The Incidence of Renal Artery Stenosis in Patients with Significant Stenosis of Lower Extremity Arteries

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ABSTRACT

The purpose of this study is to evaluate the unity of renal artery stenosis and peripheral vascular disease and to find the frequency of incidental renal artery stenosis in the patients with peripheral vascular disease. In this study,it was included 1502 patients that were sent from cardiovascular surgery department to radiology department to do lower extremity digital substraction angiography and found on at least one segment 50% stenosis and more. The arteries of lower extremity were evaluated by dividing into three segments as aortoiliac, femoropopliteal and infrapopliteal. Segments were classified as unisegment and multisegment. Multisegments were named aortoiliac+femoropopliteal, aortoiliac+infrapopliteal, femoropopliteal+infrapopliteal and aortoiliac+femoropopliteal+ infrapopliteal. Patients with 50% stenosis and more of renal artery are decided. The unity of renal artery stenosis and the segmental disease of peripheral artery were compared by using Chi-Square test. It was found evident renal artery stenosis in 228 (15.2%) of 1502 patients with peripheral vascular disease. The frequency of renal artery stenosis was found lesser at unisegment disease than multisegment disease (p=0.03). The renal artery stenosis was found 11.9% unisegment and %16.4 at multisegment disease. The frequency of renal artery stenosis was appeared less at infrapopliteal (6%) disease compared to the others (p=0.027). It was not found any difference between groups when the segmental groups of peripheral vascular disease was compared with right, left and bilateral renal artery stenosis (p=0.086, p=0.219). It was found higher rate of renal artery stenosis at women (23.6%, p=0.01). The frequency of renal artery stenosis is %15,2 in the patients with peripheral vascular disease. Renal artery stenosis is less at infrapopliteal segment disease. Renal artery stenosis in women is more than men at multisegment disease compared to unisegment disease.

Key words: *Atherosclerosis, renal artery stenosis, peripheral vascular disease*

Belirgin Alt Ekstremite Arter Darlığı Olan Hastalarda Renal Arter Darlığının Sıklığı

ÖZET

Bu çalışmanın amacı, renal arter stenozu ile periferik arter hastalığı birlikteliğini değerlendirmek ve periferik arter hastalığı olan hastalarda insidental renal arter stenozu sıklığını saptamaktır. Bu çalışmaya alt ekstremite arterlerine yönelik DSA yapılan ve en az bir segmentinde %50 ve üzeri stenoz saptanan toplam 1502 hasta dahil edildi. Alt ekstremite arterleri aortoiliak, femoropopliteal ve infrapopliteal olarak 3 segmente ayrılarak değerlendirildi. Segmentler tek segment ve multisegment tutulumu olarak sınıflandırıldı. Multisegmentler aortoiliak+femoropopliteal, aortoiliak+infrapopliteal, femoropopliteal+infrapopliteal ve aorto ilaik+femoropopliteal+infrapopliteal olarak isimlendirildi. En az bir segmentde %50 ve üzeri stenozu olanlar çalışmaya alındı. Segmental periferal arter hastalığı ve renal arter stenozu birlikteliğini karşılaştırmada ki-kare testi kullanıldı. Periferik vasküler hastalığı olan 1502 hastanın 228 inderenal arter stenozu saptandı. Renal arter stenozu sıklığı tek segment tutulumu olanlarda multi segment tutulumuna göre daha az bulundu (p=0.03). Renal arter stenozu sıklığı tek segment tutulumunda %11,9 ve multisegment tutulumunda %16,4 bulundu. Renal arter stenozu sıklığı diğerleriyle karşılaştırıldığında infrapopliteal tutulumda (%6) daha az bulundu (p=0.027). Sağ, sol ve bilateral renal arter stenozuyla segment tutulumları karşılaştırıldığında segment grupları arasında fark bulunmadı (p=0.086, p=0.219). Kadınlarda renal arter stenozu sıklığı daha yüksek oranda bulundu (%23.6, p=0.01). Renal arter stenozu periferal vasküler hastalığı olanlarda %15,2 sıklıkla görülmektedir. Renal arter stenozu infrapopliteal segment tutulumunda daha görüşmektedir. Multisegment tutulumu ile karşılaştırıldığında tek segment tutulumunda renal arter stenozu sıklığı kadınlarda erkeklere nazaran daha sıktır.

