

## Urological challenges in renal transplantation

N. Seneviratne and N. D. Perera

Department of Urology and Renal Transplantation, National Hospital of Sri Lanka, Colombo, Sri Lanka.

Urological evaluation is an essential component of the pre-transplantation assessment of any potential renal recipient. The main objective is to identify structural and functional abnormalities of the native urinary tract that may preclude transplantation or threaten patient or graft survival. Mainly the assessment should be tailored to determine the need for pre transplant nephrectomy and the suitability of the lower urinary tract to receive the graft. Meticulous measures taken to harvest a healthy ureter which is properly implanted with a non refluxing method is mandatory since ureteric complications could arise at any time and could be an unforgiving threat to the graft viability or even patient survival. These post operative complications are now increasingly managed by endourological or percutaneous image guided techniques which have become a part and parcel of modern urological practice. As a result, reoperation is rarely required unless all other resources have been

exhausted. Hence the true incidence of technical graft loss due to urological complications is infrequent.

### Pre transplantation assessment

#### 1. Upper urinary tract

Probably the most frequent pre-transplant surgical consideration of the upper tracts of the renal system is the need of nephrectomy with or without ureterectomy. The goals of nephrectomy are to clear a potential nidus for septicemia which becomes an issue during immunosuppression, to ameliorate hypertension and to eliminate a potential neoplastic focus (1). Table 1 summarizes the indications for pre-transplant nephrectomy.

Whenever possible the procedure should be limited to a unilateral nephrectomy to allow continued erythropoietin and urine production by the remaining kidney to buy time before the transplantation.

**Table 1. Indications for pre-transplant nephrectomy**

Indication	Rationale	Pathology
(a) Mandatory	Ongoing infection	Staghorn calculus Renal cortical abscess Resistant organisms in urine culture
	Malignant hypertension	Renovascular disease Idiopathic unresponsive to medical therapy
	To rule out malignancy	Renal Mass Acquired cystic kidney disease
(b) Preferable	Eliminate potential infection Persistent pain Haemorrhage requiring transfusion	History of pyelonephritis Polycystic kidney disease

Laparoscopy (total or hand assisted) should be and rightfully considered as the method of choice ('Gold standard') for pretransplant nephrectomy. The high success rate, low morbidity, early recovery all are considered as real advantages for this patient population (2). However, in the era of laparoscopy, bilateral simultaneous nephrectomy should be considered, minimizing the waiting time and the duration between nephrectomy and transplantation. As Lap-donor nephrectomy is considered as an advanced technique which should be practised towards the end of the learning curve of a laparoscopist, presence of an experienced general or preferably a urological surgeon could minimize complications during organ harvesting (3).

High grade vesicoureteric reflux (VUR) that is left untreated post transplantation is associated with increased urinary tract infections, even when urinary tract infections were not a problem prior to transplantation (4). Surgical options are reimplantation or nephroureterectomy. Endoscopic collagen injection has been successful in children prior to transplant which reduces the morbidity of surgery (5). Generally, ureterectomy is indicated in the presence of VUR grade III or above or presence of primary renal infections due any degree of reflux disease. If ureterectomy is contemplated the entire ureter has to be excised upto the bladder. However, the decision for ureterectomy should not be made lightly since post transplant necrosis or long strictures of the donor ureter are most easily replaced with the native ureter (6). Dilated donor ureters could also be used for bladder augmentation in children prior to transplantation.

## 2. Lower urinary tract

The ideal bladder for implantation of the transplant ureter is a continent, sterile, low-pressure reservoir that empties completely. Basic evaluation should be a good history and physical examination on irritative or voiding symptoms, urinary tract infection and haematuria followed by urine analysis, sonographic assessment of bladder volume and the post void residual volume. It is routine to do a X-ray KUB in places where stone disease is endemic as in ours as well as it gives a clue into calcified vessels (7). In the absence of a past urological history with initial evaluation being negative further investigations are generally not required. However, two groups at extremes of age are at additional risk despite the initial screening and need further evaluation.

30-40% of paediatric renal transplant recipients in contrast to 6% of adults have end stage renal disease (ESRD) secondary to or associated structural genitourinary abnormalities (8). Therefore, formal assessment of the lower urinary tract should be done in all children

before transplantation. Voiding cystourethrography is a reliable method of detecting significant abnormalities and has been shown to be a cost efficient means of initial investigation (9).

Older renal transplant candidates, particularly men above 50 years, also have an increased incidence of abnormalities of the urinary tract, although these are generally acquired. In this situation PSA estimation, sonographic evaluation of the prostate as well as non invasive measurement of the voiding efficiency by means of uroflowmetry will be invaluable initial base line investigations.

Potential recipients with underlying urological problems or whose screening investigations are suspicious obviously require more detailed studies. Additional imaging should be undertaken to establish the cause of any ureteric dilatation and hydronephrosis, which in many cases requires an assessment of vesical function. The storage and emptying properties of the bladder are studied in more detail by formal advanced urodynamics supported by a cystoscopy.

It is of prime importance that the assessment of bladder function is considered early in the management of the patient approaching end-stage renal failure. Vesical function deteriorates in most patients on dialysis. Many develop small-capacity bladders with low voiding rates. Male haemodialysis patients are most affected, with a median bladder capacity of 180 ml and maximal flow rate of 5 ml/sec, compared to 300 ml and 14 ml/sec in patients on peritoneal dialysis (10). The majority improve within 3 months of transplantation. An average increase in excess of 50% in both bladder capacity and maximal flow rate is seen (11). Unfortunately, it is difficult to predict bladder function after transplantation in an oliguric patient. However, those with pre-transplant bladder capacities of less than 100 ml and a history of urinary infection have a poor outcome and worse graft survival (10). It is critical, therefore, that patients with chronic renal impairment in whom there may be potential concerns with respect to bladder function have this formally assessed prior to transplantation.

