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ORIGINAL ARTICLE

Surgical treatment of renovascular hypertension

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ABSTRACT

Background: Renovascular hypertension is the commonest form of secondary hypertension. It occurs in less than 5 % of all hypertensive population. There are two forms of renovascular hypertension: Atherosclerotic and fibromuscular dysplasia. Renovascular hypertension is suspected when it develops suddenly in patients under 30 or over 55 years of age, or abruptly worsen in any patient. The aim was to evaluate the indications of surgical treatment of "renovascular hypertension"**.**

Methods: Twenty cases with renovascular hypertension were included. The main investigations were: Laboratory studies, Duplex ultrasound, Intravenous pyelogram, CT angiography, aortography and selective renal angiography. Indications for surgery were : complex disease of the renal artery, aneurysm, accessory renal arteries, fibromuscular dysplasia and partial damaged of one kidney. Also, atherosclerotic stenosis of the renal arteries and complete kidney damage.

Results : According to the etiology, 20 patients were divided into two groups : **Group 1(Below 30 years)(Fibromuscular dysplasia group)**which included 14 patients, (100.0%) were females, their age ranged from 18 to< 30years with the mean±SD (24.7±3.5).**Group 2(Above55 years)(Atherosclerotic group)** which included 6 patients, their age ranged from >55 to 68 years with the mean±SD(62 ±4.1), 5(83.3%)were males and 1(16.7%) was female. **Renal artery bypass graft** was done for 15 cases, **endarterectomy** in 2 cases, **endarterectomy with patch graft** in two cases and **nephrectomy** in one case. Control of hypertension was successful in 17 cases, partial control of 2 cases, while the blood pressure still high in case of nephrectomy. No mortality in both groups within 6 months follow up period.

Conclusions : Surgical treatment for renovascular hypertension is mandatory for complex disease of the renal artery, aneurysms and failure of endovascular procedures. Nephrectomy is the treatment of choice for damaged kidney.

Key wards : Renovascular hypertension, renal artery stenosis, renal artery bypass, renal revascularization**.**

INTRODUCTION

Renovascular hypertension (RVH) is a secondary form of high blood pressure caused by a narrowing of the renal artery. Renal hypertension is the most common form of secondary hypertension. Recent studies have defined significant atherosclerotic renal artery stenosis (ARAS) as a decrease of at least 60% in luminal diameter, which was found in over 6% of persons aged over 65 years. Stenosis of the renal artery (STAR) leads to hypertension and potentially to chronic renal failure. Increased risk of cardiovascular disease in (ARAS) patients may result from activation of the renin–angiotensin–aldosterone system (RAAS).[(1,2)] The two most common primary

diseases of the renal arteries are (ARAS) [1] and fibromuscular dysplasia (FMD). [3] Atherosclerosis accounts for about 90% of cases and usually involves the ostium and proximal third of the main renal artery and the perirenal aorta. [4]

Other rare causes of RVH included renal trauma, aortic dissection, arterial embolus, hypercoagulable state with renal infarction (e.g., Lupus anticoagulate), autoimmune diseases (e.g., Takayasu's arteritis, Polyarteritis nodosa) and malignancy encircling the renal artery (e.g., Renal cell carcinoma & pheochromocytoma) . [5]

Narrowing of the renal artery reduces the flow of blood to the kidney. In response, the kidney produces the protein renin. Renin is released into the blood stream and converted into an enzyme that causes sodium (salt) retention and constriction of the arterioles. Renovascular hypertention is suspected when hypertension develops suddenly in patients under 30or over 55years of age or abruptly worsens in any patient. [6]

No single test for renovascular hypertention is definitive. Imaging studies which are used for diagnosis include Intravenous urography, renal arteriography. magnetic resonance (MR) and computed tomography angiography (CTA) provide detailed images of the aorta and renal arteries. Doppler ultrasound (DUS) is operator-dependent but highly specific in competent laboratories. [7-11]

Renal artery surgery offers major benefits for patients undergoing surgical repair of the aorta or nephrectomy, and for patients with complex disease of the renal arteries, e.g. aneurysms or failed endovascular procedures. The results of surgery are found better than the results of endovascular interventions for osteal lesions, for sequential stenoses in single renal artery, and for stenoses in multiple renal arteries at the same side. Also results of surgery are better when the cause of renal artery stenosis is atherosclerosis. Metaanalysis of 47 studies compared the results of surgery vs endovascular interventions showed that surgery of renal artery stenosis has better long-term results in the control of blood pressure and renal function.[12] Surgical procedures may include aortorenal bypass grafting, endarterectomy, or occasionally extra anatomic repair using anastomosis to the hepatic or splenic arteries. [1,4,6] Fibromuscular dysplasia predominantly affects young women with normal kidney function, so renal artery revascularization in fibromuscular dysplasia is expected to be relatively successful. [13-15]

AIM OF THE WORK

The aim of this work was to evaluate the indications of surgical treatment of renovascular hypertension.

