

Vascular complication in live related renal transplant: An experience of 1945 cases

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ABSTRACT

Introduction and Objective: Among the surgical complications in renal transplantation, the vascular complications are probably most dreaded, dramatic, and likely to cause sudden loss of renal allograft. We present our experience and analysis of the outcome of such complications in a series of 1945 live related renal transplants.

Materials and Methods: One thousand nine hundred and forty five consecutive live related renal transplants were evaluated retrospectively for vascular complications. Complications were recorded and analyzed for frequency, time of presentation, clinical presentation, and their management.

Results: The age of patients ranged from 6 to 56 years (mean = 42). Vascular complications were found in 25 patients (1.29%). Most common among these was transplant renal artery stenosis found in 11 (0.58%), followed by transplant renal artery thrombosis in 9 (0.46%), renal vein thrombosis in 3 (0.15%), and aneurysm formation at arterial anastomosis in 2 (0.10%) patient. The time of presentation also varied amongst complications. All cases of arterial thrombosis had sudden onset anuria with minimal or no abdominal discomfort, while venous thrombosis presented as severe oliguria associated with intense graft site pain and tenderness. Management of cases with vascular thrombosis was done by immediate surgical exploration. Two patients of renal artery stenosis were managed with angioplasty and stent placement.

Conclusions: Major vascular complications are relatively uncommon after renal transplantation but still constitute an important cause of graft loss in early postoperative period. Aneurysm and vessel thrombosis usually require graft nephrectomy. Transplant renal artery stenosis is amenable to correction by endovascular techniques.

Key words: Live related renal transplant, renal artery thrombosis, renal artery stenosis

INTRODUCTION

Surgical complications in renal transplantation can be divided into vascular complications, ureteric complications, lymphocele formation, and general surgical problems such as bleeding and wound

infections. Out of these, vascular complications are probably the most dreaded, dramatic, and likely to cause sudden loss of renal allograft.^[1] We present our experience of such complications in a series of 1945 live related renal transplants and analyze the outcome.

MATERIALS AND METHODS

One thousand nine hundred and forty five live related renal transplants were done at our institute from June 1989 to April 2010. In cases with single renal artery and vein renal artery was either anastomosed to *internal iliac artery* (end to end) or to *external iliac artery* (end to side).

Technique of arterial anastomosis

To internal iliac artery

Anastomotic ends of both recipient and graft arteries was spatulated at opposite ends. Medial and lateral corners were approximated first using prolene 6-0 sutures. The cephalad and caudad margins were then sutured by prolene 6-0 using continuous sutures.

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To external iliac artery

The part of external iliac artery was freed of fascia. After clamping artery proximally and distally an appropriate size arteriotomy was made using aortic punch (3.5-4.5). Graft artery was spatulated, cephalad and caudad ends are approximated. Medial and lateral wall of anastomosis is completed using continuous sutures by prolene 6-0.

Venous anastomosis was done to external iliac vein by end to side technique using prolene 5-0 suture in all cases. Moreover, the surgeons have changed but the technique of anastomosis has not changed, as per our institutional protocol.

Multiple vessels were dealt with by either two/three separate anastomoses or as two joined into single pantaloon anastomosis depending upon individual anatomical findings. In all cases, ureteroneocystostomy was performed by modified Lich Gregoir technique. Immunosuppression was given according to standard international protocols varying from time to time. The immunosuppressants have changed over a period of time. Triple drug regimen of cyclosporine, azathioprine and prednisolone was used till 1998 after which azathioprin was replaced by MMF. Cyclosporine was predominantly substituted by tacrolimus in 2005.

Post operatively patients were kept in a dedicated transplant unit under careful clinical observation and monitoring. Renal function tests and other serum biochemical parameters were monitored on daily basis and if required more frequently depending on patients' condition. Two dimensional ultrasound and color Doppler were performed whenever there was clinical suspicion or evidence of suboptimal renal function. MRI/CT angiogram was done subsequently if there was suspicion of any vascular complication on color Doppler studies. Imaging studies in long-term follow up were done only if either requirement of antihypertensive drugs was escalated or unexplained deterioration of allograft function was noted.

In the present study, a retrospective analysis of inpatient and follow-up records of all these patients was evaluated.

All episodes of vascular complications were recorded. Cases in which early graft loss was secondary to acute rejection were excluded from analysis of vascular complications. All these patients were having normal vascular patency and to avoid follow-up biases these were excluded. Similarly, vascular complications like A-V fistula and pseudoaneurysm occurring after biopsy of renal allograft were excluded. Vascular complications were further divided into four categories, i.e., transplant renal artery thrombosis, transplant renal vein thrombosis, aneurysm formation, and transplant renal artery stenosis (TRAS). All specimens of allograft nephrectomy were subjected to pathological examination. Cases with thrombosis of major renal vessels in the absence

of severe rejection were included in the study. For TRAS, more than 50% stenosis of main renal artery was taken as cut-off for inclusion in the present study. The incidence, time of onset, clinical presentation, diagnosis, methods of management, and ultimate outcome of the patient and renal allograft in all these cases were studied.

