Renal Artery Stenosis in Patients with Ischemic Heart Disease

İskemik Kalp Hastalarında Renal Arter Darlığı

İsmail ATES[1]
Şeref ULUCAN[2]
Mehmet DOĞRU[1]
Zeynettin KAYA[2]
Anıl AKTAŞ SAMUR[3]
Havva Asuman YAVUZ[4]

1 Medline Private Hospital, Department of Cardiology, Antalya, Turkey
2 Mevlana University, Faculty of Medicine, Department of Cardiology, Konya, Turkey
3 Akdeniz University, Faculty of Medicine, Department of Biostatistics, Antalya, Turkey
4 Acıbadem University, Atakent Education and Research Hospital, Department of Nephrology, İstanbul, Turkey

ABSTRACT

OBJECTIVE: Renal artery stenosis (RAS) is emerging one of the cause of chronic renal failure and end-stage renal disease. The vast majority of cases in elderly are due to atherosclerotic disease. The prevalence of RAS in several population studies varies considerably. The study aimed to examine the frequency and risk factors of atherosclerotic critical RAS in patients with coronary artery disease.

MATERIAL and METHODS: This study included 762 consecutive patients (456 male and 306 female). All patients underwent coronary and renal angiography at the same time. Significant coronary stenosis is defined as ≥50% stenosis of left main coronary artery and ≥70% stenosis for the other coronary arteries.

RESULTS: A total of 355 patients out of 762 (46%) had at least one coronary vessel involved. The mean age was 62 years. The renal angiography demonstrated significant RAS (≥50%) in 68 patients (8.9%), as well severe stenosis (>80%) in 5 patients. Systolic blood pressure was higher in patients who have significant RAS (p= 0.001). Patients with significant RAS were also more frequently diabetic (73.5% to 26.7%, p=0.001), had dyslipidemia (86.8% to 50%, p= 0.001) and were being treated with statins (72.1% to 28.7%, p= 0.001). The presence of significant RAS was associated with a reduced eGFR (p= 0.001).

CONCLUSION: In patients with ischemic heart disease, screening of the patients with impaired renal functions, diabetes mellitus, advanced age, dyslipidemia and increased pulse pressure is useful for the detection of RAS.

KEY WORDS: Renal artery stenosis, Ischemic heart disease, Cardiac catheterization

ÖZ

AMAÇ: Renal arter darlığı (RAD) kronik böbrek hastalığı ve son dönem böbrek yetmezliği nedenleri içinde yer almaktadır. Yaşlılarda sıklıkla aterosklerotik hastalığa bağlı olarak ortaya çıkmaktadır. RAD prevelansı çeşitli popülasyon çalışmalarında değişiklik göstermektedir. Bu çalışma, koroner arter hastalığı olan hastalarda aterosklerotik ciddi RAD sıklığı ve belirleyicilerini araştırmayı amaçlamıştır.

GEREÇ ve YÖNTEMLER: Çalışma popülasyonu 762 hastadan (456 erkek, 306 kadın) oluşmaktadır. Tüm hastalara aynı seansta koroner ve renal anjiyografi işlemi uygulanmıştır. Anlamlı koroner arter hastalığı sol ana koroner arterde ≥%50 darlık, diğer koroner arterlerde ≥%70 darlık olarak tanımlanmıştır.

BULGULAR: En az bir koroner arterde darlık 762 hastanın 355'inde (%46) görülmüştür. Ortalama yaş 62 dir. 68 hastada (%8,9) en az bir renal arterde anlamlı RAD (≥%50) saptanmış olup 5 hastada RAD ciddi olarak (>%80) değerlendirilmiştir. Sistolik kan basıncı anlamlı RAD olanlarda daha yüksek saptanmıştır (p=0,001). Anlamlı RAD olan hastalar sıklıkla diabetik (%73,5 - %26,7, p=0,001), dislipidemi (%86,8 - %50, p= 0,001), ve statin tedavisi almakta olanlardı (%72,1 - %28,7, p= 0,001). Anlamlı RAD varlığı ayrıca azalmış eGFR ile ilişkiliydi (p=0,001).

SONUÇ: İskemik kalp hastalığı olan hastalarda bozulmuş böbrek fonksiyonu, diabetes mellitusu, ileri yaş,dislipidemi ve yüksek nabız basıncı olan hastaların taranması RAD tespiti açısından yararlıdır.

