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Renal transplantation: technical aspects, diagnosis and management of early and late urological complications

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Renal transplantation represents actually the most effective therapy in patients with end-stage renal failure as it is cost effective, allows for a normal life style and reduces the risk of mortality from dialysis related complications. Renal transplantation can be classified in deceased- donor or living-donor transplantation, depending on the source of the donor organ. The short-term results of transplants with kidneys from donors over 65 years old are almost similar to those with younger organs, but in these patients it is mandatory to reduce cold ischemia time. In the last years, the demand for kidney transplantation has increased dramatically, which has been associated with an increase in living-donor organ procurement, which presents several advantages. Moreover, new operative techniques have been recently developed in order to improve surgical outcomes and graft survival and to reduce the complications' rate after renal transplantation. The purpose of the present review is to evaluate the published literature regarding the technical aspects and the urological complications associated with renal transplantation.

KEY WORDS: Kidney transplantation - Kidney failure, chronic - Outcome assessment (Health Care).

Renal transplantation has been widely accepted as the most effective form of renal replacement in patients with end-stage renal failure (ESRD). The procedure is performed on patients ranging in age from 12 months to 75 years. Approximately 20% of all children and 5% of all adults with ESRD have renal failure secondary to urological disease. Urological diseases in children include vesicoureteric reflux (40%), posterior urethral valves (40%), and prune belly syndrome (10%).[1]

Chronic pyelonephritis represent the primary urological condition in adults that leads to ESRD. It is therefore not surprising that renal transplant recipients of all ages are regularly assessed both before and after transplantation by a urologist.[2] Actually, renal transplantation should be offered to all patients with advanced and irreversible renal failure, comprising stage IV disease with a glomerular filtration rate of under 30 mL/min/1.73 m^2. Nevertheless, while the number of organs available for transplantation is limited, the number of patients with ESRD is increasing.[3-5]

Renal transplantation can be classified in deceased-donor or living-donor transplantation, depending on the source of the donor organ.

In the last years, the demand for kidney transplantation has increased dramatically, which has been associated with an increase in living-donor organ procurement. Most organs still come from deceased donors, brain-dead donors, and from the non-heart-beating donor (NHBD) procurement program, which is now used by several transplant centers.[6] Generally, the gap between the supply and demand of kidneys has tended to stabilize in countries with a donation rate greater than 40 kidneys per million population, but has increased in countries with a lower donation rate. The elderly donors (>60 years) and the living-donors represent a valid solution to this problem. Moreover, the advantages of live-donor renal transplantation are several.

First, cold ischemia time is significantly shorter

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than in cadaveric-donor kidney transplantation and thus there is an almost complete absence of ischemic injury to the transplanted kidney. This results in a relative insensitivity to poor tissue matching and better long-term function. Second, kidneys harvested from living donors represent perfect organs from perfectly healthy donors, ensuring a better graft and recipient survival compared with human leukocyte antigen (HLA)–matched cadaveric transplants. Third, live-donor nephrectomy (LDN) reduces the waiting time for the recipient and therefore allows renal transplantation earlier, with the recipient still in better general condition and health.[7-9]

The purpose of the present review is to evaluate the published literature regarding the technical aspects and the urological complications associated with renal transplantation.

Materials and methods

A comprehensive literature review was performed using PubMed and Thomson-Reuters Web of Science between May 1976 and February 2014. Using free-text protocol, the following terms were applied: chronic kidney failure, renal transplantation, medical workup, laparoscopy, living donor nephrectomy, surgical techniques, urological complications.

Review articles, editorials, commentaries, and letters to the editor were included only if deemed to contain relevant information. In addition, cited references from the selected articles and from review articles retrieved in the search were assessed for significant manuscripts not previously included. Subsequently, studies published only as abstract or presented without abstract, and reports from meetings and studies not published in English were not included in the review.

The authors selected 100 articles according to the search strategy based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses Criteria (PRISMA) [10] (Figure 1).

Results

Technical aspects

Since the first successful renal transplantation,[11] surgical techniques have steadily improved and made it possible for most patients with ESRD to undergo renal transplantation. When compared to maintenance hemodialysis, renal transplantation is preferred by most patients with ESRD as it is more cost effective, allows for a normal life style and reduces the risk of mortality from dialysis related complications. Survival rates for renal transplantation have improved over the last two decades.[12, 13]

The short-term results of transplants with kidneys from donors over 65 years old are almost similar to those with younger organs. However, long-term graft survival is lower.[14] In addition, the main physiological risk factor in "older" kidneys is a prolonged cold ischemia time.[15, 16] In keeping with these observations, the modern definition of a suitable donor places less emphasis on age and more on the physical condition of the donor, especially of the organ to be donated. The aim is to reduce the possibility of discarding usable organs. Thus, there are now no absolute age limits to donation. However, a short ischemia time is mandatory, as well as careful donor selection, particularly because older donors have more comorbidity. There is a similar trend towards extending the upper age donation limit in living donors to over 55 years old.[17]

The pre-transplant evaluation evaluates potential contraindications and risk factors for transplantation.

