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Original Article

Invasive Assessment of Central Aortic Blood Pressure, Differential Impact of Beta Blocker vs. Non-Beta Blockers and their Correlation with Severity of Coronary Artery Disease in Hypertensive Patients Undergoing Coronary Angiography

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ABSTRACT

Background: Non-invasively measured brachial arterial pressure is accepted as the standard method for blood pressure measurement. However, systolic pressure varies throughout the arterial tree such that central systolic pressure is actually lower than corresponding brachial pressure. The aim of the study was to evaluate the differential effects of commonly used antihypertensive drugs on central aortic pressure measured invasively. **Methods and Results:** This was a prospective, single-centre and observational study. During the time period November 2009 to November 2010, a total of 170 patients with chronic stable angina and systemic hypertension were enrolled. Detailed medical history and physical examinations were performed. Laboratory investigations were noted. Brachial and central aortic pressures were recorded and compared. Demographic and clinical parameters were comparable among patients in different antihypertensive therapy groups. Mean systolic blood pressure (SBP) difference and mean pulse pressure (PP) ratio values between beta blocker and non-beta blocker groups were significantly different, (p<0.0001) and (p=<0.0001) respectively. Mean central SBP difference and mean pulse pressure ratio values between beta blocker arm and beta blocker combination groups arm were significantly different too, (p <0.0001 and p=0.0005 respectively). Mean SBP difference and mean PP ratio were also significantly different for beta blocker monotherapy as compared with non-beta blocker drugs individually. In each antihypertensive therapy group, moderate and severe coronary artery disease groups had significantly higher central PP levels. **Conclusion:** Different classes of antihypertensives have differential impact on central blood pressures. Central systolic and pulse pressures cannot be inferred accurately from brachial blood pressures. Thus, there is potential for under treatment or overtreatment of hypertension based on brachial blood pressure targets.
Key words: Antihypertensives, Coronary artery disease, Central aortic blood pressure, Coronary angiography, Systemic hypertension.

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INTRODUCTION

Hypertension is a major risk factor of cardiovascular disease. It is defined as prolonged elevation of brachial blood pressure.[1] Systolic pressure is usually amplified when measured peripherally. Hence, brachial pressure measured in clinical practice does not reflect true blood pressure.[2] Instead, central aortic pressure reflects cardiac afterload and perfusion and is therefore a better indicator of cardiovascular outcomes.[1] Blood pressure lowering effect of different antihypertensive drugs may be accurately assessed from central aortic pressure.[3] It has further been indicated that central aortic blood pressure is superior in predicting patient outcome compared to corresponding peripheral arterial pressure.[1] Previous studies have suggested that different antihypertensive drug classes have different effects on central aortic pressure despite similar effects on brachial arterial blood pressure.[4-6] This may be an important reason for different clinical outcomes with various classes of antihypertensives. Beta blockers are associated with higher stroke rates compared with other commonly used antihypertensives.[7,8] This may be because beta blockers despite reducing brachial arterial blood pressure adequately, fail to reduce central aortic blood pressure to the same extent as other antihypertensives.

Major studies such as the Conduit Artery Function Evaluation (CAFE) study,[3] a sub study of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT),[8] have used non-invasive radial or carotid tonometry to acquire waveforms to derive central aortic pressure. Only a few studies have used invasive direct measurements of central aortic pressure, acquired during routine diagnostic cardiac catheterization. So we proposed this study (i) to evaluate effects of commonly used antihypertensive drugs on central aortic pressure measured invasively, (ii) to study whether central aortic pressure is reduced to lesser extent with beta blockers compared to other antihypertensive drugs, (iii) to study whether beta blocker and other antihypertensive drug combinations can reduce central blood pressure to a greater extent than that achieved with beta blockers monotherapy and (iv) to study the relation between central PP and CAD severity