Anahtar kelimeler: *Ateroskleroz, renal arter darlığı, periferal vasküler hastalık*

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Received: 09.10.2011, Accepted: 06.03.2012

INTRODUCTION

Peripheral artery disease (PAD) of lower extremities is a common disease seen in many countries. It's important both in terms of morbidity and mortality. Even though precise figures related to PAD in our country is not known, considering the fact that expected mortality of PAD patients for 10 years is increased 6 times as compared to individuals with no disease, it's clearly understood that this is a critical health issue (1). The fact that it's seen in a large range of age groups plus its high morbidity constitutes a major problem in terms of community health care (2). PAD is asymptomatic in most cases. In a 5 year period, 5-10% of peripheral vascular disease patients become symptomatic (3). Atherosclerosis is a chronic disease which manifests with ischemia and necrosis in target organs due to stenosis or occlusion of peripheral vessels. It's a systemic disease which affects large and medium sized muscular arteries.

Atherosclerotic renal artery stenosis (RAS) constitutes approximately 90% of all RAS cases. Other major causes of RAS are fibromuscular dysplasia and vasculitis (Takayasu arteritis, polyarteritis nodosa etc.). Atherosclerotic RAS is one of the well established causes of secondary hypertension and end stage renal failure. It's the underlying disease in 1-5% of hypertensive patients and in 12-14% of dialysis patients (4-8). Even in cases where hypertension is under control with medical treatment, failure of improvement in RAS may lead to decrease in renal blood flow and ischemic injuries (9, 10). Therefore, it's recommended to revascularize stenosis prior to development of renal function disorder (11). Purpose of this trial is to evaluate coexistence of RAS and peripheral artery disease and to determine the rate of incidental RAS in patients with peripheral artery disease.

MATERIALS AND METHODS

A total of 1502 patients from Türkiye Yüksek İhtisas Hospital were enrolled in this trial, who were referred from Department of Cardiovascular Surgery to Department of Radiology between January 2007 and August 2009 in whom stenosis of ≥50% was determined in at least one segment by DSA (Digital Subtraction Angiography) in lower extremity arteries. Among all cases, 1246 were men and 242 were women; age range was 19 – 95 with a mean age of 62,07 years. Study protocol was approved by Turkey Yuksek Ihtisas Education and Research Hospital, Committee for Education Planning and Coordination.

Monoplane DSA equipment of Philips Integris Allura (Holland) was used for this investigation. Commonly used Seldinger technique was used for vascular access in 1502 patients. Right or left common femoral artery was preferred for access in 1461 patients and for 41 patients in whom entrance was not achieved through this site, left brachial artery was designated as the access site. In interventions realized through common femoral artery, femur head constitutes a firm structure as a means of compression; therefore this site was used to provide haemostasis. After placement of 5F vascular sheath, hydrophilic guide wire of 0.035 inch is advanced further to origin of renal artery. A total of 25 ml of contrast material was injected with 5F pigtail catheter with a rate of 12ml/sec; following initial abdominal aortography, aortofemoropopliteal arteriography was performed in a single plane. Monoplane imaging was not successful in some patients, therefore a second plane examination (oblique or lateral) was performed in these cases. All imaging findings were evaluated by two radiologist with consensus. Based on this evaluation, patients with a stenosis of ≥50% in at least one segment were enrolled in this trial. Lower extremity arteries were evaluated in 3 sections as aortoiliac, femoropopliteal and infrapopliteal segments. Separate involvements of these segments were evaluated as single segment involvement; on the other hand, aortoiliac+femoropopliteal, aortoiliac+infrapopliteal, femoropopliteal+infrapopliteal and aortoiliac+femoropopliteal+infrapopliteal classifications of these segments were regarded as multisegment involvements. RAS was determined in patients with single and multisegment involvements. Rate of stenosis was calculated by comparing minimum diameter of renal artery by diameter of normal renal artery proximal to stenosis or distal to poststenotic dilatation. Patients with a RAS of ≥50% were determined. In statistical evaluation, SPSS 16.0 program was utilized. Chi-square test was implemented to compare frequency of RAS ≥50% in patients with single and multisegment involvement in DSA. Values with $P < 0,05$ were regarded as significant.

