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Review Article

Experiences regarding intervention in renal transplantations by nephrologists

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ABSTRACT

Vascular complications after kidney transplantation occur at a rate of 1–4% cases. The commonest of these complications is graft artery stenosis. It is often detected following difficult to control hypertension and/or graft dysfunction. If detected early usually with the help of duplex Doppler ultrasonography it can be successfully treated by endovascular intervention by suitably trained specialists.

Interventions are also needed for post graft biopsy hemorrhage or arterio-venous fistula (AVF). Percutaneous transcatheter fibrated platinum coil embolization super selectively in the artery supplying the AVF can be life saving. It may improve blood pressure control and graft function in selected cases. Other endovascular interventions performed in transplanted kidneys are graft renal angioplasty with or without stenting and placement of covered stent graft.

Technological advances in noninvasive imaging like CT angiogram, contrast enhanced Doppler ultrasound and MR angiography have simplified diagnosis and follow up of these patients without compromising safety.

At our institute since January 2007, we encountered 8 cases of transplant renal artery stenosis, 6 arteriovenous fistulas and a case of extra and intrarenal pseudo aneurysm. All patients with transplant renal artery stenosis underwent angioplasty and stenting successfully both in terms of anatomical correction and improvement in blood pressure control as well as graft function. One patient had arterial stenosis and arteriovenous fistulas both and he underwent simultaneous stenting and coil embolization. Three patients with fistulas who had significant bleeding underwent successful coil embolization while 2 patients who were asymptomatic are under close surveillance. One patient each who had extra and intrarenal pseudo aneurysm underwent successful endovascular covered stent grafting and multiple coil embolization respectively. Vascular interventions in renal allograft by experienced nephrology unit can achieve good success with minimal complications.

Keywords: *Transplant renal artery stenosis, Vascular complications, Pseudo aneurysm, Arteriovenous fistula, Endovascular intervention*

INTRODUCTION

Vascular complications in renal transplant recipients are important causes of graft dysfunction associated with high morbidity and mortality. Intervention plays a major role in the management of vascular complications in renal transplants, including arterial stenoses, arteriovenous fistulas (AVF), pseudo aneurysms (PA), and thromboses. Although color Doppler ultrasonography and gadolinium enhanced magnetic resonance angiography (MRA) are useful diagnostic screening methods, conventional angiography not only remains the gold standard procedure for final diagnosis, but also enables endovascular treatment at the same sitting.

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Currently the practice of nephrology interventions in the country is divided among Nephrologists, Cardiologists and Intervention specialists. Central venous dialysis catheter insertions both tunneled and non-tunneled are done by Nephrologists while other endovascular interventions like angiography and/or angioplasty with or without stent are directed to cardiologists or interventional specialists depending on the availability. At our institute in Nadiad nephrologists perform all interventional procedures, including endovascular procedures are carried out by nephrologists. We believe that this happens only in our institute in India.

TRAS

Transplant renal artery stenosis (TRAS) is the most common vascular complication of transplanted kidney, which results in difficult to treat hypertension and often results in allograft dysfunction. Transplant renal artery stenosis (TRAS) usually becomes apparent from 3 months to 2 years after transplantation.[1]

The prevalence ranges widely from 1 to 23% in different series, reflecting the heterogeneous criteria used to establish the diagnosis, the different manner of preservation of the graft, and surgical expertise.[2]

Three different locations of transplant stenoses are anastomosis, distal to the anastomosis, and recipient iliac artery. Each type has particular predisposing causes, which include operative, hemodynamic, and immunological factors. Although surgical techniques for renal Transplantation vary by institution, transplant renal vessels are anastomosed to the recipient external (end-to-side) or to the internal iliac artery (end-to-end) and to the recipient external iliac vein (end-to-side). The vast majority of TRAS occurs within 1 cm of the anastomosis and is directly related to the surgical technique. Distal donor artery stenoses are less common and are thought to be caused by intimal injury or rejection, with the typical angiographic appearance of beaded intrarenal vessels. Recipient iliac artery stenoses are rare and result from vascular clamp injury or native atherosclerotic disease.[3]

Kinking of renal artery can also mimic a stenosis. This is mostly seen when the right kidney is transplanted due to short renal vein and long renal artery.[4]

Patients often experience accelerated hypertension of either sudden or insidious onset that is refractory to multiple drug regimens and is associated with progressive renal insufficiency in the presence of excessive diuretic use or treatment with angiotensin-converting enzyme inhibitors in the absence of rejection, ureteric obstruction, or infection. The presence of a bruit is nonspecific and may be heard in healthy transplant patients.[5]

Since more & more kidney transplantations are performed in patients at increased risk of peripheral artery disease (such as older patients and diabetic patients) the possibility of previously unsuspected proximal iliac artery disease that mimics TRAS (pseudo-TRAS) should always be taken into consideration.[6]

