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Blood Pressures may be Predictor of Cardiac Ischemia in Myocardial Perfusion Scintigraphy

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Abstract

Objective: Low diastolic blood pressure (DBP) is associated with adverse cardiovascular outcomes in patients with chronic coronary disease (CAD), but its association with ischemia is unknown. Relationship between DBP and the myocardial ischemia in myocardial perfusion scintigraphy (MPS) was investigated.

Methods: Patients with chronic coronary artery disease who underwent MPS were included. One day stress/rest gated MPI with Tc-99m MIBI protocol was applied to all patients. Blood pressures was measured before MPI. Patients were divided into 2 groups as ≤75 mmHg and >75 mmHg according to DBP. The SDS were calculated using the sum of the 17-segment.

Results: The patients with DBP ≤75 mmHG and with DBP>75 mmHG were compared, there was no significant difference in SDS (4.44±4.67 and 4.65±4.70 respectively; p=0.657). Association of DBP ≤75 mmHg with SDS appeared to be primarily among those with SBP >130 mmHg. Patients with DBP ≤75mmHg and SBP >130mmHg had different SDS (6.87±6.00 and 4.99±4.77; p=0.015) between patients with DBP >75 mmHg and SBP >130mmHg.

Conclusion: Coexistence lower diastolic blood pressures (≤75mmHg) with higher systolic blood pressures (>130mmHg) could be a predictor of myocardial ischemia in patients who underwent adenosine stress MPI.

Keywords: Adenosine; diastolic blood pressure; ischemia.

Miyokard Perfüzyon Sintigrafisinde Kan Basıncı Değerleri Kardiyak İskemiyi Öngördürebilir

Özet

Amaç: Kronik koroner hastalığı (KAH) olan hastalarda, düşük diyastolik kan basıncının (DKB) mortalite dahil olmak üzere olumsuz kardiyovasküler sonuçlarla ilişkilidir, ancak iskemi ile ilişkisi bilinmemektedir. Bu çalışmamızda düşük diyastolik kan basıncının (DKB) miyokard perfüzyon sintigrafinde (MPS) iskemi ile ilişkisi araştırıldı.

Yöntemler: Tüm hastalara tek gün TI-99m MIBI protokolü uygulandı. Kan basınçları işlemden hemen önce ölçüldü. Hastalar DKB değerlerine göre ≤75mmHg ve >75mmHg olarak iki gruba ayrıldı. 17 segment kullanılarak SDS (summed difference score) hesaplandı.

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Bulgular: DKB ≤75 mmHg olan ve DKB>75 mmHg olan hastalar karşılaştırıldığında SDS değerlerinde anlamlı bir fark saptanamadı (sırasıyla 4.44±4.67 ve 4.65±4.70; p=0.657). Fakat sistolik ve diyastolik kan basınçları birlikte değerlendirildiğinde DKB ≤75mmHg ve SKB> 130mmHg olan hastalar ile DKB>75 mmHg ve SKB>130mmHg olan hastalar karşılaştırıldığında SDS (6.87±6.00 and 4.99±4.77; p= 0.015) değerleri anlamlı olarak farklıydı.

Sonuç: Adenozin ile yapılan stres miyokard perfüzyon sintigrafisinde 75 mmHg altında diyastolik kan basıncı ve 130 mmHg üzerinde sistolik kan basıncı birlikteliği iskemi için öngördürücü olabilir.

Anahtar sözcükler: Adenozin; diyastolik kan basıncı; iskemi.

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Treatment of hypertension through reduction in blood pressure is a cornerstone for the prevention of cardiovascular events in patients with and without established coronary artery disease (CAD).[1] However, aggressively reducing blood pressure has the potential risks of hypotension. Peri-Okonny et al. found that there was a relationship between low diastolic blood pressure and angina in chronic coronary artery patients.[2] An observational study, done in real-life stable patients with coronary artery disease treated for hypertension, showed that low systolic (<120 mm Hg) and low diastolic (<70 mm Hg) blood pressures were associated with an increased risk of cardiovascular events (cardiovascular death, myocardial infarction, stroke, hospital admission for heart failure).[3] In another important study, compared with those with diastolic blood pressure between 70-80 mm Hg, primary clinical events resulting from CV death, MI, stroke or hospitalization with heart failure are higher in those with diastolic blood pressure <70 mm Hg.[4]