As the age of the transplant patients increase, more male patients exhibit benign prostate enlargement. Prior to transplant these patients have small urine outputs which are probably inaccurate to address the bladder outlet obstruction. In general it is preferable to perform a transurethral resection (TURP) after successful transplantation as lack of transurethral urine tends to predispose bladder neck stricture formation which would be an additional burden prior to transplantation. Additional advantage of a delayed prostatic surgery is

that with a post transplant diuresis some of the lower urinary tract symptoms such as poor flow could markedly improve.

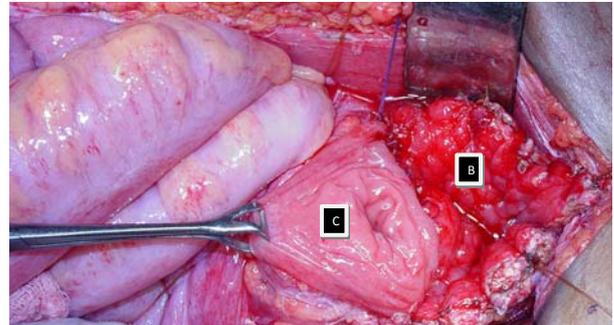
### Lower urinary tract reconstruction – bladder augmentation or urinary diversion

Many ESRD patients have defunctionalized bladders and generally of low capacity (12). Of the adult population 6% have lower urinary tract anomalies. Generally they are small bladders with detrusor irritability or large volumes with poor emptying. In this group voiding cystourethrogram and advanced urodynamics become key investigations to get an idea of the nervous and/or muscular response to volume expansion (13). But in majority of patients with abnormal vesical function, the surgically unmodified bladder can still be rehabilitated and used for transplantation with a planned strategy involving intermittent self-catheterization and/or anticholinergic therapy (if required), with good long-term results (8). Self catheterization has been far more superior and less in morbidity when compared to surgery.

On the other hand, patients with small nondistensible fibrotic bladders are unlikely to become an adequate reservoir post transplant. Therefore, bladder augmentation should be done prior to transplantation which employs a detubularized segment of caecum (Figure 1), right colon, ileum or sigmoid colon (14). Urinary tract infections are the most common complication of the augmented bladders. Regulated timed voiding and double voiding will reduce the occurrence of infections though others believe low-dose antibiotic prophylaxis will prevent symptomatic urine infections (15). Electrolytes and metabolic abnormalities are not so uncommon. Acidosis should be treated due to its contribution to metabolic bone disease. This favours gastric segments to be employed in children hoping that secretion of acid into the urinary tract offsets metabolic acidosis of chronic renal failure and may decrease the risk of urine infection. However, gastric acid production can also cause problems when stomach is interposed in the urinary tract. The use of small bowel additionally will give rise to nutritional deficiencies such as B12 as well as excessive mucous related problems. Regular drainage of augmented bladder and irrigation to remove mucous are recommended to prevent symptomatic urine infections. All these complications can be overcome if redundant dilated lower ureter is used, if available, for augmentation of the bladder in the uraemic patient (16).

The other form of dysfunctionalized bladder is the hypotonic/ atonic bladders resulting from diabetes and other causes of peripheral or autonomic neuropathy

which is common among the ageing transplant population. Problems of recurrent urinary infection and chronic retention can be avoided in such patients with regular and complete bladder emptying by clean intermittent self catheterization.



**Figure 1.** End stage renal failure due to neuropathic thick walled bladder (B) augmented with caecum and right colon (C).

Predominantly children with neurological and anatomical derangements affecting the detrusor/sphincter mechanism, in a very few, the entire bladder is deemed an unsuitable reservoir. In this case simple urinary diversion in the form of conduit of ileum, sigmoid or the caecum has been used and the transplanted ureter has been anastomosed to it (17). Although historically the initial approach to this problem was anastomosis of the ureters to the sigmoid colon (by Coffey), the procedure was abandoned due to the development of metabolic and infective complications. Since then ileal conduits, have become more widely utilized procedure.

Continent urinary diversion and neo bladder reconstruction are alternatives to conduit diversion and are being used increasingly (18). The major concern of using long bowel segments, was that it could result in bicarbonate loss causing hyperchloremic acidosis which in turn inhibits renal resorption of calcium and production of 1-25 dihydrocholecalciferol, leading to bone demineralization. This could exacerbate the existing clinical bone disease in post transplant recipients treated with steroids and calcineurin inhibitors.

Whenever possible, urinary tract reconstruction, particularly if prosthetic devices are to be used, should be completed before transplantation, to reduce the risk of infection during immunosuppression.

### Perioperative concerns

#### 1. Ureteric harvesting

Transplant ureter has a proclivity toward complications, because it receives its entire blood supply from the vessels that emanate in the hilar and upper periureteral

areolar tissue, sites that are vulnerable to injury during donor nephrectomy. Therefore, caution has to be exercised during harvesting the ureter to avoid dissection of the perihilar fat and preserving periureteric fat and areolar tissue by limiting the dissection medial to the gonadal vein. In addition if the ureteral segment is either too long and redundant or too short and under tension may compromise the blood supply.

To reduce the magnitude of the donor operation in terms of convalescence and improved cosmetic results laparoscopic donor nephrectomy was introduced in 1995 (20). Though the initial ureteric complications during harvesting was 11% lately it has dropped down to less than 2% almost reaching the conventional open figures which is less than 1% (19,20).