Laboratory studies like PRA, hypokalemia and metabolic alkalosis are nonspecific to TRAS. Doppler ultrasound though dependent on sonologist's ability and experience is the first noninvasive imaging modality of choice. Peak systolic velocity (PSV) of more than 2.5 m/s and the ratio of PSV in the transplant main renal artery and external iliac artery of >1.8 is highly suggestive of hemodynamically significant stenosis. The transplant renal artery is often tortuous hence there is often difficulty in obtaining a precise spectral quantification. Another, parameter which is less, operator dependent is to determine the intrarenal waveform. The intrarenal waveform shows flattening of systolic peak. This is called parvus-tardus waveform. This is however, not always present.[4,6]

Isotope renography (basal and after renin angiotensin system blockade) has been the most popular noninvasive screening procedure for TRAS. However, despite relatively good sensitivity (75%), the procedure is seriously limited by its poor specificity (67%).[7]

If Doppler ultrasound is positive or highly suspicious of TRAS the diagnosis can be established by either multi slice helical CT scan (MSCT) or MR Angiography (MRA). MSCT compare to MRA has advantage of better imaging but risk of radio-contrast induced nephropathy. If there is a strong suspicion of TRAS on clinical parameters and Doppler imaging patient can be subjected directly to digital subtraction angiography (DSA) and intervention if indicated can be performed simultaneously. This approach can minimize the volume of & repeated exposure to radio-contrast and avoids repeat arterial puncture. Stenosis with luminal diameter less than 70% of the proximal vessel are usually considered hemodynamically significant. It is essential to perform nonselective aorto iliac arteriography, to rule out significant disease in the proximal iliac vessel, which can mimic TRAS.[4,6]

Three different treatment modalities are available for patients with TRAS: (I) medical management is indicated if the degree of stenosis is not considered hemodynamically or clinically very significant ($<70\%$) and/or renal function has not been deteriorated significantly; (ii) surgical revascularization is indicated for cases of unsuccessful PTA or when the stenosis is not accessible to PTA; or requires surgery simultaneously for other vascular reconstruction; (iii) PTA accompanied by stent implantation (PTAS)

when necessary is a less invasive procedure and represents the preferred option even when stenosis is in hilar or distal portion of the arterial renal bed. It must be remembered that a combination of all modalities of management for better long term outcomes must be offered to patients.[1]

Contra lateral femoral artery approach or a brachial artery approach is best for accessing end-to-end anastomosis of graft artery with internal iliac artery. Ipsilateral approach is used for accessing end-to-side anastomosis with external iliac artery. The stenosis is crossed using a guide wire. Premounted balloon expandable stents accessed through a guiding catheter allows accurate placement of the stent. The primary success in terms of normalization of blood pressure and return of serum creatinine to the baseline is in the range of 63−83% and 85−90% respectively.[8] Re-stenosis rate is less than 10%. This may be further reduced by using stents coated with antiproliferative agents. However, in the setting of TRAS use of these stents is investigational.[6]

Surgery is indicated for patients with unsuccessful angioplasty or with very severe stenoses that are inaccessible to PTA. Surgical techniques include resection and revision of the anastomosis, saphenous vein bypass graft of the stenotic segment, patch graft, or localized endarterectomy. Surgery is now considered as rescue therapy and should be restricted to carefully selected cases with untreatable hypertension and at high risk of major renal or cardiovascular events. An important option, infrequently used, but in dramatic cases very useful, is auto-transplantation of the kidney with complex stenoses of graft arteries.[6]

Since January 2007, 557 kidney transplantations have been performed at our institute and among which we encountered 8 cases of TRAS, which makes cumulative incidence of 1.44% of TRAS. All except one patient had presented with reduction in graft function. Three patients developed worsening of hypertension and 3 had flash pulmonary edema. The diagnosis was suspected on the basis of strong clinical suspicion, supported by color Doppler ultrasound which was positive in 7 out of 8 patients and confirmed by CT or MR angiography. One patient also had asymptomatic intrarenal arteriovenous fistula along with TRAS. All 8 eight patients underwent angioplasty with stenting. Patient with AVF underwent fibrated platinum coil embolization to block the fistula along with angioplasty and stenting for TRAS (Fig. 1). Estimated glomerular filtration rate improved substantially in 7

