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Association between coronary artery disease severity and videocapillaroscopic findings of nail fold capillary circulation

Koroner arter hastalığının şiddeti ile tırnak yatağı kapiller dolaşımının videokapilleroskopik bulguları arasındaki ilişki

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Abstract

Aim: Endothelial dysfunction plays a significant role in the etiology of coronary artery disease (CAD), which develops due to atherosclerosis, and is a major cause of morbidity and mortality. Nail fold videocapillaroscopy (NVC) assessment is a surrogate marker of endothelial dysfunction. To the best of our knowledge, the relationship between the microcirculation features on NVC and the severity of coronary atherosclerosis has not previously been investigated. In this study, we aimed to investigate the relationship between severity of coronary atherosclerosis (shown by SYNTAX and Gensini scores) and NVC findings which is an indirect indicator of systemic endothelial damage.

Methods: The study was designed as a retrospective cohort. One-hundred consecutive patients who underwent coronary angiography (CAG) and had at least one lesion in the epicardial coronary arteries, narrowing the lumen by more than 50%, were included. Coronary angiographic images of the patients were evaluated by two experienced interventional cardiologists and SYNTAX and Gensini scores were calculated. Patients were divided into three groups according to the SYNTAX scores (SYNTAX score ≤22, between 23-32, and ≥33) and two groups according to Gensini scores (Gensini score ≥30 and <30). The NVC examinations were performed by a rheumatologist who was experienced in this field, and the reduction in capillary density, presence of dilated capillaries, giant capillary, microhemorrhage, branching, disorganization, tortuosity, avascular area, extravasation, and neoangiogenesis were investigated.

Results: Dilated capillary vessels were more common in diabetic patients (85%) than in non-diabetics (66.7%) (P=0.041). Besides, there was no significant difference in NVC parameters between patients with and without diabetes mellitus (P>0.05 for all), with and without hypertension (P>0.05 for all). There was no significant difference between the SYNTAX groups in terms of NVC findings (P>0.05 for all). The NVC findings were similar between Gensini groups (P>0.05 for all).

Conclusion: The severity of atherosclerosis surrogated by SYNTAX and Gensini scores was not related to the NVC findings. Therefore, NVC is inappropriate for determining the severity of CAD.

Keywords: Coronary artery disease, Nail fold videocapillaroscopy, SYNTAX, Gensini Score

Öz

Amaç: Ateroskleroza bağlı olarak gelişen ve önemli morbidite ve mortalite nedeni olan koroner arter hastalığının (KAH) etiyolojisinde endotel disfonksiyonu önemli rol oynar. Tırnak dibinin videokapilleroskopik (NVC) değerlendirilmesi endotel disfonksiyonun dolaylı bir göstergesidir. NVC ile değerlendirilen mikrosirkulasyona ait verilerle endotel disfonksiyonunun önemli rol oynadığı koroner arterlerdeki aterosklerozun yaygınlığı arasında bir ilişki olup olmadığı daha once araştırılmamış bir konudur. Biz bu çalışmada sistemik endotel hasarının dolaylı bir göstergesi olan NVC ile tırnak yatağının kapiller dolaşımını değerlendirererek koroner arter hastalığının yaygınlığı gösteren SYNTAX ve Gensini skorları ile muhtemel ilişkiyi araştırmayı amaçladık.

Yöntemler: Bu çalışma retrospektif Kohort çalışması olarak tasarlanmıştır. Koroner anjiyografi (KAG) yapılan ve epikardiyal koroner arterlerde lümeni %50'den fazla daraltan lezyon tespit edilmiş olan ardışık 100 hasta çalışmaya alınmıştır. Çalışmaya katılan hastaların KAG görüntüleri deneyimli iki invaziv kardiyoloji uzmanı tarafından değerlendirilerek SYNTAX ve Gensini skorları hesaplanmıştır. Hastalar SYNTAX skoruna göre ≤22, 23-32 arası ve ≥33 olmak üzere 3 gruba ve Gensini skoruna göre Gensini skoru ≥30 ve <30 olan hastalar olmak üzere 2 gruba ayrılmıştır. Çalışmaya katılan hastaların NVC incelemeleri bu konuda deneyimli olan bir romatoloji uzmanı tarafından yapılmıştır ve dev kapiller arter varlığı, mikrohemoraji, dallanma, disorganizasyon, tortiyozite, avasküler alan, extravazasyon, neogenezis, kapiller dansitede azalma ve dilate kapiller damar varlığı araştırılmıştır.

