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review

Interventional radiological management of complications in renal transplantation

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Background. *The most frequent radiologically evaluated and treated complications in renal transplantation are perirenal and renal fluid collection and abnormalities of the vasculature and collecting system. Renal and perirenal fluid collection is usually treated successfully with percutaneous drainage. Doppler US, MRA and digital subtraction angiography (DSA) are most important in the evaluation of vascular complications of renal transplantation and management of the endovascular therapy.*

Conclusions. *Stenosis, the most common vascular complication, occurs in 1% to 12% of transplanted renal arteries and represents a potentially curable cause of hypertension following transplantation and/or renal dysfunction. Treatment with percutaneous transluminal renal angioplasty (PTRA) or PTRA with stent has been technically successful in 82 to 92% of the cases, and graft salvage rate has ranged from 80-100%. Complications such as arterial and vein thrombosis are uncommon. Intrarenal A/V fistulas and pseudoaneurysms are occasionally seen after biopsy, the treatment requires superselective embolisation. Urologic complications are relatively uncommon; they consist predominantly of the urinary leaks and urethral obstruction. Interventional treatment consists of percutaneous nephrostomy, balloon dilation, insertion of the double J stents, metallic stent placement and external drainage of the extrarenal collections. The aim of the paper is to review the role of interventional radiology in the management of complications in renal transplantation.*

Key words: kidney transplantation; renal artery obstruction; radiology interventional; angioplasty, balloon

Introduction

Renal failure is treated by dialysis or renal transplantation. Renal transplantation has become the treatment of choice for end-stage renal disease (ESRD) because of long-term survival and improved life quality in cases when transplantation is performed instead of hemodialysis.[1-3] The most frequent renal transplantation complications are the following: renal and perirenal fluid collections, decreased renal function, and abnormalities of the vascular, tubular system, and renal parenchyma. Postoperative fluid collections are common, after transplantation, and they include haematomas, seromas, urinomas,

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lymphoceles and abscesses. Vascular complications of transplantation include occlusion or stenosis of the arterial or venous supply, arteriovenous fistulas, and pseudoaneurysms. Urological complications consist predominantly of urinary leaks and urethral obstruction. Percutaneous and endovascular management of these complications has become an important component in the management of transplant patients and has led to further improvement in graft salvage rates.

Perirenal fluid collections

Perinephric fluid collections are the most common complications in renal transplantation, occurring in approximately 50% of transplant patients.[4] The majority of these are asymptomatic, but approximately 15 to 20% may cause symptoms secondary to local mass effect that can produce pain, hydronephrosis, lower extremity oedema and compromise transplant function.[4,5] These fluid collections can also become secondarily infected. The majority of these collections can be detected by ultrasound (US). US-guided aspiration and drainage is essential for the correct diagnosis and management of symptomatic post transplant fluid collections. However, computer tomography (CT) often delineates fluid collections and their anatomic relationship to adjacent structures better than US, particularly in obese patients. In addition, puncture and drainage can be performed with CT guidance in cases when US fails to demonstrate access to the collection.

