Surgical aspects of renal transplantation
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Citation for published version (APA):

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The prevalence of end-stage renal failure in the Netherlands is 70 per 100 000 residents. The number of kidney transplantations in the Netherlands and at the Academic Medical Center, Amsterdam is shown in Figures 1 and 2. Kidney replacement therapy consists of dialysis and/or kidney transplantation. Haemodialysis and peritoneal dialysis can lead to long-term survival and may bridge patients to kidney transplantation. When compared with long-term dialysis, kidney transplantation increases survival and improves quality of life. Therefore, kidney transplantation is the therapy of choice for end stage renal disease. Kidney allografts are procured from both living and deceased donors. Living donation and pre-emptive transplantation in particular, result in better patient and allograft survival than does deceased donor transplantation.

History
In 1902 the first successful experimental kidney transplants were performed at the Vienna Medical School in Austria. Emerich Ullmann (1861-1937) transplanted a kidney from one dog to another. A few years later in 1906, Mathieu Jaboulay (1860-1913), professor of Surgery in Lyon, France, connected the renal vessels of a sheep's and a pig's kidney, respectively, to the brachial vessels of two patients who were dying of renal failure. Neither kidney functioned, but these were the first transplants, albeit xenografts, to be placed in humans. The techniques used to join the vessels together during transplantation were those developed...
and described by Alexis Carrel (1873-1944), who was a young surgeon in Jaboulay’s unit, and in fact, the techniques of vascular anastomosis described by Carrel are exactly the same as those still in use in kidney transplantation today\textsuperscript{10}. For these efforts, Carrel was awarded the 1912 Nobel Prize in Physiology or Medicine.

In 1936, the first deceased human kidney transplant was performed by Yu Yu Voronoy in Kherson, Ukraine\textsuperscript{11}. The donor kidney was obtained from a patient who had died after a head injury. The kidney never functioned due to an ABO blood type incompatibility. The patient died two days later. In 1954, the first successful kidney transplant between identical twins was performed by the surgeons Joseph E. Murray and J. Hartwell Harrison in the Peter Bent Brigham Hospital in Boston, USA\textsuperscript{12}. The recipient lived another seven years with this well-functioning transplanted kidney before dying of heart failure. Murray won the Nobel Prize in Physiology or Medicine in 1990. In the early 1960s successful deceased kidney transplantation was made possible by the development of the first effective drug to prevent rejection, azathioprine\textsuperscript{13}. In 1966, the first Dutch kidney transplantation was performed in Leiden by Prof. J.L. Terpstra. The recipient received his kidney from his mother\textsuperscript{14}. The 1980s and 1990s were characterised by the advent of a series of completely new immunosuppressive agents, which were used either alone or with the drugs already in use, i.e. azathioprine and prednisone. These drugs greatly improved long-term survival of the transplanted kidney\textsuperscript{15}.

Over the past decades, an increasing number of patients suffering from renal insufficiency and a stagnating number of transplants have resulted in a discrepancy between organ demand and organ supply. The excellent results of live donation have brought a dramatic increase in the numbers of living donor kidney transplantations. New surgical techniques have been developed to decrease harm to the donor and to speed up their convalescence. In recent years, minimally invasive procedures in removing donor kidneys have gained widespread acceptance and have replaced the open technique. The most commonly applied techniques are the hand-assisted and the total laparoscopic donor nephrectomy.

Figure 2. Kidney transplantation in the Academic Medical Center, Amsterdam (1986-2008)
**Current issues in renal transplant surgery**

*Hand-assisted laparoscopic donor nephrectomy*

Several surgical techniques have been described for taking a renal allograft from a live donor. The classical open donor nephrectomy is carried out retroperitoneally through a lumbotomy incision below the 12<sup>th</sup> rib. Disadvantages of this technique are a long hospital stay, prolonged postoperative pain, cosmetic problems and slow convalescence. Long-term side-effects include denervation of the abdominal wall and less frequently, intractable pain. These adverse events are a drawback for potential donors to donate a kidney. Therefore, in most centres, over the past decade the open donor nephrectomy has been replaced by less invasive techniques.

A modification of the classical open donor nephrectomy is the muscle-sparing mini-incision of approximately 7 centimetres. On comparison with laparoscopic donor nephrectomy, this approach resulted in slower recovery, more fatigue, a worse quality of life for the donor, and equal safety and function for donor and graft<sup>16</sup>.

