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Surgical aspects of living-donor kidney transplantation

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ABSTRACT

Laparoscopic living donor nephrectomy has shown less morbidity than the open approach, with less pain and analgesia requirements and allowing a quicker recovery and an earlier return to normal activity. Furthermore, many studies have shown equivalent results between both approaches in terms of graft function and recipient complications.

For these reasons, we can accept laparoscopic kidney living donor nephrectomy as the gold standard surgical technique in these patients. The implementation of this minimally invasive technique in most centers has led to an increase in the rate of this kind of organ procurement, due to its better acceptance by the donors.

In order to decide which kidney is better to extract, it is mandatory to maintain the best kidney in the donor. In equal conditions, it is advisable to perform left nephrectomy.

Aspectos quirúrgicos de la donación de vivo

RESUMEN

La nefrectomía de donante vivo por laparoscopia ha demostrado una menor morbilidad sobre el donante comparada con la cirugía a cielo abierto clásica, disminuyendo el dolor y la necesidad de analgesia y permitiendo una recuperación más rápida de los donantes.

Los diversos estudios que han comparado las técnicas de extracción renal abierta y laparoscópica demuestran que los resultados funcionales del injerto en el receptor son equivalentes, por lo que podemos afirmar que la nefrectomía por laparoscopia es el «gold» estándar para la donación de vivo en centros especializados. Por otro lado, gracias a la introducción de este tipo de cirugía mínimamente invasiva, la donación de vivo ha experimentado un gran incremento en los últimos años, por su mejor aceptación y sus ventajas respecto a la cirugía abierta.

A la hora de tomar la decisión de qué riñón extraer, es mandatorio mantener el riñón de mejores características en el donante. En igualdad de condiciones y con una vascularización similar, se prefiere la realización de la nefrectomía izquierda.

INTRODUCTION

Spain has one of the highest rates of cadaveric donation in the world. Even so, waiting lists are long with an average waiting time of around 2 years to receive a kidney. It is therefore necessary to promote other sources of kidney implantation such as living-donor, non-beating heart and marginal donor kidneys.

It is important to note that living donation is a special procedure since it is performed with healthy individuals who have selflessly given up their kidney. This requires absolute safety in the surgical procedure to prevent any short/long-term morbidity in the donor.

The traditional surgical technique for living-donor nephrectomy is open surgery using lumbotomy, which causes some morbidity due to the incision. The introduction of minimally invasive surgery in general practice has reduced this morbidity thus improving patient safety. Multiple studies have also shown other advantages such as less bleeding, faster postoperative recovery, less need for analgesic agents and better cosmetic results.[1,2]

The superior characteristics of laparoscopic surgery have had a positive impact on living donation. Since the first laparoscopic nephrectomy was performed on a living donor

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by Ratner et al in 1995,[3] this technique has gained great importance and now represents, along with open surgery, the gold standard for living-donor kidney donation in experienced centres. This has had a positive effect on the rate of living donations.[4]

Here we describe the surgical assessment of the living kidney donor and the various surgical techniques currently available for performing a safe extraction, and we analyse complications and results.

SURGICAL ASSESSMENT OF DONORS

From a surgical point of view, the assessment of living donors involves two main aspects:

1. Assessment of the viability of extraction, selecting the appropriate side for the nephrectomy.

2. Evaluation of any concomitant urological pathology that may contraindicate donation.

This assessment is made using anamnesis, careful physical examination and imaging tests.

Anamnesis

The donor's medical and surgical history must be known in order to determine the risk and difficulty of the surgery. It is important to assess previous abdominal surgeries to estimate the presence of intestinal adhesions, dissection difficulty, risk of injury to abdominal organs, etc. Another aspect to consider is the presence of associated urological disease (lithiasis, cysts or tumours) in order to assess the kidney's viability after transplantation and the donor's risk of developing renal failure.

