlation coefficients (ICC) were used to assess the agreement between BP measures and absolute CVD risk scores using a single-rater, 2-way mixed-effects, absolute agreement model. The mean ICC together with 95% CI were used to define the strength of agreement between measurement conditions as poor (<0.50), moderate (0.50–0.75), good (0.75–0.90), and excellent (>0.90) [19]. χ^2 pairwise comparison was used to investigate differences in risk category classification between clinic and before-, during-, and after-blood collection absolute CVD risk score using the McNemar test.

Results

Participant Characteristics

Participant characteristics are shown in Table 1. On average participants were middle-aged and normotensive, and most were classified as low absolute CVD risk. Approximately half of the study sample reported taking antihypertensive medications and there were 10 participants with type 2 diabetes.

BP during Blood Collection

Differences in BP measures are reported in Table 2. Clinic SBP was not different compared to SBP measured before, during, and after blood collection ($p > 0.05$ for all). However, there were differences observed for the ANOVA model; before- and during-blood collection SBP values were higher than after-blood collection SBP values ($p = 0.010$ and $p = 0.003$, respectively). Clinic and after-blood collection diastolic BP (DBP) values were lower than before- and during-blood collection DBP values. Before- and during-blood collection DBP values were higher than after-blood collection DBP values ($p = 0.048$ and $p = 0.001$, respectively). The absolute agreement between clinic and before-, during-, and after-blood collection BP was poor as indicated by the ICC (Table 2). There were no differences in BP response to blood collection based on the BP device or antihypertensive agents. Participants reported little to no anxiety or pain from blood collection (median: 1 [IQR 1–2] and 1 [IQR 1–1.5], respectively). Anxiety and pain had no effect on BP measured at the time of blood collection.

Table 3. Differences between absolute CVD risk scores calculated using research grade SBP measured at a separate clinic visit and SBP measured before, during, and after blood collection

SBP used to calculate the absolute CVD risk	Mean ± SD (%)	Mean difference from clinic absolute CVD risk (95% CI)	p value ¹	ICC (95% CI)	p value
Clinic	7.3±6.5	REF		REF	<0.001
Before-blood collection	7.6±5.9	0.3 (–1.5 to 2.1)	0.999	0.86 (0.74 to 0.92)	<0.001
During-blood collection	7.7±6.1	0.4 (–1.5 to 2.4)	0.999	0.84 (0.71 to 0.91)	<0.001
After-blood collection	7.1±5.7	–0.2 (–1.9 to 1.5)	0.999	0.87 (0.76 to 0.93)	<0.001

The total number of patients is 45. REF, reference. ¹ Comparison with clinic absolute CVD risk scores by ANOVA.

Blood Collection BP and Absolute CVD Risk Calculation

There were no differences in absolute CVD risk scores calculated using clinic SBP compared with SBP values measured at the time of blood collection. This was despite before- and during-blood collection absolute CVD risk values being higher compared to after-blood collection absolute CVD risk ($p = 0.014$ and $p = 0.004$, respectively) (Table 3). After adjusting for gender, there was no difference in the results. The mean ICC indicated good agreement between absolute CVD risk scores calculated with clinic SBP and each of the blood collection SBP, but the range for the 95% CI varied from good to excellent. There were no differences in absolute CVD risk scores between patients referred by their general practitioner and participants recruited from the general population. Due to the small numbers of participants in the moderate and high absolute CVD risk categories, these were combined to determine the potential for risk reclassification and significance for clinical management. There were minimal changes in the distribution of risk between all BP measurement conditions, with only 3 participants reclassified. Two participants were reclassified from low to moderate risk from clinic to before- and during-blood collection and 1 was reclassified from moderate to low risk from clinic to after-blood collection.

Discussion

The principal finding of this study was that absolute CVD risk scores calculated using a reference SBP were not different from absolute CVD risk scores calculated using SBP measured at the time of blood collection. Although there were small differences in SBP between before-, during- and after-blood collection, these did not result in absolute CVD risk reclassification and therefore would be unlikely to change subsequent clinical decisions. These findings are of clinical importance as BP measurement and blood collection may occur during the same consultation for assessment of the absolute CVD risk.

Before- and during-blood collection SBP values were 4 and 6 mm Hg higher than after-blood collection SBP values, respectively. To our knowledge, only 1 other study has sought to determine the potential effect of blood collection on BP and this was in young people (mean age 20 ± 2 years) [14]. However, in that study there was no actual collection of blood, and instead investigators were interested in the BP response to people simply being informed that a blood sample would be collected. This alone caused a small increase in SBP (3 mm Hg) on average, suggesting that anxiety associated with the collection of blood in itself could lead to minor BP increases, at least in this specific population of young people [14]. These investigators did not measure

anxiety, whereas our work extends this knowledge by measuring both perceived anxiety and pain, before and after blood collection. Interestingly, our participants reported little to no anxiety or pain and there was no association between anxiety or pain and the SBP measured around the time of blood collection. The low self-reported levels of anxiety and pain may be explained by our participants being middle- to older aged and familiar with routine clinical blood collection.

Numerous factors can affect the quality of SBP recorded in clinical practice, but the extent to which different SBP values may influence the assessment of absolute CVD risk is poorly understood. One study in 607 participants compared the absolute CVD risk scores derived from 3 established calculators (Framingham, QRISK2, and SCORE) [20–23] using SBP values from either clinic BP, 7-day home BP, or 24-h ambulatory BP measurements. The method of BP measurement did not markedly change absolute CVD risk estimations, with less than 10% of participants being reclassified into a different risk category. Similar to the findings of our study, those that were reclassified tended to have absolute CVD risk scores on the borderline between risk category thresholds. In our study the participant with the largest difference in SBP (19 mm Hg) during blood collection had a change in absolute CVD risk of only 1%, moving them from low to moderate risk (from 9 to 10%).

Broad et al. [24] observed comparable findings in a large study of 23,676 participants investigating the difference between absolute CVD risk scores estimated with either the exact doctor- (or nurse-) measured SBP or the SBP rounded to the nearest whole number (digit preference), which is likely to occur in clinical practice. Overall, less than 3% of the participants were misclassified to receive treatment based on absolute the CVD risk approach due to digit preference. However, less than 1% of the participants were misclassified based on the absolute CVD risk approach after taking into account those participants with an exact BP reading ending in zero. Altogether, the findings suggest that absolute CVD risk algorithms are not highly sensitive to acute differences in BP that may arise within the vicissitudes of clinical practice. Furthermore, these findings highlight the additional value of absolute CVD risk management for appropriately identifying high-risk patients and guiding treatment decisions, because the CVD risk score is less likely to be significantly influenced compared to single risk factors, especially BP.

To our knowledge, this study is the first to use an experimental design to investigate the effect of blood collection on the estimation of absolute CVD risk. A limitation of this study is the relatively low number of participants across the CVD risk categories and the lack of prior data with which to estimate study power. As such the findings should be regarded as hypothesis generating. Although both BP devices used were validated, and no significant differences were observed based on the BP device used, there remains the possibility of device-related bias in the clinic BP measurement.

In conclusion, absolute CVD risk calculation is not affected by use of SBP measured during the same consultation as blood collection compared to research grade SBP. Therefore, in clinical practice, BP measurement and blood collection could occur in the same consultation for subsequent calculation of absolute CVD risk.

Statement of Ethics

This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. All subjects provided written informed consent and the study protocol received ethical approval from the University of Tasmania Health and Medical Human Research Ethics Committee.

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