RESULTS

Segment involvements of lower extremity arteries in 1502 patients is seen Table 1. In our trial, PAD was observed to be coexistent in 412 patients (27,5%) with

***Table 1**. Segment involvements*

	n	*%*
Aortoiliac	*152*	*10.1*
Femoropopliteal	*127*	*8.4*
Infrapopliteal	*133*	*8.9*
Aortoiliak+femoropopliteal	*114*	*7.6*
Aortoiliak+infrapopliteal	*60*	*4.0*
Femoropopliteal+infrapopliteal	*463*	*30.8*
Aortoiliak+femoropopliteal+infrapopliteal	*453*	*30.2*
Total	*1502*	*100*

single segment involvement and most frequently in aortoiliac segment (10,1%) while it was observed in 1092 patients (72,5%) with multisegment involvement and most frequently in femoropopliteal+infrapopliteal segment (30,8%).

Renal artery involvement is seen in Table 2. Renal artery involvement was right-sided in 15 of 412 patients (3,6%) with single segment involvement determined by DSA, left-sided in 23 patients (5,5%) and bilateral in 11 cases (2,6%). Renal artery involvement was determined as right-sided in 73 of 1090 patients (6,6%) with multisegment involvement, left-sided in 78 patients (7,1%) and bilateral in 28 patients (2,5%) (p=0,086). In RAS cases coexisting with single and multisegment artery involvements, no significant difference was seen in terms of right, left and bilateral involvement. No significant difference was found between the degree of segment involvement and right, left and bilateral RAS involvements (p=0,219). Renal artery involvement was found in 49 of 412 patients (11,8%) with single segment involvement as determined by DSA and in 179 of 1090 patients (16,4%) with multisegment involvement (p=0,03). Rate of RAS is significantly higher in multisegment involvements as compared to single segment involvement. Additionaly rate of RAS was significantly lower in infrapopliteal segment involvement (6%), as compared to other peripheral artery involvements.

DSA revealed renal artery involvement in 171 of 1260 male patients (13,6%) and in 57 of 242 female patients (23,6%) (p=0,01). Rate of male patients was considerably high; in spite of a lower risk of PAD in women, a higher rate of RAS was observed in less number of patients.

DISCUSSION

Atherosclerosis is a chronic disease manifesting with ischemia and necrosis in target organs caused by stenosis or occlusion in peripheral arteries. Even though precise figures related to PAD in our country is not known, considering the fact that expected mortality of PAD patients in 10 years is increased 6 times as compared to individuals with no disease, it's clearly understood that this is an important health issue (1). Atherosclerosis is a systemic disease involving peripheral arteries in addition to large and medium size muscular arteries (Figure 1). The fact that it's seen in a large range of age group and its high morbidity constitutes a major problem in terms of community health care (2). PAD and RAS is commonly seen concurrently because both have a common basis, namely atherosclerosis. Since the disease causes acute failure in renal functions, it's critical to establish the diagnosis in early stages.