ANAHTAR SÖZCÜKLER: Renal arter darlığı, İskemik kalp hastalığı, Kardiak kateterizasyon

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Correspondence Address:
İsmail ATEŞ
Özel Medline Antalya Hastanesi, Kardiyoloji Bölümü, Antalya, Turkey
Phone : +90 532 205 83 29
E-mail : drates07@gmail.com

INTRODUCTION

Renal artery stenosis (RAS) is one of the leading causes of chronic kidney disease and is often unrecognized (1,2). The vast majority of cases in elderly are due to atherosclerotic disease usually in the presence of widespread disease affecting the coronary vessels, cerebral vasculature, and/or the vessels supplying the lower limbs (3,4). RAS is generally associated with changes in left ventricular mass and function and increased risk of cardiovascular disease (5,6).

Clinical diagnosis of RAS is often difficult. Clinical manifestations of RAS (resistant hypertension, renal failure, acute decompensated heart failure) are often attributed to other causes. The clinical diagnosis of atherosclerotic RAS remains problematic. This makes it difficult to make the diagnosis and determine the exact prevalence of RAS (7).

Reported RAS prevalence varies greatly because of different study populations and selection criteria (hypertension, ischemic heart disease, peripheral artery disease (PAD), chronic kidney disease) (8). The recent guidelines recommend screening the renal arteries at the same time as coronary angiography, especially in patients with a risk of atherosclerotic RAS (9, 10).

The study aimed to examine the prevalence and predictors of atherosclerotic significant RAS (≥50%) in patients with coronary artery disease.

METHODS

Between May 2007 and December 2012, a total of 762 patients referred to the coronary angiography laboratory with suspected ischemic heart disease underwent coronary and renal angiography at the same session. Patients with accessory renal arteries, acute coronary syndrome, end-stage renal failure and inadequate image quality were excluded from the study. Significant coronary stenosis was defined as ≥50% stenosis for the left main coronary artery and ≥70% stenosis for the other coronary arteries (11). Selective renal and coronary angiography was performed and evaluated by two independent cardiologists. For measurement, the outer diameter of the catheter was taken as reference and then the decrease in luminal diameter of the imaged renal artery was expressed as the percentage. Significant RAS was defined as ≥50% narrowing in one or both of the main renal arteries. The Ethics Committee approved the study protocol and informed consent was obtained from each patient.

Demographic and clinical characteristics of the patients were recorded. The glomerular filtration rate (GFR) was calculated with the Modification of Diet in Renal Disease (MDRD) formula (12).

STATISTICAL ANALYSIS

All statistical analyses were performed using SPSS v. 18.0 for Windows (SPSS, Inc., Chicago, IL, USA). Demographic and clinical characteristics were given as mean ± SD and percentage. The normal distribution of the data was evaluated and then categorical variables were compared using the chi-square test. The Mann-Whitney U test was used to evaluate non-parametric variables. Multivariate logistic regression analysis was used to determine the independent predictors of RAS. A p-value <0.05 was considered statistically significant.

RESULTS

The study included 762 consecutive patients (456 males and 306 females). All patients underwent coronary and renal angiography at the same time (Table I). The mean age of the studied patients was 62 years. The most frequent accompanying chronic disease was hypertension (55.6 %). Dyslipidemia was present in 53.3% and diabetes mellitus in 30.8% of patients while 23.4% patients were smokers. Mean serum creatinine was 0.79 mg/dL and eGFR (MDRD) was 97 ml/min/1.73 m^2. A total of 355 (46%) patients had at least one coronary vessel involved (one vessel in 127 cases; two vessels in 92; three vessels in 120; LMCA in 16 patients). The renal angiography demonstrated significant RAS (50%) in 68 patients (8.9%), as well as severe stenosis (80%) in 5 patients. The level of RAS was often ostial (89%). There was often single renal artery involvement (unilateral in 87% and bilateral in 13%). Total occlusion of the renal artery was rare (n = 3). There was no complication during renal angiography. Transient contrast-induced nephropathy was observed in 10% of the patients