In patients, whose ESRD is caused by either a congenital (*i.e.*, posterior urethral valve, spina bifida, prune belly syndrome, vesico-renal reflux, bladder exstrophy, VATER syndrome) or an acquired malformation (shrunken or neurogenic blaer) of the lower urinary tract, the abnormality should be corrected before transplantation.[18, 19] In patients with sphincter insufficiency (*e.g.*, neurogenic bladder) or absent bladder, supravesical urinary diversions must be performed, such as conduits or continent catheterisable pouches. Artificial sphincters may be an alternative. In low-compliance bladders, pharmacological therapy (*e.g.*, parasympathicolysis), with or without intermittent self-catheterisation, is necessary. If these methods fail, bladder augmentation and continent pouches are successful alternatives following transplantation.[20, 21]

A laparoscopic bilateral nephrectomy should be considered in presence of poorly controlled hypertension, heavy proteinuria, and recurrent urinary tract infections associated with vesicoureteral reflux.[22] Unilateral or bilateral nephrectomy is also necessary, if there is not enough space for the trans-

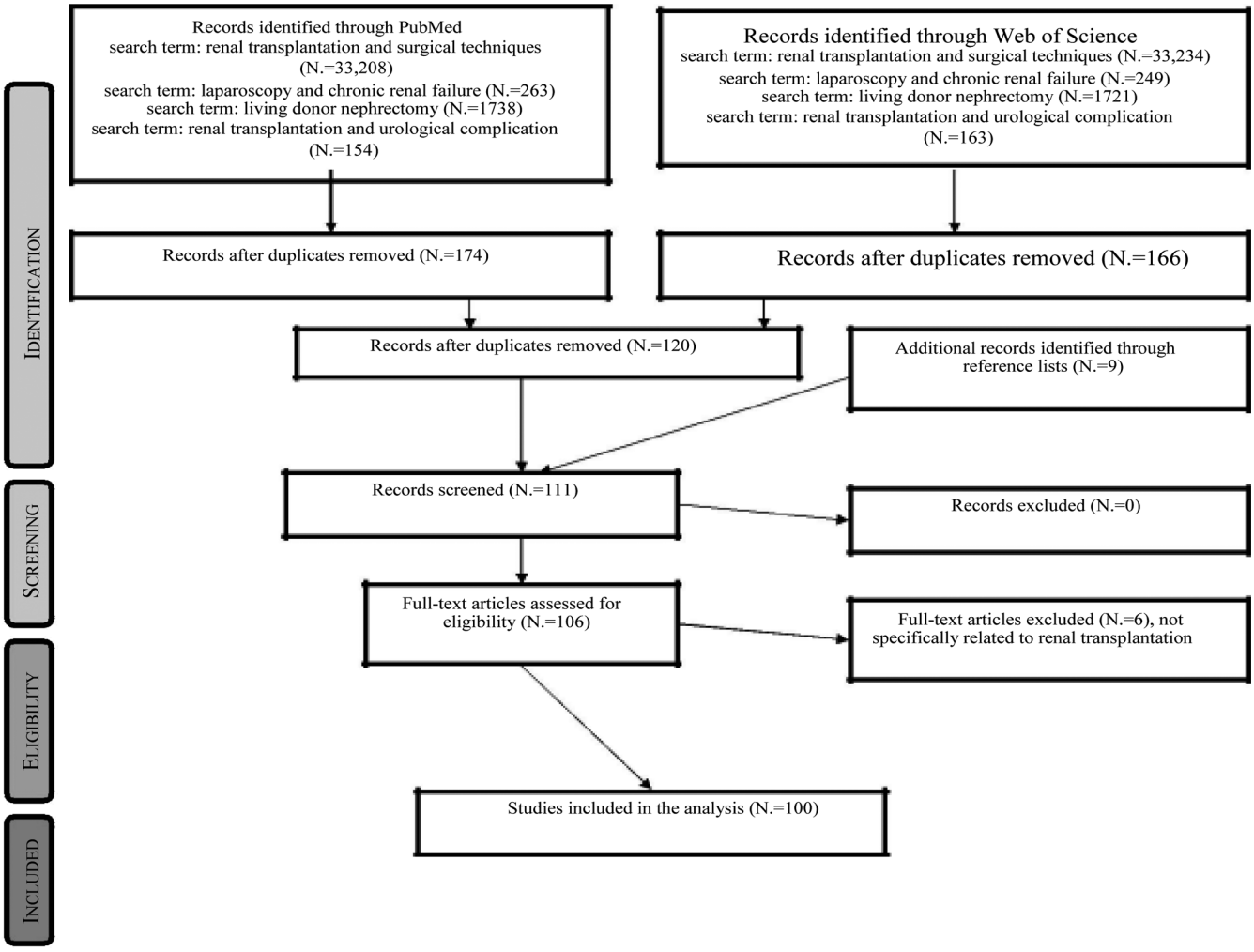

Figure 1.—The authors selected 100 articles according to the search strategy based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses Criteria (PRISMA).