Lymphoceles

Lymphocele formation is a late complication of renal transplantation caused by lymphatic obstruction or leak. It can occur in up to 15% of renal transplantations.[6,7] Simple needle aspiration of the fluid using sterile technique will make the diagnosis. At biochemical analysis, a lymphocele has the same levels of protein, urea nitrogen, creatinine, electrolytes, and occasionally, lipids as serum, so differentiation from urinoma, haematoma, seroma, or abscess is possible.[8-10] Most lymphoceles are discovered incidentally, are small or sterile and asymptomatic, and do not require therapy. If symptomatic, they are usually secondary to local mass effect, with compression of the urethra resulting in hydronephrosis, compression of the iliac vein with resultant lower extremity oedema, or deep venous thrombosis, or a combination of both. Only rarely cases do secondary compression of renal artery lead to postoperative hypertension. Symptomatic lymphoceles can be treated with either percutaneous or surgical techniques. Despite the relatively high success rates of surgical treatment (90% success rate), open surgery carries more risks, greater morbidity and longer hospitalisation.[10-13] The operation of choice is laparoscopic peritoneal marsupialisation (fenestration) of the cyst into the peritoneal cavity. The major advantage of the laparoscopic approach is the absence of postoperative *ileus*, with the opportunity to continue the enteral immunosuppressive regimen and a lower recurrence rate (4%).[5,13] Percutaneous therapy varies from simple aspiration to placement of a drain (Figures 1a, 1b), with or without sclerotherapy. Percutaneous needle aspiration is the usual technique for diagnosis, but simple percutaneous aspiration of the lymphocele results in 80%-90% recurrence rate and an infection of 25%-50%.[5,14-16] Indwelling catheter drainage alone has been reported in most series as reaching cure rates of 50%-80%.[8,12,17,18] The introduction of a sclerosing agent in conjunction with catheter drainage has improved success rates to 79%-94%, with recurrence rate up to 31%.[9,10,12,19-22] A number of agents, including povidone iodine, bleomycin, alcohol, doxycycline and talc have been used for sclerosis, but none of these agents universally. The major advantage of percutaneous

drainage and sclerotherapy is the very low incidence of major complications. The most frequently reported complication is secondary infection of the lymphocele, with reported rates of 7%-17%.[14,23-25] The major disadvantages of percutaneous drainage and sclerotherapy are the need for multiple treatments and the requirement of the catheter to be left in place for a significant period of time.

Urinomas

Urinomas due to extravasations of urine from the renal pelvis, urethra, or ureteroneocystostomy usually occur in the first 1-3 weeks following transplantation and may result from of disruption of the ureterovesical anastomosis, incomplete bladder closure, ischemia of the collecting system, post biopsy injury, or severe obstruction. The diagnosis is usually made by US or CT. Characterisation of the fluid can be achieved by obtaining a sample via US-guided aspiration and determining the creatinine concentration of the sample. After confirmation of the diagnosis, percutaneous catheter placement is indicated. Anterograde pyelography is the best test for confirming the source of leak. It is discussed in the section on urinary complications.

Haematomas

Postoperative perirenal haematomas occur frequently but are usually small and asymptomatic and should be considered a normal sequel to surgery.[6,26] In US, the acute haematoma appears as a fluid collection with echogenic debris. Later the clot lysis-decreased echogenicity appears. The CT appears as fluid collection with hyper attenuating areas prior to intravenous contrast material administration, a finding which is consistent with fresh blood. Size, location, and growth determine the significance of these collections. An increase in size may indicate the need for interventional management or surgery. Large haematomas can cause symptoms secondary to mass effect but usually only present a problem when they become secondarily infected. If the patient is asymptomatic and there are no signs of infection, these collections can be treated conservatively if the haematoma does not increase in size. Aggressive interventional percutaneous drainage can successfully resolve an infected haematoma but larger calibre drains (12 or

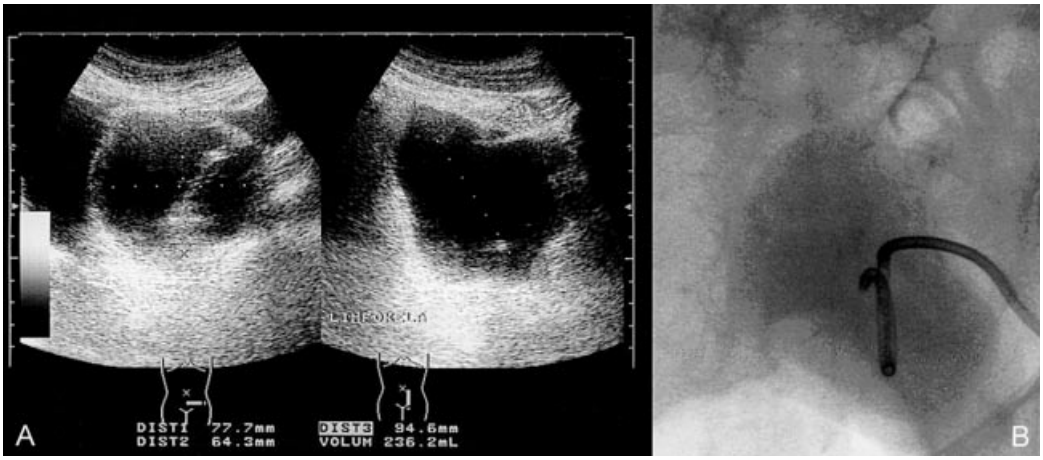

Figure 1. Lymphocele. a. US image demonstrates a large hypoechoic fluid collection with single septation in the left side of the pelvic cavity. **b.** Percutaneous catheter drainage (X-rays)

