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The Relationship Between the Internal Carotid Artery Resistive Index and the Myocardial Performance Index

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ABSTRACT

Objective: The carotid resistive index (RI) represents carotid vascular resistance. The myocardial performance index (MPI) is an echocardiographic parameter that reflects cardiac functions. The present study aimed to assess the relationship between carotid hemodynamics, measured by the internal carotid artery RI, and overall cardiac functions, assessed by the MPI in the general population.

Material and Methods: A total of 284 consecutive patients were enrolled in this cross-sectional study. Transthoracic echocardiography and carotid Doppler ultrasonography were performed on each participant. Patients were divided into two groups: the low carotid RI group (RI≤ 0.7) and the high carotid RI group (RI> 0.7).

Results: The MPI was significantly higher in the high carotid RI group than in the low carotid RI group (0.44 ± 0.11 vs. 0.41 ± 0.06, p= 0.014). Logistic regression analysis demonstrated that age [odds ratio (OR)= 1.127, 95% confidence interval (CI)= 1.046-1.214; p= 0.002], and the MPI (OR= 1.286, 95% CI= 1.060-1.520, p= 0.019) were independently associated with high carotid RI.

Conclusion: Age and the MPI were independent predictors of high internal carotid artery resistance in the general population.

Keywords: Carotid artery, myocardial performance index, vascular resistance, internal carotid artery resistive index

ÖZ

İnternal Karotis Arter Direnç İndeksi ile Miyokardiyal Performans İndeksi Arasındaki İlişki

Giriş: Karotis direnç indeksi (Dİ), karotis vasküler direnci temsil eder. Miyokardiyal performans indeksi (MPİ), kardiyak fonksiyonları yansıtan ekokardiyografik bir parametredir. Bu çalışmada genel popülasyonda, internal karotis arter Dİ aracılı ölçülen karotis hemodinamisi ile MPI tarafından değerlendirilen genel kardiyak fonksiyonlar arasındaki ilişkiyi değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Bu kesitsel çalışmaya toplam 284 ardışık hasta alındı. Her katılımcıya transtorasik ekokardiyografi ve karotis Doppler ultrasonografi yapıldı. Hastalar iki gruba ayrıldı; düşük karotis Dİ grubu (Dİ≤ 0.7) ve yüksek karotis Dİ grubu (Dİ> 0.7).

Bulgular: MPİ, yüksek karotis Dİ grubunda, düşük karotis Dİ grubuna göre anlamlı derecede daha yüksekti (0.44 ± 0.11'e 0.41 ± 0.06, p= 0.014). Lojistik regresyon analizi, yaşın [odds oranı (OR)= 1.127, %95 güven aralığı (GA)= 1.046-1.214; p= 0.002] ve MPİ'nin (OR= 1.286, %95 GA= 1.060-1.520, p= 0.019) bağımsız olarak yüksek karotis Dİ ile ilişkisini gösterdi.

Sonuç: Yaş ve MPI, genel popülasyonda yüksek internal karotis arter direncinin bağımsız belirleyicileriydi.

Anahtar Kelimeler: Karotis arter, miyokardiyal performans indeksi, vasküler direnç, internal karotis arter direnç indeksi

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INTRODUCTION

The resistive index (RI) is a Doppler sonographic measurement that reflects the resistance of a vessel. The RI of the internal carotid artery (ICA) is not only associated with the severity of atherosclerosis (1) but also can predict cardiovascular adverse events over three years (2). The RI is a parameter that can be easily measured without the need for a high-resolution ultrasound probe (2). Previous studies have focused on renal RI, which is calculated by renal blood flow (3). The renal RI has been investigated properly in various clinical conditions, including atherosclerotic renovascular disease (4), systemic hypertension (4), diabetes (5), ischemic heart disease, and heart failure (6), and is considered an atherosclerotic marker. Similarly, the carotid RI was found to be associated with atherosclerosis (1). However, no studies have been conducted to investigate the link between carotid artery RI and cardiovascular events.

The myocardial performance index (MPI) is an echocardiographic parameter that reflects cardiac performance comprehensively, including systolic and diastolic functions (7). This index has been studied in several conditions, including systemic hypertension (8), diabetes (9), ischemic heart disease, heart failure (10,11), and renal vascular resistance (12). The relationship between carotid artery resistance and left ventricle functions has yet to be studied. The purpose of this study was to assess the relationship between the MPI, which measures cardiac functions, and the carotid RI, which measures atherosclerosis and cerebral hemodynamics.