plant kidney, or if there are complications, such as cyst infection, cyst rupture with/without haematuria, pain, or abdominal girth.[6]

All potential donor must be checked for infectious diseases, malignant tumors, vascular conditions and risk factors such as age, renal diseases, peripheral artery disease, cerebral occlusive vascular disease, diabetes mellitus, obesity, coagulopathies, psychiatric diseases.[6]

Infections, which should be considered as a possible exclusion criteria for renal transplantation, include human immunodeficiency virus-1, -2 (HIV-1, HIV-2), hepatis C (HCV), hepatitis B surface antigen (HBsAg), anti-HBc, acute hepatitis, cytomegalovirus (CMV), Epstein-Barr virus (EBV) (only in pediatric recipients), active syphilis, viral infection, sepsis, tuberculosis, infections of unknown etiology. Nevertheless, in an HCV-positive recipient, transplant is allowed following informed consent.

A previous history of malignancy is not usually a contraindication for organ donation. However, there are some absolute contraindications that make a donor unsuitable for transplant. These are active cancer or a history of metastatic cancer and cancers with high recurrence rates, such as advanced breast carcinoma, melanoma, leukemia, or lymphoma. With other cancers, if less than 10 years has elapsed since completion of treatment, a careful risk-benefit as-

sessment must be done of the risk of disease transmission versus mortality on the waiting list. The donor shortage has led to many transplant programs accepting donors after only 5 years' absence of recurrent malignancy.[23]

Successful renal transplants have been performed with kidneys affected by small, low-grade renal carcinomas that were completely excised. Recipients of organs from donors with a history of malignancy must be informed and carefully monitored.[24]

Important risk factors for organ failure are a prolonged history of diabetes mellitus or serious hypertension with retinal vascular damage. Factors for excluding potential donors or for considering a donor as a single- rather than a multi-organ donor include:

— previous myocardial infarction;
— coronary bypass and angina;
— severe systemic vascular disease;
— events of long-lasting hypotension;
— oliguria;
— long-lasting intensive care stay.

Acute renal failure is not itself a contraindication but these kidneys may be used after careful assessment.[25]

A short life expectancy and conditions that interfere with compliance (*e.g.*, severe psychiatric disease) are not acceptable risks for long-term success of transplantation.

As a result of the shortage of kidneys for transplantation, the increasing demand for transplantable grafts and the increasing numbers of elderly patients, the use of kidneys from older donors has become widely accepted.[25-27]

Dual kidney transplantation

There is a well known and amply demonstrated negative effect of an age-related low nephron mass on graft survival, especially in kidneys transplanted from "expanded criteria" donors. This carries an inherent risk of poor long-term outcome, but has been balanced by transplanting both donor kidneys into a single recipient (dual kidney transplantation, DKT).[6, 28]

Although no randomized prospective studies comparing the results of single and dual kidney transplantation from elderly donors have been published, several authors have reported acceptable graft survival and renal function with the utilization of DKT, sometimes when those kidneys have been considered unacceptable to others.[28-32]

The rationale for dual marginal kidney transplantation is based on two conflicting concepts. Firstly, kidneys with a small nephron mass undergo hyperfiltration and glomerular hypertension, which causes progressive glomerulosclerosis.[33] A single marginal kidney has a reduced renal mass and a suboptimal number of nephrons, which are further reduced by cold ischemia time, transplant trauma, and the potential nephrotoxicity of immunosuppressive therapy. Simultaneous transplantation of both kidneys to the same recipient may increase nephron mass and prevent kidney damage.

Secondly, marginal kidneys have a functional reserve only verifiable after transplantation. In addition, the glomerular filtration rate of a transplanted kidney often increases post transplant.[34-36] Dual transplantation is redundant because it shortens the organ pool.

These two opposing concepts would seem to suggest that kidneys judged unsuitable based on function or histology should either both be transplanted into a single recipient or both be discarded.[37]

However, if the kidneys are appropriately evaluated,[38] DKT represents a means of increasing the number of transplants performed by widening the donor pool.