14 Fr) are usually required. Immediate postoperative haematoma can be secondary to graft rupture or injury to the vascular pedicle. Emergency surgery is mandatory in these cases.

Perirenal abscess

Perirenal abscess is an uncommon early complication of renal transplant. When a patient has fever and US or CT demonstrates perirenal collection with air, the diagnosis of perirenal abscess is clear. The treatment of abscess is based on antibiotics together with a percutaneous or surgical drainage procedure depending on the size of the abscess and the clinical course. Bouali *et al* and Lang report success rates of 67% and 96% in a series of 31 and 33 cases of abscesses treated percutaneously together with low rate in complications.[27,28] Percutaneous drainage under US or CT guidance avoids the risk inherent in surgery and anaesthesia, saves considerable time and meets greater patient acceptance. We recommend insertion of a percutaneous catheter into abscess to obtain a specimen for culture, and to drain the pus-filled cavity in order to hasten recovery and shorten the duration of anti-microbial therapy.

Vascular complications

Vascular complications are found in less than 10% of renal transplant recipients, but they are an important cause of graft dysfunction.[6,29-35] The most frequent vascular complications of renal transplantation include stenosis, thrombosis, arteriovenous fistulas, aneurysms, and pseudoaneurysms in the graft artery and in the recipient iliac arterial system. In contrast to other causes of transplant dysfunction, vascular complications are associated with high morbidity and mortality. The diagnostic screening methods are ultrasound with duplex and colour Doppler modes and three-dimensional (3D) gadolinium (Gd)-enhanced magnetic resonance angiography (MRA).[36,37] Digital subtraction angiography (DSA) remains the standard procedure for final diagnosis and checking endovascular treatment of vascular complications. Endovascular management is the initial treatment of choice for vascular complications in renal transplantation.

Renal artery stenosis

Stenosis, the most common vascular complication of renal transplantation, occurs in 1%-12% of transplanted renal arteries and represents a potentially curable cause of hypertension following transplantation and/or renal dysfunction.[30-34,39-42] The cause of transplant renal artery stenosis (TRAS) is multifactorial and includes surgical technique (clamp injury to the vascular endothelium, perfusion pump cannulation injury of the donor vessel, faulty suture technique), angulations due to disproportionate length between graft and iliac artery, kinking of the renal artery, type of allograft, immunological factors, and cytomegalovirus arteritis.[40,41] In long-standing transplants, progression of underlying arteriosclerosis in the recipient iliac artery can also be a source of arterial stenosis. The incidence of renal artery stenosis is more common in cadaver transplant (most renal allografts originate in cadavers), and it can occur as early as two days or as late as several years after the procedure.[38,43] In cadaver transplant, allograft revascularisation is usually performed as an end-to-side anastomosis with the external iliac artery. When a living, related donor is used, an end-to-side anastomosis with the external iliac artery (AIE) may still be used, but an end-to-end anastomosis with the internal iliac artery (AII) is often preferred.[44] The clinical presentation often mimics that of rejection, but a diagnosis of renal allograft arterial stenosis may be strongly suggested on the basis of sonography and

