Outcome following renal autotransplantation in renal artery stenosis

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Abstract Introduction: With significant advances in the area of interventional radiology, angioplasty and stenting have become preferred first-line treatment in patients with significant renal artery stenosis. However, not all patients have favorable anatomy to undergo minimally invasive treatments, and reconstruction of the renal artery is an option. In select cases, either improved renal function or maintenance of existing function and sometimes resolution of hypertension can follow surgical treatment.

Material and Methods: This was a prospective observational study conducted from August 2010 to June 2016. Patients <45 years of age with uncontrolled hypertension secondary to renovascular hypertension (RVH) and refractory to medical management and renal arterial disease unfavorable for percutaneous intervention were included in the study. All patients were evaluated thoroughly using computed tomography angiography and diethylenetriaminepentaacetic acid renal scan. Patients underwent autotransplantation either into the right or left iliac fossa. Some kidneys required bench reconstruction of the renal artery and/or its branches before being implanted into either iliac fossa.

Results: Nine patients were included in the study. The mean age was 27 years. Seven were males and two were females. Five patients had bilateral renal artery stenosis. After autotransplantation, initially five patients became free of antihypertensive medicines, but on the follow-up, two patients showed rising trend of blood pressure. The evaluation revealed narrowing at anastomosis site in both patients with salvageable kidney function in one patient. Angioplasty with stenting was done in this patient while the second patient underwent secondary nephrectomy. At 2 years of follow-up, four patients required no antihypertensive medicines.

Conclusion: Autotransplantation can be a successful treatment of severe RVH and should be considered in patients with renal arterial disease unfavorable for percutaneous intervention.

Keywords: Atherosclerosis, fibromuscular dysplasia, renal autotransplantation, renovascular hypertension

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INTRODUCTION

Renovascular hypertension (RVH) is generally suspected in newly diagnosed relatively younger patients with uncontrolled hypertension or in patients >55 years of age with new onset of high blood pressure and absent family history.^[1,2] In the vast majority of patients, antihypertensive medicines followed by percutaneous angioplasty (PTA) with or without stenting are used to manage RVH. The appeal of PTA and stenting lies in the fact that it is minimally invasive and can be repeated with less morbidity in experienced hands. It is the procedure of choice in ostial or focal, main or branch stenosis of the renal artery of atherosclerotic or fibromuscular disease (FMD).^[3] In certain patients, it becomes difficult to manage RVH using percutaneous procedures due to either complex lesion or difficult anatomy. In these patients, renal autotransplantation (RAT) plays an important role in managing RVH. Irrespective of the nature of treatment, a patient is labeled to have successful revascularization only when renal function and blood pressure either stabilize or improve following the intervention.^[3-8] While it is claimed that RVH is curable, any obvious benefit of either PTA or RAT has not been found in curing RVH in recent studies.^[9] Some studies have further quoted that placement of kidney in iliac fossa during RAT increases the risk of atherosclerosis of renal vessels and its consequences in such kidneys.^[10]

We conducted this study to assess the role of RAT while managing patients with complex lesions arising from different etiologies which were either difficult to manage or failed with the combination of PTA and antihypertensive medicines. We also evaluated the outcome of RAT in RVH in this small cohort resulting from different etiologies.

MATERIALS AND METHODS

After approval from the institutional ethics committee, this study was conducted from August 2010 to June 2016. This was a prospective interventional study. Young patients (<45 years) diagnosed to have RVH with uncontrolled hypertension and renal arterial disease unfavorable for PTA were included in the study. Patients were explained the study, and informed consent was obtained in their native language. All patients were preoperatively assessed with detailed clinical history, number, and types of antihypertensive medications required to manage hypertension, body mass index (BMI), and hematological investigations including lipid profile. Vessels were evaluated using computed tomography with angiography, and diethylenetriaminepentaacetic acid (DTPA) scan was used for baseline renal function assessment. Details about lesions and patency of renal, iliac, and other arteries were assessed on angiography.