PATIENTS AND METHODS

Patients:

This study occurred within 63 months period from October 2014 to January 2020.Twenty patients with renovascular hypertension were included. All cases were admitted to The Vascular Surgery Unit in Alexandria Main University Hospital, Faculty of Medicine and Department of Experimental and Clinical Surgery, Medical Research Institute, Alexandria University, Egypt. After approval of The Ethical Committee of the Faculty of Medicine, Alexandria University, an informed consent was taken from every patient. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: Failure of medical treatment of hypertension, failure of endovascular revascularization of the kidney, ischemic nephropathy and cardiac destabilization syndromes.

Exclusion criteria: Bilateral renal damage and malignant tumor of the kidney.

Methods:

All patients were subjected to the following:

History taking and clinical examination: Including assessment of headache, hypertension, tiredness, confusion, vision changes, nausea and vomiting, angina like chest

pain and congestive heart failure. Bruit in the epigastrium or on the flanks.

Laboratory investigations: Including renal function tests, glycemic profile (fasting, postprandial & HbA1c) and serum cholesterol & triglyceride levels. Control of type 2 diabetes mellitus with oral antidiabetics for 3 months before operation and control of high cholesterol and triglycerides by Atorvastatin for 3 months before operation were done.

Preoperative medical treatment for hypertension: All patients received 4 antihypertensive drugs including: angiotensin receptor blockers (ARB), B–blockers, calcium channel blockers and diuretics.

Imaging studies: Including Duplex ultrasound, intravenous pyelogram, CT angiography, aortography and selective renal angiography were done.

Surgical treatment: Bypass graft or endarterectomy with or without patch graft and nephrectomy for complete kidney damage.

Follow up of the patients for 6 months postoperatively.

Statistical analysis of the data:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0**. (**Armonk, NY: IBM Corp**)** Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation. The used tests were **Chi-square test, Fisher's Exact, Student t-test, Paired t-test and ANOVA with repeated measures.** Significance of the obtained results was judged at the 5% level.

RESULTS

Demographic data:

A series of 20 patients with (RVH) were included in this study within 63 months period from October 2014 to January 2020. Patients were divided into two groups: **group I**: **(Fibromuscular dysplasia group)** which included 14 female patients with (RVH) due to fibromuscular dysplasia (FMD). Their age ranged from 18–to<30 years with the mean±SD (24.7±3.5) years. **Group II: (Atherosclerotic group)** which included 6 patients with (RVH) due to atherosclerosis. Their age ranged from >55 to 68 years with the mean±SD (62 ±4.1) years. Sex incidence for both groups was 15 females and 5 males. (Table 1)

Clinical presentation:

The main symptoms included: headache in (20/20,100%) of patients, early fatigue in (14/20, 70%) of patients, vertigo in (11/20,55%) of patients, impaired vision in (10/20,50%) of patients, dyspnea in (10/20,50%) of patients, nausea &vomiting in (9/20, 45%) of patients and angina like chest pain in (8/20,40%)of patients, Table 3.

The main signs included: Hypertension in (20/20,100%) of patients, bruit in the abdomen or the flanks in (10/20,50%) of patients and left ventricular hypertrophy in (7/20,35%) of patients, Table 2.

Laboratory Investigations:

Laboratory Investigations were done for all patients. Renal function tests were normal in all patients. All patients in group II **(Atherosclerotic group)** were hypercholestrolemic and hypertriglyceridemic, but during the study they were controlled by anticholestrolemic drugs Ator vastatin.

