Do Cardiovascular Risk Factors and Severity and Complexity of Coronary Atherosclerosis Predict Aortic Pulse Pressure during Cardiac Catheterization?

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Abstract

Keywords

- coronary artery disease
- atherosclerosis
- aortic pulse pressure
- cardiovascular risk factors
- SYNTAX score
- aspirin
- cardiac catheterization
- aging

Pulse pressure (PP), estimated from the peripheral blood pressure measurements, has been linked with adverse cardiovascular events. But, the association of PP and coronary artery disease is not well studied. There is a lack of data on the association of invasively measured aortic PP and cardiovascular risk factors and severity of coronary atherosclerosis. We determined the predictive factors of aortic PP during cardiac catheterization. Electronic medical records from 2010 to 2013 were retrospectively reviewed. A total of 368 patients were eligible. The data on demographics, cardiovascular risk factors, coronary lesion characteristics, and medication use was collected. On multivariable regression analysis, aging ($\beta = 0.34$, $p = 0.001$, 95% confidence interval [CI] 0.14–0.53) and prior aspirin use ($\beta = 5.09$, $p = 0.015$, 95% CI 0.99–9.18) were associated with higher aortic PP. Increasing estimated glomerular filtration rate ($\beta = -0.52$, $p = 0.040$, 95% CI -0.90 to -0.23) was associated with lower aortic PP. Severity and complexity of coronary lesions, SYNTAX score, and number of obstructed vessels were not associated with aortic PP. Aging, prior aspirin use, and declining renal function were associated with an increase in aortic PP. Aortic PP may not predict the severity and complexity of coronary atherosclerosis. Therefore, the risk of adverse cardiovascular events associated with an elevated aortic PP may not be mediated by the severity of coronary atherosclerosis.

Pulse pressure (PP) (systolic blood pressure – diastolic blood pressure) is a function of left ventricular stroke volume and compliance of arterial system.¹ The reflection of waves at branch points of major arteries, such as aorta, results in superimposition of forward waves generated from left ventricular ejection and augmentation of systolic blood pressure and PP.^{1,2} These branch points are located close to the peripheral arteries, which results in amplification of periph-

eral pulse waves and PP.² Thus, central (or aortic) PP, estimated using noninvasive means by measuring carotid–femoral peripheral pulse wave velocity, M-mode ultrasound derived aortic diameter, and stiffness are less accurate than the PP measured directly in the aorta during cardiac catheterization (CC).^{3–5} Aortic PP, an indicator of aortic stiffness, has been associated with adverse cardiovascular events (including myocardial infarction) and all-cause mortality.^{6–11} The

mechanisms linking aortic PP and increased cardiovascular morbidities have not been clearly elucidated. Several theories such as elevated aortic PP leading to endothelial dysfunction, coronary atherosclerosis, left ventricular hypertrophy, increased afterload, increased myocardial oxygen demand, and decreased coronary perfusion have been proposed, all of which could increase the risk for adverse cardiovascular events.^{1,6}

The data on the association of PP and cardiovascular risk factors are conflicting.^{8,12–15} The link between PP and extent of coronary atherosclerosis is not well studied. For example, very few studies have shown that an increase in aortic PP is associated with the presence of obstructive coronary artery disease (CAD) and lesions in the right coronary artery and its branches.^{3,15,16} But, these studies lack comprehensive assessment of cardiovascular risk factors and severity and extent of CAD. Synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) score, an angiographic tool for grading CAD complexity and severity, grades coronary anatomy based on coronary lesion characteristics such as number of lesions, coronary segments involved, lesion location, presence of calcification and thrombus, lesion length, and coronary dominance.^{17,18} It provides a comprehensive assessment of coronary atherosclerosis and thereby helps to determine revascularization approaches.^{17,18} The association of invasively measured aortic PP and cardiovascular risk factors and extent of CAD has never been assessed in conjunction. Given that PP is a predictor of future adverse cardiovascular events, we predicted an association between aortic PP measured invasively and major cardiovascular risk factors and extent of severity and complexity of CAD.

Methods

A retrospective cross-sectional study was conducted at an urban community teaching hospital in Brooklyn, NY. The study protocol was approved by the hospital's institutional review board, and a waiver of patient informed consent was granted. Electronic medical records, CC reports, and laboratory data were retrospectively reviewed for the period January 2010 to December 2013. The CCs were performed by a cardiologist certified in interventional cardiology. In addition to age and gender, patients were grouped based on the presence or absence of cardiovascular risk factors such as hypertension, smoking, and hypercholesterolemia. Patients were further stratified based on their comorbidities such as congestive heart failure, diabetes mellitus (DM), prior CAD, peripheral arterial disease (PAD), cerebrovascular accident (CVA), and transient ischemic attack (TIA) at baseline. Use of medications such as aspirin, β -blockers, calcium channel blockers, nitrates, angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACE-I/ARBs) before hospitalization was noted for each patient.

