The Relation Between Aortic Pulse Pressure and Coronary Artery Disease

Aortik Nabız Basıncı ile Koroner Arter Hastalığı Arasındaki İlişki: Koroner Anjiyografik Çalışma

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ABSTRACT

Objective: Pulse pressure (PP) is a significant marker of cardiovascular morbidity.We investigated the relation between aortic PP and the presence and extent of coronary artery disease (CAD) in patients undergoing diagnostic coronary angiography (CAG).

Patients and Method: The study group consisted of 550 patients (363 men, 187 women).We evaluated patients in two different groups, PP < 60 mmHg and ≥ 60 mmHg.

Results: In univariate analysis gender and presence of hyperlipidemia showed no statistically significant differences between both groups. However, the ratio of patients having diabetes mellitus, hypertension or smoking were significantly higher in ≥ 60 mmHg PP group. The mean age was 55.2 ±11.9 in < 60 mmHg PP group and 61.3±9.3 in the other group (p<0.01). Although systolic blood pressure level was higher in ≥ 60 mmHg PP group (160.4±21.1 vs. 126.4±13.5, p< 0.001), diastolic blood pressure level showed no significant differences between both groups (78.3±13.5 vs. 80.3±10.2, p= 0.32). In the <60 mmHg PP group, the ratio of normal CAG was significantly higher, and also, the critically CAD rate was lower than the other group. In multivariate analysis, smoking [odds ratios (OR) 2.344, 95% confidence intervals (CI), 1.416-3.879], male gender (OR 5.858, 95% CI, 3.425-10.019) and PP ≥60 mmHg (OR 25.788, 95% CI, 14.001-47.498) were evaluated as an independent indicators of CAD.

Conclusions: In our study, we demonstrate that, aortic PP ≥60 mmHg is related to the risk of critically CAD as an independent factor.

Key Words: Coronary Artery Disease, Pulse Pressure, Coronary Angiography.

ÖZET

Amaç: Nabız basıncı (NB) kardiyovasküler mortalitenin önemli bir belirtecidir. Tanısal amaçlı koroner anjiyografi (KAG) uygulanan hastalarda aortik NB ile koroner arter hastalığı (KAH) varlığı ve yaygınlığı arasındaki ilişki araştırılmıştır.

Hastalar ve Metod: Çalışma grubu 550 hastadan oluşmuştur (363 erkek, 187 kadın). Hastalar NB<60 mmHg ve ≥60 mmHg olmak üzere iki ayrı grupta değerlendirilmiştir.

Bulgular: Tek değişkenli analizde cinsiyet ve hiperlipidemi varlığı gruplar arasında istatistiksel olarak anlamlı fark görülmedi. Ancak, diyabetes mellitus, hipertansiyon ve sigara içimi NB ≥60 mmHG grubunda daha sık idi. Ortalama yaş NB <60 mmHg grubunda 55.2 ±11.9 iken, diğer grupta 61.3±9.3 olarak bulundu (p<0.01). Sistolik kan basıncı NB ≥60 mmHg grubunda daha yüksek iken (160.4±21.1 vs. 126.4±13.5, p< 0.001), diyastolik kan basıncında gruplar arasında anlamlı fark görülmedi (78.3±13.5 vs. 80.3±10.2, p= 0.32). <60 mmHg grubunda normal KAG oranı daha yüksek, kritik KAH oranı ise daha düşük saptandı. Çok değişkenli

analizde sigara içimi [odds ratios (OR) 2.344, %95 confidence intervals (CI),1.416-3.879], erkek cinsiyet (OR 5.858, %95 CI, 3.425-10.019) ve NB ≥ 60 mmHg (OR 25.788, %95 CI, 14.001-47.498) olması KAH'ın bağımsız belirteçleri olarak bulundu.

Sonuç: Önceki çalışmalarda NB ile KAH arasındaki ilişki çok değişkenli analizde kaybolmuş olsa dahi, çalışmamızda aortik NB'nin ≥60 mmHg olması kritik KAH riski ile ilişkili bağımsız bir faktör olduğu gösterilmiştir.

Anahtar Kelimeler: Koroner Arter Hastalığı, Nabız Basıncı, Koroner Anjiyografi.