Diabetes mellitus type 2 was present in all patients of group II (**Atherosclerotic group**), HbA1c was totally uncontrolled ranging between (9.0 – 10.50) %, with the mean +SD (9.7 ± 0.7). After 3 months of treatment with oral antidiabetics, there was a statistical significant decrease of HbA1c. It ranged from (7.10 – 8.0)%, with the mean +SD (7.7 ± 0.3), p=0.001 .Also, fasting and postprandial blood glucose showed statistical significant decrease in their levels after oral antidiabetics (p<0.001, p<0.001) respectively, Table 3.

Measurements of blood pressure:

For both groups, there was a statistically significant decrease in systolic and diastolic blood pressure in the three studied periods (Before medical treatment, after 3 months of antihypertensive drugs and immediate after surgery), Table 4.

Imaging studies:

Duplex ultrasound for evaluation of the renal arteries was done for all patients. It visualized stenosis in 4patients and occlusion in 2 patients due to atheromatous changes in renal artery in patients of group II **(Atherosclerotic group)**.

CT angiography was done in (18/20, 90%) of patients. It was diagnostic in (13/14, 92.86%) of patients in group I &(5/6, 83.33%) of patients in group II).

Aartography: It visualized osteal lesions and multiple renal arteries in 4 patients of group II **(Atherosclerotic group)**.

Selective renal angiography was done in 3 patients of group I (**Fibromuscular dysplasia group)**.It showed beads of string in the renal artery.

Intravenous pyelogram: It showed no uptake & no excretion of the dye in two patients, one patient in each group, Table 5.

Indications of surgery: Surgical interventions were done for patients with complex disease of the renal artery, aneurysm of the renal artery, fibromuscular dysplasia, atherosclerotic renal artery stenosis, complete kidney damage and failure of endoplasty in one patient.

Surgery of the renal artery:

In all operations, renal arteries were reconstructed, Table 5.

Renal artery bypass graft was done for 15patients (aorto – renal) using PTFE in 8 patients and great saphenous vein bypass in 7 patients for revascularization of the kidney. Case 1 (Figure 1(A,B,C&D) & case 2 (Figure 2). Endarterectomy was done in two patients. Endarterectomy with patch graft was done in two patients. Nephrectomy was done in one patient.

Post operative control of hypertension was successful in 17 patients down to the normal level without any drugs. In two patients, partial control of the blood pressure was done with treatment with two antihypertensive drugs. The blood pressure was still high in the patient with nephrectomy.

Post operative control of diabetes mellitus, cholesterol & triglycerides.

No mortality was detected in all patients within 6 months follow up period.

Case 1:

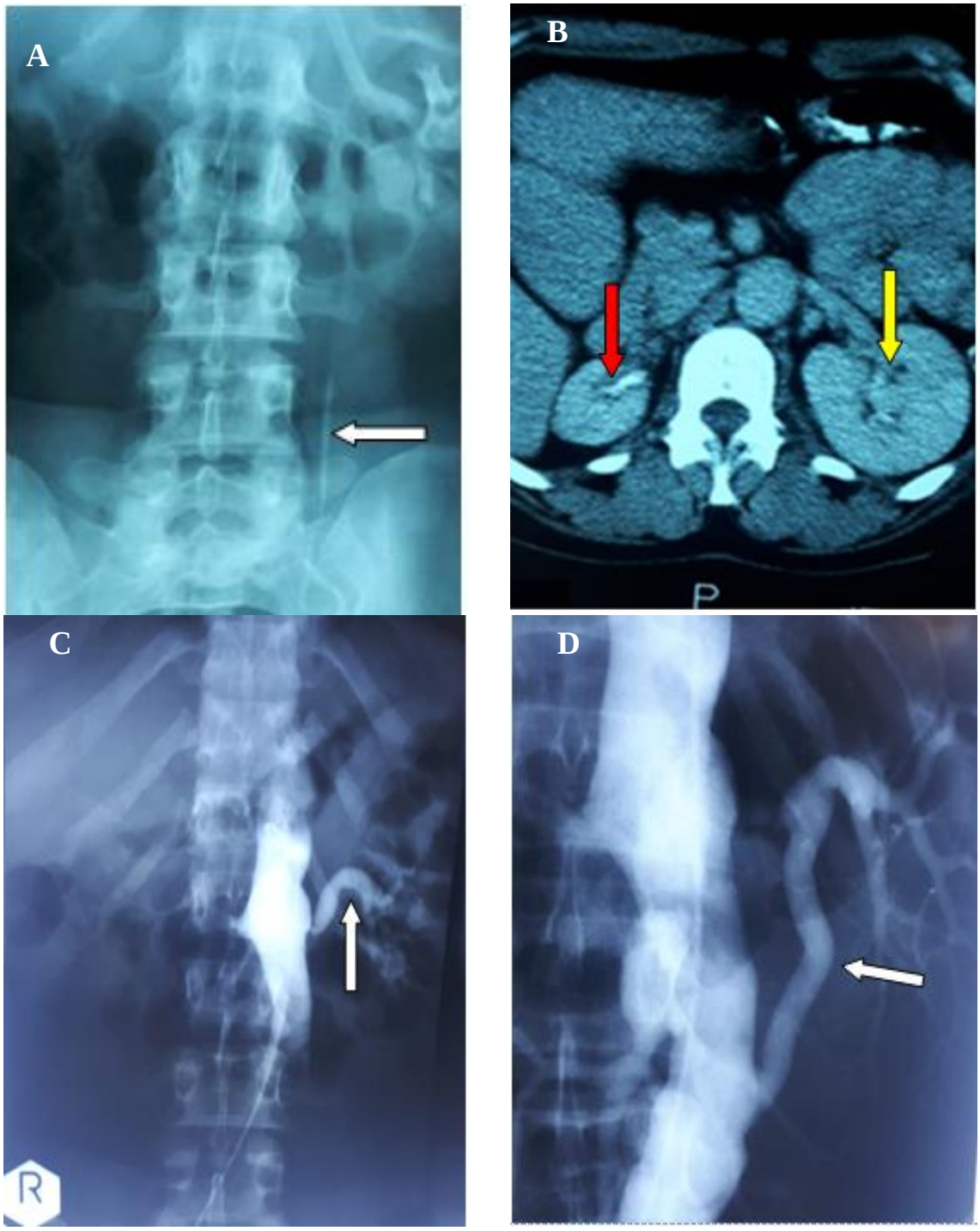

Figure 1:

Case 1

Fig. (1): A) Intravenous urogram showing non functional right kidney and functioning left kidney (The arrow showing dye in the left ureter) Preoperative . **B)** CT abdomen showing atrophy of the right kidney, occlusion of the right artery (red arrow) and functioning left kidney with stenosis of its renal artery (yellow arrow). Preoperative. **C)** Abdominal aortography showing occlusion of the right renal artery and atrophy of the right kidney with stenosis of the left renal artery (Preoperative). **D)** Postoperative aortography showing. a graft from the aorta to the hilum of the left kidney (Gortex graft 6 mm). The arrow showing the graft.

Figure 2

Case 2

Fig. (2): Postoperative aortography showing normal right renal artery , stenosis of the left renal artery plus attenuated left accessory renal artery and patent aortodistal renal artery bypass graft from the abdominal aorta to the Hilum of the left kidney . The arrow showed the graft (Gortex graft 6 mm)

Table (1): Demographic data of patients with (RVH) in both groups (total No=20)

	Group I Fibromuscular dysplasia group (18-<30 years)	Group II Atherosclerotic group (>55–68 years)	Test of sig.	p
Age (years)				
Range	18.0 – 29.0	56.0 – 68.0	t=20.803*	<0.001*
Mean ± SD.	24.7 ± 3.5	62 ± 4.1		
No.	14	6		
%	70.0	30.0		
Gender				
Male	0(0.0%)	5(83.3%)	χ^2= 15.556	FEp <0.001*
Female	14(100.0%)	1(16.7%)		

t: Student t-test χ^2: **Chi square test** FE**: Fisher Exact**

p: p value for comparing between the studied groups

*: Statistically significant at $p \leq 0.05$

Table (2): Clinical presentation of patients with (RVH) in both groups (total N0=20)

Items	No.	%
Symptoms		
Headache	20	100
Fatigue	14	70
Vertigo	11	55
Impaired vision	10	50
Dyspnea	10	50
Nausea and vomiting	9	45
Angina like chest pain	8	40
Signs		
hypertension	20	100
Bruit of the abdomen or flanks	10	50
Left ventricular hypertrophy	7	35

Table (3): Comparison between the glycemic profile in group II before and after 3 months of oral antidiabetics

