RESEARCH ARTICLE / Araştırma Makalesi

Evaluation Of Clinical Outcomes and Coronary Artery Disease In Patients Scheduled For Endovascular Intervention Due To Lower Extremity Ischemia

Alt Ekstremite Iskemisi Nedeniyle Endovasküler Girişim Planlanan Hastaların Klinik Sonuçları ve Koroner Arter Hastalığı Açısından Değerlendirilmesi

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Abstract

Objective In this study, clinical outcomes and coronary artery disease in patients diagnosed with peripheral occlusive artery disease who were scheduled to have an endovascular intervention procedure were investigated.**Sakarya Med J, 2018, 8(2):266-271)**

Materials and Methods 114 peripheral artery disease patients who were planned to undergo an endovascular intervention due to stenosis of 70% or more in any one of lower limb arteries between January 2013 and August 2017 and underwent coronary artery angiography at the same time were included in this study. Patients were divided into three groups according to the degree of the stenosis in their coronary arteries. Group 1: patients without CAD or having <40% of stenosis, Group 2: patients having equal or more than 40% but less than 70% of stenosis, Group 3: patients with ≥70% of stenosis. The groups were retrospectively compared in terms of age, gender, lipid profiles (total cholesterol, LDL, HDL, and triglyceride), other diseases (hypertension, diabetes mellitus, and chronic obstructive pulmonary disease), lower extremity amputation, and mortality.

Results The mean age was 66.56 ± 11.65. 100 of the cases (87.7%) were male. Eight of the cases (7.0%) had coronary artery disease with a stenosis of 40-70%, and 75 patients (65.8%) had significant coronary artery disease with stenosis of 70% and above. 61 (53.5%) of the cases had hypertension, 31 (27.2%) had diabetes mellitus, 78 (68.4%) cases had dyslipidemia, and 10 (8.8%) cases had chronic obstructive pulmonary disease. The mortality rate was 17.5% (20 patients) in patients who could be followed up for one year. The mean age of group 1 was statistically significantly lower than the other two groups. No significant difference was found between the groups in terms of other clinical outcomes.

Conclusion Because of the high incidence of coronary artery disease in patients with peripheral occlusive artery disease, it is important to screen these patients via routine coronary artery angiography to decrease cardiovascular mortality and morbidity.

Keywords Peripheral artery disease; coronary artery disease; coronary artery angiography

Öz

Amaç Bu çalışmada, endovasküler girişim planlanan periferik tıkayıcı arter hastalığı teşhisi konulan hastalarda koroner arter hastalığı ve klinik sonuçları incelendi. **(Sakarya Tıp Dergisi, 2018, 8(2):266-271).**

Gereç ve Yöntem Ocak 2013 ile Ağustos 2017 tarihleri arasında alt ekstremite arterlerinin herhangi birisinde %70 ya da daha fazla stenoz nedeniyle endovasküler girişim planlanan ve aynı zamanda koroner anjiografisi yapılan 114 periferik arter hastalığı olgusu çalışmaya dahil edilmiştir. Hastalar koroner arter stenoz derecesine göre üç gruba ayrıldı. Grup 1: Koroner arter stenozu olmayanlar veya <%40 stenozis olanlar, Grup 2: ≥ 40% ve <70% stenozis olanlar, Grup 3: ≥70% stenozis olanlar. Gruplar yaş, cinsiyet, lipit profilleri (total kolesterol, LDL,HDL, trigliserit), ek hastalıklar (hipertansiyon, diabetes mellitus, kronik obstruktif akciğer hastalığı), alt ekstremite amputasyonu ve mortalite açısından retrospektif olarak karşılaştırılmıştır.

Bulgular Ortalama yaş 66.56±11.65'tir. Olguların 100'ü (%87.7) erkekti. Olguların 8'sinde (%7.0) %40-70 arası darlık olan koroner arter hastalığı, 75'inde (%65.8) %70'in üzerinde darlık olan önemli koroner arter hastalığı saptandı. Olguların 61'i (%53.5) hipertansiyon, 31'i (%27.2) diyabetes mellitus, 78'ü (%68.4) dislipidemi, 10'u (%8.8) kronik obstrüktif akciğer hastalığına sahipti. Mortalite oranı bir yıllık takibi yapılabilen hastalarda %17.5 (20 hasta) bulundu. Grup 1'de yaş ortalaması diğer iki gruptan istatistiksel olarak anlamlı düşük çıktı. Gruplar arasında diğer klinik sonuçlar açısından anlamlı fark bulunmadı.