MATERIALS AND METHODS

Study design and population

A single-centre, observational, cross-sectional study was conducted at our tertiary-care centre in India between November 2009 and November 2010. Patients with chronic stable angina and systemic hypertension admitted for coronary angiography (CAG) were screened for enrolment. Inclusion criteria were: (i) normal left ventricular ejection fraction (LVEF) by echocardiography, i.e. LVEF ≥50% and (ii) ongoing therapy with beta blocker only or another antihypertensive monotherapy (angiotensin converting enzyme inhibitor [ACEI]/ angiotensin receptor blocker [ARB]/ dihydropyridine type of calcium channel blocker [CCB]/ diuretic) or beta blocker + another antihypertensive (ACEI/ARB/CCB/ diuretic) drug for at least three months. Exclusion criteria were: (i) patients with hypertensive urgency (i.e. SBP>180 mmHg or DBP>110

mmHg); (ii) patients with acute coronary syndrome (ACS) (ST-segment elevation myocardial infarction [STEMI]/non-STEMI/unstable angina) and (iii) ongoing therapy with drugs from three or more antihypertensive classes. Patients were categorized into three groups according to the class of the ongoing antihypertensive drug. These groups were: (i) beta blocker (BB Arm) monotherapy (n=49); (ii) non-beta blocker (NBB Arm) monotherapy such as ACEI (n=4)/ARB (n=6)/ CCB (n=8)/diuretic n=0) and (iii) combination of beta-blocker with another antihypertensive (CBB Arm) (n=103). All patients were on statins and antiplatelets. Written informed consent was obtained from each patient prior to the start of the study.

Laboratory investigations

All patients underwent detailed history and physical examination. Routine blood investigations included hemoglobin, total leucocyte count, differential leukocyte count, blood urea, serum creatinine, serum sodium/potassium and random blood sugar tests. Serum lipid profile was also investigated. 2-D echocardiography was performed to identify patients with LVEF >50%, which was the inclusion criteria. Nitrates have short duration of action. Hence, patients prescribed nitrates were not administered nitrates on the day of CAG in order to eliminate any confounding effect on blood pressure. Only a few patients complained of angina during CAG so they were administered sublingual nitrate after measurement of central aortic pressure and brachial arterial pressure.

Blood pressure assessment

Brachial blood pressure was measured in triplicate in the right arm using a mercury sphygmomanometer cuff. The patient was rested in a seated position for 5 min before assessment of BP. Diastolic pressure was recorded on disappearance of Korotkoff sounds. The average of the three measurements was recorded as brachial systolic and diastolic blood pressure. Pulse pressure was calculated as the difference between brachial systolic and diastolic pressures.

Central aortic pressures were recorded while performing CAG in the catheterization laboratory. CAG was performed through femoral (mostly) or radial approach. Before CAG was performed, central aortic systolic and diastolic pressures were recorded with the angiographic catheter tip in the ascending aorta. The distal end of the angiographic catheter was connected to the transducer dome (Medex Medical Ltd., Haslingden, Lancashire, UK) in order to ensure no air remained inside the pressure line. Central aortic systolic and diastolic blood pressures were recorded from the aortic pressure waveforms that appeared on the display monitor

Data collection and analysis

Demographic and clinical profiles of the patients were compared between the groups to assess whether parameters were comparable. Pulse pressure (PP) was calculated as SBP-DBP for brachial and central blood pressures. Central PP and brachial PP were calculated. SBP difference was calculated as brachial SBP-central SBP. This value denotes the amount of blood pressure augmentation that occurs when the pressure wave travels from central aorta to the brachial vasculature. PP ratio was calculated by dividing brachial PP with central PP (i.e. central PP: brachial PP). These observed and calculated hemodynamic data were compared between different groups of patients.

Coronary artery disease (CAD) correlation assessment

The relation of central PP to CAD severity was assessed. Severity of CAD was determined on the basis of maximum coronary stenosis assessed visually by two cardiologists at the time of coronary angiography. Patients with mild CAD were excluded as atherosclerotic disease is unlikely to significantly affect aortic stiffness and thus the central pulse pressure. The groups formed were: (i) normal coronary (n=19,); (ii) moderate CAD: 50%–89% stenosis (n=71) and (iii) severe CAD: ≥90% stenosis (n=36). As antihypertensive drugs also affect central blood pressure differentially, we studied the blood pressure values among groups of different CAD severity separately in 'BB group', 'NBB group' and 'CBB group'. The blood pressure values of moderate CAD group and severe CAD group were compared with those of normal coronary group.

Statistical analysis

The statistical evaluation of data was done using the Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 12. Continuous variables are expressed as mean ± standard deviation and discrete variables as percentages. Continuous variables were compared using Student t test. Categorical variables were compared using either Chis-square test or Fisher exact test. A p value of <0.05 was considered as statistically significant and an adjusted odds ratio with 95% confidence interval was used for assessment.