More than a decade after the first report of DKT from an adult deceased donor,[39] many centers now perform DKT using various organ selection criteria and surgical techniques,[40-44] including the extra- or intraperitoneal bilateral placement of the two kidneys [41-44] through two separate Gibson incisions or one midline incision.[42-44]

In 1998, Masson *et al.*,[45] were the first to transplant both adult donor kidneys unilaterally (monolateral or ipsilateral) into the same iliac fossa. Their reasoning was that this would reduce the surgical trauma and thus facilitate the immediate postoperative recovery of the patient, and also leave the contralateral iliac fossa intact for a further transplantation procedure in the event of graft loss. Extraperitoneal unilateral placement through a single Gibson incision presents several technical hurdles, such as more extensive vessel dissection and a higher risk of renal vein thrombosis (RVT) due to compression by the two kidneys.

Therefore, surgeons are often reluctant to perform the unilateral technique in DKT due to technical doubts and potential surgical complications, which could lead to graft loss.

Moreover, the small numbers of published studies with limited or no explanation of technical details,[46, 47] and the relatively small number of transplants performed unilaterally [46, 48] do not encourage those who may wish to perform DKT using the unilateral approach.

However, unilateral placement of both kidneys considerably reduces the operating time and surgical trauma (using a single Gibson incision) in comparison to standard DKT techniques.[28, 49]

In 2007, Kayler *et al*. described an alternative technique for UDKT in patients with minimal abdominal vascular access [50] in which the renal arteries of the right and left donor kidneys were anastomosed end-to-end to the donor's internal iliac artery and external iliac artery of an iliac Y-graft on the back table. Thereafter, the common iliac artery of the Y-graft was anastomosed to the recipient's external iliac artery end- to-side. A contraindication to this technique is represented by the atherosclerosis which characterizes many marginal donors, making it impossible to use an iliac artery graft. In addition, such a technique can only be applied if each kidney has only one renal artery. In such cases, the unilateral technique should be converted to a standard bilateral technique.

Moreover, Stratta *et al*.[43] have documented the potential risk of DKT in recipients >60 years old due to the longer period of anesthesia required and the surgical risks associated with the longer bilateral DKT procedure, suggesting only patients <60 years of age for DKT.

Laparoscopic living-donor nephrectomy

Laparoscopy has revolutionized the field of surgery. Many procedures previously performed with the open technique are now being performed with the laparoscopic approach. Decreased pain, shorter hospital length of stay, and a lower incidence of wound infections are some of the benefits associated with laparoscopy.[51] Similarly, organ transplantation has revolutionized the care for many patients with end-organ failure. As scientific advancements progress, a select group of solid-organ recipients can be candidates and receive the well-known benefits of laparoscopic procedures.[52]

Since the early 1990s, laparoscopic techniques have been successfully adapted for various open urologic procedures, including laparoscopic living-donor nephrectomy (LLDN) which was first described in 1995.[53, 54] Because laparoscopy is generally considered to be less invasive than open surgical techniques, laparoscopy may be preferable if it can be demonstrated to achieve the same result with the same safety for the patient. While pure laparoscopic donor nephrectomy is feasible, some surgeons for reasons of safety prefer hand-assisted laparoscopy for living-donor nephrectomy (LDN),[55] with either a trans- or retroperitoneal approach. With the introduction of laparoscopy into LDN, some centers have reported an increase in the numbers of renal transplants from living donors.[9, 56-58] For the United States, the United Network of Organ Sharing (UNOS) reported that in 2005, 83% of all LDNs were performed laparoscopically.[59]

Selecting an appropriate donor for LDN requires a careful evaluation and the involvement of various medical disciplines. Prospective donors need to be of good general health and at low risk of co-morbidity resulting from removal of one kidney. Thus all acute and chronic diseases, including malignancy, need to be ruled out. In addition, a prospective donor has to be fit to undergo surgery and have acceptable renal anatomy, including the vascular supply.[60, 61]

Irrespective of the chosen technique of LDN, the left kidney is generally preferred for renal transplantation by most surgeons because of its longer vein, which facilitates the vascular anastomotic procedure.[9, 53, 54, 62-66] The right kidney is selected when significant anatomic variations of the left renal vascular supply are seen on preoperative donor angiography,[9, 53, 54, 67-70] or if split renal function on nuclear scintigraphy is <40% in the right kidney, according to the principle that the kidney with the better function remains with the donor.[67-70]

The use of live-donor kidneys with double renal arteries has increased and this anomaly is no longer considered a contraindication since it can be transplanted with a minimal risk of technical failure.[9, 70, 71]

In 2010 Greco *et al*.[9] have demonstrated that both laparoscopic and open (OLDN) techniques of donor nephrectomy have comparable complications and equal functional graft outcomes. Laparoscopic techniques of donor nephrectomy may have advantages in postoperative recovery and duration of pain, but these differences are difficult to quantify and difficult to assess in their impact on long-term outcome. Laparoscopic techniques of donor nephrectomy have reported disadvantages in terms of longer operating time (OPT) and longer warm ischemia time (WIT).