## 2. Ureteric anastomosis

Implantation of the transplant ureter is usually done by one of two techniques. Choice of technique appears largely related to institutional preference. In the Leadbetter-Politano technique, which is an intravesical method requires a larger anterior cystotomy to visualize interior of the bladder, creation of a 2-3 cm long submucosal tunnel hence requiring a longer length of the donor ureter dissection (21). Implantation of the ureter is done superior-medial to the native ureteric orifice over the trigone rendering the accessibility of endoscopic instrumentation and stenting when indicated. This is probably of less importance in the present era with the availability of interventional radiological techniques that allow this to be done percutaneously.

Extravesical implantation Lich-Gregoir technique, which is the standard technique in many units worldwide requires a small extra vesical myotomy on the lateral surface of the bladder where the ureteroneocystostomy is done followed by a tunnel created over the ureter by approximating the two seromuscular flaps (22,23). This method which was originally described for the correction of vesicoureteral reflux was introduced to clinical transplantation by MacKinnon in 1968 (24). The method gained popularity due to the shorter length of ureter and less dissection, lower incidence of urinary leakage and stenosis although adequate randomized studies are lacking (25). Subsequent transurethral instrumentation or cannulation is also easy considering the site of the neoureterocystostomy which is now redirected at posterolateral wall of the bladder.

The two techniques have no difference apparent in early or late complications in relation to obstruction, stenosis, haematuria and urinary tract infections except urinary leakage which is more common with the extravesical technique (26). In addition, there does not appear to be

any substantial need to attempt a nonrefluxing anastomosis. The incidence of reflux on voiding cystography is similar in both tunneled and non-tunneled implants (23% v 29%). Urinary tract infections occur with similar frequency in patients with or without reflux into the transplanted ureter (27). Despite this, it has been suggested that reflux may be associated with poorer graft survival independent of infection.

Despite well established ureteroneocystostomy techniques, Whelchel and Cosmi in 1975 and Hughes in 1987 advocated the use of ureteropyelostomy connecting the ipsilateral recipient native ureter to the donor renal pelvis (28). This created a wide anastomosis with less chance of stricture or obstruction. However, the major complication of ureteropyelostomy being infected urinoma and the greater risk of vascular disruption owing to extension of infection into hilar vessels rendered this technique to be used sparingly. Alternatively, Hamburger in 1962 introduced ureteroureterostomy where donor ureter is anastomosed to the native lower ureter (29). These two alternative techniques are particularly useful if ureteroneocystostomy is not feasible owing to a shortened donor ureter due to a surgical misadventure during organ procurement.

## 3. Stenting the anastomosis

A double-pigtail polyurethane stent is inserted during the ureterovesical anastomosis to ensure free drainage urine despite anastomotic oedema to avoid ureteral distension which can lead to necrosis of the ureter. Routine use of a stent in extravesical ureteroneocystostomy has a significantly lower urological complication rate than those with nonstented anastomoses from 10% to 1%. Largest series of five randomized, controlled trials individually found stented anastomoses to have a lower complication rate and this was confirmed by metanalysis of these trials (30). Use of a stent has shown to increase the chance of urinary tract infection as high as 79% when compared to 54% in nonstented recipients (31). However, there are many large series showing that routine use of the stent is more cost effective in the long-term. Stent is usually kept for 4-6 weeks prior to removal using a flexible cystoscopy. However, recent reports suggested that 2 weeks are sufficient and the stent which has been left tied in to the catheter can be removed together on the 8-10 days avoiding another hospital admission.

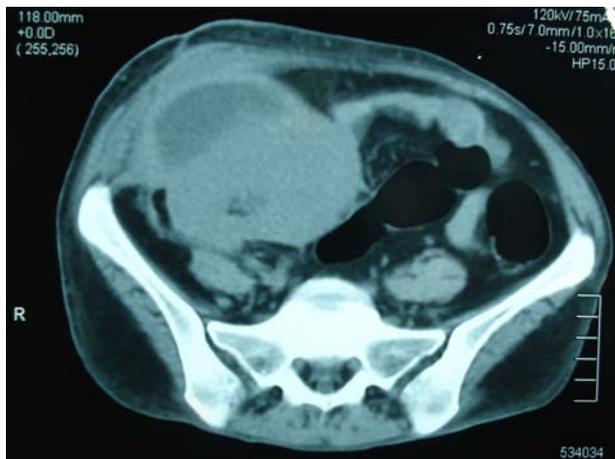
## Postoperative complications

The true incidence of urinary complications widely varies between institutions depending on the definitions used

to classify them. After excluding urinary tract infections as a urological complication generally the true reported incidence of urological complications varies from 2.5%-15% resulting in occasional graft loss (32).

### 1. Ureteric obstruction

Ureteral obstruction is the most common urinary complication. It commonly presents during the early postoperative period due to blood clots, oedema and/or haematoma that exacerbate the narrowing in a relatively tight submucosal tunnel, technical errors such as malrotation and extrinsic compression by the spermatic cord/round ligament or due to perigraft fluid collection in the form of urinoma (Figure 2), haematoma or lymphocele. Late ureteric obstruction is also reported due to chronic ischaemia.