The presence of CAD was determined based on the history of documented myocardial infarction or coronary artery stent placement. Patients with a history of coronary artery bypass graft surgery were excluded given that the presence of graft vessels would have confounded the hemodynamic variables.

Patients were also stratified based on renal function and body mass index (BMI). Renal function was determined by calculating estimated glomerular filtration rate (eGFR, mL/min/1.73 m²) using Cockcroft–Gault equation, and patients were divided into three groups: ≥ 90 , 60 to 89, and < 60 mL/min/1.73 m², respectively. BMI was determined by kg/m², and patients were divided into three groups: ≤ 25 , 25.1 to 35, and > 35 kg/m². The laboratory data such as B-type natriuretic peptide (BNP), fasting low-density lipoprotein (LDL), high-density lipoprotein (HDL), and total cholesterol during hospitalization were obtained for each patient.

The number of vessels with obstructive lesions ($\geq 50\%$ stenosis), presence of lesions with $< 50\%$ stenosis, 50 to 70% stenosis, or $> 70\%$ stenosis in the major epicardial (i.e., left main, left circumflex, left anterior descending, right main and right posterior descending), and minor epicardial arteries (i.e., obtuse marginal, diagonal, and ramus) were noted for each patient from the CC reports. The presence of lesions was divided into left circulation lesions (lesions in left main, left circumflex, left anterior descending, or branches of any of these arteries) and right circulation lesions (lesions in right main, right posterior descending, or branches of any of these arteries). The dominance of coronary circulation was also noted for each patient. In our institution, the calculation of SYNTAX score is performed using an algorithm,¹⁸ and its documentation is standard in these reports. Patients were divided into SYNTAX score tertiles (1–6, 7–14, and > 14).

During CC, proximal aortic pressures were measured using 5 to 6F fluid-filled diagnostic angiography catheters (Cordis, Bridgewater, NJ). Aortic PP was calculated by subtracting aortic diastolic from aortic systolic pressure. Left ventricular ejection fraction (LVEF) was measured for all patients using contrast ventriculography at the time of coronary angiography. Patients on intra-aortic balloon pump or pressors for hemodynamic support, any degree of valvular stenosis, aortic systolic pressure < 90 mm Hg or diastolic pressure < 40 mm Hg and heart rate < 50 bpm or > 110 bpm were excluded due to probable hemodynamic compromise. Patients with mild systolic dysfunction (i.e., LVEF $< 40\%$) on contrast ventriculography were also excluded based on the guidelines.¹⁹ A total of 709 cases were reviewed and 368 were eligible.

Statistical analysis was done using IBM SPSS Statistics 20 (Armonk, NY). Univariate analysis was performed using the chi-square test for categorical variables, and analysis of variance or *t*-test for continuous variables. Pearson correlations were done between continuous variables and PP. All risk factors with two-sided $p < 0.05$ on univariate analysis were entered into a multivariable linear regression model to assess combined effects, which then calculated Beta (β) coefficients.

Results

Patient demographics, risk factors, and medication use are summarized in ►Table 1. Coronary lesion characteristics, cardiac interventions, and laboratory data are summarized in ►Table 2.

►Table 3 shows univariate analysis of mean aortic PP and major cardiovascular risk factors and medications. ►Table 4

Table 1 Summary of patient characteristics

Demographics, cardiovascular risk factors, and medication use	Number, (n = 368 patients [%])
Hypertension	295 (80.2)
Smoking	183 (49.7)
Hypercholesterolemia	207 (56.2)
eGFR (mL/min/1.73 m ²)	
≥90	168 (45.6)
60–89	105 (28.6)
<60	95 (25.8)
BMI (kg/m ²)	
≤25	105 (28.5)
25.1–30	114 (30.9)
>30	149 (40.6)
Diabetes mellitus	166 (45.1)
Gender	
Male	146 (39.6)
Female	222 (60.3)
Age (y)	
≤50	65 (17.6)
51–70	176 (47.8)
≥71	127 (34.5)
COPD/Asthma	64 (17.3)
Prior coronary artery disease	121 (32.8)
Peripheral arterial disease	24 (6.5)
CVA/TIA	30 (8.1)
STEMI	59 (8)
NSTEMI	82 (22.2)
Unstable angina	42 (11.4)
Aspirin	210 (57.1)
Statins	186 (50.5)
Beta-blockers	193 (52.4)
ACE-I/ARBs	146 (39.6)
Calcium channel blockers	79 (21.4)
Nitrates	64 (17.4)