	Before treatment	After 3 months of treatment	t	p
HbA1c (%)				
Range	9.0 – 10.50	7.10 – 8.0	7.412*	0.001*
Mean ± SD.	9.7 ± 0.7	7.7 ± 0.3		
FBG (mg/dl)				
Range	230.0 – 275.0	135.0 – 165.0	12.237*	<0.001*
Mean ± SD.	257.7 ± 16.2	147.8 ± 11.9		
Postprandial glucose(mg/dl)				
Range	290.0 – 330.0	170.0 – 190.0	17.827*	<0.001*
Mean ± SD.	311.3 ± 14.5	177.5 ± 8.2		

t: Paired t-test

p: p value for comparing between **Before treatment** and **After 3 months of treatment**

*: Statistically significant at $p \leq 0.05$

Table (4): Comparison between the measurements of blood pressure in both groups according to the three studied periods

Measurement of blood pressure	Before medical treatment	After medical treatment	After surgical treatment	F	p
Systolic (mmHg)					
Group I	$241.4^{a} \pm 15.6$	$186.4^{b} \pm 9.3$	$139.3^{c} \pm 19.1$	264.948*	<0.001*
Group II	$236.7^{a} \pm 12.1$	$181.7^{b} \pm 4.1$	$135.8^{c} \pm 13.2$	117.891*	<0.001*
$t(p_0)$	0.663 (0.516)	1.593 (0.129)	0.401 (0.693)		
Diastolic(mmHg)					
Group I	$175.0^{a} \pm 10.9$	$116.4^{b} \pm 6.3$	$87.9^{c} \pm 9.3$	455.746*	<0.001*
Group II	$175.0^{a} \pm 10.5$	$111.7^{b} \pm 11.7$	$85.0^{c} \pm 3.2$	155.946*	<0.001*
$t(p_0)$	0.0 (1.000)	1.193 (0.248)	0.721 (0.480)		

t: Student t-test

p_0: p value for comparing between **Group I** and **Group II**

F: F test (ANOVA) with repeated measures, Sig. bet. periods was done using **Post Hoc Test (adjusted Bonferroni)**

p: p value for comparing between different period

Means with **Common letters** are not significant (i.e. Means with **Different letters** are significant)

*: Statistically significant at $p \leq 0.05$

Table (5): Imaging and surgical reconstruction of stenosed renal arteries in 20 patients with "renovascular hypertension" (RVH)

Imaging	No.	%
Duplex ultrasound	20	100
CT angiography	18	90
Aortography	4	20
Selective renal angiography	3	15
Intravenous pyelography	2	10
Surgical reconstruction		
Aorto–renal bypass graft	15	75
Endarterectomy	2	10
Endarterectomy with patch graft	2	10
Nephrectomy*	1	5

NB: The two cases of occluded renal artery :Nephrectomy was done in one case*. The other case was not removed because it was completely atrophic.

DISCUSSION

Renovascular hypertension has been recognized for more than 80 years, when seminal experimental studies demonstrated that progressive occlusion of the renal vessels produces a rise in systemic arterial pressure. These data established a central role of the kidney in blood pressure regulation and

provided one of the most widely studied models of "angiotensin-dependent" hypertension [4]

Renovascular disease is characterized by unilateral or bilateral renal artery stenosis (RAS). In Western populations 90% of RAS is caused by atherosclerotic renal artery stenosis (ARAS), and 10% by fibromuscular dysplasia (FMD). ARAS affects 7% of North Americans aged over 65 years and the incidence is rising due to aging, obesity, diabetes, and hypertension. FMD affects 0.4% of the population and is seen in younger patients .Reduced renal perfusion causes progressive chronic kidney disease (CKD) and drives neurohormonal activation with subsequent resistant hypertension, end-stage kidney disease, and death. [16]

In the present study**,** we aimed to evaluate the diagnosis and indications of surgical treatment of renovascular hypertension.

A series of 20 patients with (RVH) were included in this study. Patients were divided into two groups: **group I**: (**Fibromuscular dysplasia group)** which included 14 female patients with (RVH) due to fibromuscular dysplasia (FMD). Their age ranged from 18–to<30 years . **Group II: (Atherosclerotic group)** which included 6 patients with (RVH) due to atherosclerosis. Their age ranged from >55 to 68 years . Sex incidence for both groups was 15 females and 5 males.