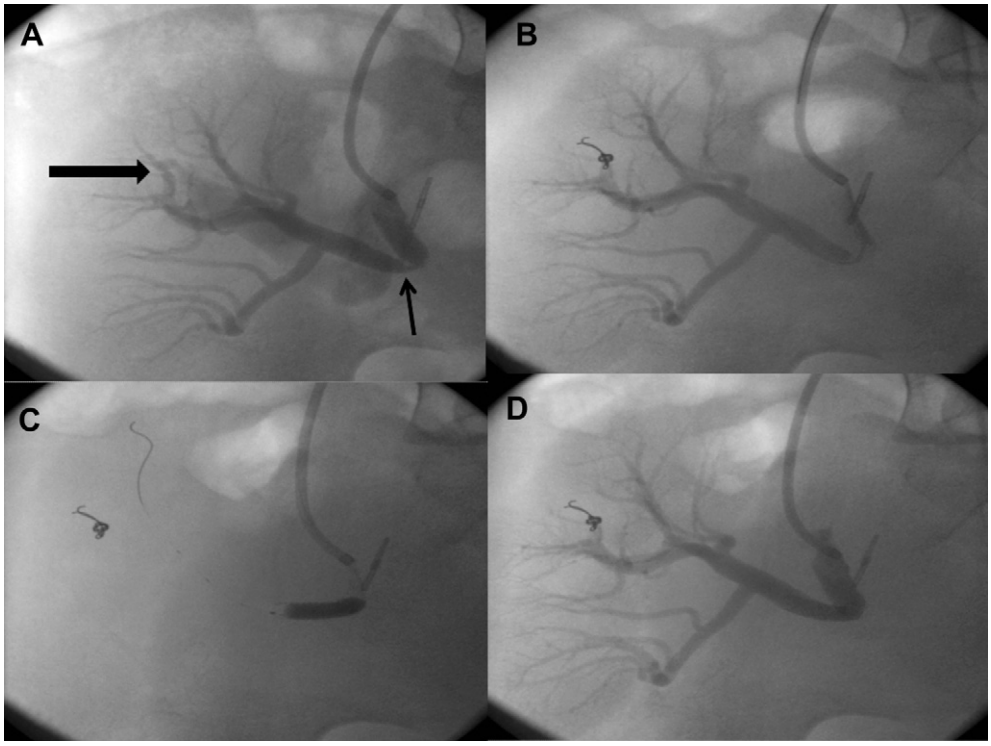

Fig. 1 Percutaneous endovascular management of transplant renal artery stenosis & post biopsy intrarenal AV Fistula (AVF) (A) Note: stenosis thin arrow & AVF thick arrow; shows filling of draining vein in arterial phase. (B) Super selective coil embolization to block AVF. (C) Balloon mounted stent being deployed. (D) Post angioplasty & angio-embolization result showing adequate dilatation of the stenosis and blocked AVF.

out of 8 patients from mean eGFR 51.71 ± 17.16 to 74.31 ± 18.7 ml/min after intervention. Antihypertensive drug requirements came down in 4 patients; in remaining patients the blood pressure was better controlled with the same number of drugs. There was no instance of clinically significant contrast induced nephropathy in our patients.

GRAFT THROMBOSIS

This uncommon complication can occur most often as an early event, but also can be a late event, a devastating clinical condition leading to graft loss. Renal artery thrombosis (RAT) onset most often follows a technical problem such as intimal dissection, kinking or torsion of the vessels. Risk factors include poor cardiac output, hyper acute rejection, unresponsive acute rejection, and a hypercoagulable state. It presents with a rapid onset of anuria. In cases of segmental or branch artery thrombosis leads to segmental infarct. This may be asymptomatic or have graft dysfunction. It may rarely present with calyceal urinary fistula. When RAT occurs as a late event, it could be attributed to severe graft artery stenosis or it may be a complication of endovascular procedure. Graft thrombosis, either arterial or venous, is a rare complication, with a reported prevalence of 0.5−6.2%; however, it is a major cause of graft loss in the early (<1 week) post-transplantation period.[8]

Renal artery thrombosis usually stems from the surgical technique as a result of torsion, kinking, or angulation of the anastomosis or dissection of the arterial wall. In renal artery thrombosis, flow in both main and intrarenal arteries is completely absent at color Doppler flow US and radionuclide imaging shows absent perfusion. Renal artery thrombosis is an early (within the first 2 days post-transplantation) technical complication that leads to graft loss and requires allograft nephrectomy. Fortunately, renal artery thrombosis is uncommon. A kink in the renal artery, severe dehydration, hypotension, hyper acute rejection, hypercoagulable states and a prolonged warm ischemia time may precipitate this devastating complication. Size discrepancy between donor and recipient renal arteries also increases the risk of renal artery thrombosis. An abrupt onset of anuria during the first 1−2 days after surgery is a sign of arterial thrombosis.[4,5]