Bulgular: Diyabetes mellitusu olan hastalarda (%85) dilate kapiller diyabetes mellitusu olmayan hastalardan (%66,7) daha yaygındı (P=0,041). Diyabetes mellitusu olan/olmayan (hepsi için P>0,05), hipertansiyonu olan/olmayan hastalar arasında NVC parametreleri bakımından anlamlı bir fark saptanmadı (hepsi için P>0,05). SYNTAX skoruna göre gruplar arasında NVC parametreleri bakımından anlamlı bir fark saptanmadı (hepsi için P>0,05). Gensini skoruna göre gruplar arasında benzer NVC bulguları saptandı (hepsi için P>0,05).

Sonuç: Koroner arter hastalığının yaygınlığını belirlemede kullanılan SYNTAX ve Gensini skorları ile NVC parametreleri arasında ilişki yoktur. Bu yüzden NVC parametrelerinin koroner arter hastalığının şiddetini belirlemede kullanılması uygun değildir.

Anahtar kelimeler: Koroner arter hastalığı, Tırnak yatağı videokapilleroskopi, SYNTAX, Gensini skoru

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Introduction

Coronary artery disease (CAD) is one of the most common causes of morbidity and mortality in Turkey as well as in the world, and the most prominent etiological factor is atherosclerosis in 85% of patients. Atherosclerosis is a progressive process that is based on endothelial dysfunction and progresses to plaque rupture and thrombosis, causing narrowing and occlusion of the vessel lumen. The endothelial layer covers the inner surface of all vascular structures and has vital functions in the maintenance of blood circulation in the organism. In the capillaries which perfuse the tissues, vessel walls consist of the endothelium, a single-layered cellular arrangement. Endothelial dysfunction plays a significant role in the development of atherosclerosis, which is considered as a systemic disease. Many parameters that indirectly indicate endothelial dysfunction have been studied previously in patients with CAD. Reduction in flow-mediated dilatation (FMD), which reflects endothelial function, has been shown with the presence and severity of CAD previously [1-3]. Gümüşel et al. [4] have shown a strong negative correlation between the Gensini score and FMD in CAD patients. It has been reported that FMD and coronary calcification score, which reflects endothelial dysfunction noninvasively, may provide complementary information in predicting the prevalence and severity of CAD graded by Gensini and SYNTAX scores [5].

Nail fold videocapillaroscopy (NVC) is a noninvasive method used as a complementary test to confirm the diagnosis and to monitor the efficiency of treatment in rheumatic diseases such as systemic sclerosis (SSc) and systemic lupus erythematosus (SLE) by examining the capillary structures in the nail fold [6-13]. The videocapillaroscopic analysis is now included in the ACR / EULAR classification criteria for systemic sclerosis [14]. Reduction of peripheral tissue perfusion is usually associated with microvascular injury in SSc, which can be demonstrated by different methods [15]. In SSc, the association of NVC findings with disease activity, pulmonary HT, efficacy of medical treatment, and involvement of internal organs has been shown previously [7,16-18].

To the best of our knowledge, the relationship between microcirculation on NVC and the severity of coronary atherosclerosis has not previously been investigated. In this study, we aimed to investigate the relation of the severity of coronary atherosclerosis, shown by SYNTAX and Gensini scores, with NVC findings as an indirect indicator of systemic endothelial damage.

Materials and methods

Two experienced interventional cardiologists evaluated coronary angiography images of the patients and calculated the SYNTAX and Gensini scores.

Gensini score

Gensini score indicating the severity and extension of coronary atherosclerosis in CAD patients was calculated as previously described in the literature [19]. This method scores and classifies the severity and extent of the stenosis in epicardial coronary arteries due to atherosclerosis. According to Gensini scoring system, 1-25% stenosis scores 1 point, 26-50% stenosis scores 2 points, 51-75% stenosis, 4 points, 76-90% stenosis, 8 points, 91-99% stenosis,16 points, and total occlusion, 32 points. In addition, each lesion in the epicardial coronary arterial system is multiplied by a factor representing the importance of its localization. The patient's score is multiplied by 5 if the lesion is in the left main coronary artery (LMCA), multiplied by 2.5 in the proximal left anterior (LAD) or in the left circumflex (LCx) artery lesions, multiplied by 1.5 in the middle segment of the LAD and LCx lesions, multiplied by 1 in the distal segment of LAD and LCx, or in the first diagonal and optuse marginalis (OM) branch, or in the right coronary artery lesions, or in the posterior descending artery (PDA) lesions, and multiplied by 0.5 in the second diagonal or OM branch lesions. The total Gensini score is calculated by summation of the scores from all coronary lesions.