However, the available evidence suggests that the longer WITs do not result in reduced graft function or survival, with the caveat that follow-up for transplantations following laparoscopic donor nephrectomy is still considerably shorter than for the open donor techniques.

Based on the actual evidence, both LLDN and OLDN can be considered standard of care in experienced hands. LLDN seems to offer advantages in terms of measured blood loss, postoperative analgesic requirements, and length of hospital stay, and disadvantages in terms of surgical time and WIT. Whether the advantages outweigh the disadvantages cannot be assessed definitively at present long-term follow-up data on graft survival and randomized clinical trials comparing OLDN and LLDN are missing and will require further evidence. Thus, at present, individual judgment and experience will determine the technique.

The robotic-assisted approach has been used in several centers to procure the living donor kidneys with good results. This technique offers the advantage of replicating the movements of the surgeon's hands with the robotic instruments, which allows the use and application of well-known open surgical techniques to the laparoscopic approach. The lack of studies, the cost of the robot and the increased operative time represent the main disadvantage of this technique.

Laparoscopic renal transplantation

Studies on laparoscopic renal transplantation are still few and limited to case reports or studies with low level of evidence.

In 2001, Meraney *et al*.[72] have performed the first laparoscopic renal autotransplantation in animal models, obtaining good results and considering vascular anastomoses to be feasible in laparoscopic surgery when performed by expert hands. Moreover, laparoscopic urterovesical reimplantation is already considered a valid alternative to open surgery for reconstructive urologicl surgery.[73]

In 2002, Hoznek *et al*.[74] have reported a case of robot-assisted laparoscopic renal transplantation, using the robotic system only to perform the vascular and ureteral anastomosis and demonstrating the feasibility of robotic assisted kidney transplantation.

The first laparoscopic transplantation of a kidney from a living donor has been described in 2009 by Rosales *et al*.[75] The authors explain the advantages of a laparoscopic approach by reducing the surgical trauma and the morbidity owing to the small surgical incisions.

Actually, laparoscopic renal transplantation is still a very complex technique, which can be performed only in well selected patients.

Urological complications: diagnosis and management

In the early era of kidney transplant, surgical complications are a major cause of graft loss. With the improvement of surgical techniques, the frequency of these complications has dropped significantly and currently, it is estimated that in large transplant centers the incidence of surgical complications is less than 5%. Post-transplant urologic complications are unusual, with the range of 2.5% to 27% in most series, and can cause significant morbidity and mortality. Urologic complications are the most common surgical complication after renal transplantation, causing significant morbidity and mortality. Results have improved over the past decade as a direct application of less invasive endourologic diagnostic and therapeutic techniques of the surgical complications.[76]

Urological complications following renal transplantation can be divided in early and late complications.

Early complications (Table I) include: general complications (wound healing, haemorrhage, haematuria, incisional hernia); urinary fistula; arterial thrombosis; venous thrombosis.

Late complications (Table II) include: ureteral obstruction; reflux and acute pyelonephritis; kidney stone; transplant renal artery stenosis; arterio-venous fistulae and pseudo aneurysms after renal biopsy; lymphocele.

Early urological complications

General complications.—Wound complications after kidney transplantation are a frequent occurrence, and although they do not generally affect graft or patient outcomes, they are a considerable source of morbidity, delaying hospital discharge and requiring re-hospitalization or re-operation in up to a third of cases.[77]

The experience of the surgeon and co-morbidities play an important role in determining the risk of such complications occurring. Since the introduction of mycophenolate mofetil to the immunosuppres-

TABLE I.—*Early urological complications.*

Complications	Risk factors	Diagnosis	Therapy
General complications:			
- Wound complications	Surgical, experience, co-morbidities, obesity, immunosuppressive therapy	Physical examination	Medical for small lesions without infections Surgical for big lesions with infection
- Hemorrhage and hematuria	Acetylsalicylic acid, poorly prepared transplant hilus, multiple renal arteries, renal biopsies and hyper-acute rejection	Physical examination, blood test, sonography, CT	Large hematoma or active bleeding requires surgical drainage
- Incisional hernia	Age, obesity, diabetes, hematoma, rejection, re-operation through transplant incision and finally m-TOR inhibitors	Physical examination, CT	If symptomatic, hernioplasty with or without synthetic mesh
Urinary fistula	Ischemic necrosis of the ureter	Biochemical analysis of the liquid, abdominal ultrasound and nuclear renal scan, cystography	Placing nephrostomy and/or a vescical catheter and double J-stent; uretero-ureteral anastomosis; Ureteroneocystostomy; polar nephrectomy and omental plasty
Arterial thrombosis	Atherosclerosis, unidentified intimal rupture, poor suture technique, kinking if the artery is longer than the vein or the anastomosis is incorrectly sited, multiple arteries, and pediatric transplants	Physical examination, DMSA renal scintigraphy, by ultrasound Doppler, and even with arteriography	Immediate surgical exploration, nephrectomy
Venous thrombosis	Angulation of the renal vein or anastomotic stricture, dehydration, venous compression by lymphocele or hematoma, progression of ipsilateral iliofemoral thrombophlebitis, nephropathy	Hematuria, or anuria and is diagnosed by Doppler or technetium scan	Thrombectomy, transplantectomy