Physical examination

Abdominal palpation, examination of existing scars. In men over 40, a PSA test and a rectal examination are indicated in order to screen for prostate cancer.[5]

Imaging tests

Imaging tests that provide information on renal morphology are needed, which allow clinicians to carefully evaluate the renovascular anatomy (presence of multiple pedicles, vascular malformations, etc.). There is no evidence as to which available imaging test is the best (CT angiography, DIVAS, MRI), therefore, the information that each provides and their possible side effects must be assessed. High-resolution CT angiography evaluates vascularisation in detail, detecting small vessels down to 1mm in diameter. It also performs multiplanar reconstructions for the careful evaluation of renal, vascular and urinary morphology.[6] The spatial resolution of MRI is not as powerful as high-resolution CT, and therefore vessels smaller than 2mm may go unnoticed.

DIVAS allows for very accurate evaluation of the donor's renovascular tree but is an invasive imaging test associated with high radiation and it does not provide information on renal morphology and possible associated anatomical abnormalities.

It is important to assess potential donors with a radiologist to get the most detailed description possible of the vascular tree prior to surgery. This will prevent any major vascular injuries and complications.

There is no need to routinely calculate the relative function of each kidney. In those cases where glomerular filtration is close to the lower limit or there is a discrepancy in size, isotopic renography can be performed to confirm the relative function and determine on which side to perform the extraction.

SELECTING THE KIDNEY TO BE EXTRACTED

When deciding which kidney to extract, the kidney with the best characteristics is required to remain in the donor. Under equal conditions and with similar vascularisation, a left nephrectomy is preferred in living donation as it provides a longer renal vein, which eases implantation. The indication for a right living kidney nephrectomy by laparoscopy has been a subject of debate. In studies published during the early implementation of this technique, nephrectomy by right laparoscopy caused a greater risk of vascular complications, mostly venous (thrombosis), greater graft loss and longer duration of delayed graft function. This is all attributed to the shorter venous length, which hindered vascular anastomosis during organ implantation.[7,8] More recent studies have reported similar results for both sides in both donors and recipients[9] In a randomised prospective study recently published by Minnee et al, results for left and right laparoscopic nephrectomies were compared for donors and recipients. The only statistically significant difference observed was the longer surgical time needed for left nephrectomies.[10] In our centre, 20% of living-donor laparoscopic

nephrectomies performed to date have been right nephrectomies. The results for donors and recipients have been equivalent to left nephrectomies.[11]

Another controversial issue is the existence of multiple vascular pedicles in the donor, which supposedly increases the risk of thrombosis after implantation. Despite being technically more difficult, there is evidence that these surgeries can be performed without added risk. Disick et al retrospectively analysed the results of 39 cases of living-donor nephrectomies with vascular malformations and multiple pedicles without observing differences in donor or recipient evolution.[12] In any case, the maximum number of arteries for accepting a kidney has not been established, since living-donor transplants have been performed with up to four arteries. The discretion of the surgeon assessing the difficulty of the case and his experience in this field will determine whether a transplant is feasible or not.

SURGICAL TECHNIQUES

Open living-donor nephrectomy

Open nephrectomy can be performed through various surgical approaches (median or subcostal laparotomy, lumbotomy) and may be transperitoneal or extraperitoneal. The most commonly used technique is extraperitoneal lumbotomy and, as mentioned above, this is the reference technique with which new surgical procedures are compared.

Patients are placed in the lateral decubitus position, angling the operating table at the level of the navel to better expose the lumbar fossa. An incision is made at the twelfth rib, with or without resection, until the renal fossa is reached. Careful extraperitoneal dissection of the kidney is then performed. First, the ureter is identified and dissected to the junction of the iliac veins and then sectioned. Subsequently, the vascular pedicle is dissected. First, the artery is bound, and then the vein. The pedicle is sectioned and then bench perfusion of the kidney is performed, with a very low warm ischaemia time.

When using this surgical technique, care must be taken when creating access to avoid injuring the peritoneum and the pleura. As this is an extraperitoneal technique, the risk of injury to intra-abdominal organs is low. This approach is a major assault on the abdominal wall since it sections the three muscles that form it, which can result in significant postoperative pain, a longer hospital stay and poor cosmetic results. Long-term complications include denervation of the abdominal wall, development of eventrations and chronic pain.