RESULTS

This study recruited 212 patients. Prior to data analysis 42 patients were excluded. Out of these, 21 patients had uncontrolled blood pressure, 9 patients had low hemoglobin and 12 patients had raised serum creatinine. The study flow is depicted in **Figure 1.**

Demographic characteristics

The mean age for the BB, NBB and CBB groups were 55.06, 56.29 and 55.64 years, respectively. Males contributed to 39 (79.6%), 12 (66.7%) and 74 (71.8%) patients in BB, NBB and CBB groups, respectively. Diabetes was the most prevalent risk factor in all groups with 14 (28.6%), 5 (27.8%) and 35 (34.0%) patients in BB, NBB and CBB groups, respectively. Mean height, weight, body mass index (BMI), total cholesterol, glucose and creatinine levels did not differ much among the groups. The demographic characteristics of the study population are detailed in Table 1.

Hemodynamic data

Comparison of hemodynamic parameters between all three study groups after treatment

Heart rate, brachial SBP, brachial DBP, brachial PP, central SBP, central DBP and central PP were comparable among all the groups. Significant SBP difference was observed for BB vs. NBB arm (p <0.0001) and the

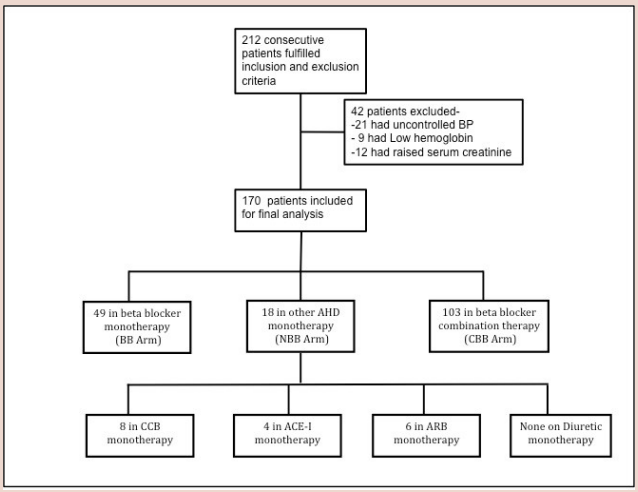

Figure 1: Study flow chart.

Table 1: Baseline demographic profile of various study groups.

Characteristic	BB Arm (*n*=49)	NBB Arm (*n*=18)	CBB Arm (*n*=103)
Age (mean ± SD, years)	55.06	56.29	55.64
<60, n (%)	38 (77.6%)	11 (61.1%)	69 (70.0%)
≥60, n (%)	11 (22.4%)	7 (38.9%)	34 (33.0%)
Male, n (%)	39 (79.6%)	12 (66.7%)	74 (71.8%)
Diabetes, n (%)	14 (28.6%)	5 (27.8%)	35 (34.0%)
Smoker, n (%)	14(28.6%)	4 (22.2%)	31(30.1%)
Alcohol intake, n (%)	6 (12.2%)	2 (11.1%)	8 (7.7%)
Height (cm)	156.3	160.2	155.3
Weight (kg)	65.4	66.7	66.1
BMI (kg/m^2)	28.9	25.8	27.5
Total cholesterol (mg/dL)	126	115	121
Glucose (mg/dL)	112	109	113
Creatinine (mg/dL)	0.8	0.9	1.0

Values are expressed as mean ± SD.

BB–Beta blocker monotherapy, BMI–Body mass index, CBB–Beta blocker combination therapy, NBB–Non-beta blocker monotherapy.

BB vs. CBB arm, (p <0.0001). A significant difference was also observed in PP ratios for BB vs. NBB arm (p <0.0001) and BB vs. CBB arm, (p <0.0005). Hemodynamic parameters between all three study groups along with the p values are demonstrated in Table 2.

Comparison of hemodynamic parameters between beta blocker monotherapy and various antihypertensive drugs individually

No significant difference was observed in heart rate, brachial SBP, brachial DBP, brachial PP, central SBP, central DBP and central PP among all the groups. Significant SBP difference was observed for BB vs. CCB arm (p <0.0001), BB vs. ACEI arm, (p <0.0001) and BB vs. ARB arm (p <0.0001). A significant difference was also observed in PP ratios for BB vs. CCB arm (p=0.001), BB vs. ACEI arm, (p=0.001) and BB vs. ARB arm (p=0.001). Compared hemodynamic profile between various anti-hypertensive drugs monotherapy and the p values are presented in Table 3. SBP difference of study groups after treatment is depicted in Figure 2.