Single photon emission tomography (SPECT) myocardial perfusion imaging (MPI) is a well-established non-invasive study used in establishing the diagnosis, prognosis and management of coronary artery disease. Adenosine stress MPI is a non-invasive imaging modality with a wealth of accumulated data regarding both diagnosis and risk stratification of patients with CAD.[5] Adenosine has wide effects as an extracellular signaling molecule inducing vasodilation in most vascular beds, regulating activity in the sympathetic nervous system, and minimal reducing blood pressure, thus Adenosine is a pharmacologic stressor to be safe, tolerable and easily used.[5,6] Adenosine also serves as an important trigger in ischemic and its release may impart cardioprotection. Exogenous administration of adenosine may also protect heart from ischemia-reperfusion injury. Exogenous adenosine activates adenosine receptors to activate plethora of mechanisms, which either independently or in association with one another may confer cardioprotection during ischemia-reperfusion injury.[6]

The importance of DBP before adenosine stress MPI is not clear enough. The effect of DBP and its relationship with SBP on the outcome of ischemia is not clearly known. There is limited information for stress MPI on association between ischemia and DBP. Therefore, we think it is important to demonstrate the direct relationship between DBP and ischemia. Our aim is to examine the relationship between blood pressure and ischemia in MPI. We predict that low DBP and the presence of simultaneously high SBP will increase the severity and probability of myocardial ischemia in SPECT MPI.

Method

Design: This is a retrospective, single-center study.

Patients: This study was conducted in the cardiology clinic of a state hospital in Turkey between 01/01/2018 and 01/01/2019. In total, 524 patients with suspected CAD underwent SPECT MPI with adenosine were included in this study. Patients older than 18 years who received antihypertensive therapy were included.

Data collection: We obtained demographic information, complaints, medications, diabetes mellitus and hyperlipidemia family history, smoking, height (cm), weight (kg), SBP and DBP from each patient's electronic medical records. SBP and DBP was measured before MPI. Blood pressure measurements were obtained at the patients' right arm, using a manual standard mercury sphygmomanometer.

Myocardial perfusion imaging: One day stress/rest gated MPI with Tc-99m MIBI protocol was applied to all patients. Adenosine stress test were applied for all patients. 140 µg/kg/min of adenosine was administered intravenously as continuous infusion for duration of 6 min. Tc-99m MIBI was injected intravenously after 3 min of adenosine infusion. The adenosine infusion was continued for another 3 min post-injection of radiotracer. BP was measured after adenosine infusion. The stress images were acquired about 30-45 min after adenosine stress.

Dual-head gamma camera (Philips Medical Systems, Brightview Gamma Diagnost, Holland and Mediso, AnyScan S, Hungary), LEHR collimator, 64x64 matrix, 180 circular orbits was performed. The quantitative gated SPECT (QGS) program was used for the processing of the images. ischemia scores were obtained by using quantitative perfusion SPECT (QPS) package program. A 5-point scale (0=normal, 1=mildly decreased, 2=moderately decreased, 3=severely decreased, and 4=absence of segmental uptake) was used with a 17-segment model to obtain summed difference scores (SDS) for semiquantitative visual analysis. The SDS, which indicates the amount of ischemia and the degree of defect reversibility.[6,7]

Qualitative assessment of angiograms: Coronary angiograms (visual assessment) were assessed quantitatively for the presence of stenoses ≥50% in the major epicardial coronary arteries and in the >1.5 mm branches. Patients who met the 50% diameter stenosis threshold by QCA (quantitative coronary angiographic information) were designated as having significant CAD. The extent of CAD was assessed by the SYNTAX (SYNergy between PCI with TAXUS™ and Cardiac Surgery) score.[8] All diagnostic coronary angiograms were scored according to the SYNTAX score algorithm. Images were scored using the consensus opinion of 2 cardiologist with more than 10 years of clinical experience.

Ethical Considerations

Before beginning the study, a local Ethics Committee approved the study (Date: 30.05.2019 and no: 2019.68.04.15). The patients were informed about the study. 'Informed consent' was received from all patients. Permission was obtained from the institution to use patient information. The study was conducted in accordance with the Declaration of Helsinki.

Statistical Methodology

PASW Statistics 18 for Windows program was used for data input and statistical analysis. Mean, standard deviation, min-max and frequency were used to state results. Normality was checked. Independent Sample T-test (or Mann Whitney U test) for two groups comparison was used. Chi-square analysis was used for categorical data comparison. Statistical significance was accepted as $p<0.05$.