***Table 2**. RAS freguency in segments*

Segments	*RAS*			
	Right n(%)	*Left n(%)*	*Bilateral n(%)*	*Total p(0.027)*
Aortoiliac	*2(1.3)*	*11(7.2)*	*5(3.3)*	*18*
Femoropopliteal	*10(7.9)*	*9(7.1)*	*4(3.1)*	*23*
Infrapopliteal	*3(2.3)*	*3(2.3)*	*2(1.5)*	*8*
Aortoiliak+femoropopliteal	*6(5.3)*	*8(7)*	*5(4.4)*	*19*
Aortoiliak+infrapopliteal	*2(3.3)*	*3(5)*	*1(1.7)*	*6*
Femoropopliteal+infrapopliteal	*33(7.1)*	*33(7.1)*	*10(2.2)*	*76*
Aortoiliak+femoropopliteal+infrapopliteal	*32(7.1)*	*34(7.5)*	*12(2.6)*	*78*

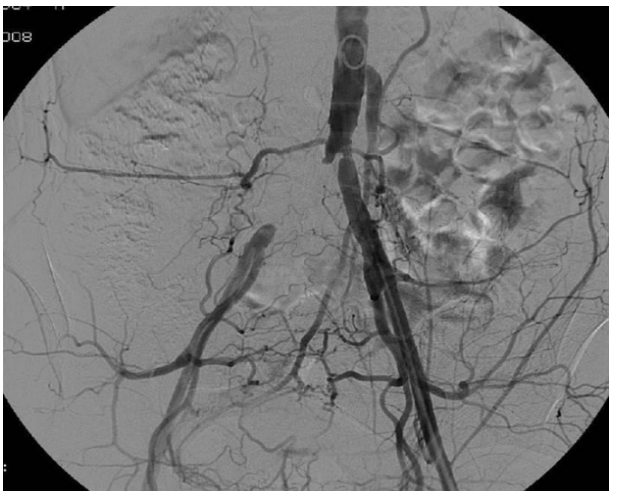

Figure 1*.Aortoiliac segment involvement. Right common iliac artery occluded from origin, significant stenosis in proximal portion of left common iliac artery*

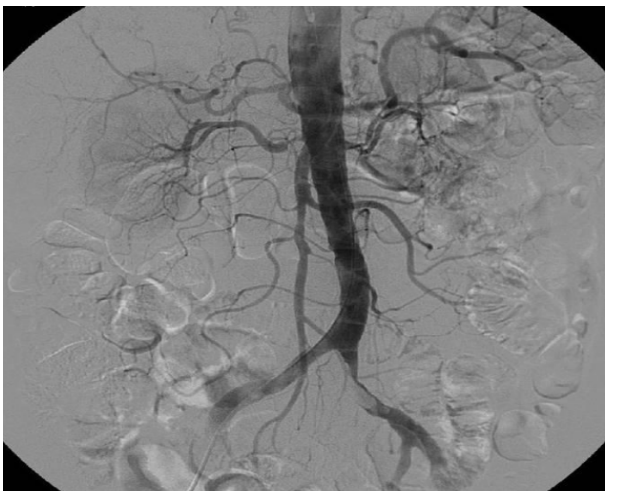

Figure 2*. Irregularities in diameter and contour of lower extremity arteries seen in angiography. Severe stenosis in both renal arteries. Severe stenosis in left common iliac artery.*

RAS is frequently diagnosed incidentally during investigation of peripheral vascular diseases (12). Atherosclerotic renal artery disease constitutes around 90% of all renal artery stenosis cases (Figure 2). Even in cases where hypertension is under control with medical treatment, failure of improvement in renal artery stenosis may lead to decrease in renal blood flow and ischemic injuries (9, 10). Therefore, revascularization of stenosis is recommended prior to development of renal function disorder (11). In several trials in literature, concurrent RAS was determined in 7.5-60% of symptomatic PAD cases, as shown by diagnostic angiography (13-25). Our results also indicate that RAS is a frequent finding in PAD patients; RAS was found in 228 of 1502 PAD patients (15.2%) which was determined as a significant rate. Variable results related to rate of RAS in above mentioned literature is due to varying degrees of stenosis and inclusion of patient groups with atheroma plaque without a significant stenosis in several trials. In different trials based on stenosis >50 % and >60%, rate of RAS is 14-42%. Differences between these rates are due to selection of patient population and differences in standards. As indicated by results of these trials, incidental RAS is frequently seen in asymptomatic patients.