Comparison of hemodynamic profile between patients with normal coronaries and, moderate and severe of CAD on beta blocker monotherapy

No significant difference was observed in heart rate, brachial SBP, brachial DBP, brachial PP, central SBP and central DBP among all the groups. Central PP was significantly for normal coronaries vs. moderate CAD (p=0.01), normal coronaries vs. severe CAD, (p=0.05) and moderate CAD vs. severe CAD (p=0.01). A significant difference was also observed in PP ratios for normal coronaries vs. moderate CAD (p<0.0001), normal vs. severe CAD, (p<0.0001) and moderate CAD vs. severe CAD (p<0.0001). Comparison of hemodynamic profile between groups and the p values are detailed in Table 4 and illustrated Figure 3.

Comparison of hemodynamic profile between patients with normal coronaries and moderate CAD on non-beta blocker monotherapy

No significant difference was observed in heart rate, brachial SBP, brachial DBP, brachial PP, central SBP, central DBP, central PP and PP ratios between patients with normal coronaries and moderate CAD on non-beta blocker monotherapy. Compared hemodynamic parameters between the groups are demonstrated in Table 5 and illustrated Figure 4.

Comparison of hemodynamic profile between patients with normal coronaries and patients with moderate CAD on beta blocker combination therapy

No significant difference was observed in heart rate, brachial SBP, brachial DBP, brachial PP, central SBP and central DBP among all the groups. Central PP was significantly lower for normal coronaries vs. moderate CAD (p=0.009), normal coronaries vs. severe CAD, (p=0.0004) and moderate CAD vs. severe CAD (p=0.08). A significant difference was also observed in PP ratios for normal coronaries vs. moderate CAD (p=0.006) and normal vs. severe CAD, (p=0.002). The hemodynamic parameter between the groups and the p values are given in Table 6 and illustrated in Figure 5.

Table 2: Comparison of hemodynamic parameters between all study groups after treatment.

Parameter	BB Arm (*n*=49)	NBB Arm (*n*=18)	CBB Arm (*n*=103)	*P* Value (BB vs NBB)	*P* Value (BB vs CBB)	*P* Value (NBB vs CBB)
Heart rate (bpm)	64.6±4.5	63.2±4.9	64.5±3.4	0.27	0.88	0.16
Brachial SBP (mmHg)	131.4±13.0	129.3±15.8	137.2±14.2	0.58	0.04	0.03
Brachial DBP (mmHg)	79.8±5.9	78.3±7.0	82.3±7.9	0.87	0.05	0.04
Brachial PP (mmHg)	51.2±9.9	51.5±10.0	54.5±12.3	0.91	0.10	0.30
Central SBP (mmHg)	125.7±12.8	119.3±14.1	127.7±13.9	0.04	0.39	0.02
Central DBP (mmHg)	80.8±6.0	78.8±6.7	82.7±7.3	0.24	0.11	0.03
Central PP (mmHg)	44.2±10.5	39.5±9.4	45.3±12.0	0.10	0.58	0.05
SBP difference (mmHg) (Brachial SBP- Central SBP)	5.7±2.1	10.0±2.4	9.5±1.8	<0.0001	<0.0001	0.30
PP ratio	1.15±0.10	1.30±0.08	1.20±0.07	<0.0001	0.0005	0.99

Values are expressed as mean ± SD.

BB–Beta blocker monotherapy, Bpm–beats per minute, CBB–Beta blocker combination therapy, DBP–Diastolic blood pressure, NBB–Non-beta blocker monotherapy, PP–pulse pressure, SBP–Systolic blood pressure.

Table 3: Comparison of hemodynamic parameters between beta blocker group with monotherapy of various antihypertensive drugs.

