Relationship between Inter-Arm Blood Pressure Difference (IAD) and severity of Coronary Artery Disease.

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Abstract:

Aims & Objectives:
Patients of coronary artery disease (CAD) present with raised blood pressure (BP), especially increased systolic blood pressure (SBP) due to atherosclerosis. Inter-arm blood pressure difference (IAD) in SBP of more than 10 mm Hg is considered abnormal. Measuring BP is a simple technique that requires nothing except for a sphygmonanometer, its investigative usefulness for CAD and relationship with future cardiovascular endpoints.
remains unidentified. Clinically, measuring IAD and ankle-brachial index (ABI) may be used to quantify atherosclerosis. Hence, we aimed to define the prevalence of significant IAD in patients with suspected CAD and to assess the relationship of IAD and ABI with the severity of CAD. **Materials & methods:** We recruited 106 subjects of both sexes between 25-75 years, posted for coronary angiography on the clinical suspicion of CAD with at least one cardiac risk factor/ an abnormal ECG. Standard procedure and formula were used to measure BP, ABI and calculate IAD. The Gensini score was used to assess the extent and severity of CAD. Coronary risk factor evaluation was done using the subject’s clinical, biochemical and anthropometric data.

**Results:** Severe CAD was established in 56.1% based on Gensini score. The mean systolic IAD (15.17±0.43 mm Hg) was above the normal cut off of = 10 mmHg. Whereas the mean diastolic IAD and ABI were within normal limits. A strong positive correlation existed between Gensini scoring and systolic IAD (p =0.0001, r =0.442).

**Conclusions:** Systolic IADs were significantly increased in symptomatic CAD patients and correlated with its severity. Thus assessing IAD may facilitate risk stratification and help reduce adverse events in CAD patients.

**Keywords:** Coronary artery disease, Blood pressure, Inter-arm difference, Ankle-brachial index.


**INTRODUCTION**

An increase in the inter-arm systolic blood pressure difference can be easily identified during routine clinical examination. Generally, the right arm blood pressure (BP) is a few mm of mercury higher than that of the left arm.\(^1\) However, a difference in systolic BP of more than 10 mm Hg between arms is considered abnormal. For many years, Hypertension society guidelines have recommended routine bilateral BP measurement \(^2\), nevertheless the adoption of the same in primary care practice is negligible till date.\(^3\) Similarly ankle brachial index (ABI) measurement is one of the less expensive and readily available markers for atherosclerosis in primary care setting. Several population-based cohort studies \(^4\text{--}5\); have already established a consistent relationship between low ABI and prevailing coronary artery disease (CAD) and cerebrovascular disease. Among the diseases related to atherosclerosis, coronary artery disease (CAD) is vitally important because of its high prevalence and mortality.\(^6\) According to a WHO survey, in India an alarming 24.8% people die annually due to various cardiovascular diseases, among which CAD is the leading cause.\(^7\)

Patients of CAD have increased arterial stiffness due to atherosclerosis. Thus the loss of arterial elastic properties paves way for increase in pressure oscillations, which is evidenced as an irregular rise in systolic BP.
with slight variation in diastolic BP.

Since the compliance of the conduit arteries differ along the arterial tree, it will be interesting to observe pressure fluctuations vary between the arms.\textsuperscript{[8]} Inter-arm BP difference (IAD) and ankle brachial index (ABI) may serve as a useful tool in quantifying systemic atherosclerosis and thus an abnormal IAD and ABI, is linked together with both atherosclerotic risk factors and imminent cardiovascular disease.\textsuperscript{[9-10]}

Although measuring blood pressure of all limbs with a sphygmomanometer is very simple, easy and cheap, its investigative utility for CAD and relationship with future cardiovascular endpoints remains largely unknown. Hence, the objective of defining the prevalence of significant inter-arm BP difference and ankle brachial index in patients with suspected CAD and assessing their relationship with severity of CAD, via the study.

**MATERIALS & METHODS**

**Study design area & duration**

This cross-sectional clinical investigation was done in the department of physiology in conjunction with the department of cardiology at SRM Medical College, Hospital & Research Centre, Potheri, Kattankulathur, for a period of two months.

**Ethical Consideration**

The study was started after getting approval from the institutional ethical committee (Ethics Clearance Number: 944/IEC/2016) and was conducted stringently following the ethical guidelines for biomedical research on human subjects by Central Ethics Committee on Human Research (CECHR), Indian Council of Medical Research (ICMR)- 2000 and those as contained in “Declaration of Helsinki”.