**Figure 2.** *Transplanted kidney complicated with a urinoma.*

Clinical diagnosis is made in the presence of oliguria, graft tenderness, urinary tract infection progressing to sepsis and rising creatinine levels. When routine ultrasonography is performed, pelvicalyceal dilatation is detectable at some stage in as high as 57% of transplant recipients (33). In fact, at least some fullness of the collecting system will be seen in virtually all patients with a stent in-situ if scanning is performed with a full bladder. Hence, a post void scan should be taken to assess the collecting system true dilatation. Only a small percentage (10%) of those with dilatation will ultimately be found to be obstructed (33,34). Antegrade pyelography is probably the preferred method for investigation of the patient with deteriorating renal function and dilatation of the pelvicalyceal system (35). Isotope renography is not useful unless used serially to monitor the progress. Combined Whitaker test which is a pressure-flow study which measures pressure of the renal pelvis as well as the intravesical pressure improve the diagnostic accuracy of antegrade pyelography, as is illustrated by the fact that up to 25%

of patients with apparent narrowing of the ureter do not have mechanical obstruction (34). In cases in which there appears to be any evidence of narrowing, and therefore possible obstruction, an antegrade stent is inserted (36). An improvement in renal function suggests that obstruction had been present. Unfortunately, in the majority of cases, chronic rejection has been found to be the underlying cause, with subsequent progressive decline in the remaining renal function over time. Long-term success has been reported with the treatment of ureteric strictures by percutaneous antegrade dilatation using 6-8 mm angioplasty balloon catheter and placement of double J- stenting alone (37). This appears most effective in those presenting early within 3 months of transplantation, when 50% to 75% of strictures occur. Success rates in excess of 70% have been reported in this group; in contrast to less than 30% with late presentations (38). The late presenters require open surgery whereby the ipsilateral native ureter or a tubularised bladder segment is anastomosed to the obstructed transplant collecting system.

### 2. Urinary leak

Urinary leak may result from faulty handling of donor ureter, undue tension during anastomosis, ureter or renal pelvis blowout due to obstruction, invasive wound infection, distortion by pelvic haematoma or rarely due to sluggish blood flow during an episode of rejection. Clinical features such as oliguria, fever, pain and swelling over the graft site, perineum, scrotum or labia, cutaneous urinary drainage with elevated serum creatinine can suggest a leak. These become apparent during the first month of transplant and can be readily diagnosed by high creatinine content of the drained fluid. Once suspected subsequent management is done depending on the site and the degree of disruption. The three potential sites of leak in descending order of frequency are at the ureter at the neoanastomosis, the bladder at the end of the anterior cystotomy or the ureteral hiatus or renal pelvis. Diagnosis is aided by ultrasonography which will demonstrate a perigraft fluid collection where as gravity cystography will demonstrate a fistula (Figure 3). Also cystometrography should be considered in patients in whom high voiding pressures may be contributing to a leakage at the ureterovesical anastomosis. However, an antegrade pyelogram will be needed if cystogram is normal. Nuclear renography scan will show evidence of isotope extravasation.

Distal lesions from the ureterovesical junction are usually managed aggressively, whereas lesions in the more proximal ureter tend to be managed conservatively. An abscess or urinoma must be drained by either percutaneous approach or by an open surgical approach.

At the same time combining a diverting nephrostomy with antegrade ureteral stent leads to an 87% leak closure rate (39). Failing which retrograde stenting can be achieved with the availability of the flexible cystoscopy/ureteroscopy. However, larger urine leaks or drainages that do not settle by 6 weeks following stenting needs open surgical repair in the form of reimplantation, pyeloureterostomy or Boari flap repair. On the other hand, vesical fistulas are generally controlled expectantly by bladder decompression with an indwelling catheter for 2-6 weeks. Rarely substantial size vesical fistulas need early exploration and primary repair. Renal pelvic wall necrosis is a rarity occurring due to vascular insufficiency due to inadvertent hilar dissection during organ procurement. This will require urgent open surgical restoration in the form of pyeloureterostomy with the native ureter, a Boari flap or direct pyelovesicostomy (40). It can be presumed that these early leaks reflected technical problems rather than extensive ureteric necrosis.



**Figure 3.** *Cystogram showing evidence of urinary leak at neoureterocystostomy of the transplanted kidney.*

### 3. Urolithiasis

Urolithiasis is a relatively rare complication after renal transplantation. Risk factors include metabolic disease, ureteric stenosis, the use of nonabsorbable suture material, and prolonged stenting resulting in encrustation. The incidence appears to be approximately 1% (41). Higher rates have been reported, but they appear to be attributable to untreated hyperparathyroidism and the use of nonabsorbable sutures for the ureterovesical anastomosis or a metabolic cause. Clinical diagnosis may be difficult because of denervation of the graft may not give rise to classical pain syndromes. Investigation of deteriorations in graft function, urinary tract

infections, and haematuria lead to the diagnosis in the majority of cases. The majority of calculi are less than 1 cm in diameter, with staghorn calculi being an unusual occurrence. As in the native urinary tract, the majority of calculi can be treated with shock wave lithotripsy (ESWL), percutaneous nephrolithotomy or flexible ureteroscopy and lithotripsy (42). Localization during SWL can be a little more difficult than in the native kidney. Generally, a prone position is required although the close proximity of the kidney to the skin can create problems in focusing the shock waves. Refractory cases which are rare, need open surgery. Urolithiasis related to primary hyperoxalosis results in renal failure, which must be treated by combined liver and renal transplantation.

Kidneys have been transplanted knowingly containing a renal stone (43). Asymptomatic potential donor may be suitable for kidney donation if the stone is less than 1.5 cm in size, single stone and metabolic causes of stone formation has been excluded in the recipient. The stone has to be removed *ex vivo* prior to transplantation by means of ureteroscopy or percutaneous surgery (44,45).