Mini-incision living-donor nephrectomy

After the introduction of laparoscopic surgery, modifications to open surgery were developed in an attempt to compete with laparoscopic surgery. Thus, mini-incision nephrectomy was developed, which consists of performing an anterior, flank or posterior nephrectomy, with an incision of about 7cm in length. This is also considered minimally invasive surgery.

Patients are placed in the lateral decubitus position, with the operating table angled for better access to the renal fossa. The incision is made at the eleventh rib, and unlike the traditional lumbotomy, the muscles of the abdominal wall are dissected to avoid injury to the intercostal nerves that lie between the internal oblique and the transversus muscles of the abdomen. Once inside the renal fossa, the peritoneum must be retracted medially. Renal dissection is performed as in conventional surgery, but with greater difficulty due to the reduced space.

Numerous randomised studies have been published that compare mini-incision surgery with traditional open and laparoscopic surgery. The surgical time required for the former is somewhat greater than in conventional surgery, although it does offer lower morbidity (less need for morphine and faster recovery). If we compare it to laparoscopic surgery, the donors require more analgesia and recover more slowly. No differences have been found in renal function results in the recipient when comparing the three techniques.[13]

Laparoscopic living-donor nephrectomy

As previously mentioned, open laparoscopy is the gold standard surgical technique for living-donor nephrectomies in specialised centres. We will now describe the surgical technique used in our centre.

The patient is placed in right or left lateral decubitus, depending on the case, horizontally at 15º with respect to the traditional open lumbotomy posture. A discreet opening of the operating table angle is made between the twelfth rib and the iliac crest. Before placing the patient in the final position, a vesical catheter is inserted and both lower extremities are wrapped in compression devices to facilitate venous return. A prophylactic dose of broad-spectrum intravenous antibiotics must have been administered one hour before surgery.

When starting the intervention, three ports are inserted, forming a triangle. The first 12mm port, placed on the paramedian line at the level of the navel, shifted 8cm

towards the flank and outside the anterior rectus abdominis muscle, will be used to perform the pneumoperitoneum and the insertion of an optical trocar. This trocar must be placed just above the navel, since abdominal distension will cause caudal displacement of the incision location when performing the pneumoperitoneum. After placing the trocar and verifying its correct position in the abdominal cavity, carbon dioxide insufflation is performed to obtain intraperitoneal pressure of 12-15mm Hg, which is maintained throughout the intervention. Immediately afterwards, the two other trocars are placed under direct vision: a 5 mm trocar in the left hypochondrium (10cm above the optical trocar) and a third 10 mm trocar in the iliac fossa (10cm below the optical trocar).

Once the trocars are placed, the colon is shifted medially to expose the retroperitoneum. Bipolar forceps held in the left hand are commonly used for dissection, with monopolar scissors or a Ligasure® held in the dominant hand. After that, the gonadal vein and ureter are identified and the latter is released to the junction with the iliac vessels where, with prior distal clipping, it is sectioned.

The ureter is then dissected proximally up to the lower renal pole. The caudal release of the kidney allows for a safe approach to the renal hilum from below. It is important to postpone dissection of the upper pole until the end of the intervention so as to maintain a renal anchor point that facilitates the dissection of the vessels. The gonadal vein is dissected proximally up to the renal vein, where it is also sectioned with Ligasure®. It is essential to achieve the maximum possible renal vein length, which means the suprarenal vein will also have to be sectioned, in addition to possible lumbar branches that often exit the lower edge of the renal vein. The artery is located behind the renal vein, and in most cases is wrapped by a lumbar vein. The dissection of this lumbar vein facilitates the dissection of the renal artery reaching up to the ostium in the aorta. It is very important to release all the surrounding tissue completely, being especially careful to prevent traction, which may produce spasms in the arterial wall.

In most cases, a fourth accessory port is needed during the operation. This port is placed on the left flank and is used by the second assistant to lift the lower pole of the kidney. This manoeuvre allows better visualisation of the renal vascular pedicle, facilitating its dissection. In addition, this move leaves both hands free to dissect the vessels safely and comfortably.