Sonuç Periferik tıkayıcı arter hastalığı olan hastalarda koroner arter hastalığı prevalansının yüksek olması nedeniyle bu hastalarda tarama amaçlı rutin koroner arter anjiografi yapılması kardiyovasküler mortalite ve morbiditenin azaltılması açısından önemlidir.

Anahtar Kelimeler Periferik arter hastalığı; koroner arter hastalığı; koroner arter anjiografi.

Introduction

Peripheral arterial disease (PAD) is a form of systemic atherosclerosis that is reflected in the clinic. Systemic atherosclerotic diseases are known to be associated with poor clinical outcome. It has been widely known that hypertension (HT), diabetes mellitus (DM), dyslipidemia (DL) and chronic obstructive pulmonary disease (COPD) are the major risk factors for PAD.[1,2] Other arterial systems as well as peripheral arterial systems are highly involved in this disease.[1] Coronary artery disease (CAD) is seen more frequently in patients having PAD.[3,4,5] This increase can reach up to 83%.3

Nowadays, endovascular therapy for peripheral arterial disease is rapidly and widely adopted as a preferred strategy by interventional radiology and surgical branches.[6,7,8,9,10] Avoiding evaluation of coronary artery stenosis in peripheral arterial disease patients who were not planned a surgical treatment may affect mortality and morbidity adversely. The increase in cardiovascular (CV) mortality and morbidity in patients with PAD is associated with the severity of PAD.[11] In patients with critical PAD, mortality from coronary artery disease was found to be 18.7% within 10 years.[12] In another study, this ratio has been reported to be about 15%, which was further elevated in patients with DM, HT and HL.[13] Cardiovascular disease was detected in 34.5% of patients having COPD along with PAH.[2] On the other hand early mortality and morbidity due to CAD is important in patients who has undergone surgical reconstruction for PAD.[14] Hence, it is important to manage risk factors in individuals having PAD and to perform coronary angiography (CAG) for early diagnosis of CAD. In this study, we retrospectively investigated the incidence of CAD, clinical outcomes, and the need for CAG for diagnostic purposes in patients with PAD requiring endovascular intervention.

Materıals and Methods

In our study, a total of 114 patients who have been performed an endovascular intervention due to PAD and were undergone CAG between January 2013 and August 2017 were evaluated, retrospectively. Before the investigation, the approval was obtained from the Ethics Board. Among patients who had been accepted to our clinic due to cladicatio complaints, peripheral artery angiography was performed in those who had a significant stenosis determined by the Doppler USG. Peripheral artery disease patients who had a stenosis of 70% or more in the lower extremity arteries determined by peripheral arterial angiography, and because of this, underwent an endovascular intervention were included in this study. 40-70% of stenosis in any one of left anterior descending coronary artery (LAD), circumflex coronary artery (CX) or right coronary artery (RCA) or their combinations has been considered "Noncritical CAD", while 70% or more stenosis has been considered "Critical CAD".[15,16] Patients were divided into three groups according to the degree of the stenosis in their coronary arteries. Group 1: patients without CAD or having <40% of stenosis, Group 2: patients having 40% or more and having <70% of stenosis, Group 3: patients with ≥70% of stenosis.

45 years of age and above for males and 55 years of age and above for females were considered to be at risk for atherosclerotic CAD.[16] The diagnosis of HT was based on either at least two blood pressures measured regularly at hospital admission ≥ 140 / 90 mm Hg or the use of any antihypertensive drugs. Patients were considered DM if they had previously been diagnosed with DM or had at least two fasting blood glucose values ≥ 126 mg / dL or those using antidiabetic medication. Blood lipid values were recorded from biochemical data obtained from the hospital's

records. Dyslipidemia is defined as the fact that blood total cholesterol level is over 200 mg/dl, triglyceride (TG) level is over 200 mg/dl, low density lipoprotein (LDL) level is over 130 mg/dl and high density lipoprotein (HDL) level is under 35 mg/dl. TG / HLD ratio was considered significantly elevated when the ratio was above [4]. The diagnosis of COPD was considered if they had previously been diagnosed with COPD or the forced expiratory volume in the first second measured by spirometry is lower than 75% of the forced vital capacity. Major amputation was defined if it occurs in proximal to the ankle, while minor amputation was defined when it occurs in distal to the ankle. The mean follow-up time for patients was 21.8±12.0 months.