Patients were placed in the right or left lateral position with the kidney bridge elevated initially to facilitate renal dissection in the extraperitoneal plane. Either a single incision starting from the middle of the 11th rib to midline in the lower abdomen or a standard flank incision excising the 11th rib followed by a Gibson incision to facilitate placement of the kidney in the iliac fossa was used. Complete mobilization of the kidney as for a donor nephrectomy was carried out taking care to preserve the ureteral collaterals. Mannitol was administered while the vessels were being dissected, and 5000 units of heparin administered just before the vessels were clamped. On completion of the nephrectomy, renal hypothermia was achieved with a combination of surface cooling with ice slush and renal perfusion using Ringer lactate at 4°C mixed with 5000 units of heparin. The ureter was not disconnected unless bench surgery was deemed necessary. Perfusion of a polar artery was sometimes required. Perfusion was considered adequate when the irrigant return from the renal vein was clear, and the kidney attained uniform cooling and uniform paleness. Bench dissection was done to reconstruct adequate caliber renal artery. While bench reconstruction was being carried out, a second team prepared the iliac fossa. Internal and/or external iliac artery (EIA) was used depending on the surgeon's preference and the vascular anatomy. In case branch reconstruction was needed, branches of the internal iliac artery were used as an ex vivo graft for reconstruction and subsequently reanastomosed to the main internal or external artery. In some patients, the inferior epigastric artery was used for a second vessel anastomosis. After reconstruction of vessels on the bench, the kidney was briefly reperfused to check the integrity of the reconstructed artery and its branches and the adequacy of parenchymal perfusion. Kidney was then transferred to the iliac fossa. The vein was anastomosed to external iliac vein in end-to-side manner initially. End-to-end anastomosis of renal artery was done to iliac artery. In case of accessory artery, anastomosis was done to EIA in end-to-side manner or the inferior epigastric artery. The ureter was reimplanted on urinary bladder in modified Lich-Gregoir manner in those patients where the kidney was removed and vascular reconstructon was performed on bench. If no bench repair was necessary, the ureter as mentioned earlier was not disconnected, and while the kidney was placed into the iliac fossa, gentle arc of ureter was achieved ensuring no twist to its passage into the bladder. After confirming hemostasis, the wound was closed in layers leaving a drain.

On the postoperative period, particular attention was given to maintenance of adequate systolic blood pressure.

Serial evaluation of hematological and renal parameters was done, and the need for antihypertensive drugs was monitored. Ultrasonogram (USG) with Doppler was done postoperatively immediately and 24 h later to assess renal arterial flow and if there was any intrarenal dampening of flow. It was repeated before discharge and during each follow-up visit. Angiography was done if any abnormality in flow was detected on Doppler. Postoperative DTPA was done to assess adequate perfusion and excretion of autotransplanted kidney.

At subsequent follow-up, clinical examination, laboratory testing, and ultrasonography were done. Blood pressure was monitored, and the antihypertensive requirement was adjusted if needed. Any complication or need of intervention following surgery was noted. Criteria described by Cambria *et al.* were used for the assessment of the effect on renal function, and criteria described by Dean *et al.* were used to assess long-term effect on blood pressure.^[3,11] Patients were evaluated initially every 2 weeks till 3 months and every month thereafter till 6 months. At 3 months and 1 year, DTPA scan was repeated. After 6 months, patients were asked to keep follow-up 3 monthly.

RESULTS

Nine patients were studied in detail. All were relatively young with the mean age of 27.45 \pm 11.47 years (mean \pm standard deviation). Seven patients were male and two were female. All were nonsmokers. None of the patients had hypercholesterolemia, except patient (single) with atherosclerosis. All patients were diagnosed with uncontrolled hypertension. One patient had stroke and another presented with pulmonary edema and were diagnosed to be due to RVH. The mean BMI was 23.25 kg/m². All these patients were started on antihypertensive drugs but even on the combination of three to four antihypertensive drugs, which consisted of diuretics, calcium channel blockers (CCBs), α and β blockers, and hypertension remained uncontrolled. Patient with atherosclerosis was started on lipid-lowering drugs.

Initial evaluation with USG revealed difference in kidney size. Mean preoperative serum creatinine level was 1.39 mg% \pm 0.39 mg%. Five patients had marginally deranged serum creatinine (upper cutoff for normal 1.4 mg%) [Table 1].

Five patients had bilateral renal arterial stenosis whereas four patients had unilateral involvement. In five patients with bilateral stenosis, two had a nonfunctioning opposite kidney. In three patients, the contralateral kidney had decreased function (i.e., split function <15%). Five patients had involvement of renal artery and its branches on angiography, which was difficult to manage with PTA. Single patient with Takayasu's disease (TD) had aneurysms in main artery. In a child with neurofibromatosis, pheochromocytoma was ruled out. In all five patients with either nonfunctioning or poor functioning contralateral kidney, initially nephrectomy was done. Postnephrectomy, no significant improvement in hypertension was noted. All patients were optimized and were posted for RAT. Minimal interval between nephrectomy and RAT was 6 months.