Results

Patient characteristics were demonstrated in Table 1. There were 98 patients in the case of monotherapy and 352 patients in the case of combination. The arterial blood pressure was 138±18/76±11 mmHg and the pulse rate was 75±12 beats/min before adenosine infusion. The hemodynamic response to adenosine infusion was a slight reduction in SBP (mean 9.9±6.6 mmHg) with a increase in heart rate (mean 8.6±3 beat per minute).

As expected, patients with lower DBP tended to have lower SBP and less frequent use of antihypertensive medications. When the patients with DBP ≤75 mmHG and with DBP>75 mmHG were compared, there was no significant difference in SDS (4.44±4.67 and 4.65±4.70 respectively; p=0.657).

DBP Cross-Classified With SBP: After stratifying the study sample by SBP categories, SDS outcomes varied according to baseline DBP levels (Table 2). The association of lower DBP (≤75 mm Hg) with SDS appeared to be primarily driven by excess risk among those with an SBP >130 mm Hg. Patients with DBP ≤75mmHG and SBP >130mmHG had different SDS between patients with DBP >75 mmHG and SBP >130 mmHG (6.87±6.00 and 4.99±4.77; p=0.015).

After stratifying the study sample by SYNTAX score categories (Table 3), lower DBP was not associated with myocardial ischemia both in the group with SYNTAX score ≥1 and with SYNTAX score=0. The relationship between DBP ≤75mmHG with SBP>130 mmHG and ischemia could not be assessed in the group with SYNTAX score≥1 because the number of samples was low. These results were consistent, demonstrating that: lower DBP with higher SBP may a risk factor for elevated SDS and ischemia in SPECT MPI.

The SYNTAX score indicates the anatomical severity in coronary angiographic evaluation and evaluates >50% diameter. In our study; as the complex structure of coronary artery disease increased, the severity of ischemia increased. There was a positive correlation between SYNTAX score and SDS (p=0.00, r=2.99). SDS was 5.74±4.8 in SYNTAX score=0 group and 9.25±6.1 in SYNTAX score ≥1 group (p=0.00).

When patients were divided into two groups as ≤65 and> 65 years old, in the> 65 age group SBP (150±25 versus 143±24, p=0.01), SDS (5.2±5 versus 4.3±4, p=0.03), SYNTAX scores (7±6 versus 3.5±3, p=0.02) were significantly higher. However, there was no difference in DBP (82.4±10.7 versus 82.3±10, p=0.9). In the patients older than 65 years; SDS was 5.6±3.6 in patients with DBP≤75mmHg, and 5.1±5 in patients with >75mmHg (p =0.6). There was no difference between SBP <130mmHg+DBP ≤75mmHg and SBP> 130mmHg+DBP ≤75mmHg in SDS (3.69±3 and 6.03±3 respectively, p=0.05). In addition to DBP and SBP interaction, the increased frequency and complexity of coronary artery disease may have an effect on the SDS in our patients over 65 years of age.

Discussion

This study showed that coexistence lower DBP with higher SBP could be a predictor of myocardial ischemia in patients who underwent adenosine stress MPI. We evaluated the association between DBP and ischemia in SPECT MPI with-

Table 1. Patient characteristics

	DBP≤75 mmHh (n=130)	DBP>75 mmHg (n=394)	p
Age (yrs)	56.68±12.30	59.05±10.96	0.060
Female/Male	88/42	265/129	0.927
SBP (mmHg)	127.45±22.29	151.98±22.18	0.000
Smoking (%)	33.06	66.4	0.007
Diagnosed diabetes (%)	22.9	77.1	0.467
Lipid medication (%)	26	74	0.547
SYNTAX score (min-max)	3.05±7.17 (0.00-37.00)	5.37±8.27 (0.00-40.50)	0.137
SDS	4.44±4.67	4.65±4.70	0.657

Values are mean±sd. or %, DBP: Diastolic blood pressure; SBP: Systolic blood pressure; SDS: Summed difference score.

Table 2. Diastolic blood pressures stratified by systolic blood pressures

	SBP≤130mmHg			SBP>130mmHg		
	DBP≤75mmHg (n=83)	DBP>75mmHg (n=79)	p	DBP≤75mmHg (n=47)	DBP>75mmHg (n=315)	p
SDS	3.06±2.98	3.29±4.15	0.684	6.87±6.00	4.99±4.77	**0.015**

Significant values are indicated in bold. DBP: Diastolic blood pressure; SBP: Systolic blood pressure; SDS: Summed difference score.