The first laparoscopic donor nephrectomy was performed in 1995 by Ratner and colleagues<sup>17</sup>. This technique has led to a significantly shorter hospital stay, fewer postoperative analgesic requirements, improved cosmetics and a quicker return to work. Compared with the open technique, laparoscopic donor nephrectomy is associated with less donor morbidity and similar allograft function and overall safety, but with increased costs<sup>18</sup>.

Hand-assisted laparoscopic donor nephrectomy was first utilised to minimize the learning curve of the total laparoscopic donor nephrectomy. Potential advantages of hand-assisted laparoscopic donor nephrectomy over conventional laparoscopy include the ability to use tactile feedback, less kidney traction, rapid kidney removal and shorter warm ischemic periods<sup>19,20</sup>. In addition, the introduction of hand-assisted laparoscopic donor nephrectomy broadens the indications for laparoscopic living donor nephrectomy to include obese donors and donors who have had previous abdominal surgery<sup>21</sup>.

There is an ongoing discussion whether right or left donor nephrectomy is to be preferred. Most centres prefer to use the left kidney for live kidney donation because the renal vein is longer which is advantageous during implantation. However, some surgeons prefer the right kidney because it is easier to recover than the left kidney and the risk of splenic laceration is decreased<sup>22</sup>. There are no prospective studies comparing the potential benefits of left- and right-sided laparoscopic donor nephrectomy. For this reason we decided to conduct a prospective single-centre randomised trial performing either a left or a right sided hand-assisted laparoscopic donor nephrectomy.

**Quality of life**

The steadily increasing demand for kidney transplantation has prompted consideration of ways to expand the pool of potential donors. The first option is the increased usage of the
so-called expanded-criteria deceased kidneys. These kidneys come from donors who are either over the age of 60 or donors who are over the age of 50, with two of the following characteristics: a history of hypertension, cerebrovascular injury as cause of death, or a creatinine level at any time higher than 130 mmol/L. The second option is the increase in healthy volunteers willing to donate a kidney, which has the largest quantitative effect. The use of older living donors remains controversial because of the physiological decline in glomerular filtration rate that begins in the third decade of life, and of the increased risk of surgical complications for the older kidney donor. However, data regarding quality of life of older living donors is lacking. In this thesis we present a prospective analysis of this issue.

Surgical complications

The overall incidence of surgical complications after kidney transplant is low, especially when compared with non-kidney transplants such as liver or pancreas. Vascular and urological complications are the most common.

Vascular complications can involve the donor vessels (renal artery thrombosis, renal vein thrombosis), the recipient vessels (iliac artery thrombosis, deep venous thrombosis), or both, and may result in significant morbidity.

Renal artery thrombosis occurs early after transplantation in about 1% of cases, usually in small-calibre arteries. Typically, it occurs secondary to a technical problem, such as intimal dissection or kinking or torsion of the vessels. Diagnosis is made with colour flow Doppler studies. Nephrectomy is generally indicated, especially if thrombosis occurs in the perioperative period. Arterial stenosis occurs in 2-10% of cases and is associated with vascular rejection. It can occur within months or years following transplantation, and is associated with the abrupt onset of hypertension. Assessment with duplex ultrasonography has a high sensitivity (87.5%) and specificity (100%). First-line treatment for clinically important lesions consists of percutaneous interventional techniques, usually angioplasty with or without a stent. Surgery is reserved for stenoses that do not respond to radiological intervention.

Venous thrombosis occurs in 0.5-4% of cases. Causes include angulation or kinking of the vein, compression by haematoma or lymphocele, anastomotic stenosis, extension of an underlying deep venous thrombosis, and hypercoagulation. It usually results in graft loss. Again, duplex ultrasonography is the best diagnostic tool.

Venous thromboembolic complications that affect the recipient vessels (deep venous thrombosis and pulmonary embolism) are not uncommon. The incidence of deep venous thrombosis is close to 5%; the incidence of pulmonary embolism is 1%. Usually two peaks in incidence are reported, one early in the postoperative period (likely related to operative factors), and a second peak around 4 weeks (perhaps related to a rising haematocrit level). Risk factors include recipients over the age of 40, diabetes, thrombophilic disorders, and a history of deep venous thrombosis.
Multiple renal arteries are present in 12-33%, while multiple renal veins are present in 5-10% of the donors\textsuperscript{28,29}. Implantation of kidneys with multiple vessels is associated with an increased incidence of vascular complications which could be prevented by additional vascular reconstructions during implantation. Therefore, as part of this thesis, we assessed the impact of additional vascular reconstructions on graft survival.