RESULTS

In our series out of 1945 recipients of live related kidneys with age ranging from 6 to 56 years (mean age 42), major vascular complications occurred in 25 (1.29%) patients. Table 1 summarizes the overall incidence of these complications.

Time of presentation

Out of these complications, the earliest to occur were major vascular thrombotic events. All the cases of renal vein thrombosis occurred within first 5 (mean = 3) days after transplantation. Out of 9 cases of renal artery thrombosis, 7 cases presented within first week, one diagnosed at 30 days post transplant secondary to sepsis and shock and another case occurred 3 years later as part of generalized atherosclerotic process leading to embolization of renal artery. Two cases of renal artery aneurysm formation were diagnosed in second and third week after transplantation. There were 11 cases of TRAS with 2 cases occurring within first 3 months (mean 49 days) and 9 cases occurring more than 6 months (mean 8.5 months) after transplantation [Table 2].

Clinical features

Transplant renal arterial or venous thrombosis had most dramatic presentation. All cases of arterial thrombosis [Figure 1] had sudden onset anuria with minimal or no abdominal discomfort, while venous thrombosis presented as severe oliguria associated with intense graft site pain and tenderness. Hematuria was recorded in two

Table 1: Incidence of vascular complications in our series

Complication	Number	%	% of total
Transplant artery thrombosis	9	36	0.46
Transplant vein thrombosis	3	12	0.15
Aneurysm formation	2	8	0.10
Transplant artery stenosis	11	44	0.58
Total	25		1.29

Table 2: Time of presentation of complications in our series

Complication	Time of presentation
Transplant artery thrombosis	7 cases in 1 st week, 1 at day 30, 1 at 3 years
Transplant vein thrombosis	3 days (mean)
Transplant artery stenosis	Early - 49 days Late - 8.5 months
Aneurysm formation	16.5 days (mean)

cases of renal vein thrombosis. Both cases of renal artery aneurysm [Figure 2] had similar presentation with failure of serum creatinine to return to baseline. One patient who was diabetic had severe wound infection with purulent discharge requiring open drainage and later secondary closure of the wound, while in the other patient there was no obvious sign of infection. Color Doppler studies within first week after surgery were normal in both cases but repeat studies done later in second and third weeks diagnosed aneurysm formation. Aneurysms were confirmed by pathological examination to be of mycotic origin.

Early renal artery stenosis presented as severe hypertension with rising serum creatinine in two patients. All late renal artery stenosis presented with escalation in requirement of antihypertensive drugs, but the graft function was stable.

Management

Management of cases with vascular thrombosis was done by immediate surgical exploration but unfortunately all the cases required graft nephrectomy. The time frame to exploration was 1-7 days. In all these cases, histopathology revealed cortical necrosis. Unfortunately, no kidney was having any viable parenchyma left during the preoperative assessment with biopsy, and therefore, no salvage procedures could be undertaken. Histopathology of artery was not done in any of the cases.

In both the cases of transplant renal artery aneurysm, external iliac artery was used for anastomosis and both of them had associated thrombosis and contained rupture. These cases were dealt with surgical exploration and nephrectomy. Both patients required Dacron graft placement to bypass damaged external iliac artery. First patient had large hematoma formation and sepsis which led to demise at the end of third postoperative week due to catastrophic hemorrhage. In this patient, the graft nephrectomy was difficult and external iliac artery was torn during the procedure. Tear was repaired using 5-0 prolene sutures. The hemorrhage took place at the site of anastomosis and artery repair. This was secondary hemorrhage with infection as the probable cause. The second patient succumbed a few months later to dialysis related complications.

Two patients of renal artery stenosis who presented early were taken up for angioplasty and stent placement [Figures 3 to 6]. Both of them responded well with improved graft function and near normalization of blood pressure. Patients who presented late were managed by medical treatment alone as they had stable renal function although the requirement of antihypertensive medication was more than usual.

DISCUSSION

The etiology of various vascular complications in renal transplant surgery is multifactorial. While some cases can



Figure 1: MR angiogram showing sudden cut off in graft artery just distal to anastomosis site at external iliac artery



Figure 2: MR angiogram showing pseudoaneurysm in external iliac artery

be attributed to technical misadventures, other recipient related factors such as hypercoagulopathies and decreased cardiac output may be equally important.