TABLE II.—*Late urological complications.*

Complications	Risk factors	Diagnosis	Therapy
Ureteral obstruction	Multiple arteries, donor's age, cold ischemia time, delayed graft function, and CMV infection	Physical examination, blood test, ultrasound, antegrade pyelogram	Percutaneous nephrostomy, ureteral meatotomy, percutaneous ureteral dilation, ureteral stent, ureteroneocystostomy, ureteropyelostomy, ureteroureterostomy
Reflux and acute pyelonephritis	Surgical procedure, lower urinary tract infections	Physical examination, blood test, ultrasound, cystography	Endoscopic injection, uretero-ureteral anastomosis, ureterovesical re-implantation
Kidney stone	Urinary infection, ureteral obstruction	Physical examination, blood test, ultrasound non-injected CT scan	Ureteral stent or percutaneous nephrostomy, ESWL, percutaneous, open nephrolithotomy; ureterolithiasis
Transplant renal artery stenosis	Donor and recipient age, expanded criteria donor, delayed graft function, ischemic heart disease and induction immunosuppression	Physical examination Doppler sonography	Medical treatment, transluminal dilatations, with or without stenting, open surgery
Arterio-venous fistulae and pseudo aneurysms after renal biopsy	Infection, surgical technique	Doppler ultrasound MRI, angiography	Angiography, selective embolisation
Lymphocele	Surgical technique obesity, immunosuppressant agents	Physical examination ultrasound, CT	Conservative, percutaneous drainage, laparoscopic/open surgery

sive armamentarium, replacing the antimetabolite prodrug azathioprine, reports have associated certain forms of wound healing complications (wound dehiscence, impaired healing, lymphocele, and incisional hernia) with the use of these agents. When mammalian target of rapamycin (mTOR) inhibitors (sirolimus, everolimus) became available, these findings have been observed increasingly.

Meticulous surgical technique, a cautious use of m-TOR inhibitors in obese patients (BMI>32 kg/m^2), and avoidance of high exposure to m-TOR inhibitors, coupled with close monitoring, can ensure that wound healing disorders remain infrequent and do not disrupt the patient's recovery.[77]

Risk factors for haemorrhage include acetylsalicylic acid, poorly prepared transplant hilus, multiple renal arteries, renal biopsies and hyper-acute rejection. A large haematoma or active bleeding requires surgical drainage. Following drainage, the ureterovesical anastomosis must be checked and an ureteral stent may be inserted.[6]

After transplant biopsy, an arterio-venous fistula (AVF) can occur. Selective percutaneous embolisation is necessary for large AVF and for recurring haematuria. Clotting may cause ureteral obstruction, increasing the risk of hematuria. Dialysis may be necessary if ureteral stenting or percutaneous nephrostomy are ineffective.[78]

Risk factors for incisional hernia include age, obesity, diabetes, haematoma, rejection, re-operation through transplant incision and finally m-TOR inhibitors. In presence of symptomatic incisional hernias, an hernioplasty with or without synthetic mesh has to be suggested.[6, 79, 80]

Urinary fistula.—Urinary fistulae are the most common early complication. They occur in 3-5% of cases in which a double J-stent has not been used. They can occur on the ureter, bladder, or parenchyma. The most frequent cause is ischaemic necrosis of the ureter.[6, 81, 82]

For being the most common surgical complication of kidney transplantation, urinary fistula is easily diagnosed. In doubtful cases, where there is need to exclude the lymphocele as main differential diagnosis, biochemical analysis of the liquid is characterized by having elevated levels of creatinine, urea and potassium.

Urinary leak are often suspected because of increased drainage from the wound.

Early urinary leaks can be divided into two types: the first usually occurs within the first 1 to 4 days and is almost always related to technical problems with the implantation. In this case, the ureter has usually pulled out of a tunnel caused by excessive tension at the anastomosis. This complication appears to be more common with the extravesical ureteroneocystostomies without ureteral stent.[83]

The second type of early ureteral leak, usually presents between 5 and 10 days, is associated with distal ureteral ischemia, which may be a consequence of injury during the donor nephectomy, technical causes such as tunnel hematoma or distal stripping of the blood supply.[84]

Radiographic tests of help include an abdominal ultrasound and nuclear renal scan. The ultrasound is nonspecific for evaluating patients with suspected urinary fistula after kidney transplantation as it can only reveal a fluid collection (anechoic image) around the graft. A renal scan demonstrating extravasation is the most sensitive method to differentiate a urine leak from other fluid collections such lymphoceles or hematomas. A cystography should be performed if a bladder leak is suspected.