Abbreviations: ACE, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular event; eGFR, estimated glomerular filtration rate; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction; TIA, transient ischemic attack.

shows univariate analysis of mean aortic PP and coronary lesion characteristics, CC indications, and laboratory data. ►**Table 5** shows the Pearson correlation of aortic PP with age, eGFR, BMI, BNP, LDL, HDL, total cholesterol, and SYNTAX score.

Subsequently, multivariable linear regression analyses were performed to determine the association of aortic PP with cardiovascular risk factors and lesion characteristics. In the regression model, aortic PP was the dependent variable and other independent variables included were age, eGFR,

gender, BMI, prior CAD, aspirin, β -blockers, statin, lesions < 50% stenosis, lesions > 70% stenosis in minor epicardial arteries, calcified lesions, and non-ST elevation myocardial infarction (NSTEMI).

Of the above variables, age ($\beta = 0.34$, $p = 0.001$, 95% CI 0.14 to 0.53), eGFR ($\beta = -0.52$, $p = 0.040$, 95% CI -0.90 to -0.23), and prior aspirin use ($\beta = 5.09$, $p = 0.015$, 95% CI 0.99 to 9.18) were independently associated with aortic PP. Lesion characteristics and SYNTAX score were not associated with aortic PP.

Table 2 Summary of patient characteristics

Coronary lesion characteristics, CC interventions, and cardiac markers	Number, (n = 368 patients [%])
Number of obstructed vessels	
0	107 (29.1)
1	90 (24.4)
2	95 (25.9)
3	76 (20.6)
Lesions with >70% stenosis in major epicardial arteries	190 (51.6)
Lesions with >70% stenosis in minor epicardial arteries	109 (29.6)
Lesions with 50–70% stenosis in major epicardial arteries	110 (29.8)
Lesions with 50–70% stenosis in minor epicardial arteries	62 (16.8)
Lesions with <50% stenosis in epicardial arteries	233 (63.3)
Vessels with diffuse disease	188 (51.1)
Calcified lesions	57 (15.5)
Bifurcation lesions	31 (8.4)
Coronary dominance	
Left	35 (9.5)
Right	321 (87.2)
Lesions in left circulation	202 (54.9)
Lesions in right circulation	150 (40.7)
Stent or angioplasty	125 (33.9)
BNP (pg/mL)	288 patients
<100	159 (52.2)
≥100	129 (44.8)
Total cholesterol (mg/dL)	
≤200	118 (32.1)
>200	250 (67.9)
LDL (mg/dL)	
≤130	270 (73.4)
>130	98 (26.6)
HDL (mg/dL)	
<50	224 (60.9)
≥50	144 (39.1)
SYNTAX score	238 patients
1–6	80 (33.6)
7–14	77 (32.3)
>14	81 (34.1)

Abbreviations: BNP, B-type natriuretic peptide; CC, cardiac catheterization; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SYNTAX, synergy between percutaneous coronary intervention with taxus and cardiac surgery.

Discussion

In this study, aging, declining renal function, and prior aspirin use were associated with an increase in aortic PP. The coronary lesion characteristics, severity, and complexity of CAD and distribution of lesions in coronary circulation (i.e., left vs. right circulation) were not associated with aortic PP.

The association of severity and complexity of CAD and aortic PP remains unknown. In our study, mean aortic PP was greater among patients with one or two obstructed vessels compared with those with no obstructed vessels. Also, patients with three obstructed vessels had a greater aortic PP compared with those with zero, one, or two obstructed vessels. However, overall the difference was not significant.