After the vascular dissection, a 6cm umbilical median laparotomy is performed, which allows the introduction of the left hand into the peritoneal cavity. Left-handed surgeons insert the right hand through an oblique incision in the iliac fossa. This move allows for smooth traction of the kidney, offering better exposure of renal vessels for clipping and sectioning with greater accuracy. When using a small incision adjusted to the size of the surgeon's hand, the placement of gauze around the wrist and in contact with the abdominal wall is enough to maintain a seal, and therefore the use of any Handport®-type device is not necessary.

There are various types of vascular clips: Hemolock®, metal staples and endovascular staplers. The use of 2 Hemolocks® in the proximal end prior to sectioning is sufficient, although it is important to keep them separated to prevent the clips from slipping, which may have fatal consequences.

The kidney is extracted through the assistance incision and perfused with saline or preservation solution if a delay in the implantation is anticipated. With this technique, our centre achieved a mean warm ischaemia time of 2.5 minutes.

After finishing the surgery, haemostasis of the entire surgical site is reviewed and a Jackson-Pratts type drain is placed so as to exit through one of the trocar openings. In the immediate postoperative period, it is common for drainage to be productive during the first few hours due to the accumulation of fluid within the abdominal cavity that shifts as the patient moves.

Patient care is the same as for a nephrectomy for any other reason.

There are a series of considerations when performing right laparoscopic nephrectomy: the available vein is much shorter, the dissection of the renal artery must be extended in its retrocaval portion and the presence of the liver hinders the process. The trocars are placed in a mirror image of those for a left nephrectomy. However, when starting the intervention, a fourth 5mm port needs to be added in the epigastric region in order to introduce a clip that is attached to the inside of the abdominal wall, allowing the liver to be separated without difficulty. The surgical sequence is the same as for left nephrectomy.

Laparoscopic surgery has a number of disadvantages compared to open surgery because it requires a learning period with a somewhat steep learning curve. In addition, there is a risk of injuring intra-abdominal structures (intestines, large vessels) during the introduction of the trocars or during the surgery. There is also a risk of intestinal herniation by the ports and eventrations.

Lastly, the material necessary to carry out these procedures represents a high cost in consumables. However, this cost is offset by the reduced average hospital stay of donors.

The rate of conversion to open surgery ranges from 0% to 13%, according to various series.

Hand-assisted laparoscopic living-donor nephrectomy

This surgical technique was developed to overcome the steep learning curve involved in pure laparoscopic surgery. The name refers to the insertion of the hand throughout the surgery process to facilitate surgical manoeuvres and provide greater safety by allowing immediate control of bleeding caused by injury to the large vessels. The incision for inserting the hand can be made at different locations, with the optional use of devices that assist in maintaining the pneumoperitoneum, according to surgeon preference.

The hand-assisted organ extraction technique is not included in this section because the incision is made at the end of the intervention and is only used for the extraction of the organ itself.

Retroperitoneoscopic living-donor nephrectomy

This technique was developed to reduce intra-abdominal handling, thus reducing complications in that area. Using this approach, the space is reduced and the anatomical view is different from the transperitoneal, making it somewhat difficult. Possible disadvantages are the risk of pneumomediastinum, pneumothorax, pneumopericardium and gas embolism.

Robot-assisted living-donor nephrectomy

The use of robot-assisted living-donor nephrectomy, pure and hand-assisted, has been reported but experience is minimal. Using the robot's instruments, finer movements can be performed with greater mobility than with conventional laparoscopy, although at greater cost.

Surgical techniques under development

Recently, new minimally invasive surgical techniques have been introduced into surgical practice such as NOTES (Natural Orifice Transluminal Endoscopic Surgery[14]) and LESS (Laparo endoscopic Single-Site Surgery). These have provided positive results for both the donor and recipient. Cane et al published the results of 17 living-donor nephrectomies using LESS compared to controls using conventional laparoscopy controls. The results of this study showed no significant differences between these techniques.[15] Furthermore, the results of eight living-donor NOTES hybrid transvaginal nephrectomies performed by our team were presented this year. The mean warm ischaemia time was 4.5 minutes and there were no complications in the donors or any changes in graft function.[16] Despite these encouraging results, these types of techniques should still be considered experimental and more evidence is required before their general use can be accepted.