The incidence of urological complications is reported to be 2–10\%\textsuperscript{30}. The two major urological complications after renal transplantation are urinary leakage and obstruction, often located at the ureterovesical junction or in the distal transplant ureter. Classically, the two major aetiological factors for urological complications after transplantation are surgical-technical factors and distal transplant ureteric ischaemia. Surgical-technical factors include poor harvesting and ureterocystostomy techniques. Preservation of the periureteral vessels and fat, reduction of ureteral length, avoiding large incisions in the bladder, avoiding external ureteral compression by the vas deferens, and creating a watertight urinary anastomosis, all decrease the incidence of urological complications\textsuperscript{31}.

Ureteral obstruction may present early or late. Early obstruction may result from distal obstruction, clot, oedema, or technical problems associated with the ureteroneocystostomy. Late obstruction is generally due to fibrosis from chronic ischemia and may result in hydronephrosis, which is easily detected by ultrasonography. If a percutaneous nephrostomy catheter and expectative management do not resolve the problem, surgical revision of the ureteroneocystostomy may be required. Splinting the ureterocystostomy results in a lower postoperative urological complication rate\textsuperscript{32,33}. However, in a routine splinting protocol the number needed to treat in order to prevent one urological complication is considerable, ranging from 10 to 30. To effectively identify patients at high risk of a urological complication, we tried to identify potential risk factors with the ultimate aim of introducing a selective splinting protocol.

**Graft survival**

One-year kidney graft survival has increased remarkably during the past 30 years, mainly due to substantial reduction in early rejection episodes and graft losses within the first few months after transplantation. The reasons for the high long-term graft survival rates among recipients of living donor kidneys are not completely understood. There are certainly benefits from elective surgery, when the donor and recipient are in optimal condition, and of using living, related kidneys with minimal ischaemia-reperfusion damage. Still, grafts that continue to function one year after transplantation fail at an inexorable rate of about 5\% per year, so that on average, half of all primary kidney transplants that survive the first post-transplant year will be lost within 13 years. Surprisingly, the rate of late graft failure has changed little over the years. Today’s 5-year graft survival rates for living donor transplant recipients are 80\% (Figure 3). For recipients of deceased kidneys the results are around 70\%\textsuperscript{34}.
A group particularly liable to end stage renal failure is the population of the Dutch Caribbean with an estimated prevalence of 145 per 100,000 residents\textsuperscript{35}, one of the highest in the world. In 1998, the St. Elisabeth Hospital in Curaçao and in 2003 the Dr. Horacio E. Oduber Hospital in Aruba, began a collaboration with the Academic Medical Center in Amsterdam, the Netherlands, the Eurotransplant Foundation, Sanquin Diagnostic Services and the Dutch Transplantation Working Group in order to set up a structured transplantation programme for patients in the Dutch Caribbean who would otherwise need lifelong dialysis. These patients were offered the opportunity to be put on the Eurotransplant waiting list to receive a deceased donor kidney or to participate in the living donor transplantation programme, if a living donor became available. The results of this unique transplantation programme are discussed in this thesis.

**Aim of this thesis**

This thesis focuses on some surgical aspects of kidney transplantation. The studies described in part I are examined in order to assess the outcome of the hand-assisted laparoscopic donor nephrectomy technique for kidney retrieval and in part II to assess recipient outcome with a focus on urological complications.

**PART I: Hand-assisted laparoscopic donor nephrectomy**

To address the role of hand-assisted kidney donation, we first compared this technique with open donor nephrectomy (Chapter 2). The results of a randomised trial comparing right and left donor nephrectomy in living kidney transplantation are presented in Chapter 3. The risk factors for delayed graft function after hand-assisted laparoscopic donor nephrec-
tomy are described in Chapter 4. In Chapter 5 the surgical outcome and quality of life in older living donors is examined.

**PART II: Surgical technique and outcome**

The outcome of additional vascular reconstructions performed during kidney transplantation is described in Chapter 6. Chapter 7 contains the results of potential risk factors for implementing a selective stenting ureterocystostomy protocol. The results of a 5-day external stented ureterocystostomy protocol are reported in Chapter 8. In Chapter 9 the 10-year results of a transatlantic kidney transplant airlift between the Dutch Caribbean and the Netherlands are presented. Chapter 10 contains summaries in English and Dutch.

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