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Renal artery stenosis: a single center experience

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ABSTRACT

Objectives: Renal artery stenosis (RAS) is among the most common causes of secondary hypertension. Prevalence of RAS are seen in end-stage renal disease (ESRD) patients with hypertension between 1-10%. In our study, we evaluated the data of patients with RAS who were followed up with medical treatment and stenting.

Methods: In our study, patients who were thought to have renal artery stenosis (RAS) with renal artery doppler ultrasonography were scanned with contrast-enhanced Magnetic Resonance Angiography (MRA). Fifty-three patients (10 received medical therapy, 43 applied invasive procedure) who diagnosed with RAS evaluated.

Results: Follow-up times were 15 (12-84) months in patients who received medical therapy, and 12 (10-96) months in patients who treated with invasive therapy ($p = 0.583$). Median ages were 56 (19-74) years in medical treatment group, and 60 (15-77) years in invasive therapy group ($p = 0.955$). Compared with the beginning of treatment, diastolic hypertension was decreased of 12.5% in invasive treatment group opposite medical therapy group ($p = 0.040$), so eGFR was increased of 5.94% in invasive treatment group.

Conclusions: In recent years, several studies about survival in patients with RAS was observed that there was no significant difference between the medical and invasive treatment. Clinical, laboratory, and individual characteristics should be considered in treatment choice.

Keywords: Chronic renal failure, hypertension, renal artery stenosis

Renal artery stenosis (RAS) is the most common causes of ischemic nephropathy and secondary hypertension (renovascular hypertension-RVH). Ischemic nephropathy is one of the causes of end-stage renal disease. Instead of prevalence of RAS are seen in end-stage renal disease (ESRD) patients with hypertension between 1-10%. Atherosclerotic renal artery disease or fibromuscular dysplasia are frequently detected in the pathophysiology [1, 2]. Angiography is still the gold standard method for diagnosis. In addition, Doppler ultrasonography, computed tomography with angiography, magnetic resonance angiography (MRA), etc. are used in methods. RAS patients may present clinically with ischemic nephropathy, resistant hypertension, and unstable cardiac symptoms (such as recurrent angina attacks, pulmonary edema). Renovascular hypertension (RVH) is seen in 7% of patients over 65 years of age. The incidence of RVH in patients with coronary artery disease or aortoiliac disease is more than 50% [3, 4]. The debate about the ef-

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fectiveness and superiority of medical and interventional treatments continues. In addition, which treatment option will be offered to which patient is important in terms of kidney and patient survival [5, 6].

In our study, clinical and laboratory data, kidney functions and response to treatment of patients diagnosed with RAS and receiving medical and interventional treatment evaluated, retrospectively.

METHODS

Patients

Eighty patients (25 females, 55 males) with suspected RAS, resistant hypertension (using at least three antihypertensive drugs, one diuretic), diabetes, coronary artery disease or chronic renal failure screened by renal doppler ultrasonography between 01.07.2018-30.06.2021. Because it is an easy, non-invasive method, patients with suspected RAS were first examined with renal Doppler ultrasonography for preliminary evaluation, considering their prognosis. Patients with suspected RAS [resistive index (RI) > 0.70] by renal doppler ultrasonography were scanned with contrast-enhanced MRA. Treatment, clinical and laboratory data of 53 patients (18 females, 35 males) who diagnosed with RAS by MRA evaluated retrospectively. All of our patients had atherosclerotic RAS. Interventional treatment applied in patients with renal artery stenosis of 80% or more, as in the CORAL study [7]. Other patients were followed up with medical treatment. Patients under the age of 18 and receiving renal replacement therapy were excluded from the study. Glomerular filtration rate (eGFR) calculated according to the Modification of Diet in Renal Disease (MDRD) formula [8]. Renal functions were evaluated according to serum urea and creatinine values before treatment and at the last follow-up.

Renal Doppler Ultrasonography

Renal doppler ultrasonography data performed using an angle of ≤ 60 degrees. Peak systolic flow (PSF) and end diastolic volume (EDV) were measured at 4 sites: trunk of the renal artery, hilum (renal pedicles), segmental and interlobar regions. PSF also calculated for the aorta These ultrasonic measurements made ≥ 3 times in each position and the averages of the measured values were used for the analyses. RI calculated using the formula RI = (PSF-EDV)/PSF. Patients with RI index > 0.70 evaluated with MRA. MRI angiography was performed in the second step in those with suspected RAS in the study, as it visualized vascular structures, differentiated soft tissue better, and was less nephrotoxic. Ethics committee approval obtained from our unit (09.02.2022, 2022-1 / 12).