Patients with significant RAS were older, had a history of hypertension more commonly and received more antihypertensive drugs. Systolic blood pressure was higher in patients who had significant RAS (p= 0.001), but the diastolic blood pressure was lower (p= 0.001). Nonetheless pulse pressure was higher in patients with significant RAS (68.5 mmHg) than in the remaining patients (50 mmHg) (p=0.001). Patients with significant RAS were also more frequently diabetic (73.5% to 26.7%, p=0.001), had dyslipidemia (86.8% to 50%, p= 0.001) and were being treated with statins (72.1% to 28.7%, p= 0.001). The presence of significant RAS was associated with a reduced eGFR (p= 0.001) (Table II). Patients with significant RAS had more PAD (p=0.001) and chronic renal failure (p=0.001). The study also showed patients with significant RAS had more frequent CAD, especially two or three vessel disease. 82.3% of patients with significant RAS had at least one-vessel coronary involvement; 27.9% of them had two-vessel disease, 30.9% three-vessel disease and 4.4% LMCA disease. On the other hand 17.7% of patients with significant RAS had noncritical coronary stenosis (< 70% in at least one vessel) or normal coronary artery.

DISCUSSION

This study has shown that the prevalence of RAS is 8.9% in patients undergoing coronary angiography and who have cardiovascular risk factors. Impaired renal functions, diabetes mellitus, advanced age, dyslipidemia and increased pulse pressure are the risk factors for the RAS. Performing renal angiography after cardiac catheterization seems to be appropriate in patients with these risk factors.

Table I: Demographic and angiographic characteristics of patients with RAS and controls.

		Whole population (n=762)	Without RAS (n=694)	With RAS (n=68)	P
Age	(years)	62[54-69]	61[54-68]	69[61-75]	0.001
Gender					
Male	(n,%)	456(59.8)	416(59.9)	40(58.8)	0.857
Female	(n,%)	306(40.2)	278(40.1)	28(41.2)	
Smoking	(n,%)	178(23.4)	161(23.2)	17(25)	0.738
Diabetes	(n,%)	235(30.8)	185(26.7)	50(73.5)	0.001
Weight	(kg)	77[70-85]	76[70-85]	80[70-85]	0.498
Height	(cm)	167[60-170]	167[160-170]	165[160-172]	0.427
Body Mass Index	(kg/m^2)	27[25-29]	27[25-29]	28[25-30]	0.365
Number of antihypertensive drugs	(n)	1[0-1]	1[0-1]	1[1-2]	0.001
On antihypertensive treatment	(n,%)	414(54.3)	353(50.9)	61(89.7)	0.001
Systolic blood pressure	(mmHg)	130[120-140]	130[120-140]	140[134-144]	0.001
Diastolic blood pressure	(mmHg)	80[70-81]	80[74-84]	70[65-80]	0.001
Pulse pressure	(mmHg)	50[40-60]	50[40-60]	68.5[60-70]	0.001
Hypertension	(n,%)	424(55.6)	363(52.3)	61(89.7)	0.001
Cholesterol	(mg/dL)	193.5[177-214]	190[176—212.3]	205[196.3-230]	0.001
Dyslipidemia	(n,%)	406(53.3)	347(50)	59(86.8)	0.001
Creatinine	(mg/dL)	0.79[0.69-0.90]	0.78[0.68-0.90]	0.94[0.79-1.29]	0.001
cGFR(MDRD)	($ml/min/1.73m^2$)	97[82-110]	98[85-112]	73.5[55.5-89.7]	0.001
On statins	(n,%)	248(32.5)	199(28.7)	49(72.1)	0.001
On anti-platelet agents	(n,%)	485(63.6)	422(60.8)	63(92.6)	0.001
On diuretics	(n,%)	166(21.8)	143(20.6)	23(33.8)	0.012
On beta blockers	(n,%)	306(40.2)	270(38.9)	36(52.9)	0.024
On ACE inhibitors	(n,%)	210(27.6)	180(25.9)	30(44.1)	0.001
On calcium blockers	(n,%)	120(15.7)	101(14.6)	19(27.9)	0.004
On alpha blockers	(n,%)	12(1.6)	11(1.6)	1(1.5)	0.990
On ARB	(n,%)	113(14.8)	96(13.8)	17(25)	0.0.13
CAD extent					
No CAD lesion	(n,%)	162(21.3)	160(23.1)	2(2.9)	0.001
No significant lesion	(n,%)	245(32.2)	235(33.9)	10(14.7)	0.001
One-vessel	(n,%)	127(16.7)	114(16.4)	13(19.1)	0.570
Two-vessel	(n,%)	92(12.1)	73(10.5)	19(27.9)	0.001
Three-vessel	(n,%)	120(15.7)	99(14.3)	21(30.9)	0.001
LMCA	(n,%)	16(2.1)	13(1.9)	3(4.4)	0.165
Peripheral vascular disease	(n,%)	47(6.2)	34(4.9)	13(19.1)	0.001
Chronic renal failure	(n,%)	40(5.2)	17(2.4)	23(33.8)	0.001
Stroke	(n,%)	2(0.3)	1(0.1)	1(1.5)	0.171
Myocardial infarction	(n,%)	105(13.8)	90(13)	15(22.1)	0.038