In the present study, seventy percent of the patients had fibromuscular dysplasia, their age were below 30 years and all were females. Phukan et al 2017 [17] dedicated that fibromuscular dysplasia (FMD) is a nonatheromatous disease affecting the small‐ and medium‐sized arteries. It affects mostly the renal and internal carotid arteries. FMD is very often seen affecting the renal arteries, 60%–75% cases. The prevalence of FMD is 4.4%–6.6%, most commonly in females.

The explanation of the younger age and higher percentage of the fibromuscular dysplasia in the present study is that In Egypt, the average of life expectancy is about 71 years. That is why doctors do not search for RAS as diagnosis of hypertension in elderly as they consider it essential hypertension .On the other hand, doctors search meticulously for RAS as cause of secondary hypertension in younger age especially in young females . That is why the number of FMD in our study was higher than the number of patients with atherosclerosis; which is not matches with the literature.

In the present study, thirty percent of the patients had atherosclerosis ,their age were above 55 years and 83.3% were males Textor [4] dedicated that The dominant cause (at least 85%) of RVD in western countries is atherosclerotic renal artery stenosis (ARAS). This often develops as part of systemic atherosclerotic disease affecting multiple vascular beds, including coronary, cerebral and peripheral vessels. Community based studies suggest that up to 6.8% of individuals older than 65 have ARAS more than 60% occlusion. Screening studies indicate rising prevalence of detectable ARAS in hypertensive subjects from 3% (ages 50-59) to 25% (above age 70) with older ages. Clinically significant atherosclerotic RVD often is manifest by worsening or accelerating blood pressure elevations in older individuals with pre-existing hypertension.

The explanation of the younger age of the atherosclerotic group in the present study may be due to different life style, fatty food intake, lack of exercise, smoking, diabetes and obesity. This needs culture behavior changes.

In the present study, the main clinical picture of renovascular hypertension in both groups was (hypertension and headache) in 100% of cases. It was highly suspicious and the diagnosis was confirmed by imaging (Duplex ultrasound, CTA, selective renal angiography and I.V. pyelography). They were diagnostic and this was matched with what was mentioned in the literature.[1,7-11]

Regarding the preoperative medical control of the blood pressure, all patients received antihypertensive drugs. They received 4 antihypertensive drugs including: angiotensin receptor blockers (ARB), B–blockers, calcium channel blockers and diuretics for 3 months before surgical operation. Although there was a

statistical significant decrease in blood pressure after 3 months of treatment ($p<0.001$) .However , the surgical intervention caused immediate normalization of blood pressure.

This result was in agreement with Dupey and Ricco (2019) [6] who dedicated that surgical revascularization can provide immediate improvement in kidney function and normalizing the blood pressure in RAS patients. They stated that the main goal of renal artery surgery in patients with RAS is to treat resistant hypertension. In patients with renal artery aneurysm (RAA), renal artery surgery aims to either protect from rupture or to treat concomitant hypertension.

In the present study, the indications of surgery included complex disease of the renal artery, aneurysm, FMD, atherosclerotic renal artery stenosis and failure of angioplasty.

In the present study, renal artery bypass graft was done for 15patients (75%) using PTFE graft in 8patients and great saphenous vein bypass graft in 7patients to revascularise the kidney, endarterectomy in two patients (10%), endarterectomy with patch graft in 2 patients (10%) and nephrectomy in one patient (5%) due complete kidney damage.

Steuer et al 2019.[18] and Balk et al 2007.[19] mentioned that the indications and surgical procedures for surgical repair of renal artery stenosis similar to the indications in the present study

In the present study, surgical repair of the renal arteries was successful in all patients in both groups: either in patients with atherosclerosis (ARAS) or in patients with (FMD). All reconstructions were durable.

In present study, complete damaged kidney in one patient was removed and this was in accordance with Thomaz et al[20] who stated that in patients with renovascular hypertension nephrectomy of the atrophic kidney is a procedure which results in improvement of arterial hypertension and of the renal functions.

CONCLUSIONS

Intervention is better to be early enough to reserve the kidney functions and prevent renal damage. Surgical reconstruction for the treatment of (RVH) due to atherosclerosis is often effective. Treatment of (FMD) can be surgical or via angioplasty. Surgery has lower incidence of restenosis than angioplasty. The surgical treatment is mandatory for complex disease of the renal artery, aneurysms and failure of endovascular procedures. In damaged kidney, nephrectomy is mandatory.

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Contributors

All authors have approved the final article.

Authorship

All authors have made equal contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

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