Magnetic Resonance Angiography (MRA)

Breathing exercises were given to the patients for 20-30 seconds. A 4-hour fasting recommended to reduce the effect of bowel peristalsis. Non-contrast and contrast-enhanced series should be obtained in the same phase of respiration. The patient's arms should be elevated above the head to avoid artifact formation. MR contrast material was not used in cases with a GFR below 30 ml/min. Meglumine gadoterate preferred as a contrast agent in patients with mild to moderately impaired renal function with a GFR of 30-60 ml/min. To detect renal masses and incidental adrenal lesions that may cause hypertension, T1 axial (phase-in-phase-out) field of view (FOV) 30-35 cm, slice thickness 5-6 mm, inter-slice spacing 0.5-1.5 mm; fat suppressed T2 axial FOV 30-35 cm, slice thickness 5-6 mm, inter-slice spacing 0.5-1.5 mm; T1 coronal oblique fat-suppressed 3D gradient echo, FOV 35-50 cm, section thickness 1.6-3 mm were taken.

In standard extracellular agents, the contrast dose was 0.15-0.2 mmol/kg, at a rate of 2-3 ml/sec. followed by an injection of 20-30 ml of saline. Dynamic sections obtained from the aorta by administering 1-2 ml of contrast material followed by 20-30 ml of saline as a test dose. By placing the region of interest (ROI) on the upper abdominal aorta, 3D images obtained automatically after sufficient contrast enhancement appeared in this area. During the 3-4 seconds before the acquisition of the images, the patient was held for breath and was asked to hold his breath until the end of the examination.

The images then transferred to the workstation and processed. Processing method maximum intensity projection (MIP) algorithm was used. With MIP, images obtained in different thicknesses and planes similar to conventional angiography. T1 axial dynamic 3D contrast series also reformed. In order to evaluate the venous structures, sections obtained in the venous

phase following the arterial phase. Venous structures also evaluated with coronal 3D sequence and T1 coronal sections with late contrast. Considering the patient's clinical status, kidney functions response to medical treatment and arterial structure, balloon or stent application performed in patients with 70% or more stenosis.

Statistical Analysis

Data were expressed as median value (minimum, maximum). The percentage changes of the measurements made after the treatment compared to the baseline measurements made before the treatment calculated. Mann Whitney-U, Chi-square and Fisher's exact tests were used for comparison between groups. A p value less than 0.05 considered significant. Statistical analyzes performed using the SPSS v20 software program (SPSS, Chicago, IL, USA).

RESULTS

In our study, the data of patients diagnosed with RAS between August 31, 2018 and September 30, 2021 evaluated retrospectively. The disease detected in 66.2% (53 patients) of 80 patients who thought to have renal artery stenosis. The mean age was 56 (19-74) years in the medical treatment groups (MTG) and 60 (15-77) years in the interventional treatment groups (ITG).

In the ITG group, stent was applied to 9 patients, bypass to 2 patients, and percutaneous transluminal renal angioplasty to 32 patients. There was no difference in age distribution of both groups (p = 0.955). Sixty-three percent of MTG patients had unilateral stenosis and 37% had bilateral stenosis, 54.2% of ITG patients had unilateral and 45.8% had bilateral stenosis (p = 0.725). Gender distribution between groups was similar (p = 0.475). The mean duration of hypertension disease in those receiving medical treatment was 5 (1-20) years, and 6 (1-30) years in interventional treatment group. Use of antihypertensive drug medication was similar in the MTG and ITG [3 (3-4) and 3 (3-5), p = 0.332, respectively]. Among the antihypertensive treatments administered, the use of calcium channel blockers was intense in both groups (71.7% of all patients), but no difference observed in terms of antihypertensive treatments in both groups (p > 0.05). Duration of hypertension was similar in both groups (p = 0.583). The duration of smoking did not differ between the two groups [MTG 0 (0-120) pack/year, ITG 0 (0-80) pack/year, p = 0.920]. Pretreatment serum urea and creatinine values were higher in the ITG [serum creatinine 1.34 (0.50-10.20) mg/dL in ITG, p = 0.232; serum urea 49 (14-179) mg/dL, p = 0.317].

When the mean glomerular filtration rates (eGFR) before treatment evaluated according to MDRD, it was 54.8 (4.5-150) ml/minute/m^2 in patients with ITG and 87.05 (18.90-126.80) ml/minute/m^2 in patients with MTG. There was no significant difference in eGFR values of both groups (p = 0.312). No significant difference shew between the sizes of both kidneys measured by renal doppler ultrasonography. Right kidney sizes evaluated by MRA were smaller in ITG (p = 0.008). No difference observed between the systolic and diastolic blood pressure values of the patients, the decrease in the percent change in diastolic blood pressure values detected more significant in the post-treatment ITG group [-12.50 (-50-11.11), p = 0.040]. When the percent change in eGFR before and after treatment compared, a mean increase of 5.94 (-42.46-186.55) detected in patients with ITG after treatment (p = 0.043). None of the patients had received renal replacement therapy prior to the treatment process. During the follow-up period, progression of chronic renal failure was seen in three (11.1%) patients with MTG and six (12.5%) patients with ITG, and the patients included in the chronic dialysis program (p = 1.00) (Tables 1 and 2).