Renal vein thrombosis is also an early (within the first 2 days post-transplantation) technical complication that most often leads to graft loss and requires allograft nephrectomy. Renal vein thrombosis can occur as a result of compression of the renal vein by fluid collection, propagation of a deep venous thrombosis from the ileofemoral vein, coagulopathy, hypovolemia, and surgical technique. Fortunately, renal vein thrombosis is also uncommon. The initial clinical presentation includes sudden oliguria or anuria, graft tenderness and swelling, and edema of the lower extremities that is more pronounced in the ipsilateral thigh and leg. Diagnostic methods include nuclear scan, ultrasound, angiography, and surgical exploration. In renal vein thrombosis, color Doppler flow US shows completely absent venous flow and an abnormal arterial signal with a plateau like reversed diastolic flow.[4,5]

Catheter-based angiography, MR angiography, or MR venography may be performed to confirm the diagnosis. Graft loss is inevitable if the diagnosis of graft thrombosis is delayed. In patients with renal vein thrombosis, thromboembolic and septic complications or graft rupture resulting from the high venous pressure may cause death.[4,5]

Since January 2007, we encountered 2 cases of graft renal arterial thrombosis with incidence of 0.36%. Both patients presented with anuria following engraftment. One patient had extension of thrombus into iliac artery which needed sapheno femoral bypass and successfully retransplanted later on. Both patients needed graft nephrectomy. The other patient unfortunately died of sepsis later on. One patient in our experience suffered venous thrombosis, presented with graft site pain and tenderness, fever and acute graft dysfunction. The diagnosis was confirmed by MR angiogram and underwent graft nephrectomy.[4,5]

INTRARENAL ARTERIOVENOUS FISTULA (AVF) AND PSEUDO ANEURYSM (PA)

Despite advances in noninvasive diagnostic tests and techniques, core needle biopsy is still considered the standard technique for diagnosing renal transplant dysfunction. Biopsy-related renal vascular complications include AVF resulting from simultaneous laceration of the adjacent artery and vein, and PA due to isolated arterial injury. Occasionally, AVF and PA can occur simultaneously. The frequency of these complications is estimated to be between 1% and 18%.[9]

These vascular complications are easily detected with color Doppler flow and duplex Doppler US. Characteristic US findings in patients with AVFs include focal areas of disorganized color flow outside the borders of the normal renal vasculature. Spectral analysis may show increased arterial and venous flow, with high velocities and low impedance − the classic waveform of AVFs. A dilated draining vein may also be visible. Pseudo aneurysms appear as simple or complex renal cysts on gray-scale US images, but intracystic flow and alternating jets at the neck can be appreciated on color Doppler flow images. MR angiography can be a useful adjunct when US findings are inconclusive.[3,5]

It has been reported that 70% of all AVFs resolve within 1−2 years, but that 30% persist or become symptomatic. Persistent or symptomatic AVFs can result in persistent hematuria or transplant dysfunction as the result of marked arteriovenous shunting stemming from an intrarenal "steal" phenomenon. Enlarging pseudo aneurysms can rupture.

Transcatheter embolization is the treatment of choice for both symptomatic AVFs and enlarging pseudo aneurysms. Super selective embolization performed with a coaxial catheter and a metallic coil minimizes the loss of functioning allograft tissue. It also allows the occlusion of targeted vessels in a precise and definitive manner. In AVFs with high blood flow, temporary balloon occlusion of the draining vein may be necessary during coil embolization to prevent coils from making their way into the systemic circulation. Pseudo aneurysms with a narrow neck may be embolized with coils tightly packed within the sac itself. This technique allows preservation of flow in the distal renal artery.[3,5]

We have encountered 6 AVFs following graft biopsies. Three had presented as hemorrhage following biopsy. One was asymptomatic detected when angiography was done for difficult to control blood pressure. 2 remaining patients were detected during routine Doppler examination were completely asymptomatic. Three patients with bleeding were successfully managed with fibrated platinum coil embolization. Two asymptomatic patients are being followed by color Doppler ultrasound. The patient with RAS plus AVF had angioplasty and stent as well as coil embolization at the same sitting.

EXTRA RENAL PSEUDO ANEURYSMS

Extra renal pseudo aneurysms are extremely uncommon in patients with renal transplants (<1% of patients)[10]; when they do occur, however, they can be devastating because of their potential for rupture. Extra renal pseudo aneurysms may result from surgical techniques or infection and usually occur at the site of the arterial anastomosis. These pseudo aneurysms may be asymptomatic or may manifest clinically as a large, pulsating mass accompanied by abdominal pain. Hypertension or allograft dysfunction may be seen owing to the extrinsic compression of renal vessels. Color Doppler flow and duplex Doppler US can easily depict the pseudo aneurysms, whose features are the same as those of their intrarenal counterparts.

We have reported a case of intrarenal pseudo aneurysm treated successfully with multiple coil embolization.[4] The placement of an endovascular covered stent graft maybe an option in patients with an iliac artery pseudo aneurysm. We have reported as case of recurrent pseudo aneurysm of the graft artery successfully treated with covered stent graft.[11]

CONFLICTS OF INTEREST

All authors have none to declare.

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