RAS: Renal artery stenosis; **cGFR:** Calculated glomerular filtration rate, **MDRD:** Modification of diet in renal disease, **ACE:** Angiotensin converting enzyme, **ARB:** Angiotensin receptor blocker, **CAD:** Coronary artery disease, **LMCA:** Left main coronary artery.

Table II: Predictors of renal artery stenosis.

	P	QR	95%CI-lower	95%CI-upper
Age	0.049	1.036	1.000	1.074
Diabetes (yes)	0.000	4.197	2.194	8.029
Pulse Pressure	0.000	1.056	1.034	1.078
Dyslipidemia (yes)	0.007	3.049	1.365	6.811
cGFR	0.000	0.964	0.950	0.979
Significant lesion (no)	0.026	2.508	1.116	5.636

cGFR: Calculated glomerular filtration rate.

The prevalence of RAS has been identified in several studies with varying frequency (3.6-18%). These differences could be associated with the patient selection and diagnostic approach. Marc Antoni et al. (8) have found the RAS prevalence 5.4% in their study that had similar patient selection criteria to ours. They identified the risk factors for RAS as PAD, impaired renal function, advanced age, dyslipidemia, CAD (coronary artery disease) severity and wide pulse pressure. We also similarly identified impaired renal function, advanced age, dyslipidemia, and increased pulse pressure as absolute risk factors for RAS. Nevertheless, diabetes mellitus, which is a major risk factor for atherosclerotic vascular disease, can be accepted as a relative risk factor for RAS.

In another study, Buller et al. (7) performed renal angiography after cardiac catheterization in 851 patients who had at least one major risk factor such as severe hypertension, unexplained renal dysfunction, acute pulmonary edema due to hypertension and severe atherosclerosis. Renal artery atherosclerosis was found in 39% of the patients, but ≥ 50% stenosis was observed in 14.3%. In our study, the reason for the relatively low prevalence of RAS may be related to the selection of patients regardless of RAS risk factors.

In a study performed by Kobo et al. (13), the significant RAS prevalence was found to be 9.1% in 450 patients who had risk factors such as PAD, resistant hypertension, renal failure and pulmonary edema. Although these results are compatible with ours, our prevalence of RAS could be higher than what we found if we had selected the patients using the criteria of the Kobo et al. study.

The different results of the prevalence of RAS varying from 3,6% to 18% may be explained by the selection of different criteria for the studies and the number of the patients.

Bazemore TC et al. investigated the relation of pulse and systolic and mean blood pressure with severe renal RAS (14). The study demonstrated that severe RAS was associated with a lower diastolic BP and a higher pulse pressure (14). This can be explained by the maintenance of kidney perfusion by higher pulse pressure. We showed that pulse pressure was higher in patients with significant RAS, and this was consistent with the mentioned study.

Although hypertension, antihypertensive therapy with multiple drugs, multiple CAD, PAD and the history of MI were not determined as a primary risk factors in our study, the patients who had the mentioned risk factors had statistically significantly higher rates of RAS. These patients should be carefully evaluated for RAS.

We also found that the prevalence of RAS is higher in patients who are using antihypertensive and antiatherosclerotic therapy with antiplatelet drugs, ACEI or ARB, beta blockers, CCB and statins. The patients who take such medications should be evaluated in terms of RAS.

Using anti-hypertensive and statin therapy provides important clues for the detection of RAS in patients with ischemic heart disease. According to the results of the study, ACE inhibitor or ARB, beta-blocker, CCB, and statin use was more common in patients with RAS. They seem to be predictors for the diagnosis of RAS but establishing a direct relationship does not seem appropriate.

Study Limitations

The limitations of our study are that DSA was not used for the screening of the renal arteries, the relatively lower number of patients, and including patients in the study regardless of the specific risk factors mentioned above.

CONCLUSION

Although the prevalence of RAS varies in different studies, we think that screening patients who have impaired renal functions, diabetes mellitus, advanced age, dyslipidemia and increased pulse pressure is useful for RAS detection. Further studies designed with a higher number of the patients who have specific risk factors for RAS are needed.

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