Table 3 Univariate analysis of pulse pressure

Demographics, cardiovascular risk factors and medication use		Pulse pressure mean $\pm$ SD (mm Hg)	SEM	Difference of mean	95% CI of mean or difference of mean	p-Value
Hypertension						
Present (n = 295)		61.52 $\pm$ 20.53	1.19	-3.53	-8.82 to 1.76	0.190
Absent (n = 73)		57.99 $\pm$ 20.84	2.43			
Smoking						
Present (n = 183)		61.19 $\pm$ 19.86	1.46	-0.73	-4.9 to 3.5	0.734
Absent (n = 185)		60.45 $\pm$ 21.38	1.57			
Hypercholesterolemia						
Present (n = 207)		61.22 $\pm$ 20.74	1.44	-0.92	-5.19 to 3.34	0.670
Absent (n = 161)		60.30 $\pm$ 20.45	1.61			
Group	Body mass index (BMI, kg/m ²)					
1	<25 (n = 105)	63.90 $\pm$ 20.27	1.98		59.97 to 67.82	0.040 ^a
2	25.1-30 (n = 114)	62.17 $\pm$ 21.22	1.98		58.23 to 66.10	
3	>30 (n = 149)	57.62 $\pm$ 20.07	1.64		54.37 to 60.87	
Group	eGFR (mL/min/1.73 m ²)					
1	$\geq$ 90 (n = 168)	55.05 $\pm$ 19.27	1.48		52.11 to 57.98	0.001 ^a
2	60-89 (n = 105)	63.07 $\pm$ 21.13	2.06		58.98 to 67.16	
3	<60 (n = 95)	68.54 $\pm$ 19.49	2.00		64.57 to 72.51	
Diabetes mellitus						
Present (n = 166)		62.84 $\pm$ 20.73	1.61	-3.68	-7.92 to 0.56	0.089
Absent (n = 202)		59.16 $\pm$ 20.42	1.43			
Gender						
Male (n = 146)		58.95 $\pm$ 20.21	1.35	4.718	0.38 to 9.05	0.033 ^a
Female (n = 222)		63.66 $\pm$ 20.95	1.73			
Age (in y)						
$\leq$ 50 (n = 65)		51.58 $\pm$ 18.33	2.27		47.04 to 56.13	0.001 ^a
51-70 (n = 176)		59.20 $\pm$ 19.08	1.44		56.34 to 62.05	
$\geq$ 71 (n = 127)		67.79 $\pm$ 21.42	1.90		64.03 to 71.55	
COPD/asthma						
Present (n = 64)		62.38 $\pm$ 22.40	2.80			0.507
Absent (n = 304)		60.49 $\pm$ 20.24	1.16			
Prior coronary artery disease						
Present (n = 121)		65.07 $\pm$ 22.34	2.03	-6.33	-11.01 to -1.64	0.008 ^a
Absent (n = 247)		58.74 $\pm$ 19.42	1.233			
Peripheral arterial disease						
Present (n = 24)		63.71 $\pm$ 19.13	3.90	-3.09	-11.65 to 5.47	0.478
Absent (n = 344)		60.62 $\pm$ 20.72	1.11			
CVA/TIA						
Present (n = 30)		63.73 $\pm$ 19.52	3.56	-3.174	-10.90 to 4.55	0.420
Absent (n = 338)		60.56 $\pm$ 20.71	1.12			
STEMI						
Present (n = 59)		55.59 $\pm$ 20.93	2.75	5.53	-0.718 to 11.78	0.080

(Continued)

Table 3 (Continued)

Demographics, cardiovascular risk factors and medication use	Pulse pressure mean $\pm$ SD (mm Hg)	SEM	Difference of mean	95% CI of mean or difference of mean	p-Value
Absent (<i>n</i> = 309)	61.12 $\pm$ 23.62	0.92			
NSTEMI					
Present (<i>n</i> = 82)	64.79 $\pm$ 21.96	2.42	−5.11	−10.17 to −0.06	0.048 ^a
Absent (<i>n</i> = 286)	59.68 $\pm$ 20.11	1.18			
Unstable angina					
Present (<i>n</i> = 42)	59.60 $\pm$ 20.54	3.17	1.38	−5.27 to 8.03	0.684
Absent (<i>n</i> = 326)	60.98 $\pm$ 20.65	1.44			
Aspirin					
Present (<i>n</i> = 210)	63.69 $\pm$ 20.82	1.43	−6.63	−10.85 to −2.40	0.002 ^a
Absent (<i>n</i> = 158)	57.06 $\pm$ 19.56	1.57			
Statin					
Present (<i>n</i> = 186)	63.33 $\pm$ 20.10	1.47	−5.01	−9.21 to −0.80	0.020 ^a
Absent (<i>n</i> = 182)	58.32 $\pm$ 20.72	1.54			
Beta-blocker					
Present (<i>n</i> = 193)	62.95 $\pm$ 21.43	1.54	−4.41	−8.62 to −0.19	0.040 ^a
Absent (<i>n</i> = 175)	58.54 $\pm$ 19.26	1.46			
ACE-inhibitor					
Present (<i>n</i> = 146)	61.21 $\pm$ 20.39	1.68	−0.564	−4.88 to 3.75	0.985
Absent (<i>n</i> = 222)	60.65 $\pm$ 20.66	1.39			
Calcium channel blocker					
Present (<i>n</i> = 79)	64.33 $\pm$ 22.94	1.18	−4.41	−9.52 to 0.71	0.091
Absent (<i>n</i> = 289)	59.92 $\pm$ 19.95	2.50			
Nitrates					
Present (<i>n</i> = 64)	60.55 $\pm$ 18.78	1.20	0.39	−5.17 to 5.96	0.889
Absent (<i>n</i> = 204)	60.94 $\pm$ 20.91	2.34			