RESULTS

Donor results

The biggest disadvantage of organ donation is the deleterious effect it may have on the donor. Apart from cosmetic surgery, organ donation is the only medical situation in which a healthy individual is subjected to a "mutilating" surgical procedure. As with all surgical procedures, living-donor nephrectomy is not exempt from morbidity and mortality, which must be taken into account and minimised as much as possible.

To date, scientific evidence has indicated that living donation is safe.[17] According to the United Network for Organ Sharing (UNOS), the mortality associated with nephrectomy is 0.03%. This figure has not changed in the last 15 years despite the emergence of new surgical techniques and changes in donor selection criteria.[18,19]

The rate of complications from living-donor nephrectomy is around 10%.[20] Complications that can result in the donor's death are mostly related to vascular pedicle injuries, loss of clips in the vascular stump and automatic suture defects when sectioning the vein. Upon these sudden and intense haemorrhages an immediate conversion to open surgery is necessary to repair the lesion, and they are the primary cause for conversion and delayed re-operation. Devices have been developed that offer the maximum assurance of tight vascular suture, such as the Hemolock® clips. Even so, in order to avoid disastrous consequences, clipping and kidney extraction may be performed using hand-assistance, which allow the surgeon to employ gentle traction on the renal pedicle, for controlled and safe clipping and a longer vascular length.

In a recently published study, Segev et al analysed perioperative mortality and long-term survival of 80 347

living donors, comparing the results with a control cohort. They observed higher mortality at 3 and 12 months for donors who were men, African American and/or hypertensive, without noticing significant differences in terms of age, BMI, systolic blood pressure or smoking. Mortality was greater for donors than in the control group at three months, equal at one year, and similar or lower for donors in the long term.[12]

With respect to morbidity, the first point to note is the evolution of an individual after nephrectomy. Much has been published on the subject and the vast majority of studies agree that laparoscopy offers distinct advantages over open surgery: shorter hospital stay, less postoperative pain with a consequent reduced use of analgesics, an early return to work and, above all, improved cosmetic results.[21,22] These are the main selling points for promoting living donation as an alternative to cadaveric implants. This technique is widely accepted by the public and directly affects the rate of donations, which has been on the increase in Spain in recent years.[23]

Recently, Andersen et al published a prospective randomised study that compared the quality of life of patients who underwent laparoscopic nephrectomies against those who underwent open nephrectomies. The results show less postoperative pain in the laparoscopy group, but no long-term differences were found based on the completed questionnaires. Advantages were only seen in the laparoscopy group when stratified according to conversion/reoperation.[24]

Kocak et al, using a total of 600 living-donor nephrectomies, reported a 7.2% complication rate. Based on the Clavien classification,[25] the study suggested a classification of these complications into four groups according to severity:[26]

1. Complications that do not threaten the life of the patient and require minimal or no treatment (e.g. urine retention).

2. Potentially severe complications that do not leave sequelae (e.g. prolonged ileus).

3. Any complication that incurs sequelae (e.g. splenectomy secondary to accidental spleen injury)

4. Graft loss or patient death. Among the results described in this series.

Some 95.3% of complications were included under groups 1 and 2.

Another essential aspect to assess is the effect that nephrectomy has on the donor's renal function. A slight increase in creatinine levels after nephrectomy has been reported during recovery. At six months, renal function recovery is greater than 70%.

In 1998, a study was conducted in our centre that assessed 97 living donors with an average follow-up of 17 years (unpublished data). At the end of follow-up, only six of these donors showed creatinine levels that were higher than 1.3 and none required dialysis. When assessing the six cases, we found that all had risk factors (hypertension, hyperuricaemia or obesity). Fehrman-Ekholm et al carried out a follow-up of 430 donors between 1964 and 1995. In 87% of the cases, levels of serum creatinine, proteins and red blood cells in urine were measured along with blood pressure. According to the study, none of the donors died due to kidney disease or had chronic renal failure.[27] These results were corroborated by a meta-analysis published in 2006. The conclusion of this study was that kidney donation causes a decrease in initial glomerular filtration (25%-30%) that is not accompanied by a loss of renal function or progression to dialysis within 15 years.[28]

In summary, we can conclude that living-donor laparoscopic nephrectomy is a safe procedure, although a minimal associated morbidity and mortality must be taken into account. The positive results shown by various published series should serve as a stimulus for promoting living donation as an alternative source of organs for transplantation.