Parameter	BB Arm (n=49)	CCB (*n*=8)	ACEI Arm (*n*=4)	ARB Arm (*n*=6)	*P* Value (BB vs CCB)	*P* Value (BB vs ACEI)	*P* Value (BB vs ARB)
Heart rate, bpm	64.6±4.5	65.3±3.9	66.1±4.1	65.6±4.2	0.60	0.60	0.60
Brachial SBP (mmHg)	131.4±13.0	134.1±12.1	130.2±10.2	130.1±12.7	0.82	0.82	0.82
Brachial DBP (mmHg)	79.8±5.9	82.2±6.2	80.4±6.7	80.3±7.1	0.84	0.84	0.84
Brachial PP (mmHg)	51.2±9.9	51.9±7.8	49.8±8.8	49.8±7.2	0.73	0.73	0.73
Central SBP (mmHg)	125.7±12.8	124.0±11.0	120.0±13.2	120.1±13.7	0.32	0.32	0.32
Central DBP (mmHg)	80.8±6.0	81.2±5.9	80.1±6.0	82.0±4.7	0.63	0.63	0.63
Central PP (mmHg)	44.2±10.5	42.8±11.2	39.9±12.2	38.1±8.9	0.17	0.17	0.17
SBP difference (mmHg) (Brachial SBP- Central SBP)	5.7 ± 2.1	10.1±2.4	10.2± 2.1	10.0±1.8	<0.0001	<0.0001	<0.0001
PP ratio	1.15 ± 0.10	1.21±0.07	1.24± 0.09	1.30± 0.09	0.001	0.001	0.001

Values are expressed as mean ± SD.

ACEI–Angiotensin converting enzyme inhibitors, ARB– angiotensin receptor blocker, BB–Beta blocker monotherapy, Bpm–beats per minute, CBB–Beta blocker combination therapy, DBP–Diastolic blood pressure, NBB–Non-beta blocker monotherapy, PP–pulse pressure, SBP–Systolic blood pressure.

Table 4: Comparison of hemodynamic profile between patients with normal coronaries and, moderate and severe of CAD on beta blocker monotherapy.

Parameter	Normal coronaries (*n*=5)	Moderate CAD (*n*=20)	Severe CAD (*n*=10)	*P* Value (Normal coronaries vs Moderate CAD)	*P* Value (Normal coronaries vs Severe CAD)	*P* Value (Moderate CAD vs Severe CAD)
Brachial SBP (mmHg)	122.0±14.4	134.7±14.2	131.0±14.5	0.08	0.27	0.08
Brachial DBP (mmHg)	75.2±7.5	82.0±7.6	80.0±7.5	0.08	0.26	0.08
Brachial PP (mmHg)	46.8±12.2	52.7±12.1	49.0±12.2	0.34	0.74	0.34
Central SBP (mmHg)	113.6±14.0	129.9±13.9	124.6±14.2	0.02	0.17	0.02
Central DBP (mmHg)	76.4±7.0	83.3±7.0	80.0±7.1	0.06	0.36	0.06
Central PP (mmHg)	30.4±12.0	46.6±12.1	44.6±12.0	0.01	0.05	0.01
PP ratio	1.73±0.18	1.13±0.18	1.10±0.18	<0.0001	<0.0001	<0.0001

Values are expressed as mean ± SD.

CAD-Coronary artery disease, DBP–Diastolic blood pressure, PP–pulse pressure, SBP–Systolic blood pressure.

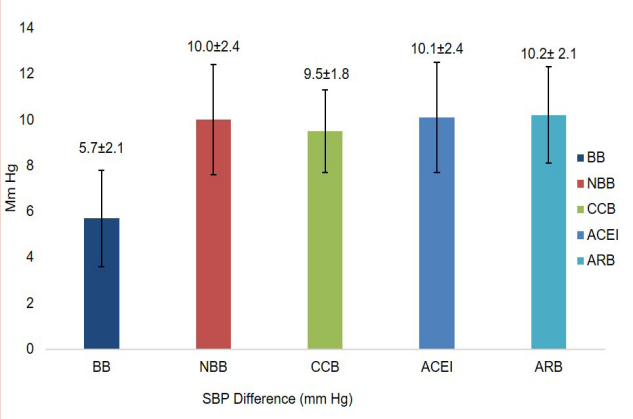

Figure 2: SBP difference of study groups after treatment. [BB- Beta blocker-;NBB- non beta blocker; CCB- Calcium channel blocker; ACEI- ACE inhibitor; ARB- Angiotensin receptor blocker].