biopsy. A renal allograft biopsy is generally performed prior to angiography in order to rule out chronic rejection of other forms of renal parenchyma disease. Doppler US has become the preferred screening modality for stenosis of the transplanted renal artery.[45] Doppler ultrasound has been reported to have a sensitivity of 85% to 100% and specificity of 86% to 100% in the diagnosis of TRAS.[5,44-48] Data suggest that this technique is highly accurate, but is highly dependent upon the experience of the ultrasonographer. In obese patients, colour Doppler evaluation can be difficult and MRA or CT angiography can be helpful as an adjunctive non-invasive diagnostic test for TRAS. The gold standard for diagnosis of transplant renal artery stenosis remains DSA, being diagnostic in 93% of cases.[49] It should be performed in patients with clinical and Doppler US findings of TRAS or in patients with clinical findings of stenosis despite normal US results. However, it is invasive and in patients with marginal renal function it can induce acute tubular necrosis secondary to contrast toxicity. A useful alternative to nephrotoxic iodinated contrast agents is provided by CO^2 or Gadolinium DSA.

The options available to correct stenosis of the renal artery include conservative treatment, transluminal angioplasty (PTRA) with or without stenting and surgery. If the stenosis is relatively minor and the blood pressure controllable with medication, it is reasonable to continue with conservative treatment. The conservative option becomes particularly attractive if the lesion is unsuitable for PTRA or when PTRA is used but it fails. Surgery should only be undertaken for graft arterial stenosis if the other alternatives of PTRA or conservative treatment are not appropriate. PTRA has become accepted as the initial procedure of choice in the treatment of renal allograft arterial stenosis, both in allograft renal and native iliac artery stenoses (Figures 2a, 2b, 2c). The best approach to end-to-end anastomoses (AII) is from the contralateral-femoral artery, whereas end-to-side anastomoses (AIE) are usually more accessible from an ipsilateral approach. Non-selective pelvic arteriography was performed to exclude inflow lesions by means of a femoral approach as previously described. A narrowing of greater than 50% of the luminal diameter was considered haemodynamically significant. All patients who underwent interventional radiological treatments received intra-arterial boluses of heparin (5000 IU) during the procedure. The technical success of PTRA was defined as a residual stenosis of less than 30%

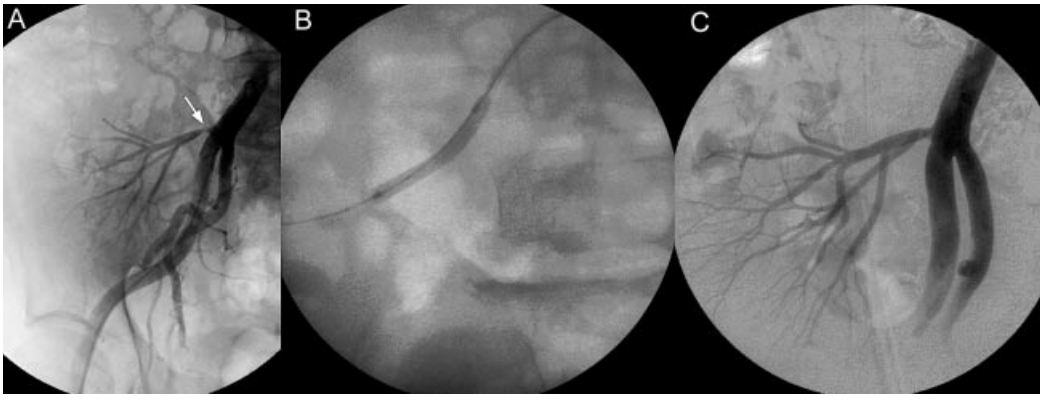

Figure 2. Transplant renal artery stenosis. **a.** Cadaver renal transplantation, with a single renal artery and end-to-side anastomosis to the right external iliac artery. Arteriogram shows a stenosis of the transplant renal artery (arrow). **b.** Balloon dilatation. **c.** Repeat arteriogram after PTRA with 5-mm diameter angioplasty balloon.