Abbreviations: ACE, angiotensin converting enzyme; BMI, body mass index; CVA, cerebrovascular event; eGFR, estimated glomerular filtration rate; NSTEMI, non-ST elevation myocardial infarction; SD, standard deviation; SEM, standard error of mean; STEMI, ST elevation myocardial infarction; TIA, transient ischemic attack.

^a*p* < 0.05.

among all four groups. But, there was a trend toward increasing mean aortic PP with increasing number of obstructive vessels. Philippe et al, in a study of 99 patients, have shown a positive association between invasively measured aortic PP and the number of diseased (>50% stenosis) coronary vessels.¹⁵ But, they only assessed major coronary vessels (i.e., left anterior descending, left circumflex, and right main arteries) and did not stratified their patients based on eGFR. In contrast, we looked at all major coronary vessels and their branches to get complete assessment of atherosclerosis in coronary circulation. We stratified the presence of CAD based on different degrees of obstruction (<50%, 50–70%, and >70% stenosis) to give more comprehensive assessment of severity of coronary lesions. In addition, we also assessed patients based on the degree of renal function (i.e., eGFR), which in our study was an independent predictor of aortic PP. These findings suggest that aortic PP may not be associated with

the extent of CAD determined by number of obstructed vessels.

Our study showed an increase in aortic PP in patients with lesions >70% stenosis in minor epicardial arteries, lesions with <50% stenosis in major and minor epicardial arteries and calcified lesions on univariate analysis. These findings are likely due to confounding factors, as they were attenuated after multivariable adjustment in regression model. Similarly, SYNTAX score, divided into three categories, was not associated with aortic PP. There was a nonsignificant correlation between SYNTAX score and aortic PP (*r* = 0.029). The presence of lesions with > 70% stenosis in major epicardial arteries and 50 to 70% stenosis in major or minor epicardial arteries was not associated with aortic PP. The above findings collectively suggest that aortic PP is not associated with both the extent of severity and complexity of CAD.