Transplant renal artery thrombosis

Thrombosis of renal artery in the transplanted kidney is an uncommon complication with reported incidence ranging from 0.5% to 3.5%.^[2] Sudden reduction or cessation of urine output is usually the only mode of presentation with no other clinical signs or symptoms to suggest the diagnosis. A very high degree of suspicion is therefore required in early postoperative period to make a timely diagnosis of transplant renal artery thrombosis. It is a useful strategy to get an immediate ultrasound and color Doppler done whenever there is sudden decrease in urine output in early postoperative period before attributing it to other more common causes such as acute rejection or ATN.

Transplant renal artery thrombosis is usually caused by technical reasons which result in compromise of the arterial lumen and hence cause abnormal flow dynamics. Twisting



Figure 3: MR angiogram showing stenosis at anastomosis site in internal iliac artery



Figure 4: Digital subtraction angiography (DSA) of the same patient

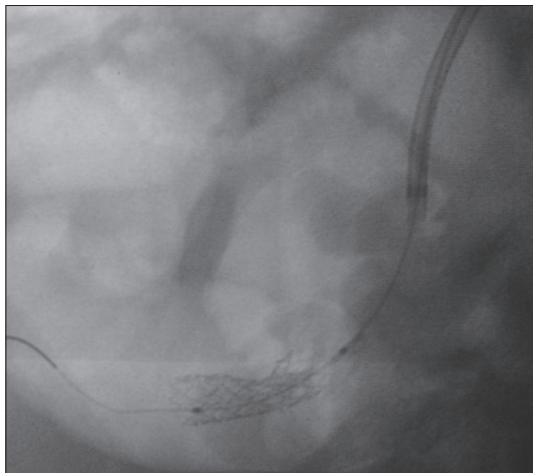


Figure 5: DSA after deployment of endovascular stent

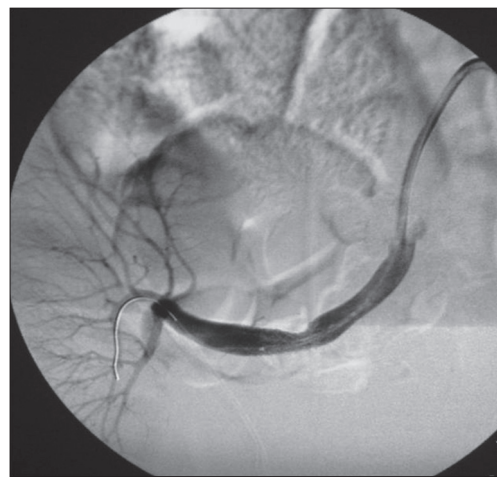


Figure 6: Final DSA showing normal blood flow in graft artery

or kinking at the site of anastomosis and injury to intima resulting in dissection are likely to increase chances of this complication. Poor cardiac output, thrombophilic states, severe ATN, or acute vascular rejection may be contributing factors.^[3] Administration of OKT3 has been found to increase risk of thrombosis in allograft artery, especially when used in combination with high doses of methylprednisolone.^[4,5] Transplant renal artery thrombosis is a surgical emergency and only hope to save the transplanted kidney is by immediate exploration with restoration of the blood flow to the kidney. A few cases of graft salvage in transplant renal artery thrombosis with endovascular catheter directed thrombolysis with or without angioplasty have been reported.^[2] More commonly by the time diagnosis is confirmed, it is already too late and graft nephrectomy is the only option left.

In our series, we diagnosed 9 cases of main renal artery thrombosis. It appears that the cases which presented within first week after transplant had one or the other technical cause as etiological factor. The two cases presented at 1 month and

3 years after transplantation. They had other unrelated events leading to this complication as mentioned earlier.

Transplant renal vein thrombosis

Thrombotic occlusion of the renal vein in transplanted kidney has a reported incidence up to 6%.^[6] Presentation of transplant renal vein thrombosis is more dramatic with sudden onset of oliguria and hematuria associated with pain or intense discomfort over graft area. In severe cases, graft swelling and rupture can result in catastrophic hemorrhage. Technical factors play most important role in the etiology of transplant renal vein thrombosis, especially in the setting of right donor kidney because of short and thin-walled renal vein. Other contributing factors include various hypercoagulopathic states such as deficiency of antithrombin III, protein C, or protein S. Diagnosis is confirmed by color Doppler which shows lack of flow in the renal vein. Other findings include swollen graft, a clot covering the lateral margin of the kidney, and reverse diastolic flow in arterial waveform. Emergent exploration is required to do venous thrombectomy and restore blood flow. If that is not possible, nephrectomy is done to save patient.