### 4. Urinary retention

Postoperative urinary retention in renal transplant recipients may cause problems in their management. The more frequent acceptance of older males for transplantation has resulted in an increasing number of patients who are at risk of urinary retention as a result of benign prostatic enlargement. Low urine outputs while on dialysis may mask the development of bladder outflow obstruction. Assessment is also difficult due to reduced bladder volumes as a result of oliguria or anuria. However, recommendation has been to avoid prostatic surgery in patients who are approaching end-stage renal failure or who have recently commenced dialysis. In this situation there is a substantial risk of urethral stricture and bladder neck contracture when urine production is low in ESRD. It is preferable to closely observe the patients at risk once the catheter has been removed after transplantation. If any difficulties or problems are encountered, intermittent clean self catheterization is immediately instituted. Patients continue with this until a normal voiding pattern is re-established. When inadequate bladder emptying persists or if the patient continues to suffer symptoms of bladder outflow obstruction, a transurethral resection of the prostate or bladder neck incision is performed 4 to 6 weeks later from the time after stent removal. Patients with atonic bladders or peripheral neuropathies affecting detrusor function are also managed by early catheter removal with immediate institution of self

catheterization. If and when residual volumes are small this can be stopped, although it may need to be continued on a long-term basis.

### 5. Erectile dysfunction

Sexual dysfunction is a common finding in end-stage renal disease, occurring in approximately 70% of either sex of haemodialysis patients compared to 9% of the general population. The prevalence of erectile dysfunction between dialysis and renal transplant recipients varies from 21% and 43% (46). Co-existing neuro-endocrine dysfunction including diabetes, hypertension, peripheral vascular disease and their drug treatments together with psychological factors are the major contributors to erectile dysfunction. Neuroendocrine and psychological disturbances are frequently reversed by transplantation, with nearly 50% of those with erectile dysfunction before transplantation subsequently regaining potency (47). The sole reason being depression and disturbances of the hypothalamo-pituitary gonadal axis which both substantially reduced after transplantation. However, elevations of serum prolactin and reduced testosterone can persist despite transplantation in 25-57% of patients, although in these cases improvements in erectile function usually occur with hormonal supplementation (48). Intracavernosal self-injection of PGE1 is well accepted and tolerated by kidney transplant patients with more than 90% response rates. It poses no apparent risks to the transplanted kidney and could be a good modality to treat erectile dysfunction in kidney transplant recipients (49).

After transplantation, vasculogenic factors appear to be the most important in erectile dysfunction. Mechanisms include renal failure associated with atherosclerosis and hypoxia, which may lead to structural changes in the contractile smooth muscle and collagen and elastin components of the erectile tissue. The resulting loss of elasticity may be a direct cause of veno-occlusive dysfunction (50). Renal transplantation may impair penile arterial blood supply. The blood supply to the corporeal bodies is from the internal pudendal arteries, which are branches of the internal iliac arteries. Arterial inflow from only one side may be adequate for an erection. However, this may not be the case if atherosclerosis or other effects of prolonged uraemia have restricted the circulation. Similarly, use of the internal iliac artery at the time of retransplantation, when the contralateral vessel was used or ligated at the previous transplant operation, carries a risk of vasculogenic impotence (51). It is believed that, if possible, these vessels should not be used in this situation. If use of the internal iliac artery may prove necessary, the patient needs to be advised of the potential risk to potency before surgery (52). Treatments of

vasculogenic impotence include revascularization and implantation of penile prostheses (53). Vascularisation is performed in few centres and success rates are limited, probably because of fibrosis and other changes within the corporeal bodies as a result of chronic ischaemia that has already taken place by the time of surgery. Penile prostheses while overall the most successful treatment, can be associated with an increased risk of infection as a result of immunosuppression (54).

### 6. Malignancy

Genitourinary cancers are the second most common tumours in transplant recipients with prostate cancer and renal cell carcinoma being the most common (55). Unlike the more common skin malignancies, genitourinary tumours have a significant impact on both graft and patient survival. During an average follow-up of 2.5 years, 25044 (3%) of 831804 transplant recipients developed cancer compared with an expected number of 21185 in respect to the general population (56). Younger than 35 years was considered as high risk for genitourinary malignancy due to their long lifespan.

#### Renal tumours

On the basis of the existing literature, it is very difficult to give a reasonable estimate of the prevalence of renal tumours among chronic dialysis patients awaiting transplantation (57). Acquired renal cystic disease (ARCD), renal adenoma, renal cell carcinoma (RCC) and oncocytoma were found in 33%, 14%, 4.2% and 0.6% of cases respectively among over 800000 patients followed up beyond a decade (56,57). On multivariate analysis, ARCD was positively associated with male sex and longer dialysis duration and negatively associated with peritoneal dialysis. On average 0.5% pre transplant patients develop RCC signifying the greater risk of malignant renal tumours over the general population. Transplantation is believed to be an effective and justifiable therapy for RCC patients based on data from North American and European Transplant Registries. Long-term follow-up revealed that only 10% subsequently developed metastatic disease and that there was a 5-year graft survival rate of 63% (58). Duration of dialysis before transplantation was not a determinant of recurrence of RCC. Since tumour stage is an important predictor of recurrence it would therefore seem reasonable to consider that no waiting period would be necessary for patients who have low-stage (pT1-pT2), incidentally discovered tumours. However, patients with a higher stage (pT3 and above) or symptomatic presentations should remain disease free for at least 2 years before consideration for transplantation (59,60). Similar criteria can be applied to other patients with non RCC.

ARCD is a progressive disease characterized by the continuous replacement of the atrophic parenchyma by small cysts. Adenoma and carcinoma are seen in the kidneys of 5% to 19% of patients with ARCD (61). These tumours are often multifocal, with those reported generally being small and asymptomatic. The distinction between adenoma and carcinoma has been based on the tumour diameter (less than 3 cm generally considered an adenoma and that 3 cm or greater to be carcinoma). It is reasonable to screen potential transplant recipients with ultrasound if and when they have been on dialysis for 3 to 5 years, repeating this every 3 years and continuing after transplantation. Nephrectomy should be performed if suspicious lesions are detected. If an RCC is found, the contralateral kidney should also be removed. Tumour size and stage would then determine the timing of subsequent transplantation.