after angioplasty and no flow-limiting intimal flap. Clinical success was defined as more than 15% reduction in serum creatinine level, more than 15% reduction in mean diastolic blood pressure with the number of anti-hypertensive medications equal to that before PTRA, or more than 10% reduction in mean diastolic blood pressure with a reduction in the number of anti-hypertensive medications.[40] Technical success has ranged from 82% to 93%, and graft salvage rates have ranged from 80%-100%.[30-34,41-50] Although up to 20% of cases will develop recurrent stenosis, but are usually amenable to repeat PTRA,[30-34,39,43,50] periprocedural morbidity is generally low, and significant complications have been reported in 0% to 12% of cases.[44,51] Complications are usually related to puncture site complications and rarely to distal extremity embolisation, extensive arterial dissection, renal artery thrombosis and renal artery rupture.[30-34,39,43,50] The success of stent placement used in combination with PTRA for a wide variety of vascular lesions suggests that deployment of metallic stents may be useful in those with recurrent stenosis of the transplant renal artery, failure to satisfactorily eliminate the stenosis after repeat balloon dilatation, intimal dissection with luminal compromise, and stenosis involving the renal arterial ostium (Figures 3a, 3b, 3c, 3d). Stent deployment in six patients with recurrent stenosis was evaluated in retrospective study.[52] At almost three years post procedure, all arteries were patent without significant stenosis, and no additional interventions were required. The role of stent placement for the treatment of TRAS and its effect on long-term patency has yet to be investigated.

Renal artery thrombosis

Renal artery thrombosis is an uncommon complication of transplantation and usually occurs in the early postoperative period, almost invariably leading to graft loss. The most common causes are faulty surgical anastomoses, persistent hypotension, dehydration, and procoagulant conditions such as lupus anticoagulant, severe acute rejection, and progression of a stenosis to thrombosis. Spontaneous late thrombosis of the renal artery is a rare event, and renal artery stenosis is an obvious risk factor. Thrombosis of long-term grafts after intervention such as angiography or attempted angioplasty is more common than spontaneous renal artery thrombosis. Renal artery thrombosis after PTRA may be minimized by keeping the patient well anti-coagulated during the procedure and by the intra-arterial administration of nitro-glycerine in order to prevent vascular spasm. The diagnosis is relatively simple when duplex and colour Doppler techniques fail to demonstrate intra renal venous and arterial flow, with angiography providing confirmation prior to intervention.[53] In selected cases, the early diagnosis of vascular thrombosis may en-

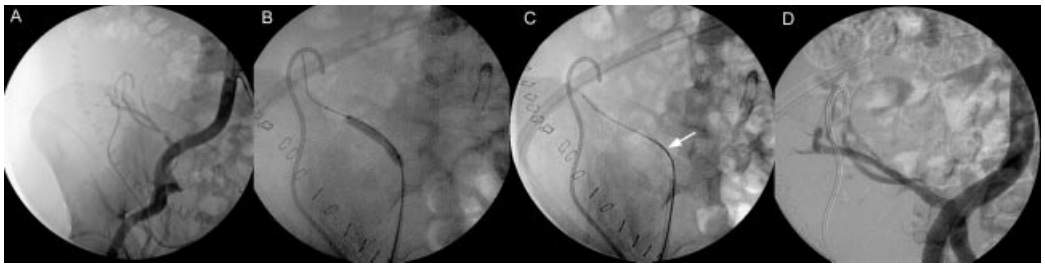

Figure 3. Transplant renal artery stenosis. **a.** Cadaver renal transplantation, with end-to-side anastomosis to the right external iliac artery. Arteriogram shows a stenosis of the transplant renal artery. **b.** Balloon dilatation. **c.** Metallic stent after incomplete PTRA (arrow). **d.** Repeat arteriogram after procedure shows a widely patent transplant renal artery with no residual stenosis.

able graft salvage thrombolytic treatment or clot aspiration. The use of thrombolytic therapy in treating renal artery thrombosis has been reported as successful.[44,54,55]