MATERIALS and METHODS

Patients and Study Design

Four hundred sixty-seven patients who were examined in the cardiology outpatient clinic between July 1, 2020 and December 1, 2020 were included in this prospective single-center study. Individuals with a history of stroke, carotid artery stenosis, severe left ventricular systolic dysfunction (left ventricular ejection fraction (LVEF)< 30%), severe valvular heart disease (valvular stenosis and regurgitation), chronic atrial fibrillation or flutter, coronary artery disease, pulmonary hypertension, infectious or inflammatory disease, malignant disease, reduced glomerular filtration rate (GFR) (<30 mL/min/1.73 m2), chronic hepatic disease, and pregnancy were excluded. Two hundred eighty-four patients were included in the study and 183 patients were excluded from the study.

The study was approved by the local ethics committee (Issue no: 48670771-514.10, Date: 30.06.2020). Informed consent was obtained from each patient. The research was conducted in accordance with the Declaration of Helsinki.

Transthoracic Echocardiography

Transthoracic echocardiographic examinations were performed according to the recommendations of the American Society of Echocardiography (13). Measurements were taken from the participants in the left decubitus position with a VIVID 7 (GE-Vingmed, Horten, Norway) echocardiography device using a 3.5 MHz cardiac probe.

M-mode and Doppler echocardiographic parameters, including interventricular septum thickness (IVST), posterior wall thickness (PWT), left atrium diameter, transmitral E-wave velocity (E), and A-wave velocity (A) were measured. Tissue Doppler parameters, such as early (Em) and late (Am) diastolic mitral annular velocities, peak systolic mitral annular velocity (S), isovolumetric contraction and relaxation, and ejection times were measured. Left ventricular ejection fraction was measured by using the modified Simpson method (14). Velocities over three cardiac cycles were averaged. The MPI was calculated following the formula; MPI= (isovolumetric contraction time + isovolumetric relaxation time)/ejection time (Figure 1).

Carotid Doppler Ultrasonography and the Internal Carotid Artery Resistive Index

The carotid Doppler sonography was performed with the Philips IU-22 system using a 5-MHz linear array probe. Examinations were performed after a 15-minute resting period in a supine position. The pulsed-Doppler indicator was placed in the internal carotid artery. Doppler ultrasonography parameters, including peak systolic (PSV) and end-diastolic velocities (EDV), RI, and pulsatility index were measured automatically using the inbuilt software (Figure 2). The RI was defined as (PSV-EDV)/PSV (15). The mean value of right and left internal carotid artery RIs were used for analysis. Zero point seven was set as the cut-off value for RI (low carotid RI≤ 0.7 and high carotid RI> 0.7) (16).

Statistical Analysis

SPSS 22.0 (SPSS v22.0 for Windows, Chicago, IL, USA) was used for analysis. The normal distribution was evaluated using the Kolmogorov–Smirnov test. Continuous parameters were expressed as mean ± standard deviation or median (min-max) and compared using the independent samples t-test or Mann–Whitney U test regarding distribution. Categorical parameters were expressed as numbers (percentages) and compared using the Chi-square test. The reliability analysis was used for intra-observer variability of MPI measurements. All significant parameters ($p< 0.1$) were selected for the multivariable model. Logistic regression analysis with a forward conditional method was performed. A p-value of <0.05 was considered significant.

RESULTS

In the present study, the low carotid RI group (RI≤ 0.7) included 218 patients (153 male; mean age= 60.5 ± 9.5 years), and the high carotid RI group (RI> 0.7) included 66 patients (47 male; mean age= 63.7 ± 10.4 years). Patients in the high carotid RI group were significantly older than those in the low carotid RI group (p= 0.017). Other demographic and laboratory parameters were similar between the two groups except for age. These variables are shown in Table 1.

Interventricular septum thickness and PWT were significantly higher in the high carotid RI group than in the low carotid RI group (11.5 ± 1.9 vs. 10.9 ± 2.0, p= 0.036 for IVST; 12.1 ± 1.9 vs. 11.3 ± 1.8, p= 0.002 for PWT). Em and S velocities were significantly lower in the high carotid RI group than in the low carotid RI group (5.2 ± 1.8 vs. 5.8 ± 1.9, p= 0.022 for Em velocity; 6.3 ± 1.6 vs. 6.9 ± 1.4, p= 0.002 for S velocity). The MPI was significantly higher in the high carotid RI group than in the low carotid RI group (0.44 ± 0.11 vs. 0.41 ± 0.06, p= 0.014). The comparison of transthoracic echocardiographic parameters of the patients is shown in Table 2.

Univariate and multivariate binary logistic regression analysis demonstrated that age [odds ratio (OR)= 1.127, 95% confidence interval (CI)= 1.046-1.214; p= 0.002)], and the MPI (OR= 1.286, 95% CI= 1.060-1.520, p= 0.019) were independent predictors of high carotid RI (Table 3).