Table 4 Univariate analysis of pulse pressure

Coronary lesion characteristics, CC interventions, and cardiac markers	Pulse pressure Mean $\pm$ SD (mm Hg)	SEM	Difference of mean	95% CI of mean or difference of mean	p-Value
Number of obstructed vessels					
0 vessel (n = 107)	57.57 $\pm$ 19.75	1.91		53.78 to 61.36	0.120
1 vessel (n = 90)	61.41 $\pm$ 22.17	2.33		56.77 to 66.06	
2 vessels (n = 95)	60.59 $\pm$ 19.90	2.04		56.54 to 64.64	
3 vessels (n = 76)	64.97 $\pm$ 20.37	2.33		60.32 to 69.63	
Lesions with > 70% stenosis in the major epicardial arteries					
Present (n = 190)	61.06 $\pm$ 21.10	1.53	−0.58	−4.86] to 3.69	0.788
Absent (n = 178)	60.48 $\pm$ 20.33	1.54			
Lesions with > 70% stenosis in minor epicardial arteries					
Present (n = 109)	64.14 $\pm$ 21.60	2.07	−4.79	−9.43 to −0.14	0.043 ^a
Absent (n = 259)	59.35 $\pm$ 20.18	1.26			
Lesions with 50–70% stenosis in the major epicardial arteries					
Present (n = 110)	61.45 $\pm$ 19.19	1.83	−0.95	2.36 to −5.60	0.689
Absent (n = 258)	60.50 $\pm$ 21.36	1.34			
Lesions with 50–70% stenosis in the minor epicardial arteries					
Present (n = 62)	64.03 $\pm$ 21.79	2.76	−3.92	−9.59 to 1.75	0.175
Absent (n = 306)	60.12 $\pm$ 20.45	1.17			
Lesions with < 50% stenosis in epicardial arteries					
Present (n = 233)	62.48 $\pm$ 20.60	1.35	−4.70	−9.13 to −0.278	0.037 ^a
Absent (n = 135)	57.77 $\pm$ 20.63	1.80			
Vessels with diffuse disease					
Present (n = 188)	62.26 $\pm$ 21.96	1.60	−2.88	−7.14 to 1.38	0.185
Absent (n = 180)	59.38 $\pm$ 19.15	1.45			
Calcified lesions					
Present (n = 57)	67.12 $\pm$ 21.64	2.86	−7.47	−13.32 to −1.62	0.012 ^a
Absent (n = 311)	59.65 $\pm$ 20.40	1.17			
Bifurcation lesions					
Present (n = 31)	61.35 $\pm$ 18.06	24	−0.63	−8.28 to 7.03	0.873
Absent (n = 337)	60.73 $\pm$ 20.96	31.15			
Dominance ^b					
Left (n = 35)	62.89 $\pm$ 22.07	3.73	2.14	−5.10 to 9.38	0.561
Right (n = 321)	60.75 $\pm$ 20.53	1.14			
Lesions in left circulation					
Present (n = 202)	62.13 $\pm$ 20.69	1.45	−2.90	−7.15 to 1.33	0.179
Absent (n = 166)	59.22 $\pm$ 20.46	1.58			
Lesions in right circulation					
Present (n = 150)	61.64 $\pm$ 20.32	1.65	−1.38	−5.69 to 2.92	0.526
Absent (n = 218)	60.25 $\pm$ 20.84	1.41			
Stent or angioplasty					
Present (n = 125)	59.38 $\pm$ 20.65	2.01	3.62	−1.50 to 8.73	0.165
Absent (n = 243)	63.00 $\pm$ 20.54	1.64			

(Continued)

Table 4 (Continued)

Coronary lesion characteristics, CC interventions, and cardiac markers	Pulse pressure Mean $\pm$ SD (mm Hg)	SEM	Difference of mean	95% CI of mean or difference of mean	p-Value
BNP (pg/mL, n = 288)					
<100 (n = 159)	60.17 $\pm$ 20.26	1.60	4.07	−0.71 to 8.85	0.095
$\geq$ 100 (n = 129)	64.24 $\pm$ 20.79	1.83			
Total cholesterol (mg/dL)					
$\leq$ 200 (n = 118)	61.57 $\pm$ 20.73	1.90	1.08	−3.52 to 5.68	0.645
>200 (n = 250)	60.49 $\pm$ 21.08	1.33	1.08	−3.52 to 5.68	0.645
LDL (mg/dL)					
$\leq$ 130 (n = 270)	60.78 $\pm$ 21.38	1.30	0.64	−4.42 to 5.70	0.804
>130 (n = 98)	60.14 $\pm$ 23.07	2.33			
HDL (mg/dL)					
<50 (n = 224)	60.15 $\pm$ 21.12	1.41	1.09	−3.27 to 5.45	0.623
$\geq$ 50 (n = 144)	59.06 $\pm$ 20.25	1.68			
SYNTAX score (n = 238)					
1–6 (n = 80)	62.28 $\pm$ 20.29	2.49		57.31 to 67.24	0.943
7–14 (n = 77)	61.95 $\pm$ 20.94	2.41		57.13 to 66.76	
>14 (n = 81)	62.23 $\pm$ 19.95	2.21		57.82 to 66.65	

Abbreviations: BNP, B-type natriuretic peptide; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SYNTAX, synergy between percutaneous coronary intervention with taxus and cardiac surgery.

^a $p < 0.05$.

^bOnly comparing left and right dominant coronary circulation (not codominant circulation).

Differences in aortic PP have been linked with presence of lesions in left versus right coronary arteries and their branches. In a study by Khoueiry et al, higher aortic PP was observed among patients with presence of isolated obstructive lesions ($\geq 50\%$ stenosis) in the right coronary artery and its branches compared with those with lesions in the left coronary artery and its branches.³ These findings were attributed to both systolic and diastolic flow in right coronary arterial system (right coronary artery and its branches), which makes it susceptible to atherosclerosis due to changes in PP. However, Khoueiry et al did not substratify their