SYNTAX score

The SYNTAX score has been developed as a combination of several predetermined angiographic classifications aimed at grading coronary atherosclerotic lesions based on the number, functional impact, localization, and complexity of the lesions [20]. This scoring system is intended to assist in risk classification of patients with severe coronary lumen stenosis who require revascularization and the selection of patients for appropriate revascularization technique [20-22]. It was used in the SYNTAX study for the first time. In this study, the rates of long-term cardiovascular events differed between treatment strategies (coronary artery bypass grafting (CABG) vs percutaneous coronary intervention (PCI)) and among the groups categorized into tertiles according to the SYNTAX score as well. According to the results of the first published SYNTAX trial, the event rates were similar in patients with low (0-22) and moderate (23-32) SYNTAX score tertiles for CABG and PCI, but the rate of long-term adverse cardiovascular event was significantly higher in the PCI group compared to the CABG group in patients with a high SYNTAX score (≥33 indicating most complex disease) [23].

NVC findings

NVC examination of the patients was performed by a rheumatologist who was experienced in capillaroscopy in Rheumatology Clinic by Video Cap 3.0 device. Reduction in capillary density, dilated capillaries, giant capillary structures, microhemorrhage, branching, disorganization, tortuosity, avascular area, extravasation, and neoangiogenesis were investigated [24,25].

Study population

As a result of the sample size analysis based on other research findings in the literature, the minimum number of participants in each group was determined as 17 with a 95% confidence level and 80% power.

The study included 100 consecutive patients who underwent coronary angiography (CAG) and who had ≥50% stenosis in epicardial coronary arteries. Patients were divided into groups according to heart failure (EF ≥50% and EF <50%), presence of HT and DM, SYNTAX score (<23, 23-32, ≥33) and Gensini score (<30 and ≥30) and compared in terms of NVC parameters.

Patients with chronic diseases such as systemic sclerosis, chronic renal failure, chronic liver disease,

decompensated congestive heart failure, any malignancy, dilated cardiomyopathy, congenital heart disease, and pregnant women were excluded from the study.

Statistical analysis

Numerical variables were presented as mean, standard deviation and minimum-maximum values. Categorical variables were given as numbers and percentages. Pearson's chi-square test was used to compare the categorical variables between the study groups. Statistical analyses were performed with Jamovi (Version 0.9.5.12) computer software. $P<0.05$ was considered statistically significant.

Results

The study included 100 patients, 31 females 69 males. The age of patients ranged from 38 to 89 years with a mean age of 62 (11) years. Forty patients had diabetes mellitus (DM), 52 had hypertension (HT).

The highest and lowest SYNTAX scores were 53 and 2, respectively. The mean SYNTAX score of the patients was 18.6 (12.6). According to the SYNTAX scores, 68 had a score of 22 or less, 20 had a SYNTAX score of 23-32, and 12 had a SYNTAX score of 33 or higher.

The highest and lowest Gensini scores were 242 and 4, respectively, with a mean Gensini score of 63.0(49.2). When the patients were divided into 'mild-moderate CAD' and 'severe CAD' groups according to the Gensini score, 27 patients had a Gensini score of <30 and 73 had a Gensini score of ≥30.

In the NVC evaluation of the patients, 16 had reduced capillary density, 74 had dilated capillary structures, 2 had giant capillaries, 4 had microhemorrhage, 36 had branching, 7 had disorganization, 73 had tortuosity, and 15 had an avascular area, one had extravasation, and one had neoangiogenesis.