In a trial conducted by Metcalfe (16) et al., rate of atherosclerotic renal artery disease in patients with peripheral artery disease in femoral region (42.1%) is higher than in patients with peripheral artery disease in iliac (39.7%) and distal regions (38.1%). On the other hand, in the trial performed by Androes (26) et al. on 200 patients, coexistence of RAS in patients with aortoiliac segment involvement was found to be significant (p= 0,031). Also in a trial realized by Özkan (19) et al. on 629 patients, coexistence of RAS and aortoiliac segment involvement was found to be significant as compared to coexistence with femoropopliteal, distal segment and multisegment involvement. Ahmed (27) et al. reported that RAS is highly associated with iliac and femoropopliteal atherosclerotic disease in their trial conducted on 212 patients. Our trial results showed that RAS in infrapopliteal segment involvement (6%) is significantly less than other peripheral artery involvements (p=0.027).

In a trial conducted by Metcalfe (16) et al., rate of atherosclerotic renal artery disease in patients with PAD in ≥ 3 segments (43,4%) was found to be higher than in patients with single segment involvement (8%). In trials conducted by Missouris (20) et al. and by Androes (26) et al., coexistence of multisegment involvement and RAS was found to be significant (p=0,0015, p=0,001); on the other hand, in the trial realized by Özkan (19) et al. on 629 patients, coexistence of aortoiliac segment involvement and RAS was found to be significant as compared to femoropopliteal, distal segment and multisegment involvements. Results of most of the trials in literature

indicated above and our results show that rate of RAS in multisegment involvement is significantly different from single segment involvements.

Bilateral renal artery involvement was found in 24 patients (12%) in a trial conducted by Androes (26) et al. but no differentiation was realized in this trial in terms of single and multisegment involvement. In a trial conducted by Shakeri (21) et al., in 37 arteries with stenosis among 88 renal arteries (42%), 9 were right-sided (24.3%), 4 were left-sided (10.8%) and 24 were bilateral (64.9%). In the trial realized by Pillay (28) et al. on 98 patients, bilateral RAS was found in 34 patients and unilateral stenosis with equal numbers on both sides were found in 64 patients. These trial results and our findings indicate that in RAS accompanying single and multisegment involvements, there is no significant difference between right, left and bilateral involvements. No statistically significant result was found between rate of RAS classified according to levels and right, left and bilateral involvements. No similar comparison exists in the literature.

In the trial conducted by Özkan (19) et al., gender was found to be insignificant in contrast to trial conducted by Metcalfe (16) et al. In the trial realized by Androes (26) et al., RAS was found to be statistically significant in women. Also in the trial conducted by Missouris (20) et al., a significant relation was found between female gender and existence of RAS (P=0,04). In a trial conducted by Przewlocki (24) et al., a correlation was found between RAS and female gender (p=0,009). Similar to previous trials, rate of men in whom radiography was performed to diagnose PAD was shown to be higher than women (29, 30). As indicated in our trial, percentage of male patients is considerably high. Even though the risk of PAD is lower in women, higher rate of RAS was determined in less number of patients.

In conclusion, incidence of RAS in patients with peripheral artery disease is 15.2%. Rate of RAS is lower in infrapopliteal segment involvement. It's more frequent in multisegment involvement as compared to single segment involvement and in women as compared to men. Our results indicate that incidental RAS is a frequent finding in patients with PAD diagnosed by DSA. Therefore, investigation and determination of RAS in angiographies of patients referring with PAD symptoms will enable early diagnosis and early intervention of the disease, without additional costs and examinations.

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