Table 3. Diastolic blood pressures stratified by SYNTAX score

	SYNTAX score ≥1			SYNTAX score=0		
	DBP≤75 mmHh (n=10)	DBP >75 mmHg (n=49)	p	DBP ≤75 mmHh (n=26)	DBP >75 mmHg (n=56)	p
SDS	9.90±7.12	9.12±5.98	0.718	5.23±3.79	5.98±5.29	0.518

DBP: Diastolic blood pressure; SBP: Systolic blood pressure; SDS: Summed difference score. SYNTAX: SYNergy between PCI with TAXUS™ and Cardiac Surgery.

in subcategories of SBP. Vasodilator stress MPI is used as a method for evaluating cardiovascular risk. A study showed that lower resting SBP and DBP conferred prognostic value for mortality in patients undergoing vasodilator PET MPI.[9] The authors concluded that for patients undergoing vasodilator MPI, a lower resting BP is independently associated with mortality on follow-up. BP is a major determinant of myocardial oxygen-demand, but little information is available regarding the changes in BP during myocardial ischemia. Similar to cerebral perfusion, most of myocardial perfusion occurs during diastole, therefore decreased diastolic pressure and flow may cause myocardial ischemia.[10] Some sources have shown a higher risk of adverse outcomes at both high and low DBP, which is of concern because the lower targets in the hypertension guidelines might result being treated to the point of diastolic hypotension.[11] In multicenter, cross-sectional analysis of patients with chronic CAD, Peri-Okonny et al. found that very low DBP was associated with an increased odds of angina. In our study, there were 130 patients with DBP ≤75mmHg and 86 patients with DBP ≤70mmHg. The authors concluded that in the treatment of hypertension it may be prudent to ensure that DBP levels do not fall to <70 mm Hg.[10,11] In our study, when SDS values were compared, it was 4±4 in patients with DBP <70 mmHg and 4±4 in patients with DBP ≥70 mmHg, and no significant difference was found. According to the results of our study, we found that lower DBP alone did not affect the myocardial ischemia in SPECT MPI.

In our study, we found that although lower DBP alone does not cause ischemia, it can cause ischemia when SBP≥130mmHg is added to DBP≤75mmHg. Previous studies have reported an association between pulse pressure and the incidence of major cardiovascular events. This is because pulse pressure correlates with vascular endothelial function, arterial stiffness, volume status, and autonomic nervous system activity.[12] Pulse pressure is a surrogate of aortic stiffness and has strong prognostic value in many settings. In a study particularly among adults with an SBP

>120 mm Hg, and thus elevated pulse pressure, low DBP was associated with high troponin levels.[13] However, in our study, no difference was found in SDS values when SBP >120mmHg and <120mmHg were compared in patients with DBP ≤75mmHg (p=0.215). Difference in SDS values increases as SBP exceed 130mmHg.

Hypotension may lead to cardiac ischemia through supply–demand mismatch or promotion of coronary artery thrombosis. This may occur more commonly in patients with obstructive coronary artery disease than in patients without obstructive coronary artery disease.[10,14] When the coronary angiography results were evaluated in our study, SDS values were higher in patients with SYNTAX score ≥1 as expected (SDS=5.75±4.7 in SYNTAX score=0 and SDS=9.25±6.1 in SYNTAX score ≥1; p=0.00). However, when DBP≤75mmHg and >75mmHg were compared in both SYNTAX groups (=0 and ≥1), we could not find a significant difference in SDS (Table 3).

Limitations

The current study had some shortcomings. This was an retrospective study, and inferences might not reflect direct causal effects between DBP and myocardial ishemia. The interplay between DBP, SBP, coronary perfusion pressure, coronary flow, and myocardial wall stress cannot be fully analyzed in a retrospective study. Aortic stiffness and LVH were not considered. High aortic stiffness reduce myocardial perfusion pressure and may contribute to development of myocardial ischaemia.[15] LVH is independently associated with presence of myocardial ischemia in patients with non-obstructive CAD.[16] In addition, because adenosine is not used in patients with SBP <90mmHg, the number of samples was low. Patients who underwent exercise stress testing using treadmill were excluded, because blood pressures increase with exercise and the effect of low DBP on cardiac ischemia will be shadowed. Therefore, the results of our study are not suitable for SPECT MPI using exercise stress testing with the treadmill.

Conclusion

Our results suggested that coexistence DBP≤75mmHG with SBP>130mmHG may cause myocardial ischemia in adenosine stress MPI. Low DBP and the presence of simultaneously high SBP may be predictive of the myocardial ischemia in vasodilator MPI.

Ethics Committee Approval: Approval was obtained from local clinical research ethics committee in order to conduct the research (Date: 30.05.2019 and no: 2019.68.04.15).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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