Intrarenal arteriovenous fistulas and pseudoaneurysms

Intrarenal arteriovenous fistulas and pseudoaneurysms are occasionally seen after biopsies. They occur in 1%-18% of renal biopsy.[5,56,57] Intrarenal arteriovenous fistulas may appear when an artery and vein are lacerated; pseudoaneurysms result when only the artery is lacerated. Arteriovenous fistulas within the kidney are usually asymptomatic, and normally resolve spontaneously. When lesions are sizable, marked arteriovenous shunting may result in renal ischemia, hypertension or hematuria.[6,57] They are easily identified at colour and Doppler US. Helical CT is a good alternative when US cannot define the nature of the lesion. However, a negative US and CT evaluations does not exclude the diagnosis, and, if clinical suspicion remains, these patients should be evaluated with angiography. When symptomatic or large, intrarenal arteriovenous fistulas and pseudoaneurysms may be effectively treated with selective arterial catheterisation and embolisation. Transcatheter embolisation is a safe and effective alternative to surgery; however, it may result in a segmental infarction and impaired renal function if the feeding vessel is embolised. Treatment requires superselective embolisation in order to preserve the maximum amount of renal parenchyma (Figures 4a, 4b). A potential complication is occlusion of the main renal artery due to migration of the embolising agent. Coils are typically chosen as the embolic agent for arteriovenous fistulas because of the greater control in deployment when compared to Gelfoam embolisation.[3] Perini *et al*[58] performed embolotherapy in 21 patients with renal allografts and vascular complications. Technical success was achieved in 20 of 21 patients (95%) without serious complications, and no long-term graft dysfunction was noted in 58% of those treated.

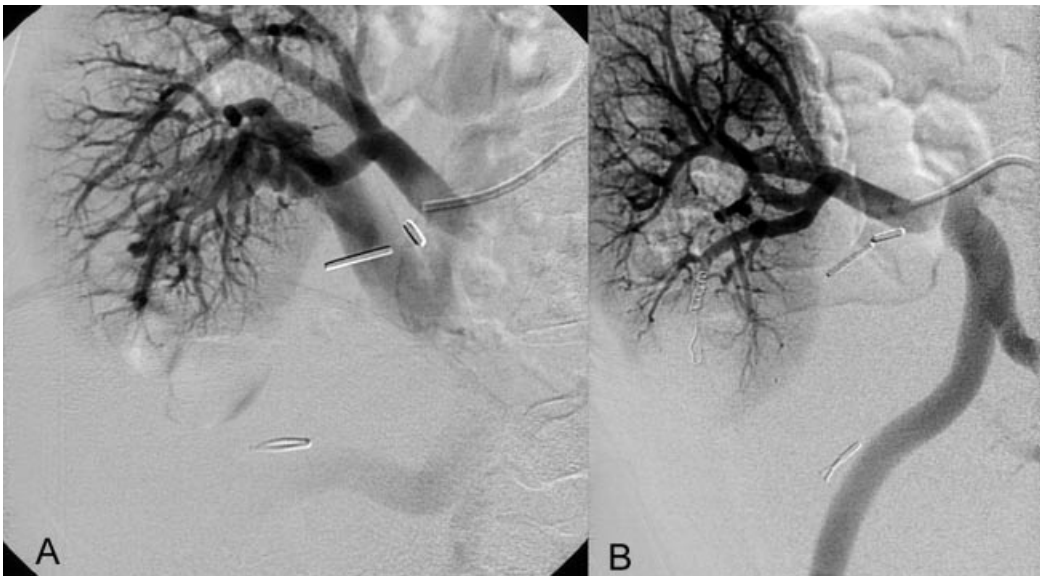

Figure 4. Intrarenal arteriovenous fistula following biopsy. **a.** Angiogram obtained with selective injection of the main renal artery shows early filing of the transplant renal vein. **b.** On an angiogram obtained after subselective embolization with coils, early draining veins are not visualized.