Recipient results

Initially, the first published series reported an incidence of early graft loss that was higher in kidneys extracted laparoscopically compared to those obtained through open surgery (2.9% according to the University of Maryland[29] and 5.4% according to Johns Hopkins University[30]), with a ureteral complication rate around 10%. In 1999, Nogueira et al presented a retrospective series that reported a difference in creatinine levels at the first month post-transplant that favoured traditional open extraction.[31]

In 2001, the first randomised prospective study was published comparing open living-donor nephrectomy to the laparoscopic approach.[32] This study showed that creatinine levels were higher for laparoscopic nephrectomy during the first three months post-transplant.

To date, multiple published studies have compared the results using the three techniques described: pure laparoscopic nephrectomy, hand-assisted laparoscopic

nephrectomy and open surgery. The most experienced teams monitor their patients for up to five years, with positive results that are comparable among the three groups.[33] A meta-analysis published in 2003 concluded that there were no differences in graft evolution even during the first year post-transplant.[34] Another meta-analysis published in 2007 only compared pure laparoscopic surgery to hand-assisted.[35] Once again, the results for graft renal function and its complications in the recipient were similar for both techniques.

It is important to note that none of the published studies to date have reported differences in graft renal function at one year, regardless of the extraction technique.

It is also important to assess why the kidneys of the initial series had worse graft function during the first three months post-transplant. To answer this question, most studies have focused on evaluating the effect that pneumoperitoneum has on renal perfusion. Several experimental studies have observed that the increase in intra-abdominal pressure decreases renal flow.[36-38] This decrease in blood flow is greater when located cortically with respect to the medulla.[39] In order to diminish this effect, various measures for performing nephrectomies have been proposed.[40] One measure would be to increase intraoperative intravenous perfusion, which has been shown to be effective in experimental studies.[41] Another measure is to avoid arterial spasms by topical application of papaverine. Azcher et al have confirmed its usefulness in experimental studies.[42] A third factor to consider is optimisation of surgical manoeuvres during nephrectomy. The late release of the posterior face of the kidney and avoidance of renal artery traction improves organ perfusion. The less the organ is handled, the better its condition upon implantation. Other manoeuvres, such as reducing intra-abdominal pressure below 15mm Hg, have not been shown to be clinically effective.

Lastly, the effect that warm ischaemia has on the transplanted kidney's function must be assessed. Laparoscopic nephrectomy usually causes an increase in warm ischaemia time, especially when performed without an assistance incision, but in most cases this ischaemia time is around five minutes.[43] However, this slight increase in warm ischaemia time has no clinical significance. Simforoosh et al performed a prospective study comparing renal graft evolution according to warm ischaemia time. Their conclusion was that, with warm ischaemia times under 10 minutes, there were no differences in the evolution in the recipient's creatinine levels.[44]

To minimise injury due to ischaemia-reperfusion, it is important to minimise warm ischaemia times, protect the kidney with mannitol infusions, use diuretics in the donor during extraction and infuse a large amount of crystalloids (3.5-4 litres) during the intervention.[45]

RECOMMENDATIONS

As already mentioned, living-donor nephrectomy is a special surgical procedure since it is performed in healthy individuals seeking to benefit another person. As such, one must minimise the risks as much as possible. There are various safe surgical techniques with positive results for both the donor and recipient, so we must therefore use the surgical technique that, in our hands, provides the most security for the donor. Living donation programmes should be carried out in specialised centres by trained professionals in order to achieve and maintain safety and positive results.

CONCLUSION

Living kidney donation is a procedure that is not exempt from risk. Nevertheless, extraction by laparoscopy allows us to offer donors minimal morbidity and mortality with excellent results for both the donor and recipient. The emergence of this type of surgery has increased the number of living donors by decreasing donor morbidity, which allows us to safely promote this source of organs.

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