If it is possible to localize the fistula, it is worth trying nephrostomy and/or a vesical catheter and double J-stent. Stented re-implantation is possible if necrosis is very distal and the ureter is long enough. Percutaneous techniques like nephrostomy associated to antegrade ureteral stenting works in 40% of a much selected group of patients presenting with small fistulae from the distal ureter. Otherwise uretero-ureteral anastomosis is performed using the patient's original ureter. Nevertheless, this technique can results in ureterohydronephrosis of the native kidney after ureter ligation for reconstruction. Ureteroneocystostomy *de novo* is used for reimplantation defects or for small distal ureteral necrosis and it remains an important option for urinary fistulae management. Vesical fistulae can be treated by suprapubic or transurethral catheter. Calyceal fistulae may be treated by DJ-stent and vesical catheter. In most cases, polar nephrectomy and omental plasty are necessary.[6, 85]

Mortality directly related to the fistula or to its correction was high in the early transplantation era and nowadays is reported to range from 0% to 8%.[85]

Arterial thrombosis.—The incidence of arterial thrombosis is 0.5% in the first post-operative week.

Risk factors include atherosclerosis, unidentified intimal rupture, poor suture technique, kinking if the artery is longer than the vein or the anastomosis is incorrectly sited, multiple arteries, and paediatric transplants. It should be suspected if there is primary non-function or sudden anuria.[6, 86, 87]

The hallmark of renal artery thrombosis is the absence of blood perfusion of the parenchyma, which can still be identified intra-operatively. In the post-operative period the most common clinical presentation is the sudden interruption of urinary flow, without pain in the graft. The renal perfusion should be evaluated by DMSA renal scintigraphy, by ultrasound Doppler, and even with arteriography, if needed.[88] The immediate surgical exploration may allow in a few cases, revascularization and recovery of the graft, especially if the diagnosis of arterial thrombosis is done before closing the incision. The loss of the graft is the most common consequence and nephrectomy should be performed.

Venous thrombosis.—Venous thrombosis is rare, occurring in 0.5% of kidney transplants in adults and in 2.5% in paediatric patients. As causative agents related are: angulation of the renal vein or anastomotic stricture, dehydration, venous compression by lymphocele or hematoma, progression of ipsilateral iliofemoral thrombophlebitis should also be considered. Late cases of renal vein thrombosis have been associated with recurrence of membranous nephropathy. It is suspected by primary non-function, haematuria, or anuria and is diagnosed by Doppler or technetium scan. Salvage thrombectomy has a very poor success rate and transplantectomy is often necessary.[89, 90]

Late urological complications

Ureteral obstruction.—Ureteral obstruction and ureteral leakage are the most common urinary complication after renal transplantation with an incidence of 3-8%.[91]

There are three causes of ureteral dilatation: 1) vesical high pressure with thickened bladder wall or urinary retention, which is treated by bladder drainage; 2) vesicorenal reflux, which is not an obstruction; 3) ureterovesical stenosis due to scar formation and/or poor surgical technique. These comprise 80% of ureteral stenoses. Most occur during the first year post transplant, although the risk of occurrence increases with time to 9% of transplant patients at 10 years. Risk factors include multiple arteries, donor's age, cold ischemia time, delayed graft function, and CMV infection.[6]

The clinical presentation includes pain over the surgical site, decreased urine volume leading to oligoanuria and rise in blood pressure secondary to impaired renal function.

Diagnostic tests shows gradual rise in serum creatinine. The ultrasound demonstrates pyelocaliectasis or ureteropyelocaliectasis in most of cases. Nuclear scintigraphy is less sensitive because the obstructed kidney also displays impaired radionuclide uptake, a sign often present in allograft rejection. When the diagnosis is unclear the antegrade pyelogram must be performed in order to determine the level of stenosis, degree, and length.[92]

The treatment must be instituted as early as possible to avoid loss of renal graft function.

Initially the percutaneous nephrostomy must be done to restore renal function to normal. Afterwards, stenosis ureteral at the site of bladder reimplantation can be addressed by several endourology techniques such as ureteral meatotomy or percutaneous ureteral dilation with balloon followed by implant of stent at the ureter.

However, open surgery is still considered the gold standard. In distal ureteral obstructions a ureteroneocystostomy by extravesical Lich-Gregoir modified techniques can be performed.

When there are multiple, long stenosis of the ureter or even poor vascularization, it is necessary to perform the anastomosis of the renal pelvis with the host ureter (ureteropyelostomy) or the ureter with the host ureter (ureteroureterostomy). However, the last technique has a higher rate of stenosis. When the native ureters cannot be used, the "Boari flap" should be done joining the short ureteral stump or the renal donor pelvis, allowing an adequate distance to the bladder.