Five patients (55.56%) had single renal artery bilaterally whereas in four patients (44.45%), accessory renal arteries were noted. These patients required bench reconstruction of renal vessels. One patient with FD suffered fatal myocardial infarction at the time of releasing clamps. Details of angiography findings and intraoperative reconstruction are given in Table 2.

Postoperative patients were monitored to maintain adequate blood flow to the autotransplanted kidney. For the initial postoperative period, blood pressure was managed using nitroglycerin perfusion. Perfusion was titrated to maintain adequate blood pressure. Four patients with prolonged bench dissection and single kidney suffered perioperative transient acute kidney injury. Urine output was adequate in all patients. Initially (at 6-month visit), five patients became free of antihypertensive medicines. At 9-month follow-up, one patient with neurofibromatosis showed worsening hypertension and raised serum creatinine level. Doppler revealed significant

Table 1: Preoperative details of clinical features in patients who had undergone renal autotransplantation	1: Preoperative details of clinical features in patients who ha	ad undergone renal autotransplantation
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n	Age/sex	Preoperative creatinine	Preoperative BP	Side affected	Preoperative split function (right:left)
1	25/female	1.2	190/110	U/L (left)	68:32
2	43/male	1.5	170/100	U/L (left)	14:86
3	19/male	1.8	180/100	B/L	100:0
4	35/male	1.6	160/90	B/L	12:88
5	45/male	1.7	200/110	U/L (right)	100:0
6	17/male	1.1	180/100	B/L	96:4
7	23/male	0.7	170/100	B/L	90:10
8	28/male	1.8	190/100	B/L	100:0
9	12/male	1.1	160/100	U/L (right)	32:68

BP: Blood pressure, B/L: Bilateral, U/L: Unilateral

n	Angiography finding	Diagnosis	Surgery	Reconstruction	Anastomosis
1	Right-normal Left-stenosis at ostium and proximal portion with aneurysm in proximal portion of segmental artery Accessory left renal artery- + Narrow in its proximal portion	TD	Left autotransplant	Main and segmental artery- reconstructed using hypogastric artery Accessory artery- inferior epigastric artery	Main artery- E-E anastomosis with IIA Accessory Artery- end to side with EIA
2	Right- small kidney with normal artery Left- stenosis with 90% occlusion at the origin and narrowing in single segmental artery	FD	Left autotransplant	Main artery- reconstructed using hypogastric artery Segmental artery- reconstructed using graft of distal hypogastric artery	Main art- E-E anastomosis with IIA
3	Right- ostial lesion with 90% occlusion Left- nearly completely occluded	FD	Left nephrectomy	Main artery- diseased portion excised and anastomosed directly with hypogastric artery	-
4	Right -near completely occluded Left- near complete occluded with collateral present	FD	Left autotransplant and right nephrectomy	Main artery- diseased portion excised and double barrel side to side anastomosis with adjacent collateral One collateral anastomosed with EIA	Main art- E-E anastomosis with IIA Collateral- end to side with EIA
5	Right renal artery ostial 90% occlusion	Atherosclerosis	Right autotransplant	Main artery- diseased portion excised and anastomosed directly with hypogastric artery	Main art- E-E anastomosis with IIA
6	Right-90% occluded with extension into segmental vessel Left- almost completely occluded Right subclavian 50% stenosis and aortoarteritis	TD	Right autotransplant with left nephrectomy	Main artery- reconstructed using hypogastric artery Segmental artery- reconstructed using graft of distal hypogastric artery	Main art- E-E anastomosis with IIA
7	Right renal artery- 80% occlusion distal to the origin Left renal artery -complete occlusion SMA (Superior mesenteric artery)- also involved with narrowing at ostium Hazy, irregular outline of aorta. These lesion patterns were suggestive of diagnosis of aorto-arteritis	TD	Right autotransplant with left nephrectomy	Main artery stump- reconstructed using hypogastric artery	Main art- E-E anastomosis with IIA
8	Right- near complete occlusion of the main artery and its branches with reformation beyond, with collaterals Hazy, irregular outline of aorta s/o aortoarteritis Left-completely occluded	TD	Right autotransplant with left nephrectomy	Main artery- reconstructed using hypogastric artery Segmental artery- reconstructed using graft of distal hypogastric artery Collaterals anastomosed on the side to main artery	Main art- E-E anastomosis with IIA
9	Right artery- near complete occlusion of main stump and its premature branches Accessory right renal artery + Left artery- normal	Neurofibromatosis	Right autotransplant	Main artery- reconstructed using hypogastric artery Accessory artery- Inf. epigastric artery	Main art- E-E anastomosis with IIA Acc. Art- end to side with EIA