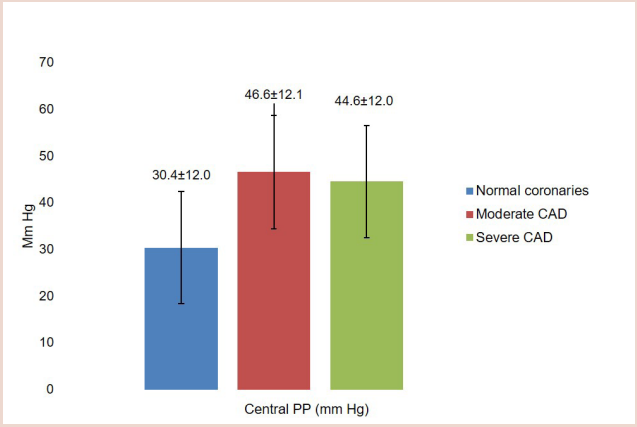

Figure 3: Central PP of patients with normal coronaries, moderate and severe CAD on beta blocker monotherapy. [CAD-coronary artery disease; PP- Pulse pressure].

Table 5: Comparison of hemodynamic profile between patients with normal coronaries and moderate CAD on non-beta blocker monotherapy*.

Parameter	Normal coronaries (*n*=2)	Moderate CAD (*n*=7)	*P* Value (Normal vs. Moderate)
Brachial SBP (mmHg)	140.0±14.2	135.4±14.4	0.70
Brachial DBP (mmHg)	81.0±7.5	80.6±7.5	0.94
Brachial PP (mmHg)	59.0±12.2	54.8±12.2	0.68
Central SBP (mmHg)	129.0±14.0	123.1±14.1	0.59
Central DBP (mmHg)	85.0±6.9	80.0±7.0	0.40
Central PP (mmHg)	44.0±12.1	43.1±12.0	0.93
PP ratio	1.33±0.18	1.28±0.18	0.73

Values are expressed as mean ± SD. * -There was a single patient with severe CAD on non beta-blocker monotherapy & hence he was excluded during analysis.

CAD-Coronary artery disease, DBP–Diastolic blood pressure, PP–pulse pressure, SBP–Systolic blood pressure.

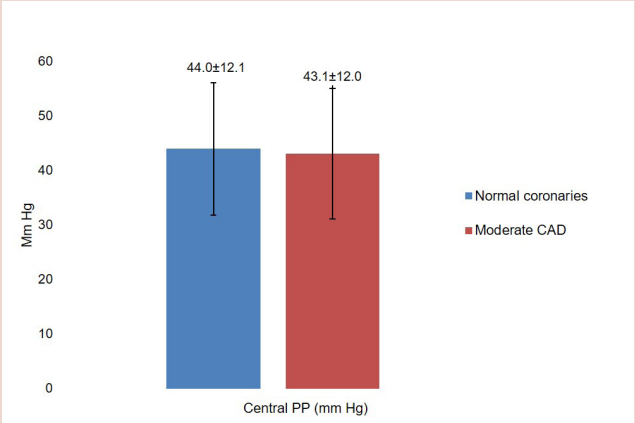

Figure 4: Central PP of patients with normal coronaries and moderate on non-beta blocker monotherapy. [PP- pulse pressure].

Table 6: Comparison of hemodynamic profile between patients with normal coronaries and patients with moderate and severe CAD on beta blocker combination therapy

Parameter	Normal coronaries (*n*=12)	Moderate CAD (*n*=44)	Severe CAD (*n*=25)	*P* Value (Normal coronaries vs Moderate CAD)	*P* Value (Normal coronaries vs Severe CAD)	*P* Value (Moderate CAD vs Severe CAD)
Brachial SBP (mmHg)	129.3±14.6	136.8±14.7	142.5±14.5	0.12	0.08	0.12
Brachial DBP (mmHg)	82.8±7.5	82.8±7.4	83.5±7.5	0.99	0.79	0.70
Brachial PP (mmHg)	46.5±12.2	53.9±12.3	58.2±12.5	0.07	0.05	0.17
Central SBP (mmHg)	118.8±14.3	127.2±14.3	133.8±14.1	0.07	0.02	0.07
Central DBP (mmHg)	84.8±7.1	82.9±7.0	83.5±7.1	0.40	0.60	0.73
Central PP (mmHg)	34.0±12.0	44.6±12.1	50.0±12.1	0.009	0.0004	0.08
PP ratio	1.37±0.18	1.21±0.17	1.16±0.18	0.006	0.002	0.25

Values are expressed as mean ± SD.

