VASCULAR COMPLICATIONS FOLLOWING RENAL TRANSPLANTATION

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Abstract

Vascular complications following renal transplantation are infrequent but important cause of graft dysfunction. If detected early the graft can be salvaged by prompt surgical or radiological intervention. They include transplant renal artery stenosis, arterial and venous thrombosis and postbiopsy arteriovenous fistula and pseudoaneurysm. In this review we will discuss the clinical presentation, diagnostic modalities and surgical and radiological interventional management of these complications.

1. Introduction

Renal transplantation is the treatment of choice for patients with endstage renal disease. Despite, continuous progress in immunosuppressive therapy, surgical technique, prevention and management of infections, vascular complication continue to account for about 3-15% of the cases of graft dysfunction.

In this article, we will discuss the causes of post operative vascular complications, their diagnostic workup and the role of surgery and minimally invasive interventional radiologic techniques for their management.

Vascular complications include:
1. Transplant renal artery stenosis (TRAS)
2. Transplant arterial and venous thrombosis,
3. Arteriovenous fistula (AVF) or intrarenal pseudoaneurysm following graft biopsy,
4. Extrarenal pseudoaneurysm

**Transplant renal artery stenosis:**

Transplant renal artery stenosis (TRAS) is the most common vascular complication following renal transplantation. Depending upon the criteria used for diagnosis its incidence varies from 1 to 23%. TRAS is a potentially curable cause of treatment refractory hypertension and graft dysfunction.

1.1. Etiology:

The stenosis is usually situated at the anastomotic site and less frequently it may found on either side of the anastomosis. The suture site stenosis is due to technical reasons and is usually stable. The lesion on the proximal donor artery is due to intimal injury caused during organ retrieval or perfusion. Less commonly they are due to atherosclerotic disease in the donor artery. Recipient arterial stenosis is due to clamp injuries or atherosclerotic disease. Kinking of renal artery can also mimic a stenosis. This is mostly seen when the right kidney is implanted. This is due to short renal vein and long renal artery. Most of these stenosis are seen between 3 and 12 months after transplantation. Stenosis occurring in the later period is due to atherosclerotic disease in the transplant renal artery or in the proximal iliac artery (pseudo stenosis).

Diffuse stenosis occurring late after transplantation is believed to be due to immunological causes or CMV infection. However, there is a lack of temporal association between rejection and the occurrence of stenosis.

Pathophysiologically, the transplant renal artery behaves like Goldblatt’s one kidney one clip model. Transplanted kidney is denervated hence sympathetic response is not elicited. The hypertension is essentially volume dependent and plasma renin activity may to low or normal.

1.2. Clinical presentation:

TRAS usually presents as worsening hypertension which is refractory to multiple medications. They may also present as creeping rise of serum creatinine or sudden deterioration of graft function following the use of ACE inhibitors. Less commonly they may present with flash pulmonary edema. Presence, of bruit
though suggestive is not specific for transplant renal artery stenosis. With increasing use of renal Doppler may cases are picked up on routine screening. Patients with iliac artery stenosis mimic TRAS. They often have weak femoral pulse.

1.3. Imaging:

Doppler ultrasound is the imaging modality of choice. It is non-invasive, easily available and is cost effective. A peak systolic velocity (PSV) of more than 2.5m/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 tortuous and 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 also called parvus-tardus waveform. This is however, not always present.?

![Figure 1 - Algorithm for post transplant renal artery stenosis management]

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Angiography. There is small but definite risk of contrast nephropathy with CT. However, the image qualities of CT are superior to that of MRI. If there is a strong suspicion of TRAS on Doppler imaging one can straight away proceed with digital subtraction angiography (DSA) and intervention if necessary can be performed at the same time. (Figure 1) Stenosis with luminal diameter less than 50% of the proximal vessel are usually hemodynamically significant. Non-selective aorto iliac arteriography should also be performed to rule out disease in the proximal iliac vessel which can mimic TRAS.

2. Treatment

Percutaneous transluminal angioplasty (PTA) with stenting is the initial treatment of choice. Contralateral 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. (figure 2) 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. Restenosis 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. Most common complication is puncture site hematoma. Infrequent but serious complications include arterial dissection, rupture and thrombosis. In such cases urgent exploration may be necessary to salvage the kidney.

Surgical revascularization should be considered for failed angioplasty and stenting. Surgical techniques include resection of stenosis and reanastomosis, saphenous vein bypass graft or venous patch angioplasty. Rare case may be managed by autotransplantation. About 20% of patients undergoing surgery experience morbidity and mortality.

3. Transplant renal artery thrombosis

Renal artery thrombosis is the least common but the most dreaded of the vascular complications. It is seen in less than 1% of all renal transplantation.
3.1. Etiology

Arterial thrombosis is usually due to technical difficulties encountered during organ retrieval and implantation. This is often due to creation of an intimal flap during donor nephrectomy or perfusion. It is also seen when there is size discrepancy and misalignment, torsion or kinking of the anastomosis. Spatulating the narrow donor artery may reduce the risk of thrombosis and stenosis.