The intra-observer variability of MPI measurements was evaluated using the reliability analysis. The MPIs of randomly selected 30 patients were measured 10 days apart. The intra-class correlation coefficient was 0.937 (p< 0.001).

DISCUSSION

Our study yielded some significant findings, which can be attributed to a variety of mechanisms. First, patients who had high carotid RI were significantly older than those who had low carotid RI. Age is associated with diastolic dysfunction of the heart (17), and carotid artery flow changes (18-21). Diastolic dysfunction of the left ventricle refers to cardiac fibrosis and collagen matrix proliferation. Collagen fibers type I and cross-linking are enhanced in the aged population (22). Buljan et al. revealed a clear connection between carotid intima-media thickness, and age in healthy adults (18). Gepner et al. demonstrated that carotid arterial stiffening accelerates with advanced age (19). Also, Hirata et al. reported that vascular stiffening enhances carotid flow augmentation and can explain the flow fluctuations in the cerebral circulation (20). Kamenskiy et al. discovered that geometric changes in carotid arteries occur with aging, including intramural elastin

Table 1. Comparison of baseline demographic and laboratory parameters of the patients

Variables	Low Carotid RI (n= 218)	High Carotid RI (n= 66)	p-value
Age (years)	60.5 ± 9.5	63.7 ± 10.4	**0.017**
Gender (male), n (%)	153 (70.2)	47 (71.2)	0.873
BMI (kg/m^2)	27.8 (19.2-47.2)	27.0 (18.6-40.8)	0.225
Systolic BP (mm Hg)	112 (88-156)	117 (81-157)	0.151
Diastolic BP (mm Hg)	71 (47-105)	72 (52 -95)	0.536
Diabetes mellitus, n (%)	59 (27.1)	24 (36.4)	0.146
Hypertension, n (%)	90 (41.3)	28 (42.4)	0.869
Hyperlipidemia, n (%)	38 (17.4)	10 (15.2)	0.665
Smoking status, n (%)	97 (44.5)	25 (37.9)	0.341
Haemoglobin (g/dl)	13.8 ± 1.7	13.5 ± 1.8	0.152
Leukocyte count, x10^3/μL	8.6 (3.4-14.2)	9.3 (84.6-14.8)	0.242
Platelet count, x10^3/μL	249.8 ± 55.2	250.7 ± 61.9	0.903
HDL cholesterol (mg/dl)	39.6 ± 10.4	39.1 ± 11.0	0.746
LDL cholesterol (mg/dl)	138.0 ± 40.9	130.4 ± 38.8	0.182
Total cholesterol (mg/dl)	198.2 ± 44.4	187.9 ± 42.6	0.097
Triglyceride (mg/dl)	143.5 (44.0-1185.0)	144.0 (45.0-789.0)	0.951

Data are presented as mean ± standard deviation, median (minimum-maximum) or number (%).
p-value was calculated using the Independent-Samples T test or the Mann-Whitney U test for continuous variables and the Chi-Square test for categorical variables as appropriate. A p-value of <0.05 was considered significant.
BMI: Body mass index, BP: Blood pressure, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, RI: Resistive index.

Table 2. Comparison of transthoracic echocardiographic parameters of the patients

Parameters	Low Carotid RI (n= 218)	High Carotid RI (n= 66)	p-value
E velocity (cm/s)	58.0 ± 17.0	55.9 ± 17.4	0.372
A velocity (cm/s)	72.4 ± 15.3	74.9 ± 16.2	0.259
E/A ratio	0.82 ± 0.27	0.78 ± 0.32	0.273
IVST (mm)	10.9 ± 2.0	11.5 ± 1.9	**0.036**
PWT (mm)	11.3 ± 1.8	12.1 ± 1.9	**0.002**
LVEF (%)	59.1 ± 8.9	57.2 ± 8.9	0.141
LA diameter (mm)	34.1 ± 4.2	33.4 ± 4.6	0.286
Em velocity (cm/s)	5.8 ± 1.9	5.2 ± 1.8	**0.022**
Am velocity (cm/s)	8.5 ± 1.7	8.2 ± 1.9	0.172
S velocity (cm/s)	6.9 ± 1.4	6.3 ± 1.6	**0.002**
E/Em ratio	9.3 ± 1.8	9.6 ± 1.9	0.336
MPI	0.41 ± 0.06	0.44 ± 0.11	**0.014**

Data are presented as mean ± standard deviation.
p-value was calculated using the Independent-Samples T test. A p-value of <0.05 was considered significant.
IVST: Inter-ventricular septum thickness, LA: Left atrium, LVEF: Left ventricular ejection fraction, MPI: Myocardial performance index, PWT: Posterior wall thickness, RI: Resistive index.