CAD-Coronary artery disease, DBP–Diastolic blood pressure, PP–pulse pressure, SBP–Systolic blood pressure

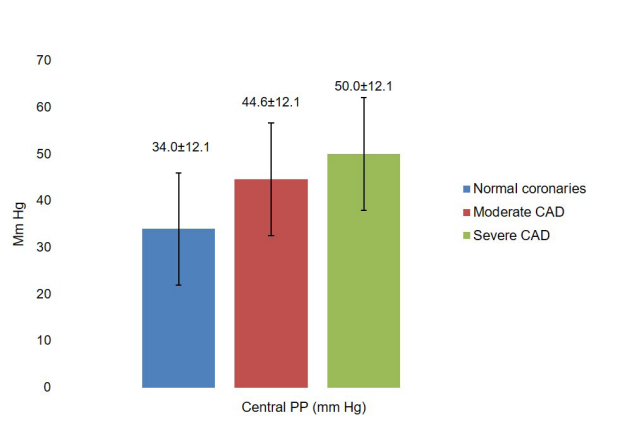

Figure 5: Central PP of patients with normal coronaries, moderate and severe CAD on combination beta blocker therapy. [CAD-coronary artery disease; PP- Pulse pressure].

DISCUSSION

In our study comprising of 170 patients, we compared invasively obtained central aortic pressures with non-invasively obtained brachial pressures. All patients had chronic stable angina with normal LVEF and underwent CAG at our institution, as it may not be ethically permitted to perform aortic catheterization in isolated hypertensive patients. Moreover, pure hypertensive patients may not give consent for invasive tests. Patients with ACS can have large fluctuation or variation of blood pressures due to hemodynamic stress or various medications. Hence, patients with ACS were excluded from the study.

SBP difference denotes the extent to which central SBP is lower than peripheral SBP. As diastolic blood pressure does not change across the arterial tree, the value of the PP ratio also indicates the extent to which central SBP is lower compared to peripheral SBP. In our study, it was observed that mean SBP difference and the mean PP ratio were significantly different from ACEI/ARB/CCB as compared to beta blocker therapy. This indicates that central aortic systolic and pulse pressures were reduced to greater extent with ACEI/ARB/CCB therapy as compared

to beta blocker therapy. Our findings are consistent with the data from previous large studies namely café,[3] LIFE[7] and ASCOT.[8] The CAFE[3] study has attributed this finding to increased pressure wave reflection from distal reflection sites. The Second Australian National Blood Pressure Trial[9] reported better prognosis for hypertensive subjects randomly assigned to an ACEI compared with a diuretic-based regimen despite no difference in brachial blood pressure control.

Interestingly, there is now convincing evidence that beta-blockers exert differential effects on brachial versus. central blood pressure, indicating that conventional beta-blockers lower central pressure to a lesser extent than brachial pressure. It should be noted that beta blockers provide anti-hypertensive action by decreasing cardiac output, inhibiting the release of renin and production of angiotensin II and blocking presynaptic α-adrenoreceptors. Conversely, beta-blockers also exhibit effects on glucose and lipid metabolism and their long-term hemodynamic effect of increasing peripheral resistance. This could explain the reason of beta blockers being less effective than other antihypertensive drugs in reducing central blood pressure as well as cardiovasvular outcomes.[10,11] However, it is also important to recognize that not all beta-blockers are identical. Atenolol is more hydrophilic betablocker and has short half-life of 6-9 hrs. Hence, it may not afford protection from life threatening arrhythmia's like lipophilic beta blockers (metoprolol) and give less protection against vascular remodelling compared to ACE inhibitors. Subsequent meta-analyses have pointed out that atenolol underperforms against other betablockers only in elderly or there is no difference.[12,13] Overall, the findings of the study indicate that diagnosis and management related treatment decisions in hypertensive patients should be based on central blood pressure, rather than brachial pressure.

Our study also compared beta blocker monotherapy with beta blocker + other antihypertensive combination therapy with respect to mean SBP difference and mean PP ratio. A significant difference in favour of combination therapy was observed. This observation may suggest that poor central SBP reduction caused by beta blockers may be further reduced by addition of ACEI/ARB/CCB. This finding contradicts the observation in the CAFE (4) study in which less central SBP reduction in the atenolol arm persisted throughout the CAFE study regardless of add-on therapy with thiazide diuretics. The relationship between CAD severity and brachial and carotid blood pressures has been previously studied by Waddell *et al.*[14] They observed significant differences in central PP between normal coronary, moderate and severe CAD groups. The study showed that carotid systolic blood pressures and carotid PP were more sensitive markers of CAD severity than brachial blood pressures. In their study, beta blockers were discontinued for 24 hrs before analysis. Our study was not able to achieve a statistically significant difference in central PP between moderate and severe CAD groups. This may possibly be justified by the fact that we failed to cease beta blocker and other antihypertensive drug therapies within sufficient time before blood pressure measurements.