TD: Takayasu's disease, EIA: External iliac artery

decreased flow across anastomosis. On functional scan, autotransplanted kidney was found to be nonsalvageable. After managing blood pressure with the addition of CCB and diuretics, nephrectomy of autotransplanted kidney was done. After nephrectomy, normal blood pressure was maintained with CCB and diuretics. In other patient with solitary functioning kidney and TD, worsening hypertension and deteriorating renal function were observed at 1 year. The evaluation revealed salvageable kidney with anastomotic stenosis. Angioplasty with stenting was done in this patient. Following this intervention, he did not require any further antihypertensive medicines. At 2 years of follow-up, four patients were free of antihypertensive medicines. Two patients required single antihypertensive medicine to maintain normal blood pressure.

Renal function was improved in four patients while in two patients function remained stable. Two patients had reduced renal function on postoperative DTPA scan. Of these, one patient required PTA, and in other patient with neurofibromatosis, nephrectomy of autotransplanted kidney was done. Mean postoperative serum creatinine at 2 years of follow-up was 1.125 mg% \pm 0.32 mg% [Table 3].

Mhaske,	et al.:	Outcome	following	renal	autotranspla	antation
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n	Postoperative BP	Postoperative intervention	Hypertension	Postoperative serum creatinine	Renal function
1	140/80	None	β-blocker	0.9	Stable
2	136/84	None	Cured	0.8	Improved
3	-	-	Intraoperative mortality	-	-
4	130/90	None	Cured	1.3	Improved
5	146/90	None	CCB	1.2	Stable
6	140/86	None	Cured	0.8	Improved
7	134/80	None	Cured	0.9	Improved
8	130/90	Angioplasty	Cured	1.5	Deteriorated
9	156/90	Nephrectomy of autotransplanted	CCB and diuretics	1.6	Deteriorated
		kidney			

Table 3: Postoperative outcomes in	terms of hypertension and renal	function at 2 years of follow-up

CCB: Calcium channel blockers

DISCUSSION

PTA and stenting are widely used for the management of RVH. There are limited indications for RAT in managing RVH. Current indications for RAT include relatively young patients with renal arterial lesions located on the main artery and intrahilar segmental arterial branches simultaneously, completely occluded renal artery in functioning kidney or tight ostial lesions that are not able to be accessed during PTA and stenotic lesion with aneurysms.^[12,13] Further, PTA may be devastating in RVH patients with associated inflammatory conditions such as TD or extensive atherosclerosis involving main and segmental vessels. In patients with atherosclerotic lesions involving the main renal artery and its intrahilar branches simultaneously, RAT is indicated, particularly if the patient has solitary functioning kidney. RAT, we feel helps preserve renal function in the long run as shown in our small cohort. It decreases the number of repeated interventions and prevents renal function deterioration over the long term. The need for anticoagulant therapy also does not arise.^[1,10] Due to these benefits, it is preferred in young patients who usually are afflicted with TD or FMD.

At 1 year of follow-up, 62.5% of patients did not require any antihypertensive drug whereas at 2 years, one patient required angioplasty following which he became normotensive. In 25% of patients, blood pressure was well controlled, and they needed only a single additional antihypertensive to achieve normal blood pressure. In combined FMD, TD, and atherosclerosis group of patients, RVH was either normalized or improved in 86.5% of patients in the study by Chiche *et al.*^[10] We found either normalization or improved blood pressure control in 87.5% of patients. There was no loss of kidney or any infarction in the immediate postoperative period. In the study by Ross *et al.*, autotransplanted kidney was lost in two patients, and in the remaining nine patients with well-functioning autotransplanted kidney, 88.89% showed improvement.^[13]

Majority of the patients (44.45%) in this study had TD. In patients with TD, 12.5% (one patient) required postoperative single antihypertensive medicine to maintain normal BP whereas 12.5% (one patient) required angioplasty at 1 year for anastomotic stenosis.