Table 3. Univariate and multivariate analyses of high carotid resistive index

Variables	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.036 (1.006-1.068)	**0.018**	1.127 (1.046-1.214)	**0.002**
Total cholesterol	0.994 (0.988-1.001)	0.098	-	-
IVST (mm)	1.161 (1.009-1.336)	**0.037**	-	-
PWT	1.279 (1.087-1.505)	**0.003**	-	-
Em velocity (mm)	0.823 (0.694-0.975)	**0.024**	-	-
S velocity	0.729 (0.592-0.898)	**0.003**	-	-
MPI	1.190 (1.010-1.376)	**0.015**	1.286 (1.060-1.520)	**0.019**

A p-value of <0.05 was considered significant.
CI: Confidence interval, IVST: Inter-ventricular septum thickness, MPI: Myocardial performance index, OR: Odds ratio, PWT: Posterior wall thickness.

degradation and fragmentation. These alterations may cause a measurable rise in blood flow resistance (21). Second, several cytokines, including transforming growth factor-β, fibroblast growth factor, and tumor necrosis factor-α may induce accumulation of the extracellular matrix, myocardial fibrosis, and vascular remodeling (23-26).

Variz et al. have evaluated carotid arterial stiffness and diastolic function of the heart in healthy subjects and found that stiffness parameter (β) and pressure-strain elasticity modulus were inversely correlated with transmitral E, E/A ratio, and septal Em and positively correlated with A wave (27). Also, carotid intima-media thickness was correlated with A wave, E/A ratio, Em, and Am. Akintunde et al. have investigated carotid atherosclerosis and diastolic dysfunction of the right ventricle in hypertensive patients and found that carotid intima-media thickness was correlated with early transtricuspid flow parameters (28). Unlike the previous studies, this research revealed a significant negative correlation between Em velocity and the carotid RI, and a significant positive correlation between the MPI and the carotid RI. Thus, to our knowledge, the present study was the first to assess the carotid RI and the MPI in the general population.

Many non-invasive markers, including carotid intima-media thickness, RI, and pulsatility index, are based on early alterations that occur in vascular wall layers, including expansion, calcification, and endothelial dysfunction (29,30). The carotid intima-media thickness is a non-invasive and reproducible measurement for discriminating and quanti-

fying sclerotic vessels (31). However, the RI and pulsatility index are more practical for quantifying changes in the carotid blood velocity waveforms. Compared to intima-media thickness, the RI is easier to measure and tends to have less interobserver and intraobserver variability. However, heart rhythm disturbances and stenosis near the measurement site are countable disadvantages that affect RI measurement. In our study, we excluded patients with atrial fibrillation and those with detectable stenosis.

The renal RI decreases with higher vascular resistance and increases with impaired vascular compliance (32,33). Mean arterial blood pressure, diastolic blood pressure, cardiac output, and preload have essential effects on the RI (34,35). We think that similar relationships between carotid RI and those factors are logically possible. However, further studies on these topics are warranted.

Staub et al. demonstrated that cardiovascular events were linked to increased carotid intima-media thickness and RI of the internal carotid artery. This could be explained by the fact that these two parameters can predict atherosclerosis (2). The MPI was also found to be effective in predicting cardiovascular mortality. This could be explained by the relationship of the MPI with arterial compliance and peripheral resistance (36). Indeed, the RI and MPI are associated with peripheral resistance and arterial compliance.

Isovolumetric relaxation time was significantly higher in patients with high renal RI (37). In this study, the MPI was independently associated with high carotid RI. Carotid vascular resistance is related to overall cardiac functions. We advise performing a Doppler ultrasonography of the carotid arteries in patients with impaired cardiac functions.

CONCLUSION

The MPI was significantly and independently associated with high carotid RI in the general population. Carotid vascular resistance is related to overall cardiac functions. We advise performing a Doppler ultrasonography of the carotid arteries in patients with impaired cardiac functions.

Limitations of the Study

The findings of the present study are obtained from a relatively small population. Larger studies are required to validate such outcomes. Also, the effects of anti-hypertensive drugs on the RI and MPI measurements, as well as carotid intima-media thickness were not assessed.

Ethics Committee Approval: This study was approved by the İstanbul Prof. Dr. Cemil Taşçıoğlu State Hospital Clinical Research Ethics Commitee (Decision Number: 48670771-514.10, Date: 30.06.2020).

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