patients based on their renal function, which is a major predictor of PP, and did not include patients who underwent CC for acute coronary syndrome (ACS) indications. In contrast, our study did not find any association with the presence of lesions in the right or left coronary arteries (or circulation) and their branches. Also, our study not only provided a comprehensive assessment of cardiovascular risk factors and coronary lesion characteristics (i.e., extent of CAD), but also included patients with ACS and non-ACS indications for CC. Of note, we had excluded patients with hemodynamic compromise in our study as discussed in the “Methods” section. The association of aortic PP and different presentations of ACS has not been previously investigated. We found that aortic PP was higher in patients with NSTEMI compared with those without NSTEMI. Although, the difference was significant on univariate analysis, the absence of significant difference on multivariate model points toward the effect of confounding factors. There was no difference in aortic PP among patients with STEMI or unstable angina and those without these presentations of ACS. Therefore, aortic PP may not be useful to predict presentations of ACS that warrant urgent revascularization. Prior use of statins and β -blockers was associated with higher aortic PP. But, these findings were probably confounded by aging due to greater likelihood of use of these medications in older patients.

Aging, a known cause of stiffness in the large vessels, results in increased PP.^{8,9,20} This increased stiffness of large vessels results from age-related mechanical changes (i.e., thinning and fragmentation of elastin fibers, calcium, and

Table 5 Pearson correlations with aortic pulse pressure

Variables	r-Value	p-Value
Age	0.313	0.001
eGFR	−0.270	0.005
BMI	−0.146	0.001
BNP	0.052	NS
LDL	−0.042	NS
HDL	0.022	NS
Total cholesterol	−0.033	NS
SYNTAX score	0.029	NS

Abbreviations: BNP, B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NS, nonsignificant; SYNTAX, synergy between percutaneous coronary intervention with taxus and cardiac surgery.

collagen deposition) in arterial wall.^{21,22} These changes lead to a rise in systolic blood pressure and a fall of diastolic blood pressure, which ultimately results in increased aortic PP.^{21,22} In our study, there was a graded increase in mean aortic PP across the three age groups (i.e., <50 , $50-70$, ≥ 71 years) as shown in ►Fig. 1. This association was independently associated with aortic PP on linear regression ($\beta = 0.34$, $p = 0.001$, 95% CI 0.14–0.53). There was a significant and positive correlation between age and aortic PP ($r = 0.313$, $p = 0.001$) as shown in ►Table 5. Although, our findings are consistent with the literature, our study was performed by measuring the PP directly in the aorta. We also gave more comprehensive account of cardiovascular risk factors, coronary lesions, and coronary circulation.

Gender differences in PP have previously been described.^{23–26} Few studies have shown that women have greater aortic stiffness compared with men.^{23,24} This increased stiffness is amplified after menopause due to hormonal (mainly lack of estrogen) changes.^{25,26} But, few studies have found contrasting evidence or no evidence.^{14,15} In our study, females had a higher mean aortic PP compared with men (63.66 vs. 58.95 mm Hg) on univariate analysis. But, this difference in aortic PP attenuated in multivariable analysis suggesting a confounding effect. Previous studies showing increased PP in females compared with males were based on indirect noninvasive measurement of aortic hemodynamics. Our findings are consistent with Phillepe et al who also suggested no evidence of gender-related differences in invasively measured aortic PP.¹⁵ Prospective studies with direct measurement of aortic PP would help to mitigate the inconsistency surrounding the association of gender and aortic PP.

The evidence on association between BMI and PP has been inconsistent.^{27,28} Both increase and decrease in BMI

have been associated with increasing PP. But, these studies were done based on peripherally obtained PP measurements. Our study found a decrease in aortic PP with increasing BMI on univariate analysis. This decrease was greater when comparing PP between groups 2 and 3 versus groups 1 and 2 as shown in ►Table 3. However, the difference was insignificant on multivariate analysis after adjustment. There was a significant negative correlation between BMI and aortic PP ($r = -0.146$, $p = 0.001$). Therefore, all cardiovascular risk factors need to be taken into account when assessing an association between BMI and aortic PP.