Fibromuscular dysplasia was seen in 33.34% patients. In one patient (11.12%), RVH was secondary to type I neurofibromatosis and atherosclerosis in yet another. In patients with FMD, successful outcome in managing RVH has already been proven. None of our patients with FMD required postoperative medication. A 91% success rate was found in FMD patients after RAT.^[14] We lost one FMD patient due to intraoperative myocardial infarction. In atherosclerosis patient, single antihypertensive medicine was required to control RVH. Postoperative outcomes as per different pathologies were also evaluated in other studies, and it was found that RVH was either cured or improved in 89% and 96% of patients in TD and FMD group patients, respectively.^[10]

Renal function was improved in 50% of patients postoperatively. It was stable at 25% and deteriorated in 25% of patients. In 50% of patients from the TD group, renal function improved whereas renal function had improved in all patients with FMD. In patients with RVH secondary to atherosclerosis, renal function remained stable postoperatively. In patients with deteriorating postoperative renal function, one of them with neurofibromatosis ultimately required nephrectomy and antihypertensive medicines for managing hypertension whereas other patient had TD and required angioplasty at 1 year. Although blood pressure normalized within a short period after angioplasty, renal function took 6 months to improve (serum creatinine decreased from 2.2 to 1.4 mg/dl). In a study from the Cleveland Clinic, postoperatively renal function improved in 93 patients (58%), remained stable in 50 patients (31%), and deteriorated in only 18 patients (11%).^[15]

In patients with RVH secondary to TD and atherosclerosis, the role of RAT is not yet completely clear. Very limited data are available in the literature regarding the role of RAT while managing RVH secondary to TD and atherosclerosis.^[12,16] In a larger study conducted to assess outcomes in TD, it was concluded that in patients with extensively involved renal arteries and complex lesions, RAT should be used as the procedure of choice.^[17] Further, these patients also need concomitant management of aortic lesions frequently, making it possible to repair all lesions surgically simultaneously. Role of RAT in the atherosclerotic lesion is limited. It is generally indicated when there is extensive lesion involving ostial or juxtaostial region, making it difficult to manage by PTA or reimplantation into the aorta and possibly in patients with lesion in solitary kidney. Although some have mentioned the generalized use of RAT while managing patients with RVH due to atherosclerosis,^[18,19] the limited use of RAT is recommended by some.^[10] As compared to outcomes seen in FMD and TD, the low success rate is seen in atherosclerosis patients with RVH. This might be due to the association of old age and simultaneous damage to intrarenal vessels and formation of intrarenal atherosclerotic emboli and increased peripheral vascular resistance.^[10]

On long-term follow-up, excellent outcomes are seen following RAT. This effectiveness and durability of RAT in managing RVH are also found in other studies.^[19] A success rate of 87.5% was seen at the end of 2 years follow-up in our study with the requirement of only single intervention for anastomotic stenosis at 1 year. We had single intraoperative mortality, which suggests that this type of surgery is not without risk. Others have also reported similar either intraoperative or immediate postoperative mortality and loss of kidney.^[10,13] This emphasizes that patient selection needs to be done with great care.

While reconstructing diseased artery some prefer use of superficial femoral artery, segment of external iliac artery or valve less superficial saphenous vein.^[10] While reconstructing renal arteries, we generally prefer free graft harvested from IIA as its caliber matches with that of the renal artery, provides adequate length, is autogenous and easily available. Further, harvesting of IIA grafts does not require another incision, and the artery from which graft is harvested is generally used for anastomosing renal artery. We generally start mobilizing IIA distally and preserve proximal most part for anastomosis with renal artery. Distal part is used as a free graft for reconstruction of diseased main or segmental artery. For polar or smaller collateral artery where side-to-side double barrel anastomosis is not feasible, we use IEA for anastomosis.

We have a small cohort, and this partly reflects the role of percutaneous procedures as first-line treatment of renovascular disease and also the relative rarity of these lesions, TD and FMD in particular.

CONCLUSION

RAT can be effectively performed in patients with severe RVH not responding to conventional treatment. This includes young patients with FMD and TD. In patients with RVH due to atherosclerosis, risk of surgery and associated morbidity need to be balanced against the role of interventional radiologic procedures.

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Conflicts of interest

There are no conflicts of interest.

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