Renal vein thrombosis

Renal vein thrombosis is an uncommon complication that usually occurs in the first postoperative week. When occurring in the early post transplant period it is usually associated with surgical complications and often results in the loss of the graft. At a later stage, when graft function has stabilised, its development may be associated with underlying disorders such as glomerulonephritis, immunosuppressive therapy, acute rejection, or extension of lower extremity venous thromboses.[9,58,59] The clinical features, with the effect on urine output, vary from primary non-functioning, similar to that seen with arterial thrombosis, to sudden loss of urine output and rising creatinine in a graft which is different than in one functioning perfectly. The clinical signs are striking, often with severe pain resulting from rapid local graft swelling. The usual outcome of renal vein thrombosis is infarction, and transplant nephrectomy is usually performed to prevent infection.[53] Whenever such a diagnosis is made, surgery is always urgent, because, apart from the necessity to relieve the pain, delay is associated with an increasing risk of graft rupture, which may result in catastrophic graft haemorrhage. The sonographic diagnosis dependents mainly on the Doppler portion of the examination. On grey-scale US images, the allograft may appear swollen and hypoechoic. At Doppler US examination, venous flow is absent, and the arterial waveform shows reversed, plateauing diastolic flow.[6,60,61] The diagnosis is confirmed by venography with selective venous catheterization and therapeutic thrombolysis. There are several case reports in the literature on the attempts to treat transplant renal vein thrombosis with arterial, venous, or a combination of arterial and venous thrombolysis and percutaneous mechanical thrombectomy, but results vary.[55,59,62] It is uncommon to achieve complete thrombolysis, but partial lysis of the vein may result in a marked clinical improvement.

Urological complications

Urological complications after renal transplantation are relatively uncommon. They predominantly consist of urinary leaks and urethral obstruction. The quoted incidence of urological complications ranges from 5% to 14%.[6,63-66] Urologic complications can be divided into early and late categories. Early complications are defined as those that occur within three months of the transplant, and late complications are those that occur after this period of time.[64] Leaks tend to occur early, although obstruction may occur at any post transplant stage. These complications must be diagnosed early, because delays in diagnosis can result in the loss of transplanted kidney as well as increased patient morbidity and mortality. The most commonly performed interventional procedure in the renal transplant patient is percutaneous antegrade nephrostomy for urinary obstruction or leak.[44,67]

Urethral obstructions

Urinary tract obstruction can occur early or late after renal transplantation and are observed in less than 5% of patients.[6,53,65,66,68] Patients with obstruction are typically asymptomatic, and the diagnosis is made during evaluation because of a rising serum creatinine level and is confirmed by ultrasound examination of the transplanted kidney. The common causes of obstruction are urethral stricture or kinking (accounting for more than 50% of obstruction), urethral blood clot, and urethral compression from lymphocele.[5,44] Less common etiologies of obstruction include oedema or narrowing at the ureteroneocystostomy, pelvic fibroses, fungal debris, or compression from an extrinsic mass such as adjacent haematoma or lymphoadenopathy. More than 90% of urethric stenoses occur within the distal third of the urethra and may appear days or years after

transplantation.[68,69] Once obstruction is suggested by US, antegrade pyelography can be obtained in order to confirm the diagnosis, to provide detailed, anatomic definition of the type and level of the obstruction, and to serve as an access route for percutaneous management. Interventional radiology treatment of urinary tract obstruction consists of percutaneous nephrostomy, balloon dilatation, insertion of double J stents, stent placement, or correction of the source of extrinsic compression of the collecting system, such as a lymphocele. If obstruction is secondary to ureteroneocystostomy oedema or urethral blood clot, external diversion through a percutaneous nephrostomy catheter often provides temporary relief of obstruction until the oedema subsides or the clot has passed spontaneously (Figure 5).[5,44,65] The nephrostomy is removed only after an antegrade nephrostogram has confirmed that the urinary tract is unobstructed.

Urethral stenosis in the early postrenal transplant period can be safely and effectively treated by percutaneous dilatation and stenting, with few side effects and long-term success.[70,71] This method is especially efficient in patients who develop urethral stenosis within three months of the transplant. In patients with urethric strictures developing three months after transplantation or later, percutaneous stenting is of limited significance and most patients require surgical correction. Bhagat *et al*[70] and Fontaine *et al*[71] reported a success rate of 69% and 62% of early obstruction (within three months) and 33% and 16% of late obstruction (after three months) in a series of 41 and 44 cases treated percutaneously with urinary diversion by percutaneous nephrostomy, balloon dilatation and urethral stenting. We advise the application of urethral dilatation to short fibrotic strictures, particularly those located at the ureterovesical junction. A high-pressure balloon, selected according to urethra and stricture size, was inserted and advanced to the stricture and inflated for 1-4 min. When the pressure dents on the balloon disappeared, the stricture had been controlled, and an 8-9 Fr double J stent was passed into the urethra (Figure 6). Usually the stent is kept indwelling for 9 to 18 weeks, after which it is removed cystoscopically.[5] However, surgical reconstruction may be required for long or recurrent stricture, and strictures refractory to balloon dilatation.

