

RESEARCH ARTICLE

Characterizing Agreement in the Level of Interarm Blood Pressure Readings of Adults in the Emergency Department (CALIBRATE Study)

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ABSTRACT

Background: Increased interarm systolic blood pressure difference (IASBPD) is one of the major predictors of cardiovascular disease. An IASBPD of > 10 mmHg is of clinical significance. However, studies have reported a high number of patients visiting the emergency department (ED) with high IASBPD and varying correlation of IASBPD to age, ethnic background, and comorbidities such as hypertension and diabetes.

Objective: The CALIBRATE study aimed to measure the IABPDs in the multiethnic patient population presenting to the ED in Qatar and to assess the distribution of IASBPD in this population. Methods: In a sitting position, two consecutive blood pressure (BP) measurements were recorded from the right and left arms for each participant using a calibrated automated machine and appropriate cuff sizes. The data were recorded using predefined data fields, including patient demographics, past medical, and social and family history. The continuous variables were reported as mean or median based on the distribution of data. The data were analyzed using Stata MP 14.0.

Results: A total of 1800 patients, with a mean age of 34 (10) years, were prospectively recruited from the ED. The median absolute systolic BP difference (Δ SBP) between the right and left arms was 6 (3 – 10) mmHg, and it was the same for the first (Δ SBP1) and the second readings (Δ SBP2). The absolute average of Δ SBP1 and Δ SBP2 was 7 (4 – 10) mmHg. The difference in systolic BP difference (SBP) of < 20 mmHg for interarm blood pressure was seen in the 95th percentile of the population. No meaningful association could be detected between the IABPD and the study variables such as age, demographics, regions of interest, and risk factors.

Conclusion: In population presenting to the ED, the IASBPD of at least 20 mmHg reached at the 95th percentile, validating the known significant difference. The utility of SBP difference can be improved further by taking the average of two individual readings.

Keywords: IASBPD, Interarm systolic blood pressure difference, Hypertension, Emergency Department, Qatar

INTRODUCTION

The presence of differing blood pressure (BP) in contralateral extremities is often mentioned as a physical assessment tool when aortic dissection (AD) is suspected.¹ Interarm systolic blood pressure difference (IASBPD) has been studied considerably in various settings, and its association with various risk factors and predictors have been explored. Several studies have reported that significant IASBPD is an important predictor of the increased risk of cardiovascular diseases.^{1,2} However, data regarding the normal distribution of IASBPD and its association with various risk factors and predictors in a multiethnic emergency department (ED) population is scarce.

The incidence of AD has been reported to be approximately 1 to 4 per 100,000 in the western population, and less than 45% of the cases are diagnosed at initial presentation, whereas 38% of the cases are missed.^{3 - 5} IASBPD is used in the ED setting as an initial screening and diagnostic tool for the detection of AD. The diagnosis of acute cardiovascular events such as AD and high-risk patient triage in the ED is both challenging and time critical. The population of Qatar, unlike the western population, is composed of young, expatriate population with an early onset cardiovascular disease load; predicting a higher prevalence of IASBPD in the non-AD group.

The straightforward maneuver of simply assessing BP in each arm, right upper extremity (RUE) and left upper extremity (LUE) is frequently executed, but data describing the sensitivity and specificity of IASBPD assessments in AD diagnosis and its normal distribution in the general population are scarce. In addition, it has been reported that in BP assessment of an extremity, a repeat systolic BP (SBP) taken in the outpatient setting tends to be approximately

3.2 points lower than the initial-measured SBP.⁶ The National Institute for Health and Clinical Excellence clinical guidelines for hypertension considers IASBPD of < 10 mmHg as normal.⁷ The difference of > 20 mmHq is found in < 4% of the population and is associated with underlying vascular diseases.⁸ However, the clinical significance and relevance of SBP difference between 10 and 20 mmHg are unknown, more so in an ED patient population. Furthermore, several studies have reported the association of IASBPD with ethnic background and genetic predisposition of the patient population. As suggested by the studies conducted, the normal distribution of the IASBPD is different between the Asian and Caucasian populations.^{9,10} However, no such study has been conducted in the Middle Eastern population.

The specificity of IASBPD in AD greatly depends on the normal prevalence; therefore, defining the normal distribution of IASBPD in the ED population in an ethnically diverse population group is important to understand the IASBPD in our population and facilitate the decision-making in patient management by uptriaging patients with abnormal IASBPD and possible AD. Therefore, the CALIBRATE study aimed to determine the normal distribution of IASBPD in the patient population visiting the ED of the largest tertiary care general hospital in Qatar.