There was no significant difference between the diabetic and non-diabetic patients in terms of NVC parameters except for the rate of dilated capillary structures, which was higher in diabetic patients than in non-diabetic patients (85% vs. 67%, $P=0.041$). NVC parameters of hypertensive and non-hypertensive patients (Table 1), low, intermediate, and high SYNTAX scores and groups with Gensini scores<30 and ≥30 were comparable among themselves ($P>0.05$ for all) (Table 2, 3).

Table 1: Comparison of CAD patients with and without diabetes mellitus and hypertension in terms of NVC findings

	Non-diabetic (n=60)	Diabetic (n=40)	*P*-value	Hypertensive (n=52)	Normotensive (n=48)	*P*-value
Giant capillaries, n (%)	2 (3.3)	0 (0)	0.52	2 (3.8)	0 (0)	0.50
Microhemorrhage, n (%)	2 (3.3)	2 (5)	0.99	2 (3.8)	2 (4.2)	0.99
Branching, n (%)	21 (35)	15 (37.5)	0.80	17 (32.7)	19 (39.6)	0.47
Disorganization, n (%)	6 (10)	1 (2.5)	0.24	5 (9.6)	2 (4.2)	0.44
Tortuosity, n (%)	42 (70)	31 (77.5)	0.41	38 (73.1)	35 (72.9)	0.99
Avascular area, n (%)	9 (15)	6 (15)	0.99	7 (13.5)	8 (16.7)	0.65
Extravasation, n (%)	1 (1.7)	0 (0)	0.99	1 (1.9)	0 (0)	0.99
Neoangiogenesis, n (%),	1 (1.7)	0 (0)	0.99	1 (1.9)	0 (0)	0.99
Reduced capillary density, n (%)	8 (13.3)	8 (20)	0.37	9 (17.3)	7 (14.6)	0.71
Dilated capillaries, n (%)	40 (66.7)	34 (85)	0.041	40 (76.9)	34 (70.8)	0.49

* The number and percentage of patients with relevant findings are presented.

Table 2: Comparison of NVC findings between the Syntax groups

	<23 (n=68)	23-32 (n=20)	≥33 (n=12)	*P*-value
Giant capillaries, n (%)	2 (2.9)	0 (0)	0 (0)	0.99
Microhemorrhage, n (%)	2 (2.9)	2 (10)	0 (0)	0.25
Branching, n (%)	25 (36.8)	7 (35)	4 (33.3)	0.97
Disorganization, n (%)	4 (5.9)	1 (5)	2 (16.7)	0.39
Tortuosity, n (%)	49 (72.1)	16 (80)	8 (66.7)	0.68
Avascular area, n (%)	11 (16.2)	2 (10)	2 (16.7)	0.83
Extravasation, n (%)	0 (0)	1 (5)	0 (0)	0.33
Neoangiogenesis, n (%),	1 (1.5)	0 (0)	0 (0)	0.99
Reduced capillary density, n (%)	11 (16.2)	2 (10)	3 (25)	0.53
Dilated capillaries, n (%)	49 (72.1)	15 (75)	10 (83.3)	0.71

* The number and percentage of patients with relevant findings are presented.

Table 3: Comparison of NVC findings between the Gensini groups

	Gensini ≥30 (n=73)	Gensini <30 (n=27)	*P*-value
Giant capillaries, n (%)	1 (1.4)	1 (3.7)	0.47
Microhemorrhage, n (%)	3 (4.1)	1 (3.7)	0.99
Branching, n (%)	26 (35.6)	10 (37)	0.99
Disorganization, n (%)	4 (5.5)	3 (11.1)	0.38
Tortuosity, n (%)	55 (75.3)	18 (66.7)	0.39
Avascular area, n (%)	12 (16.4)	3 (11.1)	0.75
Extravasation, n (%)	1 (1.4)	0 (0)	0.99
Neoangiogenesis, n (%),	0 (0)	1 (3.7)	0.27
Reduced capillary density, n (%)	13 (17.8)	3 (11.1)	0.55
Dilated capillaries, n (%)	51 (69.9)	23 (85.2)	0.12

* The number and percentage of patients with relevant findings are presented.

Discussion

To the best of our knowledge, this is the first study to investigate the association between atherosclerosis severity and NVC findings in CAD patients. According to our results, dilated capillary structures were more frequent in diabetic patients than non-diabetic patients. Other NVC findings were similar between the diabetic and non-diabetic patients. The NVC findings between hypertensive and normotensive patients, patients with low-to-intermediate and high SYNTAX scores, and patients with Gensini scores of <30 and ≥30 were also comparable.