**Study subjects, sample size & Inclusion criteria**

Around 100 patients of both sexes aged between 25-75 years who were posted for coronary angiography on the clinical suspicion of having CAD with minimum of one cardiac risk factor or an irregularity in ECG such as ST depression, negative T wave, or left bundle branch block were registered for this study. All study participants were explained in detail about the study and written informed consent was obtained from all participants.

We arrived at a sample size of 100 as the Hospital census indicate an average of 3 procedures of coronary angiography per day, thus the investigator would able to complete around 100 patients in two months period (this was a pilot project approved by the ICMR under Short term studentship). In the given period we were able complete 106 subjects.

**Exclusion criteria**

Subjects with the following conditions were excluded from the study.

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- Patients with unstable angina or myocardial infarction within the previous 4 weeks
- History of coronary revascularization
- Chronic renal disease with haemodialysis
- Confirmed cases of peripheral arterial disease

**Assessment of inter-arm blood pressure difference**

Blood pressure was measured according to guidelines published by the Indian hypertension society and Association of Physicians of India (11) on admission. In brief, it was measured at the bilateral brachial artery in supine position after the participants rested for a minimum of 5 minutes, with a standard mercury sphygmomanometer. The examiner made sure that appropriate size cuffs were used, each arm is well supported during measurements, free of clothing, and took recording only after the study subject seemed completely calm and comfortable. Measurements were taken twice in both arms in an interchanging sequence: right arm, left arm, right arm and left arm. The average mean systolic BP for each arm was then used to calculate the inter-arm difference (mean of left arm was subtracted from mean of right arm) and any value more than 10 mmHg was considered as an abnormal IAD.

**Measurement of ankle-brachial pressure index**

The ankle-brachial index (ABI) is the ratio between the systolic BP measured at the ankle and systolic BP measured at the brachial artery. The ABI indicates degree of severity of atherosclerosis in the legs, this index was at first offered for the non-invasive diagnosis of lower-extremity peripheral artery disease (PAD). (12-13) In recent years ABI has gained lime light as a predictive marker for adverse cardiovascular events and functional deficiency since it can be used an independent indicator to quantify atherosclerosis at other vascular beds, even without symptoms of PAD. (14-16)

Measurement of ABI was done in the subjects who has refrained from smoking at least 2 hours prior to testing in supine position after 5-10 minutes of complete physical and mental rest with head and heels support, at ambient room temperature of 25-27 °C. An adequately sized inflatable cuff was placed around the ankle with the lower edge of the cuff 2 cm above the superior aspect of the medial malleolus and the pressure was measured at both the dorsalispedis and posterior tibial arteries using a hand-held continuous-wave Doppler probe (8-10 MHz). The probe was manipulated near the area of pulse until a clear signal was heard, at a 45° to 60° angle to the surface of the skin. The same technique was utilized for measuring brachial artery pressure in both arms. The patient reminded still during the entire period of measurement. In people with healthy lower limb arterial circulation, the systolic pressure at the ankle is normally 10-15 mmHg higher than that recorded.
from the arm because pulse wave increases as it travels down from the heart leading to an ABI >1.10. The greater value of the two ankle pressures was used to take a ratio with the brachial artery pressure. Thus, ABI was calculated by taking ratio of the highest pressure in the leg with highest pressure in the arm. Reproducibility of the ABI measurement appeared to be good. We defined PAD as ABI < 0.9 in either leg, as reported previously. [17]

Assessing severity of Coronary artery disease (CAD)

After performing a coronary angiography, a trained cardiologist who was blinded to the study quantified the extent and severity of CAD using the Gensini score.[18] Gensini scoring is a validated measure of angiographic severity of CAD.[19] Gensini Score (GS) is a commonly utilized angiographic scoring system for calculating the extent and severity of CAD.

GS characterizes CAD taking into account 3 main parameters for each coronary lesion: severity score, region multiplying factor and collateral adjustment factor. A coronary lesion is considered significant when it causes ≥1% reduction in luminal diameter by visual assessment. The severity of the lesion is indicated by using a score of 1 to 32. 1 indicating and obstruction of 1–25%, 2 being 26-50%, with subsequent doubling of score for 75-90-99-100% obstruction. Thus, the severity score for each lesion may vary from 1 to 32. A multiplying factor was used to each lesion score based upon its location in the coronary tree, keeping in mind the functional significance of the area supplied by that segment. A collateral adjustment factor was used for those segments that were totally or 99% occluded, thus the final GS is the total of all the lesion scores. [20]