Transmission of malignancy can occur within an allograft. They may arise *de novo* or due to low grade small tumour which proliferates during the immunosuppressed period. To date there are very few (less than 50) cases of RCC reported. These tumours do not appear more aggressive than those arising in nonimmunosuppressed patients. Small tumours have been followed for several years before nephrectomy (60). During this period linear tumour growth of approximately 0.5 cm/year was observed, similar to that seen in nontransplanted ESRD patients. Successful treatment by partial nephrectomy has also been performed with continuation of immunosuppression (62).

### **Urothelial cancers**

Overall, there does not appear to be an increased risk of urothelial malignancy in renal transplant recipients. However, it has been well documented that prolonged consumption of compound analgesic agents is associated with both endstage renal disease (analgesic nephropathy) and a substantially increased risk of transitional cell carcinoma (TCC) (63). Over the past few years, a few cases of nephrogenic adenoma were reported. Although regarded as a benign lesion, nephrogenic adenoma may be difficult to distinguish from flat papillary TCC endoscopically (64). Several reports have also documented TCC in association with nephrogenic adenoma. It is therefore important to obtain biopsy specimens, even with recurrent lesions (65). Defunctionalisation of the bladder has also been identified as a potential contributing factor.

### **Prostate cancer**

Currently there is an increased incidence of this cancer in renal transplant recipients with a risk 2- to 5-fold higher than that in the general population (66). It does not appear to carry a substantial risk of carcinoma of

prostate to lead a more aggressive clinical course in patients undergoing renal transplantation. Nevertheless, this disease is potentially a significant issue in male recipients over the age of 50 years. The widespread use of serum prostate specific antigen (PSA) testing has led to an increased diagnosis of this disease in men over 50 years old. However, the use of single value of PSA over free/total (f/t) -PSA quotient as a tool to support the decision for or against a prostate biopsy, it should be borne in mind that the cut-off criteria determined for men with a normal kidney function cannot be applied to patients who suffer from kidney failure. The f/t-PSA quotient of patients with terminal renal failure is often shifted towards higher values. On the other hand, there is no statistically significant difference between the f/t-PSA quotients of kidney transplant recipients and patients with normal kidney function, therefore the same diagnostic criteria apply in this case (67).

The treatment of patients with clinically localized disease remains controversial, with similar survival rates of 10 years being reported with close observation, radical prostatectomy, and radiotherapy (68). Beyond that, possible survival advantages may be conferred by both radiotherapy and radical surgery. Therefore, it would appear reasonable to offer transplantation to patients with localized prostatic carcinoma, regardless of their treatment choice (if they are otherwise considered suitable) (69). In addition, because clinical disease progression is predictable in this group after 10 years, and highly unlikely within the first 2 to 3 years, there appears to be little rationale in deferring transplantation for the 2- to 5-year intervals, as suggested with other malignancies. In contrast, patients with metastatic disease have a much poorer outcome. These patients are usually managed with androgen deprivation therapy. Despite an initial response in 70% to 80% of patients to treatment, the mean survival duration in this group is approximately 24 to 36 months. Therefore, patients with non-localized prostatic carcinoma represent a poor risk group for transplantation despite apparent disease control by hormonal therapy at the time of consideration.

### **Transplantation using compromised donor kidneys**

Due to unavailability of renal donors readily diseased kidneys which have tumours/large cysts have been successfully transplanted. After bench surgery to excise small renal tumour less than 3 cm, have been used in patients with numerous medical co-morbidities to increase the quality of life, despite the apparent contradiction of an intuitive principle of organ transplantation (70). Large cysts that occupy considerable volume of the kidney might implicate complications after

transplantation due to its natural history. The renal grafts with cyst of Bosniak I and II have been safely transplanted with good long term results thus extending the criterion for the donor pool (71).

In conclusion, presence of a urologist in the transplant team becomes an essential prerequisite, when it comes to perioperative correction of several non parenchymal diseases of the urinary tract, laparoscopic donor nephrectomy and executing a sound ureteric reimplantation technique which all eventually contribute for prolonged graft survival. It is also necessary for a urologist to be conversant with the skills to manage the wide range of urological complications associated with renal transplantation to be a useful member of the transplant team.