The relationship of combination therapy (beta blocker+ other anti-hypertensive) and central aortic pressure needs further studies to reach a conclusion. If combination therapy reduces central blood pressures to a significantly greater extent than beta blocker monotherapy or to levels achieved with antihypertensive monotherapy, then we need not be concerned about the less central blood pressure reduction with beta blocker monotherapy. Whenever there is a compelling indication for beta blocker therapy, combination of beta blocker and ACEI/ARB/CCB should be preferred over beta blocker monotherapy for blood pressure control.

Moreover, it has been observed that ischemic threshold during a standard exercise stress test is lower in patients with stiffer aortas, independent of disease severity.[15] This data indicates that the risk of myocardial ischemia in CAD patients is related not only to the severity of coronary stenosis but also to aortic stiffness, which increases parallel to CAD severity. This suggests a reduction in large-artery stiffness and thus central pressure, may be an important therapeutic goal in the management of angina in patients with CAD.

Although it is not feasible to invasively measure central blood pressure in every hypertensive patient, the present study focuses light on the issue that central blood pressure reduction with beta blockers is inadequate. This might be a justify higher stroke rates associated with beta blockers compared to other blood pressure lowering drugs in previous outcome studies. This drawback with beta blockers might be compensated by combining other antihypertensive drugs with beta blockers. Combination therapy reduces central aortic pressure to a greater extent and thus would reduce cardiovascular events to significantly retaining all the beneficial effects of beta blockers. Larger studies with adequate follow-up may solve this issue.

Limitations

There are a few limitations of this study. Firstly, this study was only an observational study. Hence, it was not optional to randomize antihypertensive therapy. Secondly, the study was not designed to test the effect of various cardiovascular risk factors on central blood pressures. Thirdly, the type of beta blocker used and role of positional changes, sedation condition and other environmental changes was not considered while comparing brachial vs central pressure, which could have affected blood pressure readings. Further, the sample size in CAD group was too small and patients with mild CAD were excluded from the analysis. Lastly, the study was a single point cross-sectional study; so there was no follow-up of patients to assess the effect of central aortic blood pressure on cardiovascular outcomes with antihypertensive therapy.

CONCLUSION

Central aortic systolic and pulse pressures are reduced to a greater extent with combination therapy of ACEI/ARB/CCB with beta blocker compared to beta blocker monotherapy. Central systolic and pulse pressure reduction with this combination therapy is similar to the extent obtained with ACEI/ARB/CCB monotherapy. Central pulse pressure is significantly higher in patients with moderate and severe CAD compared to patients with normal coronaries. As both central pulse pressure rise and CAD severity progress parallel with aortic atherosclerosis, high central pulse pressure may be a marker of severe CAD. Different classes of antihypertensives have different impact on central blood pressures and the central systolic and pulse pressures cannot be inferred accurately from brachial blood pressures. This study underlines the potential to undertreat or overtreat hypertension based on brachial blood pressure targets.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

CAD: Coronary Artery Disease; **PP:** Pulse Pressure; **LVEF:** Left Ventricular Ejection Fraction; **CAG:** Coronary Angiography; **SBP:** Systolic Blood Pressure; **ACS:** Acute Coronary Syndrome; **CCB:** Calcium Channel Blocker; **ACEI:** ACE Inhibitor; **ARB:** Angiotensin Receptor Blocker

SUMMARY

Central aortic blood pressure (CABP) has been shown to better at predicting cardiovascular outcomes than peripheral pressure. The effect of various classes of antihypertensive agents on central aortic blood pressures is differential and may have a bearing on the cardiovascular pro-

tection afforded by them. In this study, we confirmed the differential effect of beta blocker versus non beta blocker drugs on CABP by invasive assessment in patients undergoing coronary angiography. Beta blockers were found to be less effective in reducing CABP as assessed by lower SBP difference and Pulse pressure ratio values. There was also correlation between severity of coronary artery disease and CABP. These findings have the potential for guiding the choice of initial drug therapy in hypertension and especially in those with coronary artery disease.

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