Reflux and acute pyelonephritis.—Acute pyelonephritis is a rare complication, whereas reflux in the renal cavity is more common.[6]

Reflux is found in 80% after Lich-Gregoire if the submucosal tunnel is short and in 10% if the tunnel is long. In lower urinary tract infections, the risk of acute pyelonephritis is 80% with reflux and 10% without reflux. Every reflux complicated by acute pyelonephritis should be treated with an endoscopic

injection. This has a success rate of 30-78%. If this fails, try using a uretero-ureteral anastomosis if the native ureter is not refluxive, or a ureterovesical reimplantation with a long tunnel if the original ureter is refluxive or non-usable.[93]

Kidney stone.—Kidney stones may be transplanted with the kidney or may be acquired. The incidence is less than 1% of transplants. The stones manifest themselves by haematuria, infection, or obstruction. Diagnosis may require non-injected CT scan. Some stones are eliminated spontaneously, but if stones do need to be removed, there are several options: 1) initially a ureteral stent or percutaneous nephrostomy should be placed; 2) calyceal and smaller renal stones should be treated by extracorporeal shock wave lithotripsy (ESWL); 3) larger stones should be removed by percutaneous or open nephrolithotomy; 4) ureterolithiasis should be treated by ESWL or by ureteroscopy.[94]

Transplant renal artery stenosis.—Transplant renal artery stenosis (TRAS) has an incidence of 10% (range, 1-23%). TRAS risk factors are donor and recipient age, expanded criteria donor, delayed graft function, ischemic heart disease and induction immunosuppression. It is suspected when existing arterial hypertension becomes refractory to medical treatment and/or there is an increase in serum creatinine without hydronephrosis. It is diagnosed by Doppler sonography showing high velocity >2 m/s. Treatment options include medical treatment and renal function follow-up, with interventional treatment indicated if the stenosis is >70%. Transluminal dilatations, with or without stenting, give poorer results (70%) than open surgery, which is reserved for plication or anastomotic stenosis, failure of percutaneous dilatation, and involves resection with direct implantation.[95, 96]

Arterio-venous fistulae and pseudo aneurysms after renal biopsy.—Arterio-venous fistulae are seen in 10% (range, 7-17%) of cases and are suggested by repeated hematuria. Diagnosis is by Doppler ultrasound and is confirmed by MRI or by angiography. Angiography is also the first step in treatment. Fistulae may regress spontaneously, but when persistent haematuria or when diameter >15 mm, selective embolisation should be used. Pseudo aneurysms are often due to mycotic infection and can be fatal.[6, 97]

Lymphocele.—Lymphocele comprises 1-20% of complications and it is associated with inadequate ligation of the delicate lymph vessels overlying the iliac vessels or present in the hilum. The method of renal uptake also appears to influence the appearance of lymphatic complications. Obesity and the use of some immunosuppressant agents such as m-TOR inhibitors are associated with a higher risk of lymphocele.[6] The diagnosis is confirmed by ultrasound which may show hydronephrosis, altered vascular flow by Doppler and quantify the lymphocele or the presence of other collections such as hematoma or urinoma. In cases of doubt about the aetiology, a computerized axial tomography (CT) can be performed.[98] Generally, it is asymptomatic, but there may be pain caused by ureter compression or infection. Percutaneous drainage is necessary for mild lymphocele or if there is no compression of the iliac vessels or the transplant ureter. Otherwise, laparoscopic marsupialisation is the treatment of choice and open surgery is indicated only in presence of contraindications to laparoscopy.[99, 100]

Conclusions

Renal transplantation represents actually the most effective therapy in patients with end-stage renal failure as it is cost effective, allows for a normal life style and reduces the risk of mortality from dialysis related complications. The short-term results of transplants with kidneys from donors over 65 years old are almost similar to those with younger organs, but in these patients it is mandatory to reduce cold ischemia time as well as careful donor selection, particularly because older donors have more co-morbidity. DKT represents a valid form of renal transplantation in kidneys with age-related low nephron mass, reporting acceptable graft survival and renal function also in kidneys considered unacceptable to others. Similarly to other surgical disciplines, laparoscopic procedures have been introduced and applied for renal transplantation. Nowadays, LLDN presents comparable complications and equal functional graft outcomes to open surgery, by offering advantages in terms of measured blood loss, postoperative analgesic requirements, and length of hospital stay. On the contrary, laparoscopic renal transplantation is still a very complex technique, which can be performed only in well selected patients.

Concerning the urological complications, they represent the most common surgical complication after

renal transplantation, causing significant morbidity and mortality. Nevertheless, the frequency of these complications has dropped significantly and results have improved over the past decade as a direct application of less invasive endourologic diagnostic and new therapeutic surgical techniques.

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