INTRODUCTION

Pulse pressure (PP) is a strong independent predictor of cardiovascular events, particularly in older populations, when compared with systolic blood pressure (SBP) and/or diastolic blood pressure (DBP), or mean arterial pressure (1-9). Findings obtained from Framingham Heart Study showed that, SBP rises in parallel with increasing age, when DBP shows age related increase up to the sixth decade, and declines slowly thereafter (6). A 10 mmHg increase in PP, was found to augment risk of adverse coronary events and overall cardiovascular mortality by 13% and 20% respectively (10). PP has been proved as a strong predictor of CV risk particularly when it is above 60 mm Hg (2,6,7,11). Several studies have shown an association between the presence and extent of coronary artery disease (CAD) and invasively measured aortic PP in patients undergoing diagnostic coronary angiography (CAG) (12-14). However the relation of widened PP (≥60 mmHg) with angiographically demonstrated CAD and its association to traditional major risk factors has not been fully clarified. The purpose of this study was to investigate the relation between widened aortic PP and the presence and extent of CAD in patients undergoing diagnostic CAG.

PATIENTS AND METHOD

Study Population

The study group consisted of 550 consecutive patients who underwent diagnostic CAG for possible CAD. A complete clinical history, including cardiovascular risk factors (hypertension[HT], diabetes mellitus [DM], hyperlipidemia [HLP], and smoking status) was taken from all patients before the procedure. Patients who had liver disease, renal disease, secondary HT, valvular disease, malignant neoplasm, and acute coronary syndromes within the previous 1 month were excluded. Baseline medications were continued during the procedure. Written informed consent was obtained from the each patient.

Weight and height were determined for each patient. Body mass index (BMI = weight/height ^{2}) was calculated for each participant derived from their body weight (in kilograms) and height (in meters). Fasting blood samples were taken for the analysis of glycemia, total cholesterol, HDL cholesterol, triglycerids, and LDL cholesterol. According to guidelines of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, HT was defined as SBP≥ 140 mmHg, and/or DBP≥ 90 mmHg, and/or already antihypertensive drug using (15). HLP was defined as having LDL cholesterol level ≥130 mg/dl and/or being prescribed a lipid-lowering drug. DM was defined as having fasting blood glucose of 126 mg/dl or more and/or already using antidiabetic drug. Current smoking patients were considered as smokers.

Coronary Angiography and Measurements

Coronary angiography was performed by a femoral approach using the standard Judkins technique. Coronary arteries in left and right oblique planes and cranial and caudal angles were demonstrated. Coronary arteries were judged as normal on the basis of visual assessment of the absence of any luminal irregularities, non-critical CAD (< 50% stenosis), and critical CAD (≥ 50% stenosis).

Invasive aortic SBP and DBP were measured using a standard fluid-filled system (6F pig-tail catheter) at baseline before any injection of contrast dye. Aortic PP was calculated as the difference between SBP and DBP. Left ventriculography was performed just after the measurement of pressures. Left ventricular ejection fraction (LVEF) was calculated by using area length method (16).

Statistical Analysis

All results are expressed as the mean±SD. Analysis of variance and Sudent t tests were used for comparison of normally distributed continuous variables. Differences in frequency were tested using chi-square test, or appropriate Fisher's exact tests. Multivariate regression analyses were performed to determine independent associations between PP and traditional risk factors, hemodynamic, and angiographic parameters. A p value <0.05 was regarded as significant.

RESULTS

The mean age of the 550 patients studied was 58.45±11.56 years and ranged from 32 to 79 years. There were 187 females and 363 males. The study group was divided into two groups according to PP, <60 mmHg and ≥60 mmHg. The clinical and angiographic parameters are summarized in Table 1.

There were 283 patients in PP<60 mmHg group and 267 patients in PP≥60 mmHg. The mean age was higher in PP≥60 mmHg. (61.3±9.3 vs 55.2±11.9, p<0.01)

Table 1: *Comparison of Clinical Characteristics and Angiographic Parameters of Groups, PP<60 mmHg and ≥60 mmHg*

Characteristics	PP <60 mmHg (n=283)	PP ≥60 mmHg (n=267)	p value
Age (years)	55.2±11.9	61.3±9.3	<0.01
Male/Female (n,%)	99(18)/184(33)	88(16)/179()	0.32
BMI (kg/m²)	25.9±3.8	26.7±3.2	0.49
Hypertension (n)	105	154	<0.001
Diabetes mellitus (n)	46	82	<0.001
Hyperlipidemia (n)	43	61	0.44
Smoking (n)	87	121	<0.01
LVEF (%)	48.4±7.2	50.5±5.6	0.09
<0.50 (n)	40	23	
≥0.50 (n)	243	244	<0.05
Aortic SBP (mmHg)	126.4±13.5	160.4±21.1	<0.001
Aortic DBP (mmHg)	80.3±10.2	78.3±13.5	0.32
Non CAD (n,%)	156(28)	43(7)	
Non critical CAD (n,%)	25(4)	25(4)	
One vessel CAD (n,%)	47(8)	62(11)	
Two vessels CAD (n,%)	27(4)	56(10)	
Three vessles CAD (n,%)	26(4)	72(13)	<0.001
Left main CAD (n,%)	2(0.3)	9(1)	
Medications (%)			
Antiplatelet	47.4	50.4	0.12
ß Blockers	23.5	26.5	0.36
ACE inhibitors	37.3	31.3	0.21
Calcium antagonists	19.4	16.5	0.46
Diuretics	13.2	14.2	0.37
Lipid-lowering drugs	14.5	20.3	0.17
Digoxin	3.1	4.2	0.61
Nitrats	12.2	15.7	0.16