The obtained data were evaluated using the SPSS Statistics 22 software. Continuous data have been presented as mean ± standard deviation while the categorical data have been presented as frequency (%) using Chi square test. Kolmogrow-Smirnow test was performed to evaluate whether the independent variables that affect the dependent variables were fitting to the mean. ANOVA test was performed for the groups with normal distribution while Kruscal-Wallis test was used in groups having non-normal distribution. p values smaller than 0.05 were considered statistically significant.

Results

The mean age of PAD cases was found to be 66.56 ± 11.65. Clinical outcomes of the patients are shown in table 1.

Table 1: Clinical outcomes of the patients.

	n (%)
Gender:	
Male	100 (87.7%)
Female	14 (12.3%)
Hypertension	61 (53.5%)
Diabetes mellitus	31 (27.2%)
Dyslipidemia	78 (68.4%)
COPD	10 (8.8%)
CAD:	
40-70%	8 (7%)
≥70%	75 (65.8%)
CAD:	
Single vessel	27 (23.7%)
Two vessels	26 (22.8%)
Three vessels	30 (26.3%)
Major Amputation:	
6 months	5 (4.4%)
1 year	5 (4.4%)
Minor Amputation:	
6 months	7 (6.1%)
1 year	9 (7.9%)
Mortality:	
1 year	20 (17.5%)

COPD: Chronic obstructive pulmonary disease; CAD: Coronary artery disease

100 (87.7%) cases were male and 14 (12.3%) cases were female. Of the cases, 61 (53.5%) were hypertensive, 31 (27.2%) were diabetic, 78 (68.4%) were dyslipidemic, and 10 (8.8%) were COPD patients. CAD with stenosis of 40-70% were seen in 8 cases (7.0%), and severe CAD with stenosis above 70% were detected in 75 (65.8%) of the cases. CAD was found to be in single vessel in 27 (23.7%), two vessels in 26 (22.8%), and three vessels in 30 (26.3%). Major amputation was performed in 5 (4.4%) and minor amputation in 7 (6.1%) cases within the 6 months after the

diagnosis. Major amputations were performed in 5 patients (4.4%) and minor amputations in 9 patients (7.9%) within 1 year. Out of the 14 patients who underwent amputation within 1 year, 12 patients had CAD with a stenosis over 70%, one had a CAD with a stenosis of 40-70%, and one patient had no CAD (Table 2). The mortality rate was found to be 17.5% in patients who could be followed up for one year. It has been found that mean cholesterol values were 180.48 ± 41.03, TG values were 144.93 ± 83.42, blood LDL values were 115.51 ± 34.14, and HDL values were 36.92 ± 11.31, TG/HDL rate 4.53±3,64. When the patients in group 1, group 2 and group 3 were compared, the mean age of group 1 was significantly lower than group 2 and group 3 ($p<0.05$), and there were no significant differences in terms of either other clinical characteristics or lipid levels ($p\geq0.05$) (Table 2 and Table 3).

Table 2: Comparison of clinical outcomes of patients in different groups

	Group 1 n (%)	Group 2 n (%)	Group 3 n (%)	p
Gender: Male Female	 26 (26.0%) 5 (35.7%)	 8 (8.0%) 0 (0.0%)	 66 (66.0%) 9 (64.3%)	 0.46 0.46
Hypertension	12 (19.7%)	4 (6.6%)	45(73.8%)	0.13
Diabetes mellitus	5 (16.1%)	1 (3.2%)	25 (80.6%)	0.12
Dyslipidemia	20 (25.6%)	4 (5.1%)	54 (69.2)	0.73
COPD	3 (30.0%)	1 (10.0%)	6 (60.0)	0.89
Major Amputation Minor Amputation (6 months)	 1 (20.0%) 0 (0.0%)	 0 (0.0%) 1 (14.3)	 4 (80.0%) 6 (85.7%)	 0.73 0.22
Major Amputation Minor Amputation (1 year)	 1 (20.0%) 0 (0.0%)	 0 (0.0%) 1 (11.1%)	 4 (80.0%) 8 (88.9%)	 0.73 0.16
Mortality (1 year)	5 (25.0%)	2 (10.0%)	13 (65.0%)	0.84

COPD: Chronic obstructive pulmonary disease; CAD: Coronary artery disease

Table 3: Comparison of mean blood lipid levels and mean age between patients in different groups