METHODS

Setting and design

The CALIBRATE study was a cross-sectional study with a prospective enrollment of patients visiting the ED of Hamad General Hospital (HGH) between March 1 and May 31, 2017. The HGH is a tertiary care, major academic, government tertiary care hospital with an annual attendance of more than 500,000 patients.¹¹ The study was approved by the institutional review board and the Medical Research Center (MRC) of Hamad Medical Corporation (MRC/0135/2017). Written informed consent was obtained from each participant before enrollment.

Study population

The patient population comprised adult population visiting the ED at HGH. Considering the demographic mix of the population presenting to the ED, a 1:1 of man to woman and 2:1 for Gulf Cooperation Council (GCC) countries including Saudi Arabia, Kuwait, United Arab Emirates, Qatar, Bahrain, and

Oman to nonGCC recruitment strategy was predefined. The inclusion criteria were defined as patients over the age of 18 years presenting to the ED at our hospital. Exclusion criteria included patients with (i) active bleeding, existing arteriovenous fistula, and severe distress and (ii) recent trauma or skin conditions that might affect taking the BP readings from the arms. Patients who were pregnant were also excluded from the study. Participants were screened for eligibility by the CALIBRATE team in the triage area of the ED. Those who met the eligibility criteria were briefed about the study, and written informed consent was obtained before induction.

BP measurements

The BP measurements were obtained by the CALIBRATE team, which is composed of a trained research associate and a dedicated research nurse for the study. Prior to the BP measurements, the patient was seated at rest on a chair for at least five minutes while demographic and baseline data were obtained utilizing a validated guestionnaire form. Utilizing a precalibrated oscillometric BP device (Criticare Systems Inc. CSI Model 506N3 series bedside monitor, Waukesha, WI, USA) and appropriate cuff size (adult 23-40 cm) used routinely in the ED, two consecutive sequential BP measurements were obtained in a sitting position from the right and left arms of each study participant. Two consecutive readings were obtained from one arm with a one-minute interval between the measurements before moving to the other arm. The complete set of BP measurements for an individual subject was performed by the same team to maximize accuracy and reduce any observation bias. The available evidence suggests that there is no association between IASBPD and the order of extremities in which BP was assessed.^{12,13} Therefore, the sequence of BP assessment was determined by patient comfort and preference.

The BP assessment approach described was not a truly "simultaneous" rather a sequential evaluation of BP in different extremities. There was an approximate delay of a minute or two between the assessments, as the cuff was cycled and then moved to another extremity. The approaches defined in this study were adopted because of a combination of considerations related to patient comfort, practicality, and external validity. The CALIBRATE study assessed BP in a similar manner as it is assessed in any ED in the world, maximizing the external validity of the CALIBRATE study.

Data collection

The data were recorded using predefined data fields including patient demographics, past medical history (focusing on diabetes, hypertension, hyperlipidemia, coronary artery disease [CAD], peripheral arterial disease, renal disease, treatment regimen, and therapy compliance), and social and family history. Based on the available evidence, body mass index, ambient temperature, and hand dominance were also recorded along with the participants' baseline characteristics.^{14–16} Primary outcome of the study was to categorize the IASBPD in the population of Qatar, especially focusing on the patients from the GCC and South East Asian regions.

Statistical analysis

The existing expert review evidence for categorization of IASBPD suggested cutoffs of 10 and 15 to define increasing levels of overall risk.^{13,17,18} To generate easily remembered and consistent categorical cutoffs and to continue the stepwise increase in IASBPD defined by the literature, we categorized IASBPD into <10, 10–14, 15-19, 20–24, and 25+ mmHg. The proportions of cases that have interarm difference (IAD) in the various categories were calculated. For these proportions and other proportion data, binomial exact 95% confidence intervals (CIs) were calculated.

IASBPD and the possible associations with independent variables (e.g., demographics and mean systolic BP (SBP)) were assessed with univariate and multivariate generalized linear modeling. Linear regression was used for IAD assessed as a continuous dependent variable; for categorical-based IASBPD analysis, we employed logistic regression. Linear modeling employed standard model-building techniques of stepwise covariate addition, with the use of univariate p = 0.2 to define evaluation in models. Model performance was assessed using the standard techniques for model fit, data heteroscedasticity, and model calibration as outlined in standard texts.¹⁹

The continuous variables were reported as the mean standard deviation for normally distributed data. For the IASBPD data (or any secondary data undergoing analysis) not normally distributed, central tendencies were reported in medians, with CI generation around the medians using bootstrapping.²⁰ All the analyses were performed using Stata MP 14.0 (College Station, TX, USA).