The incidence of HT, DM, smoking, and having LVEF ≥0.50 was statistically significantly much common in PP≥60 mmHg group. Both groups did not differ with regard to gender, BMI, HLP, and medications.

In angiopraphic parameters, although aortic SBP was much higher in PP≥60 mmHg (160.4±21.1 vs 126.4±13.5, p<0.001), aortic DBP showed no statistically significant difference (78.3±13.5 vs 80.3±10.2, p=0.32). Among patients having normal CAG, PP<60 mmHg group was much more than PP≥60 mmHg group (28% vs 7%). Although non-critical CAD rate was similar between both groups (4% vs 4%), critical CAD rate was statistically significant higher in PP≥60 mmHg group than the other (one-vessel CAD: 11% vs 8%, two-vessels CAD: 10% vs 4%, three vessels CAD: 13% vs 4%, left main CAD: 1% vs 0.3%, p<0.001).

When the study population was divided in two groups as having normal coronary arteries or CAD group (both critical and non-critical), SBP and PP were much higher in CAD group (150.9±12.6 vs 129.9±10.3, and 68.7±9.3 vs 53.5±7.1, p value <0.01, and <0.001 respectively), while DBP and LVEF did not differ between groups (85.6±6.9 vs 83.5±5.7, and 46.6±6.2 vs 51.8±4.7, p value 0.37, and 0.08 respectively) (Table 2).

Although in univariate analysis male gender, HT, DM, HLP, smoking and PP≥ 60 mmHg were found as statistically significant in CAD group, in multivariate analysis smoking [odds ratios (OR) 2.344, 95% confidence intervals (CI),1.416-3.879, p<0.01], male gender (OR 5.858, 95% CI, 3.425-10.019, p<0.001) and PP≥ 60 mmHg (OR 25.788, 95% CI, 14.001-47.498, p<0.001) were evaluated as an independent indicators of CAD (Table 3,4).

Table 2: *Hemodynamic Characteristics of The Study Population Acoording to Existence of CAD*

	CAD (-)	CAD (+)	p value
SBP (mmHg)	129.9±10.3	150.9±12.6	<0.01
DBP (mmHg)	83.5±5.7	85.6±6.9	0.37
PP (mmHg)	53.5±7.1	68.7±9.3	<0.001
LVEF (%)	51.8±4.7	46.6±6.2	0.08

Table 3: *Association of Risk Factors According to Existence of CAD in Univariate Analysis*

Risk factors	CAD (-)	CAD (+)	p value
Gender (n,%)			
Female	92(16)	95(17)	
Male	80(14)	283(51)	<0.001
Hypertension (n,%)			
No	91(16)	200(36)	
Yes	81(14)	178(32)	<0.01
Diabetes mellitus (n,%)			
No	140(25)	282(51)	
Yes	32(5)	96(17)	<0.01
Hyperlipidemia (n,%)			
No	142(25)	303(55)	
Yes	30(5)	75(13)	<0.05
Smoking (n,%)			
No	132(24)	210(38)	
Yes	40(7)	168(30)	<0.001
PP (mmHg)			
<0.60 (n,%)	155(28)	120(21)	
≥0.60 (n,%)	17(3)	258(46)	<0.001

Table 4: *Association of Risk Factors According to Existence of CAD in Multivariate Analysis*

Risk Factors	Odds Ratio	95 % Confidence Interval	p value
Male gender	5,858	3,425-10,019	<0.001
Hypertension	1,092	0,713-1,670	0.68
Diabetes mellitus	1,353	0,784-2,335	0.27
Hyperlipidemia	0,994	0,642-1,537	0.97
Smoking	2,344	1,416-3,879	<0.01
PP≥60 mmHg	25,788	14,001-47,498	<0.001

On the other hand, when the study group was divided in two groups having PP<60 mmHg or PP≥60 mmHg, HT (OR 2,439, 95%CI 1,567-3,797, p<0.001), DM (OR 1,814, 95% CI 1,077-3,054, p<0.05), smoking (OR 1,689, 95%CI 1,179-2,419, p<0.01), having CAD (OR 26,761, 95%CI 14,803-48,379, p<0.001), EF>0.50 (OR 3,206, 95%CI 1,732-5,935, p <0.001) were evaluated as an independent risk factors of widened PP (Table 5).