### References

1. Rosenberg JC. Indications for pretransplant nephrectomy. *Arch Surg* 1973; 107(2): 233-41.
2. Ahamed MS, Erakya I, El-Kappanya HA. Pretransplant native nephrectomy in patients with end-stage renal failure: Assessment of the role of laparoscopy. *Transplant Proc* 2003; 61(5): 915-20.
3. Darby CR, Cranston D, Raine AEG, Morris PJ. Bilateral nephrectomy before transplantation: Indications, surgical approach, morbidity and mortality. *British Journal of Surgery* 2005; 78(2): 305-7.
4. Erturk E, Burzon DT, Oriff M, Rabinowitz R. Outcome of patients with vesicoureteral reflux after renal transplantation. The effect of pretransplantation surgery on post transplantation urinary tract infections. *Urology* 1998; 51: 27-30.
5. Argun C, Tekin MI, Peskirciloglu CL, Ozkardez H. Endoscopic treatment of vesicoureteral reflux in renal transplant candidates. *Transplant Proc* 2000; 32: 609-10.
6. Zavos G et al. Ureteropyelostomy with the recipient's native ureter: A safe and efficacious alternative in managing urological complications of renal transplantation. *Dialysis and Transplantation* 2000; 29(12): 783-94A.
7. Kasiske BL et al. The evaluation of renal transplantation candidate. Clinical practice guidelines. *American Journal of Transplantation* 2001; 1(3): 25.
8. Hatch DA. Kidney transplantation in patients with abnormal lower urinary tracts. *Urological Clinics of North America* 1994; 21: 312-20.
9. Glazier DB. Evaluation of voiding cystourethrography prior to transplantation. 1996; 62(12): 1762-5.
10. Kashi SH, Wynne KS, Sadek SA. An evaluation of vesical urodynamics before renal transplantation and its effect on renal allograft function and survival. *Transplantation* 1994; 57: 1455.
11. Kashi SH, Wynne KS, Sadex SA, et al. Post-transplant bladder recovery: A prospective randomized trial of two techniques of ureteric anastomosis. *Transplantation* 1994; 57: 1523.
12. Serrano DP. Transplantation into long-term defunctionalized bladder. *J Urol* 1996; 156: 885-6.
13. Erando C. Urodynamic evaluation and management prior to renal transplantation. *Eur Urol* 2000; 38: 415-8.
14. Hatch DA et al. Kidney transplantation in children with urinary diversion or bladder augmentation. *J Urol* 2001; 165: 2265-8.
15. Blanco M et al. Outcome of renal transplant patient with augmented bladders. *Transplant Proc* 2009; 41(6): 2382-4.
16. Landau EH, Jayanthi VR, Mclorie GA. Renal transplantation in children following augmentation ureterocystoplasty. *Urology* 1997; 50: 260.
17. Cheykovska L. Kidney transplantation into urinary conduits with ureteroureterostomy between the native and transplant ureter: Single centre experience. *Urology* 2009; 73(2): 380-5.
18. Sheldon CA, Welch TR. Total anatomic urinary tract replacement and renal transplantation: A surgical strategy to correct severe genitourinary anomalies. *Journal of Paediatric Surgery* 1998; 33(4): 635-8.
19. Brown S, Biehl TR, Rawlins, Hefty TR. Laparoscopic live donor nephrectomy: A comparison between open approach. *J Urol* 2000; 165(3): 766-9.
20. Gill IS, Carbone JM, Clayman RV, et al. Laparoscopic live donor nephrectomy. *Journal of Endourology* 1994; 8: 143-8.
21. Leadbetter GW, Monaco AP, Russell PS. A technique for reconstruction of the urinary tract in renal Transplantation Surgery. *Gynaecology and Obstetrics* 1996; 123: 839-41.
22. Lich R, Howerton LW, David LA. Recurrent urosepsis in children. *Journal of Urology* 1961; 86: 554-8.
23. Gregoir W, Van Raremorter GV. Le reflux vesicoureteral congenital. *Urology International* 1964; 18: 122.

24. MacKinnon KJ, Oliver JA, Morehouse DD, et al. Cadaver renal transplantation: Emphasis on urological aspects. *Journal of Urology* 1968; 99: 486-90.
25. Butteworth PC, Horsburgh T, Veitch PS, et al. Urological complications in renal transplantation: Impact of a change of technique. *Br J Urol* 1997; 79: 499.
26. Shah S. Evaluation of extravesical and Leadbetter-Politano ureteroneocystostomy in renal transplantation. *British Journal of Surgery* 2008; 65(5): 82-3.
27. Grunberger T, Gnant M, Sautner T. Impact of vesicoureteral rellux on graft survival in renal transplantation. *Transplant Proc* 1993; 25: 1058.
28. Hughes JD et al. Ureteropyelostomy reconstruction in renal transplantation. *Journal of Urology* 1987; 138: 459-61.
29. Mangus RS, Hagg BW. Stented versus nonstented extravesical ureteroneocystostomy in renal transplantation: A metanalysis. *American Journal of Transplantation* 2004; 4(11): 1889-96.
30. Rangunathan et al. Infective complications associated with ureteral stents in renal transplant recipients. *Transplantation Proceedings* 2009; 41(2): 162-4.
31. DuBay DA. Is routine ureteral stenting cost-effective in renal transplantation. *Journal of Urology* 2004; 178(6): 2085-91.
32. Samahan M et al. Urological complications in renal transplantation. *Transplantation Proceedings* 2005; 37(7): 3075-6.
33. Kashi SH, Lodge JPA, Giles CV, Irvine R. Ultrasonography of renal allografts: Collecting system dilatation and its clinical significance. *Nephrology, Dialysis and Transplantation* 1991; 6: 358-64.
34. Kashi SH, Sadek SA, Irvine R. Does the Whitaker test add to antegrade pyelography in the investigation of collecting system dilatation in renal allografts. *British Journal of Radiology* 1993; 63: 877-81.
35. Heaf JG, Iversen J. Uses and limitations of renal scintigraphy in renal transplantation monitoring. *European Journal of Nuclear Medicine* 2000; 27: 871-8.
36. Baghat VJ. Ureteral obstructions and leaks after renal transplantation: Outcome of percutaneous antegrade ureteral stent placement in 44 patients. *Radiology* 1998; 209: 159-67.
37. Yong AA et al. Management of ureteral strictures in renal transplants by antegrade balloon dilatation and temporary internal stenting. *Journal of Cardiovascular and Interventional Radiology* 1999; 22(5): 385-8.
38. Fontaine AB, Nijjar A, Rangaraj R. Update on the use of percutaneous nephrostomy/balloon dilation for the treatment of renal transplant leak/obstruction. *J Vas Interv Radiol* 1997; 86: 49.
39. Matalon TAS et al. Percutaneous treatment of urinary leak in renal transplant patients. *Radiology* 1990; 174: 1049-51.
40. Delpizzo JJ, Jacobs SC, Bartlett ST, et al. The use of bladder for total transplant ureteral reconstruction. *J Urol* 1998; 159: 750.
41. Benoit G, Blanchet P, Eschwege P, et al. Occurrence and treatment of kidney graft lithiasis in a series of 1500 patients. *Clin Transpl* 1996; 10: 176.
42. Challacombe B et al. Multimodal management of urolithiasis in renal transplantation. *British Journal of Urology International* 2005; 96(3): 385-9.
43. Bhaduria RPS, Ahlawat R, Vijay Kumar R. Donor-gifted allograft lithiasis: Extracorporeal shockwave lithotripsy with over table module using the lithostar plus. *Urology International* 1995; 51: 55.
44. Lu HF, Shekarriz B, Stoller ML. Donor-gifted allograft uolithiasis: Early percutaneous management. *Urology* 2002; 59: 55.
45. Rashid MG, Konnak JW, Wolf JS. Ex vivo ureteroscopic treatment of calculi in donor kidneys at renal transplantation. *Journal of Urology* 2004; 171: 58.
46. Toorans AWFT. Chronic renal failure and sexual functioning: Clinical status vs objectively assessed sexual response. *Nephrology dialysis and transplantation* 1997; 12: 2654-63.
47. Peskircioglu L, Tekin MI, Demirag A, et al. Evaluation of erectile function in renal transplant recipients. *Transplant Proc* 1998; 30: 747.
48. Swaminathan S, Kanagasabapathy AS, Selvakumar R, et al. Zinc and testicular hormone profiles before and after renal transplantation. *Nephrology* 1997; 3: 289.
49. Mansi MK, Alkhudair WK, Huraib S. Treatment of erectile dysfunction after kidney transplantation with intracavernosal self-injection of prostaglandin E1. *J Urol* 1998; 159: 1927.
50. El-Bahnasawy MS. Effect of the use of internal iliac artery for renal transplantation on penile vascularity and erectile function: A prospective study. *J Urol* 2004; 172(6): 2335-9.