RESULTS

A total of 1800 patients were enrolled with a man to woman ratio of 1:1 and GCC to nonGCC resident ratio of 2:1. The mean age was 34 (\pm 10) years. The population comprised mostly of participants from Asia – Pacific region (n = 976, 54.2%) and Arabs (n = 738, 41%), whereas participants from Africa (n = 58, 3.2%), Europe (n = 15, 0.8%), North America (n = 4, 0.2%), South America (n = 1, 0.1%), and Commonwealth of Independent States (n = 8, 0.5%) formed minority of the study population. Among the Arabs, 33.4% of the participants belonged to the GCC countries, whereas 26.9% were Qatari nationals. The majority of the study population was right hand dominant (94.1%, 95% Cl, 92.8% – 95.1%). The proportion of participants with hypertension disorder was 9.2% (95% Cl, 7.9-10.7%), diabetes 7.7% (95% CI, 6.5%-9.1%), CAD 1.5% (95% CI, 0.9 – 2.1%), and hyperlipidemia 3.8% (95% CI, 2.9 – 4.7%). History of smoking was reported positive in 22.1% (95% CI, 20.2% – 24.1%), the characterisrics are summarized in Table 1.

The absolute difference between the right and the left arms SBP for the first reading (defined as Δ SBP1) was 6 (3-10) mmHg (Figure 1); same as the absolute SBP difference between the right and the left arms for the second reading (defined as Δ SBP2) 6 (3 – 11) mmHq (Figure 2). The average of Δ SBP1 and Δ SBP2 was 7 (4 - 10) mmHg in the study population (Figure 3). A significant IASBPD, defined as Δ SBP > 20 mmHq, for an average of Δ SBP1 and Δ SBP2, was detected in 60 participants (3.3%, 95% CI 2.6% to 4.3%). The difference in the SBP of < 20 mmHg for IASBPD was seen in the 95th percentile of the population with single reading (Figure 4), whereas the average of two individual readings was observed in the 97th percentile. Considering our observation, we can conclude that there will be a significant reduction in false-positive identification of significant SBP differences if there is a requirement for two RUE/LUE pairs of SBPs to be taken, with the average of these two IASBPDs used as the indicator. The proportion of patients with a Δ SBP > 20 mmHq, for either ΔSBP1 or $\Delta \text{SBP2},$ was detected in 175 participants (9.7%, 95% CI 8.4% to 11.2%).

Table 1. General characteristics of the study participants in the CALIBRATE study.

Variable	Frequency $(n = 1800)$
Age, Years ± SD	34.4 ± 10.8
Region, n (%) Africa Arab Asia – Pacific Europe North America South America CIS	58 (3.2) 738 (41.0) 976 (54.2) 15 (0.83) 4 (0.22) 1 (0.06) 8 (0.44)
Right hand dominance, n (%)	1693 (94.06)
BMI, kg/m ² ± SD	26.5 ± 5.56
Diagnosis, n (%) Chest pain Fever Gastrointestinal Genitourinary HEENT Musculoskeletal Neuropsychological Skin and soft tissue Trauma Nonspecific	183 (10.17) 140 (7.78) 289 (16.06) 118 (6.56) 338 (18.78) 273 (15.17) 155 (8.61) 158 (8.78) 99 (5.50) 47 (2.61)
Hypertension, n (%)	167 (9.28)
Diabetes, n (%)	139 (7.72)
CAD, n (%)	27 (1.50)
Hyperlipidemia, n (%)	68 (3.78)
Smoking, n (%)	398 (22.11)

SD, standard deviation; CIS, Commonwealth of Independent States; BMI, body mass index; HEENT, head, eyes, ears, nose, and throat; CAD, coronary artery disease.

There is no significant change in BP variances with increasing mean of the two SBPs, that is, the SBP variances are the same at both hypotensive and hypertensive levels. It also indicated that 95% of the time, the right arm and left arm SBP1 difference lies between -19.2 and 20.5, and 95% of the time, the right arm and left arm SBP2 difference lies between -20.47 and 20.12 (Figure 5). There is no meaningful association between the significant IASBPD and the study variables such as age, demographics, regions of interest, and risk factors. Although patients with diagnosed hypertension met the predefined criterion for significance, this difference was not clinically significant. There was no significant difference between IASBPD noted for the South East Asian or Arab population (Figure 6).