Chronic kidney disease (CKD) has been associated with increased aortic stiffness.^{29–33} But some studies have found no association of CKD and aortic stiffness or have attributed increased aortic stiffness to hypertension in those patients.^{34,35} However, none of the above studies have demonstrated the association of CKD and invasively measured aortic PP. In our study, patients with eGFR < 60 mL/min/1.73 m² had a greater aortic PP than patients with eGFR 60 to 89 and ≥ 90 mL/min/1.73 m²) as shown in ►Fig. 2. This difference persisted after adjusting for other significant cardiovascular risk factors in multivariate analysis ($\beta = -0.52$, $p = 0.040$). There was a significant negative correlation between aortic PP and eGFR ($r = -0.270$, $p = 0.005$). Although the exact pathogenesis remains enigmatic, the increased aortic stiffness in CKD results from hardening of arteries due to intimal thickening, breakdown of elastic fibers, collagen, and calcium deposition and decreased number of vascular smooth muscle cells.^{13,36} Besides traditional cardiovascular risk factors, presence of uremia is associated with the above vascular wall abnormalities in CKD patients.³⁵ Therefore, declining eGFR may serve as a marker for increased aortic PP independent of aging.

Fig. 1 The comparison of mean aortic pulse pressure among patients in different age groups. There were 65, 176, and 127 patients in the age groups ≤ 50 , 51 to 70, and ≥ 71 years, respectively.

Fig. 2 The comparison of mean aortic pulse pressure among patients based on renal function. There were 168, 105, and 95 patients with eGFR ≥ 90 , 60 to 89, and < 60 mL/min/1.73 m², respectively. eGFR, estimated glomerular filtration rate.

The data on association of nonsteroidal anti-inflammatory drug (NSAID) use and aortic PP is limited and conflicting.^{4,5,26} By measuring aortic diameter using M-mode ultrasound, Claridge et al showed that NSAIDs were associated with aortic stiffness.⁴ In contrast, Pietri et al demonstrated that low-dose aspirin results in decrease in measured pulse wave velocity and aortic augmentation index, the markers of aortic stiffness.⁵ In addition, Nair et al using peripherally measured brachial PP found no association between aspirin use and PP.²⁶ In our study, prior aspirin use was significantly associated with higher aortic PP compared with those not on aspirin. This difference was significant even after adjusting for multiple cardiovascular risk factors and coronary lesions ($\beta = 5.09$, $p = 0.015$). Although the exact mechanism needs to be elucidated, Claridge et al have shown increased levels of aminopeptide terminal of type III procollagen in NSAIDs users, which results in increased expression of collagen in vessel wall.⁴ Also, an increased breakdown of elastin fibers with NSAIDs use has also been thought to promote aortic stiffness.⁴ Whether NSAIDs are causal factor in increased aortic stiffness or are marker of high-risk population with increased vascular stiffness warrants further investigation. Also, whether our findings are applicable to NSAIDs other than aspirin needs further studies.

The presence of cardiovascular risk factors and comorbidities such as hypertension, smoking, hypercholesterolemia, DM, PAD, or CVA/TIA were not associated with aortic PP. There was no association between the presence of diffuse disease, bifurcation lesions, and nature of coronary intervention (i.e., stent vs. angioplasty). Similarly, the use of medications such as ACE-I/ARB, nitrates and calcium channel blockers was not associated with aortic PP. There was no association between aortic PP and physiological markers such as BNP, HDL, LDL, or

total cholesterol. There was no correlation between aortic PP and these physiological markers.

Regarding limitations of our study, we did not address the association of severity and control of cardiovascular risk factors with aortic PP. We assessed the risk factors at baseline, and therefore the preventive effect of those medications could have confounded the association of the risk factor profile and aortic PP in our patients. The retrospective nature of the study meant that patient data were obtained from review of electronic medical records. Counteracting this limitation is the consistency with which the CC reports are documented in our institution, which lends credibility to these findings. Angiographic interpretation of coronary arteries (such as lesion characteristics and SYNTAX score) was limited to an experienced interventional cardiologist, which eliminates interobserver variability. The investigation of possible mechanisms linking the elevated aortic PP and increased risk for adverse cardiovascular events is beyond the scope of this study.

In conclusion, our study demonstrates that invasively measured aortic PP is associated with aging and declining renal function, and is less likely to be predicted by other cardiovascular risk factors. Prior aspirin use is associated with greater aortic PP. Aortic PP is not associated with severity or complexity of coronary artery disease. Although, aortic PP is associated with increased risk of adverse cardiovascular events, this increased risk may not be mediated by the extent of coronary atherosclerosis. Therefore, aortic PP may not be a useful marker of CAD extent. Our findings will help predict patient populations with greater aortic PP and thereby at an increased risk of future adverse cardiovascular events. Additional prospective studies to further validate our findings would be valuable.

Contributions

All authors made substantial contributions to (1) conception and design, or acquisition of data, or analysis and interpretation of data; (2) drafting the article; and (3) final approval of the version to be published.

Disclosure Statement

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