DISCUSSION

Due to arterial stiffness in great vessels, PP get larger with increasing age (17). Both reductions in viscoelastic properties of the arterial wall reflected arterial pressure waves from the periphery back to central aorta increase the PP as a result of an increase in SBP and a decrease in DBP (18). Also, early return of reflected arterial waves increases after-load at end-systole and decreases coronary perfusion pressure during diasto-

Table 5: *Association of Risk Factors According to PP Level (<60 mmHg and ≥60 mmHg) in Multivariate Analysis*

Risk Factors	Odds Ratio	95 % Confidence Interval	p value
Male gender	1,574	0,926-2,675	0.09
Hypertension	2,439	1,567-3,797	<0.001
Diabetes mellitus	1,814	1,077-3,054	<0.05
Hyperlipidemia	1,092	0,713-1,670	0.68
Smoking	1,689	1,179-2,419	<0.01
CAD existence	26,761	14,803-48,379	<0.001
LVEF≥0.50	3,206	1,732-5,935	<0.001

le, in which this elastic properties of aorta represent an important determinant of coronary blood flow (19-20). CAD has been found to be substantially associated with increased aortic stiffness (21). On the other hand, DM, as a marker of atherosclerosis, is related to widened PP (22). Benetos et al. have demonstrated that in a large unselected population with a mean follow-up 19.5 years, increased PP was a strong and independent predictor of cardiovascular mortality, especially in men, whether they were hypertensive or normotensive (23). Likewise, in the Framingham Heart Study, increased PP was strongly related to the risk of CAD in a middle-aged and elderly population with no clinical evidence of CAD at baseline, over a 20-year follow-up (6).

In the present study, we have shown that ascending aorta PP is significantly associated with the presence of CAD as an independent risk factor, both in univariate and multivariate analysis. Several previous studies showed an association between the level of PP and the presence of CAD in various populations. Firstly, Lee et al. found this correlation in patients undergoing left heart catheterization before intervention for mitral valve stenosis, in which PP was obtained by either aortic or brachial measurement (13). Zakopoulos showed a correlation between the level of PP on ambulatory 24-hours blood pressure monitoring and the extent of angiographically documented CAD (24). And also, in a large population, Danchin et al. showed a correlation between aortic PP and the presence and extent of CAD in univariate analysis, where this correlation was disappeared in multivariate analysis due to strong interaction with gender (12). In our study, we also profound a positive correlation between widened PP and LVEF. The PP in large arteries is determined by the elasticity of the vessel and the stroke volume ejected by the heart. When left ventricular systolic function is impaired, due to fall in stroke volume, PP also decreases. And also, Jankowski et al. didn't show a correlation between aortic PP and CAD in patients with impaired left ventricular systolic function (25).

Further, in our study, we also propound a relationship between HT, DM, smoking, which are the traditional risk factors of CAD, and widened PP. This relationship suggests whether increased PP plays an inductive role in the development of CAD or whether a result of atherosclerosis. Is it a cause or a result of this situation? However, it is evident that widened PP, as a marker of pulsatile component of blood pressure, impairs the vascular structure, inhibits endothelium-dependent relaxation, and in relation to endothelial dysfunction, leading to atherosclerosis (26,27).

The relatively small sample size is the main limitation of this study. Secondly, we assessed the extent of CAD according to the number of of diseased coronary arteries. Some extent scores (eg. Gensini score) are believed to be better indicators of coronary atherosclerosis. This may cause a bias in relation of PP and CAD. Thirdly, treatment of patients using antihypertensive agents which may have different ability in reducing PP, were continued during measurement of aortic PP. So this may affect our findings.

In conclusion, aortic PP is independently related to angiographic CAD in patients referred to diagnostic CAG. However, due to close relationship with traditional risk factors and PP, it is difficult to comment whether PP is the cause or result of this situation. But, especially in patients with traditional risk factors, when PP is measured ≥60 mmHg, CAD must be taken into consideration. Thus, further studies are needed to confirm this hypothesis.

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