DISCUSSION

Renal artery stenosis is the most common cause of renovascular hypertension. Controlling blood pressure is the main goal in renal artery stenosis, reduces mortality and morbidity. Studies performed that renal artery stenosis was found between 5.1-6.8% in patients who underwent renal angiography. In patients with coronary artery or aortoiliac disease, the rate of RAS was found to be 50% or more [8-11]. The most common cause of RAS is atherosclerosis. It is seen between 12-45% of the cases. Fibromuscular dysplasia is the second most common cause of RAS and is detected

Table 1. Clinical and laboratory characteristics of patients undergoing medical and interventional treatment

	MTG (n = 10)	ITG (n = 43)	*p* values
Age (n)	56 (22:74)	60 (25:77)	0.955
Duration of HT (year)	5 (1:20)	6 (1:30)	0.583
Comorbidities, n (%)	10 (100%)	43 (100%)	
Hypertension	8 (80%)	29 (67.4%)	
Coronary artery disease	7 (70%)	33 (76.7%)	
Type 2 Diabetes	5 (50%)	24 (55.8%)	
Peripheral artery disease Chronic kidney disease	4 (40%)	10 (23.2%)	
Smoking (pack/year)	0 (0:120)	0 (0:80)	0.920
Renal sizes (left) (RDU) (mm)	100.50 (90:117)	98 (65:125)	0.624
Renal sizes (right) (RDU) (mm)	99 (68:129)	96 (60:127)	0.480
MRA left kidney (mm)	95 (82-114)	92 (61-120)	0.326
MRA right kidney (mm)	92 (63:123)	90 (56:120)	**0.008**
Systolic blood pressure BT (mmHg)	150 (120:180)	150 (120:260)	0.498
Systolic blood pressure_pc (AT→BT)	-19.38 (-27.78:-7.14)	-14.29 (-46.15:6.67)	0.724
Diastolic blood pressure BT (mmHg)	90 (80:100)	90 (80:150)	0.125
Diastolic blood pressure_pc (AT→BT)	-11.11 (-20:0)	-12.50 (-50:11.11)	**0.040**
Serum urea BT (mg/dL)	29.50 (21:91)	49 (14:179)	0.317
Serum urea_pc (AT→BT)	-12.25 (-64:62.79)	-10.53 (-73.17:107.14)	0.617
Serum creatinine BT (mg/dL)	0.96 (0.60:3.20)	1.34 (0.50:10.20)	0.232
Serum creatinine_pc (AT→BT)	3.94 (-15.63:14.29)	-4.88 (-59.76:61.54)	0.053
eGFR (ml/dak/1.73 m^2)	87.05 (18.90:126.80)	54.8 (4.5:150)	0.312
eGFR_pc (AT→BT)	-4.26 (-32.81:25)	5.94 (-42.46:186.55)	**0.043**
Follow-up time (months)	15 (12:84)	12 (10:96)	0.955
Gender (M/F)	5/5	30/13	0.475
Smoking (Yes), n (%)	2 (20%)	8 (18.60%)	1.00
Stenosis			
Unilateral	7 (70%)	26 (60.50%)	0.725
Bilateral	3 (30%)	17 (39.50%)	

MTG = Medical treatment groups, ITG = Interventional treatment groups, HT = Hypertension, RDU = Renal doppler ultrasonography, BT = Before treatment, AT = After treatment, MRA = Magnetic resonance angiography, PC = Percent change, eGFR = Estimated glomerular filtration