	Group 1 n (%)	Group 2 n (%)	Group 3 n (%)	p
Cholesterol (mg / dL)	181.12 ± 37.73	189.83±34.82	179.41±43.16	0.83
Triglyceride (mg / dL)	140.59 ± 91.14	120.00±54.64	148.77±2.53	0.50
LDL (mg / dL)	114.38 ± 27.38	121.77±35.11	115.43±36.87	0.89
HDL (mg / dL)	38.11 ± 13.74	46.33±17.13	35.60±9.14	0.27
TG / HDL	4.41 ± 3.59	3.29±2.60	4.69±3.62	0.37
Age	62.19±15.26	70.37±13.11	68.1±9.19	0.04

Discussion

Similar to CAD, PAD is an important predictor of cardiovascular morbidity and mortality. The incidence of these events were 12% in patients having only PAD while one-year CV events were found to be as high as 21% in patients with PAD along with CAD.[17] Consistently, Sigvant et al. have reported that five-year cumulative mortality rate in patients having symptomatic PAD is 13% compared to a reference control population having a 5% mortality rate.[18] Subherwal et al. have reported a 7-year follow-up study in patients with PAD that CV mortality rate is higher (47.8%) than in patients having CAD (%36.4).[19] In a different study performed by Fowkes et al., it has been shown that the ten-year CV mortality is 18.7% for male and 12.6% for female having ankle brachial index

(ABI) < 0.9 while these values were 4.4% for male and 4.1% for female having ABI > 0.9.12 In our study, one-year mortality was 17.5%.

A report on 459 Japanese patients with critical PAD (Rutherford grade 4-6) after registering revascularization shows that 41.1% of patients have had CAD.20 Lee et al. have reported their coronary angiography data from 252 patients with critical PAD that 57.5% of the patients have severe CAD (stenosis of ≥ 70%).[15] In parallel, in our study, this value was found to be 65.8%. Due to high incidence of CAD in patients with PAD, it is necessary to evaluate these individuals in terms of CAD for early diagnosis to reduce mortality and morbidity.

Previous studies have shown that the prevalence of PAD increases significantly with aging in patients over age 50.[21,22] In our study, the mean age of the patients was 66.56 ± 11.65. In the groups with coronary artery disease, the mean age was significantly higher than the group without coronary artery disease (p=0.04). This might be the fact that the incidence of coronary artery disease increases with aging.[15] In some studies, the prevalence of PAD was similar in men and women.[22,23] In our study, this rate was higher in male population, and the exact reason of this is currently unknown.

Elevated total cholesterol, LDL and TG in addition to reduced HDL values are independent risk factors for PAH.[23] It has been shown that increased TG / HDL ratio is a strong independent predictor of CAD.[24,25] Urbano et al. have reported that PAD risk is elevated by 4.7 folds when the TG / HDL ratio is above 4.[23] Consistent with these results, in our study, we found that 68.4% of the PAD patients had DL, and the TG / HDL ratio was 4.53±3.64.

HT, DM and DL were found to be strong predictors of PAD.[23] Sur et al. have found that the prevalence of HT increased with age, and this increase is associated with increased DM, DL, and high CV mortality rates.[26] HT causes an increase in arterial wall thickness and disrupts vascular endothelial function, thus leading to atherosclerosis.27 DL and DM play atherogenic roles in vascular endothelium.[28] COPD increases the tendency of thrombosis as a cause of polycythemia.[16] Pecci R et al. have reported that symptomatic PAD was present in 10.2% of patients with COPD while asymptomatic PAD was present in 24% of patients with COPD.[2] In the study conducted by Tunnel et al, HT was detected in 60% of PAD patients, 35% had DM, 15.7% had DL, and 5.7% had COPD of these patients.[16] In a similar study conducted by Bozkurt et al. HT was found in 88.7%, DM in 59.4%, and DL in 65.5% of the PAD patients.[22] In our study, we found that 53.5% had HT, 27.2% had DM, 68.4% had DL, and 8.8% had COPD of the PAD patients. Among different groups, there were no significant differences with respect to HT, DM, DL, COPD and mortality. These results suggest that PAD patients have similar risk factors for the formation of CAD.

In conclusion, our results are in concert with the current literature and show that the incidence of CAD and mortality is found to be significantly higher in PAD patients. We believe that serious strategies need to be developed for the prevention of cardiovascular mortality and morbidity in patients having lower extremity ischemia who have underwent endovascular surgery independent from the presence or severity of coronary artery disease.

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