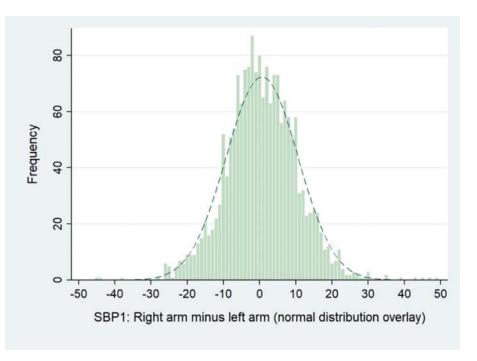


Figure 1. Distribution of the absolute difference between the right and the left arm systolic blood pressure for the first reading (Δ SBP1).

There is no clinically significant difference between the means of the BPs between the right and the left arms and also between the first and second SBP readings in the right of the left arm.

DISCUSSION

In this study, we measured the IABPD of the patients visiting the ED in Qatar and assessed the normal

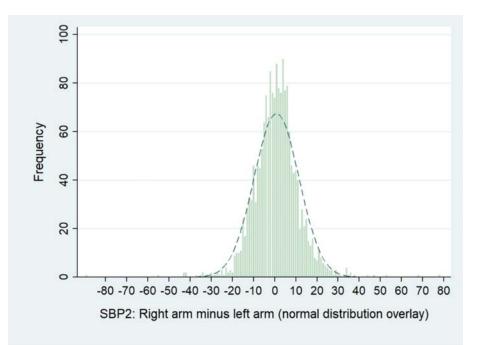


Figure 2. Distribution of the absolute difference between the right and the left arm systolic blood pressure for the second reading (Δ SBP2).

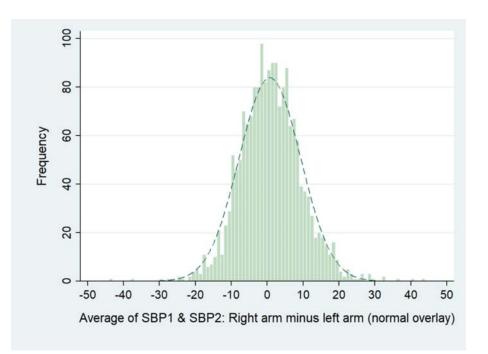


Figure 3. Distribution of the average absolute difference between the right and the left arm systolic blood pressure for the first reading (Δ SBP1) and the second reading (Δ SBP2).

distribution of IABPD in this population. The average IASBPD (Δ SBP) was 7 (4 – 10) mmHg, and the 95th percentile of the study population had Δ SBP of < 20 mmHg. The Δ SBP of < 20 mmHg was seen in the 95th percentile with a single reading that reaches up to a 97th percentile with a second reading, consistent with the findings from a large meta-analysis data.¹⁷

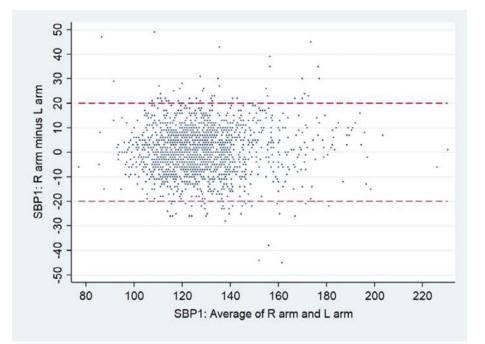


Figure 4. Bland – Altman comparison of first right and left arm systolic blood pressure (SBP1). Limits of agreement (reference range for difference): -19.209 - 20.518, mean difference: 0.654 (95% confidence interval, 0.195 – 1.114), range: 77.000 – 230.500, Pitman's test of difference in variance: r = 0.029, n = 1800, p = 0.218.

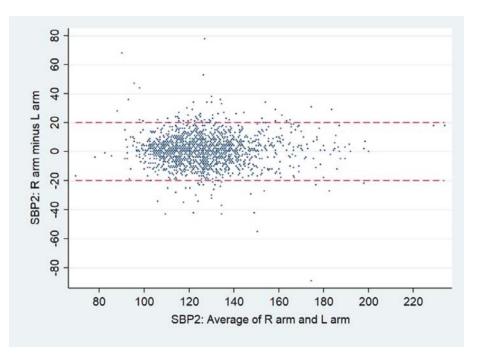


Figure 5. Bland – Altman comparison of second right and left arm systolic blood pressure (SBP2). Limits of agreement (reference range for difference): -20.470 - 22.117, mean difference: 0.823 (95% confidence interval, 0.331 – 1.316), range: 69.500 – 234.000, Pitman's test of difference in variance: r = -0.002, n = 1800, p = 0.948.