Endothelial dysfunction is an early and reversible stage in the development of cardiovascular diseases. It can be used to predict future CAD development before occurrence of atherosclerotic changes in the arterial wall [26]. Carotid intima-media thickness (CIMT) and FMD are noninvasive techniques to evaluate endothelial dysfunction [2,26]. There are studies showing that increased CIMT and decreased FMD are associated with CAD as well as studies showing that increased CIMT is associated with CAD severity [27-30].

Diabetes mellitus is a common disease with frequent complications leading to high mortality and morbidity rates worldwide. Endothelial dysfunction and angiopathy play a key role in the early stage of diabetes complications. Alterations in permeability and capillary flow affect the macrovascular and microvascular structures due to the changes in red blood cell velocity and basement membrane thickness. In patients with diabetes mellitus, increase in tortuosity and angiogenesis have been reported in NVC examination. Microcirculation angiopathy has been reported in 17% of diabetic patients and these patients deserve more attention regarding diabetic vascular complications [31]. In our study, dilated capillary vessels were found more frequently in the NVC examination of diabetic CAD patients while there was no significant difference in capillary density, the presence of giant capillaries, microhemorrhage, branching, disorganization, tortuosity, avascular area, extravasation, and neoangiogenesis compared to non-diabetic CAD patients. We believe that this was due to the presence of endothelial dysfunction underlying CAD because all patients who participated in the study had CAD.

Increased peripheral vascular resistance is associated with essential hypertension. The characteristics of microcirculation contribute to hypertension by determining peripheral vascular resistance. Nail fold videocapillaroscopic examination of hypertensive patients showed a reduction in capillary density and in velocity of red blood cells. Reduction of red blood cells velocity was associated with microcirculation impairment and end-organ damage in hypertensive patients [32]. In our study, reduction in capillary density, the presence of dilated capillaries, giant capillary, microhemorrhage, branching, disorganization, tortuosity, avascular area, extravasation, and neoangiogenesis were similar between hypertensive and normotensive patients. We believe that this was due to the small number of patients enrolled in the study.

Cardiac Syndrome X (CSX) is a clinical status characterized by typical angina pectoris and ST depression on exercise ECG test without any obstructive (≥50%) stenosis in epicardial coronary arteries on CAG. Increase in vasoconstriction sensitivity and/or impairment in relaxation in arterioles and pre-arterioles are believed to play role in the etiopathogenesis of CSX [33]. Reduction in capillary density has been reported in the NVC findings of CSX patients [34].

Coronary slow flow is defined as a delay in filling the vessel lumen by opaque material despite any stenosis in the epicardial coronary arteries on CAG [35]. The pathophysiology of coronary slow flow is implicated in small vessel disease, endothelial dysfunction, atherosclerosis, inflammation, an imbalance in vasoactive substances, and anatomical abnormalities. Nail fold videocapillaroscopic examination of patients with coronary slow flow revealed that tortuosity, microhemorrhage, and capillary dilatation were 5.7 times higher than those with normal coronary blood flow [13].

In our study, the SYNTAX and Gensini scores were calculated on CAG images to determine the severity of atherosclerosis in CAD patients with ≥50% stenosis in epicardial coronary arteries. There was no significant relation between NVC findings and SYNTAX or Gensini scores of CAD patients. Consequently, there was no significant relationship between NVC findings and the severity of atherosclerosis in CAD patients.

Limitations

The main limitation of our study was the absence of a control group with normal coronary arteries as demonstrated with CAG. The lack of a significant difference in the NVC findings between the study groups might be since there was already an underlying endothelial dysfunction, for all patients already had CAD. In addition, the number of sample size might not be high enough to reveal such a difference.

Conclusions

According to our results, there was significant relationship between diabetes mellitus, hypertension, and NVC findings in patients with CAD. Besides, we did not find any relationship between the NVC findings and SYNTAX and Gensini scores, which are used to determine the severity of atherosclerosis in CAD.

To clarify this issue, it may be more appropriate to conduct long-term intermittent NVC examinations of people with normal coronary arteries and compare NVC findings when coronary artery disease is detected, or to study where some patients have normal coronary artery disease and some patients with coronary artery disease.

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