51. Gittes RF, Waters WB. Sexual impotence: The overlooked complication of a second renal transplant. *J Urol* 1979; 121: 719.
52. Taylor RMR. Impotence and the use of the internal iliac artery in renal transplantation. *Transplantation* 1998; 65: 745.
53. Kabalin JN, Kessler R. Successful implantation of penile prostheses in organ transplant patients. *Urology* 1989; 33: 282.
54. Rowe SJ, Montague DK, Steinmuller DR, et al. Treatment of organic impotence with penile prosthesis in renal transplant patients. *Urology* 1993; 41: 16.
55. Muruve NA, Shoskes DA. Overview of genitourinary malignancies in solid organ transplant recipients. *Transplantation* 2005; 80(6): 709-16.
56. Maisonneuve P et al. Cancer in patients on dialysis for end-stage renal disease: An international collaborative study. *Lancet* 1993; 341: 93-9.
57. Mark DD et al. Prevalence of renal cell carcinoma in patients with ESRD pre-transplantation: A pathologic analysis. *Kidney International* 2002; 61: 2201-9.
58. Goldfarb DA, Neumann HP, Penn I, et al. Results of renal transplantation in patients with renal cell carcinoma and von Hippel-Lindau disease. *Transplantation* 1997; 64: 1726.
59. Choyke PL, Glenn GM, Walther MM, et al. The natural history of renal lesions in von Hippel-Lindau disease: A serial CT study in 28 patients. *Am J Roentgenol* 1992; 159: 1229.
60. Steinbach F, Novick AC, Zincke H, et al. Treatment of renal cell carcinoma in von Hippel-Lindau disease: A multicenter study. *J Urol* 1995; 153: 1812.
61. Noronha et al. Renal cell carcinoma in dialysis patients with acquired renal cysts. *Nephrol Dial Transplant* 1989; 4: 763-9.
62. Walther M, Choyke PL, Weiss G, et al. Parenchymal sparing surgery in patients with hereditary renal cell carcinoma. *J Urol* 1995; 153: 913.
63. Thon WF. De novo urothelial carcinoma of the upper and lower urinary tract in kidney transplant patients with end-stage analgesic nephropathy. *World Journal of Urology* 2004; 13(4): 254-61.
64. Kao Yu Lin. Transitional cell carcinoma in renal transplant recipients. *World Journal of Urology* 2003; 27(8): 208-12.
65. Banyafalger S, Maier U, Susani M, et al. High incidence of nephrogenic adenoma of the bladder after renal transplantation. *Transplantation* 1998; 65: 511.
66. Cormier L, Lechevallier E, Barrou B, et al. Diagnosis and treatment of prostate cancers in renal-transplant recipients. *Transplantation* 2003; 75: 237-9.
67. Kersten F et al. Shift of the f/t-PSA quotient in relation to renal insufficiency: Consequences for the early detection of prostate carcinoma in patients with terminal renal failure. *Anticancer Research* 2007; 27(4): 1945-48.
68. Markku TM, Ossi IL. Radical prostatectomy for localized prostatic carcinoma in a renal transplant patient. *Scandinavian Journal of Urology and Nephrology* 1998; 32(3): 221-2.
69. Kocack B et al. Is localized prostate cancer an obstacle for an immediate consideration for renal transplantation. A case report. *Transplant Proceedings* 2009; 41(5): 1961-2.
70. Nicol DL. Kidneys from patients with small renal tumours: A novel source of kidneys for transplantation. *British Journal of Urology International* 2008; 102(2): 188-92.
71. Grotemeyer D et al. Renal cyst in living donor kidney transplantation: Long term follow up in 25 patients. *Transplant Proceedings* 2009; 41(10): 4047-51.

## Authors

L. Niroshan Seneviratne, MS (Col), MRCS (Eng)  
Senior Registrar in Urology and Transplant Surgery

Neville D. Perera, MS (Col), FRCS (Eng), FRCS (Edin), DUrol (Lond)  
Consultant Urological Surgeon

Department of Urology, National Hospital of Sri Lanka, Colombo, Sri Lanka.