Assessment of coronary risk factors

Clinical and anthropometric data was collected from study participants. BMI (Body Mass Index) was calculated after recording patient’s weight in kilograms and height in meters, both rounded to the nearest whole number and taking the ratio of Weight (in kgs) to Height (in mt²). Risk factors included in the assessment were hypertension, hypercholesterolemia, diabetes mellitus, cigarette smoking, and family history of coronary artery disease. Hypertension was defined as systolic blood pressure≥140mmHg or a diastolic blood pressure ≥90mmHg or documented hypertension on at least two occasions in the outpatient department. Hypercholesterolemia was defined as fasting serum low-density lipoprotein cholesterol ≥ 140 mg/dL and/or triglycerides ≥ 150 mg/dL or high-density lipoprotein cholesterol ≥ 40 mg/dL, or those who are receiving lipid-lowering therapy.[21] Diabetes mellitus was diagnosed using the criteria proposed by Indian council of medical research guidelines for management of Type 2 diabetes – 2018.
STATISTICAL ANALYSIS

Data was entered and statistical analysis was done using SPSS version 21. Continuous measures were summarized using mean and standard deviation. Categorical variables were summarized by using percentages. Multivariate analysis with logistic regression and Pearson’s correlation were used to identify the relationship between inter-arm BP difference as well as ABI with severity of CAD. P-value less than 0.05 will be considered significant.

RESULTS

We measured inter-arm blood pressure difference, ankle brachial index and performed coronary angiography (CAG) in 106 stable patients with clinical suspicion of CAD. Following CAG, Gensini scoring was calculated to assess the severity of CAD. Subjects with score of 40 and above were considered to have severe CAD. We assessed clinical variables significantly associated with CAD according to simple logistic regression analysis. The following tables summarize our study findings.

Table 1: Clinical characteristics of study population

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean (n=106)</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(Years)</td>
<td>57.49</td>
<td>0.68</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>77/23</td>
<td></td>
</tr>
<tr>
<td>BMI(Kg/m^2)</td>
<td>24.20</td>
<td>0.22</td>
</tr>
<tr>
<td>Pulse rate(min)</td>
<td>80.47</td>
<td>1.17</td>
</tr>
<tr>
<td>Right SBP(mmHg)</td>
<td>130.61</td>
<td>1.92</td>
</tr>
<tr>
<td>Left SBP(mmHg)</td>
<td>114.94</td>
<td>1.36</td>
</tr>
<tr>
<td>IAD-SBP(mmHg)</td>
<td>15.17</td>
<td>0.43</td>
</tr>
<tr>
<td>Right DBP(mmHg)</td>
<td>83.33</td>
<td>1.27</td>
</tr>
<tr>
<td>Left DBP(mmHg)</td>
<td>80.57</td>
<td>1.28</td>
</tr>
<tr>
<td>IAD-DBP(mmHg)</td>
<td>2.67</td>
<td>0.29</td>
</tr>
<tr>
<td>ABI</td>
<td>1.008</td>
<td>1.02</td>
</tr>
<tr>
<td>Gensini score (mean)</td>
<td>73.9</td>
<td>12.1</td>
</tr>
</tbody>
</table>
BMI- Body mass index, SBP- Systolic blood pressure, DBP- Diastolic blood pressure, IAD- Inter-arm difference, ABI- Ankle brachial Index, M-Male, F-Female & SE- Standard error.

Table 1 shows the clinical characteristics of our study population. Severe CAD was established in 56.1% of the total study population as they had a score above 40. It is important to note that the mean systolic IAD (15.17±0.43) was above the normal cut off of ≤ 10 mmHg. However the mean diastolic IAD and ABI were within normal limits.

A look at the CVD risk factors as summarized in table 2, of the total patients 33.1% were above the age of 60 years, 81.65 were males, 83.7% had hypertension, 63.6% had diabetes mellitus, 69% had dyslipidemia, 25.4% were obese, 60.4% had family history of CVD and 22.2% were smokers.