Considering a cutoff of IASBPD exceeding 10, 29.5% (95% CI 27.4% to 31.7%) of our study population has IASBPD exceeding Δ SBP > 10 mmHg. We noted a higher proportion of the patient population with

 Δ SBP > 10 mmHg compared with 13% that is reported by a survey conducted in a healthy adult population and 19% in ED patients.^{21,22} The difference noted could be due to the difference

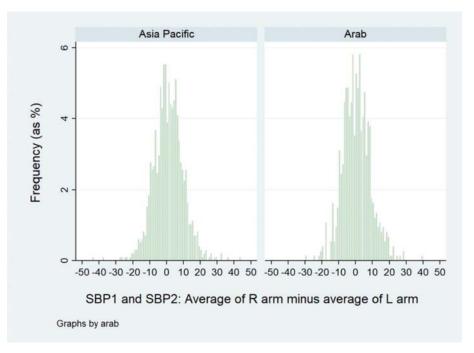


Figure 6. Distribution of the absolute average of the interarm systolic blood pressure (SBP) for patients from the Arab and Asia – Pacific regions. SBP1, SBP for the first reading; SBP2, SBP for the second reading.

in the measuring tool used in the study (a random zero sphygmomanometer)²² and the population characteristics (population-based survey²² and ethnically diverse young population in Qatar²¹). In a previous study by Grossman et al.¹² IABPD has been reported in a similar patient population of young healthy individuals and suggested that an IABPD of > 10 mmHg is not uncommon in young healthy patients.

A previous study conducted by Kristensen and Kornerup²³ suggested that the difference is more pronounced and significant in known hypertensive patients. However, considering the primary outcome of our study, we did not observe any SBP difference variation with increasing mean BP values in our study population. Similar results reported by Sharma and Ramawat²⁴ suggested that an IASBPD of < 10 mmHq is associated with risk factors such as cardiovascular diseases and endocrine/metabolic disorders. Clark et al.^{17,25} also reported that an IASBPD variation of > 10 mmHgis associated with an increased risk of cardiovascular mortality and overall mortality. However, considering a relatively younger population distribution of Qatar, we observed no statistically significant association between IASBPD and risk factors.

The CALIBRATE study has a set of limitations that should be taken into consideration. This study was conducted in a single ED in Qatar and observed a younger patient population with a mean age of 34 years. Our study has utilized a process of sequential BP monitoring using calibrated oscillometric BP devices. Although calibrated oscillometric BP devices reduce the potential of observer bias, a previous study by Fotherby et al.²⁶ revealed that simultaneous measurement of BP for IABPD reduces the variation in IASBPD in a given population and that sequential monitoring might increase the variance of IASBPD.²⁷

The importance of IABPD remains a crucial concern in an ED setting. Although studies have reported that an IABPD of > 10 mmHg is an important predictor of cardiovascular disease and all-cause mortality,^{2,28} these reports defined an elderly and more ethnically uniform population group. In an ethnically diverse young population, the observations and the associations of IABPD vary significantly, as observed in CALIBRATE. Further studies are required to define the normal distribution

of interarm BP in different ethnic groups and its association with factors that may directly or indirectly affect interarm BP.

CONCLUSION

In the population presenting to the ED, the IASBPD of at least 20 mmHg reached the 95th percentile, validating the known significant difference. The utility of SBP difference can be improved further by taking the average of two individual readings. No meaningful association could be detected between the significant IASBPD and the study variables such as age, demographics, regions of interest, and risk factors. Future studies are needed to validate the cutoff of > 20 mmHg SBP IABPD in ED patients suspected to have AD.

Conflicts of Interest

None Declared.

NOVELTY AND SIGNIFICANCE

What is new?

- 1 CALIBRATE focuses on measuring IASBPD for adult patients presenting to ED where IASBPD is clinically relevant in suspected AD cases.
- 2 This study included a large Asian and subAsian population with higher risk of cardiovascular disease pattern at relatively younger age.
- 3 The study was conducted in pragmatic approach relevant to ambulatory clinical practice.

What is relevant?

- 1 CALIBRATE is the first study in the region to assess the IASBPD in a large population group in an ED setting.
- 2 Study reported percentile data at 10, 15, and 20 mmHg IASBPD in this population, which is clinically important and shown to relate with patient-centered outcome in previous literature.
- 3 The study also assessed the difference between single measurements of IASBPD and repeated measure of IASBPD and reported the significance.

Summary

In our setting and population, the IASBPD of at least 20 mmHg reached at 95th percentile, validating the known significant difference. No meaningful association could be detected between the significant IASBPD and age,

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demographics, regions of interest, and risk factors. The utility of SBP difference can be improved further by taking the average of two individual

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