In the present study, we only had three patients who developed main renal vein thrombosis. This is much less than the incidence reported in most of the series. The probable cause for this difference may be that, this is a series of live related donors with no cases involving deceased organ donation. The incidence of main renal vein thrombosis in allografts is more in deceased donors compared to living donors. Secondly, we have always taken cuff of inferior vena cava along with renal vein during the right-sided nephrectomy and therefore never encountered any technical difficulty during anastomosis. This appears to be the predominant cause of such a low incidence of renal vein thrombosis (RVT) in this series. Moreover, most of the series have reported a higher incidence of this complication during the period when cyclosporine was initially introduced. There is evidence to suggest that higher doses of cyclosporine which were common in the early years of its use were associated with higher incidence of venous thrombosis.^[7] However, in the present series which starts from 1989 onwards we did not witness any such correlation.

Transplant renal artery stenosis

The reported incidence of TRAS is between 1% and 23% depending upon its definition and diagnostic criteria.^[8,9] It is most common vascular complication seen after renal transplantation. The time of presentation of TRAS may vary from 3 months to 2 years after transplantation. Multiple factors have been implicated in the etiology of TRAS; suturing technique, intimal trauma during harvesting, kinking or twisting of artery, and atherosclerotic lesions in donor or recipient vessels. Some studies have found association between CMV infection and TRAS.^[10]

Most common clinical presentation of TRAS is severe hypertension requiring progressively higher dosage and number of antihypertensive drugs with or without graft dysfunction. The diagnosis of significant TRAS requiring intervention is generally made when abnormal findings on color Doppler are associated with clinical picture suggestive of renal artery stenosis. Typical color Doppler findings include peak systolic velocity of greater than 2.5 m/s, intrarenal arterial waveform showing parvus-tardus pattern, and decreased resistive index.^[11,12] Once decision for intervention is taken, percutaneous angioplasty with stent placement is preferred approach with success rate approaching 80%. Surgical correction is considered only for failed cases as complication rates are high resulting in graft loss in 20% of cases.^[8] We had two cases of TRAS in the early postoperative period which required endovascular stenting as the graft function was gradually deteriorating. Both of these patients are doing well.

The low incidence (0.59%) of TRAS in our series during the long-term follow up needs to be scrutinized. On retrospection we feel that our method of doing follow-up color Doppler studies only in cases of severe hypertension or unexplained

graft dysfunction might be responsible for under diagnosing this condition in the present study. Doing imaging studies at predetermined time intervals during follow up as suggested by some authors might be more appropriate.^[13] At the same time, it must be mentioned here that the latter approach is likely to result in diagnosing additional cases of TRAS which otherwise are hemodynamically insignificant. None of these required any intervention as their graft function was stable.

Transplant renal artery aneurysm

This is a rare complication seen in less than 1% of cases after renal transplantation.^[14] Anastomotic leakage due to defective suture technique or damage to artery wall by trauma, vessel wall ischemia or infection may lead to formation of pseudoaneurysms.^[15,16] Clinically, these aneurysms are usually asymptomatic, found incidentally on Doppler study. They may however present with systemic symptoms of sepsis such as fever and anemia or may cause symptoms due to their mass effect leading to graft dysfunction.^[17] Pseudoaneurysms of transplant renal artery are potentially life threatening as their sudden rupture can lead to torrential hemorrhage.^[18]

Therapeutic options for the management of transplant renal artery aneurysms include conservative approach with careful follow up, open surgical repair/graft nephrectomy, endovascular treatment with covered stent placement to exclude aneurysm, and ultrasound-guided percutaneous injection of thrombin into the aneurysmal sac. It has been advocated that small asymptomatic aneurysms can be managed conservatively with regular monitoring,^[14] while those with symptoms or size more than 2.5 cm need intervention to prevent rupture and hemorrhage.^[19] There are reports of successful surgical excision of pseudoaneurysm and allograft autotransplantation, most of the cases require graft nephrectomy.^[20] Endovascular approach may be used to exclude aneurysm by placing a covered stent across the end to end anastomosis with internal iliac artery. Stent placement can be combined with ultrasound-guided injection of thrombin into the aneurysm to obliterate the sac.^[19,21] The present study has only two cases of renal artery aneurysm formation and in both the cases graft nephrectomy was done. Both of these patients had pathologically proven mycotic aneurysm.

CONCLUSION

Major vascular complications are relatively uncommon after renal transplantation but still constitute an important cause of graft loss in early postoperative period. Despite an early diagnosis of renal artery thrombosis and subsequent exploration, it is very difficult to salvage the graft as the acute cortical necrosis sets in within few hours of the event.

We strongly recommend obtaining an appropriate cuff of inferior venacava during the right donor nephrectomy

to minimize the complication of renal vein thrombosis. TRAS in the early postoperative period is amenable to endovascular stenting and early suspicion and aggressive management of this entity leads to graft salvage. However, TRAS developing during the long-term follow up usually does not require any intervention. Mycotic aneurysm developing in an external iliac artery anastomosis is most dreaded and life-threatening complication and needs to be dealt in aggressively.

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