Table2: Prevalence of CVD risk factors among study participants

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Percentage (%), n=106</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (above 60 Years)</td>
<td>33.1%</td>
</tr>
<tr>
<td>Male gender</td>
<td>81.6%</td>
</tr>
<tr>
<td>Obesity</td>
<td>25.4%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>63.1%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>83.7%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>63.6%</td>
</tr>
<tr>
<td>Smoking</td>
<td>22.2%</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>60.4%</td>
</tr>
</tbody>
</table>

Table: 3 Pearson correlations between Gensini score, IAD and ABI

<table>
<thead>
<tr>
<th></th>
<th>p value</th>
<th>correlation coefficient (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAD-SBP(mmHg)</td>
<td>0.0001</td>
<td>0.442</td>
</tr>
<tr>
<td>IAD-DBP(mmHg)</td>
<td>0.827</td>
<td>0.025</td>
</tr>
<tr>
<td>ABI</td>
<td>0.103</td>
<td>-0.185</td>
</tr>
</tbody>
</table>

SBP- Systolic blood pressure, DBP- Diastolic blood pressure, IAD- Inter-arm difference, ABI- Ankle brachial Index
Table 3 gives an overview of the person correlations between severity of CAD as assessed by Gensini scoring and IAD as well as ABI. It is seen that there is a strong positive correlation between Gensini scoring and systolic IAD, thus clearly establishing an association between IAD & severity of CAD (Fig:1, p =0.0001, r =0.442).

With increase in systolic IAD the severity of CAD also increases proportionally. We could not establish a similar association between diastolic IAD and Gensini score (Fig:2) and also the diastolic IAD of our patient population was well within the normal range. Similarly, we could not establish a relationship between ABI and Gensini score (Fig:3)

Fig: 1 Correlation between severity of CAD and systolic Inter-arm blood pressure difference (Pearson correlation coefficient, r = 0.442, p = 0.0001)
Fig: 2 Correlation between severity of CAD and diastolic Inter-arm blood pressuredifference (Pearson correlation coefficient, $r = 0.025$, $p = 0.827$)
The important observations established by the present study are as follows: A significantly raised systolic inter-arm blood pressure difference (IAD) exists in subjects with coronary artery disease (CAD). This increased IAD correlates with the severity of CAD (Fig: 1), the association remained even after controlling other CVD risk factors. IAD is a better indicator of severity of CAD as compared to ABI as we could not establish a significant association between Gensini score and ABI (Fig: 3). The severity of CAD was established using Gensini score. This is one of the few studies that explore the prevalence of IAD in patients with CAD and its relationship with severity of CAD, especially in Indian subcontinent.

Our results are in accordance with several studies reported from the western countries. The inter-arm difference between the systolic BP recorded from the two arms is caused by both anatomical and hemodynamic factors.
Multiple disease processes like atherosclerosis, vasculitis, radiation arteritis, fibromuscular hyperplasia, thoracic outlet compression, connective tissue disorders, dissecting aortic aneurysm, and congenital abnormalities account for raised inter-arm BP differences. However, in the lack of anatomic impediment, it has been hypothesized that the inter-arm difference in systolic BP is linked to some intrinsic property of the cardiovascular system. Variations in arterial compliance can be one reason for the inter-arm difference in systolic BP. Arterial flow is predominantly controlled by resistance vessels, as resistance increases there is an increase in mean pressure, with an equal increase in systolic and diastolic BP. Nevertheless, the blood pressure waveform augments as it travels distally from the heart, accounting for a progressive increase in SBP and a decrease in diastolic blood pressure in the arms and legs compared to aorta. However, when there is a loss of compliance (increased arterial stiffness), pressure oscillations increase resulting in an unbalanced increase in systolic BP and little change in diastolic BP. As the elastic properties of conduit arteries vary along the arterial tree, it is easy to appreciate the different pressure oscillations between the arms resulting in different recorded systolic BP. This also explains the reason for normal IAD for diastolic blood pressure (Table: 1) in our subjects and thus we were not able to establish any association between diastolic IAD and severity of CAD (Fig: 2).

Cumulatively, these evidences clearly suggest there is risk of future cardiovascular events in subjects with symptomatic CAD and the recognition of IAD by the primary care physician becomes an important part of the risk assessment in such patients.

**LIMITATIONS OF THE STUDY**

The patient population of the current study had increased likelihood of CAD on clinical grounds thus in the general population, the reported incidence of inter-arm pressure difference of 7% may actually be less than what we found.

**SUMMARY & CONCLUSION**

This study investigated the importance of inter-arm blood pressure measurements and its association with severity of CAD, and the findings have several important implications. Most importantly, the results of this study indicated that inter-arm blood pressure measurements have a clinically important role to play. If both brachial blood pressures are measured during sphygmomanometric measurement, and an imbalance is recognized, it warrants a strict follow up of the patient to avoid future cardiovascular events. Moreover, measuring of the inter-arm blood pressure difference is a easy routine clinical index that can suggest the existence and severity of CAD.
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