Table 2. Drug therapy in both groups

	MTG (n = 10)	ITG (n = 43)	*p* values
ACEinh_BT (Yes), n (%)	4 (40%)	17 (39.50%)	0.137
ACEinh_AT (Yes), n (%)	4 (40%)	9 (20.90%)	0.665
ARB_BT (Yes), n (%)	4 (40%)	14 (32.60%)	0.704
ARB_AT (Yes), n (%)	4 (40%)	10 (23.30%)	0.667
CCB_BT (Yes), n (%)	8 (80%)	30 (69.80%)	1.00
CCB_AT (Yes), n (%)	8 (80%)	25 (58.10%)	0.722
AB_BT (Yes), n (%)	4 (40%)	16 (37.20%)	1.00
AB_AT (Yes), n (%)	4 (40%)	16 (37.20%)	1.00
BB_BT (Yes), n (%)	5 (50%)	25 (58.10%)	0.730
BB_AT (Yes), n (%)	5 (50%)	21 (48.80%)	1.00
Diuretics_BT (Yes), n (%)	5 (50%)	16 (37.20%)	0.492
Diuretics_AT (Yes), n (%)	5 (50%)	13 (30.20%)	1.00
ALDOSANT_BT (Yes), n (%)	0	3 (7%)	1.00
ALDOSANT_AT (Yes), n (%)	0	1 (2.30%)	1.00
Progression of CKD n (%)	1 (10%)	4 (9.30%)	1.00
BT_DRUGS (n)	3 (3-4)	3 (3-5)	0.332
DRUGS (AT →BT) (n)	3 (2:3)	1 (1:3)	0.330

ACEI = Angiotensin converting enzyme inhibitors, ARB = Angiotensin receptor blockers, CCB = Calcium channel blockers, AB = Alpha blockers, BB = Beta blockers, Diuretics = Loop or thiazide, ALDOSANT = Aldosterone antagonist, CKD = Chronic kidney disease.

approximately 16% [12, 13].

In RAS patients, in general acceptance invasive procedure can be recommended after evaluating clinical and hemodynamics conditions in patients with stenosis above 70% [14]. Four-year survival was 89% in patients with < 75% stenosis, while survival was 57% in patients with stenosis greater than 75% [15]. In a study, renovascular hypertension was suspected in 38% of 459 hypertension patients, and RAS was detected in more than 70% of these patients. Bilateral stenosis was found in 37% of patients over 65 years of age [16].

Patients with renal artery stenosis have renal parenchymal changes including interstitial fibrosis, tubular atrophy, glomerulosclerosis, periglomerular fibrosis, and a variety of arteriolar abnormalities [17]. There are studies showing that invasive intervention improves or does not change kidney functions in RAS patients. In a study in which 76 RAS patients were evaluated (serum creatinine > 1.5 mg/dL, > 70% stenosis), it was found that renal values improved in 20 ± 11 months follow-up after stenting [18]. In another study, in which 20 RAS patients over 55 years (diagnosed by MR angiography, serum creatinine > 2 mg/dL) were evaluated, it was detected that the invasive procedure did not change their kidney functions in 6 months after the procedure [19]. In a study evaluating 96 patients with atherosclerotic renal disease with a creatinine value above 1.5 mg/dL, 70% of the patients preserved their kidney values after revascularization, and dialysis treatment was initiated in 17% of the patients [20].

The place of medical therapy and interventional therapy in the treatment of the disease is controversial. In the CORAL study, when 947 patients with renal artery stenosis evaluated after a mean follow-up of 43 months, there was no difference in renal and cardiovascular outcomes between the two groups that received medical treatment and interventional treatment (stent) [7]. In the STAR trial, 140 patients (64 medical treatments, 76 interventional treatments) examined for 2 years. No difference was found in renal survival in

patients who received medical and interventional treatment (stent) [21]. In a study which 806 patients with atherosclerosis-related renovascular disease followed for an average of 34 months, no difference detected between medical and interventional (stent) treatment in terms of renal event, cardiovascular disease, and death [22, 23].

Changes in GFR values in RAS patients undergoing medical and interventional treatment were found to be different in many studies. In some studies, a decrease in GFR after treatment was observed in those who underwent interventional procedures, while in some studies it was observed in those who received medical treatment [21, 24].

In our study, increase in diastolic blood pressure and decrease in glomerular filtration rate were more prominent in the interventional treatment group. There was no significant difference in renal survival between two groups, like other studies.

Limitations

Our study was retrospective. MRA used for the diagnosis of RAS, data of patients diagnosed with other methods or after normal angiography could not be used. In this respect, the number of our patients was less.

CONCLUSION

Finally; in patients with renal artery stenosis, interventional or medical treatment should be decided by evaluating clinical status and comorbid diseases. Patients should be followed closely in terms of kidney function and survival.

Ethics Committee Approval

This study was approved by the Bursa City Hospital Ethical Committee (approval number: 2022-1/12, date: 09.02.2022).

Authors' Contribution

Study Conception: YA, BD, SA; Study Design: YA, BD, Mİ; Supervision: YA, BD, SA, Mİ; Funding: N/A; Materials: YA,GO; Data Collection and/or Processing: YA, BD; Statistical Analysis and/or Data Interpretation: GO; Literature Review: YA, BD; Manuscript Preparation: YA and Critical Review: YA.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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