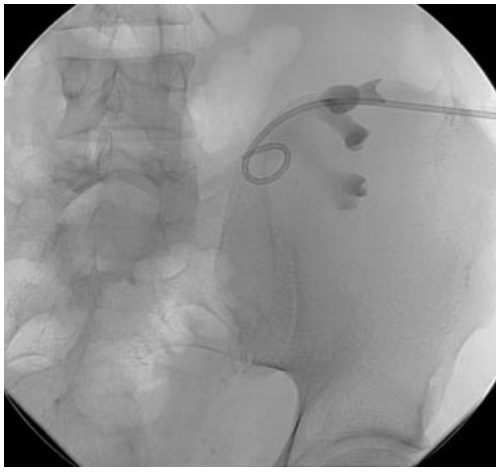

Figure 5. Urinary tract obstruction. Function is maintained by percutaneous nephrostomy.

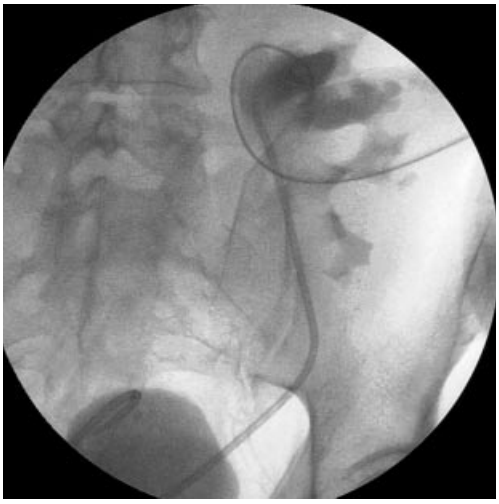

Figure 6. Urinary tract stenosis. An 8-F double J stent is placed across the stenosis after dilatation.

Urine leaks (urinomas)

Urine leaks are relatively rare complications following transplantation, occurring at the frequency of approximately 1% to 5%, and appearing in the early postoperative period as pain, swelling, and discharge from the wound.[65,68,72] Urethral extravasations producing urinoma can be caused by graft rejection, urethral necrosis due to ischemia, or inadequate surgical technique.[63] Most urine leaks occur at the ureteroneocystostomy, possibly due to vascular insufficiency, or along the anterolateral surface of the bladder where the ureteroneocystostomy has been performed.[44,68,70] Leaks may also occur from the proximal urethra, renal pelvis, or calyces secondary to distal urethral obstruction, renal infarction, or percutaneous renal biopsy. Diagnosis is usually made by US evaluation of the transplant, which reveals perinephric fluid collections that is relatively anechoic but may contain septations. Initial management should include percutaneous aspiration and fluid analysis to distinguish it from a lymphocele, which reveals an elevated creatinine level. A percutaneous nephrostogram and drainage can be both diagnostic and therapeutic, and effective in the treatment of urine leaks in renal transplant patients.[65,67,70] Definitive therapy can be carried out surgically or percutaneously with urethral stenting, double-J stents and urinary diversion by percutaneous nephrostomy.[70,71,73] Matalon *et al* have reported a success rate of 87% in a series of 23 cases of urinary leaks treated percutaneously with urinary diversion.[74] Fontaine et al treated 17 patients with transplant urinary leaks with percutaneous nephrostomy and nephroureteral stent and achieved successful closure of the urinary fistula in 10 patients (59%).[71] Benoit *et al* described successful closure of urinary leaks in all 7 patients (100%) with percutaneous nephrostomy and stent insertion.[72] The duration of catheter drainage typically ranges from 6-17 weeks.[5,65,71,74]

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