Other causes of arterial thrombosis include hyperacute rejection, presence of antiphopholipid antibody and cryoglobulins. In vitro data suggest that drugs
like cyclosporine and OKT3 may increase the risk of thrombosis but it has not been borne out in clinical practice.\textsuperscript{15,16,17,18}

Epidemiological data suggest increased risk of thrombosis in patients undergoing second transplant and those on peritoneal dialysis prior to transplantation compared to those on hemodialysis.\textsuperscript{19} Use of erythropoietin has not been associated with increased risk of vascular thrombosis.\textsuperscript{20}

3.2. Clinical presentation and diagnosis:

Patients with arterial thrombosis present with sudden cessation of urine output. Since, the transplanted kidney is denervated this is usually painless. Color flow Doppler imaging will show absence of blood flow in the kidney. Scintigraphy will show a photopenic area in the transplant bed. Arterial thrombosis can be confirmed by graft angiography.

3.3. Treatment and prevention:

Thrombosis of main renal artery results in graft loss, unless it recognized prior to wound closure. There are rare case reports of salvaging such grafts using streptokinase and heparin.\textsuperscript{21}

Aspirin, low molecular weight heparin and unfractionated heparin have been used to prevent vascular thrombosis.\textsuperscript{22,23,24} These studies show reduction in the incidence of graft thrombosis, especially in patients with antiphospholipid syndrome.\textsuperscript{14} However, most of these studies are small and retrospective. There is increased risk of hemorrhagic complication following the use of anticoagulants.

4. Renal vein thrombosis

Renal vein thrombosis (RVT) is an infrequent but disastrous complication usually occurring in the first week following the transplantation. Reported incidence varies between 0.9 to 4.5\%.\textsuperscript{25} It is often the result of poor surgical technique, perigraft fluid collections, hypovolemia and due to compression of common iliac vein between the sacrum and the right common iliac artery.\textsuperscript{26} It presents clinically as sudden onset of oliguria, hematuria, graft tenderness and swelling. Late renal vein thrombosis have been reported in association with recurrent or denovo membranous nephropathy, iliofemoral vein thrombosis and thrombophilic disorders.\textsuperscript{27,28}

On USG the graft appear swollen and hypoechoic. Doppler shows absent venous flow and renal arterial Doppler spectra shows absent or reversal of
diastolic flow. These finding are highly suggestive of RVT though absent or reversal of diastolic flow may be seen with severe vascular rejection. If in doubt the diagnosis can be confirmed by MR angiography. If suspected in the early post transplant period prompt exploration is essential to salvage the graft. Patients presenting months after transplantation, perivascular adhesions make surgical exploration difficult. Combined mechanical and chemical thrombolysis had be used to recanalize such cases.

5. Intrarenal arteriovenous fistula and pseudoaneurysm

Renal allograft biopsy is increasingly used for diagnosis of allograft dysfunction and as a protocol for monitoring the graft. Use of spring loaded biopsy gun and real time imaging has greatly increased the safety of biopsy. Vascular complications in the form of intrarenal arteriovenous fistulas (AVFs) and pseudoaneurysm are seen 1-18% of the biopsies. AVFs occur when both artery and vein are simultaneously lacerated. Pseudoaneurysm results when only the artery is lacerated. Most of these vascular complications are clinically silent and resolve spontaneously with 1-2years. Symptomatic lesions may present with hematuria when they communicate with the collecting system. Perigraft hematoma may occur when they rupture into the perirenal space. Large AVFs may cause vascular steal and result in graft ischemia. Color flow Doppler and duplex Doppler readily recognizes these complications. AVFs appear as focal areas of disorganized flow adjoining the normal vasculature. Spectral analysis shows increased arterial and venous flow, with high velocity and low resistance. Pseudoaneurysm appears as simple or complex cyst on B mode ultrasound. Color Doppler shows intracystic blood flow. They can be confirmed by multi slice CT scan or MR angiography. Superselective transcatheter embolisation is the treatment of choice for enlarging and symptomatic AVFs and pseudoaneurysm. Metallic coils are the preferred embolising material. If embolisation is not successful surgery usually ends up with partial or total nephrectomy. Biopsying the upper pole of the renal allograft with the needle directed laterally minimizes the chances of injuring the vessels or a calyx.

6. Extrarenal pseudoaneurysm

Extrarenal pseudoaneurysms are rare vascular complication but potentially devastating because of the risk of rupture. They are usually seen at the
anastomotic site. They are caused by perivascular infection or poor surgical technique. They are readily detected by Doppler USG. However, most often they present with rupture and massive bleeding. Usually they require emergency allograft nephrectomy. Excision and ligation of the external iliac artery may be necessary to control the hemorrhage. If these lesions are picked up on imaging studies they can managed by intravascular graft stenting.\textsuperscript{33}

Figure 3 - Pseudoaneurysm and AVF after renal allograft biopsy. A, Grey scale USG showing cystic lesion in the lower pole. B, Colour Doppler shows pulsatile blood flow. C, Renal angiogram showing large pseudo aneurysm. D, Super selective embolisation of the feeding artery. E, Post procedure colour Doppler shows absence of flow in the aneurysm.
References


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