LIVING DONOR NEPHRECTOMY: UNIVERSITY OF MIAMI TECHNIQUE AND CURRENT RESULTS

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Summary.- OBJECTIVES: Living-donor nephrectomy has significantly expanded the pool of renal transplant donors, allowing for a marked increase in transplantation. Improvements in antirejection medications and refinement of donor selection criteria have allowed for extremely favorable rates of graft survival. More recently, laparoscopic donor nephrectomy (LDN) has significantly reduced the morbidity of renal transplantation in the donor population. The University of Miami/Jackson Memorial Hospital Transplant Center performs a large number of living-donor nephrectomies, with increasing use of LDN and here we report our cumulative experience.

METHODS: A retrospective review was performed of all live donor nephrectomies performed over the last 10 years, including LDN. Surgical complications, both minor and major, were ascertained. Conversion from LDN to open was similarly noted. Follow up, including creatinine one year post-transplant was recorded in open donor nephrectomy (ODN) and LDN groups.

RESULTS: Over 10 years, 413 live donor nephrectomies were performed. Of these, 257 were LDN, and 156 were ODN. In two cases, LDN was converted to ODN. Three patients needed reoperation after donor nephrectomy. There were no perioperative mortalities or deep venous thrombosis. Minor complications, including hernia, fever, and C. difficile diarrhea were very rare, the most common being testicular pain in eight patients.

CONCLUSION: Our extensive experience with living donor nephrectomy, with 413 cases spanning ten years, has been very favorable. The risk of major complications was extremely low, with six reported in the series. Minor complications were similarly rare. Living donor nephrectomy is a safe and feasible method of increasing the number of renal transplantation donors with minimal morbidity.

Keywords: Donor nephrectomy. Living donor. Renal transplantation. Nephrectomy. Hand-assisted.

Resumen.- OBJETIVO: La nefrectomía del donante vivo ha aumentado significativamente el fondo de donantes para trasplante renal, permitiendo un incremento marcado de los trasplantes. Las mejorías de la medicación contra el rechazo y el refinamiento de los criterios de selección del donante han permitido unas tasas de
supervivencia del injerto extremadamente favorables. Más recientemente, la nefrectomía laparoscópica del donante vivo (NLDV) ha reducido significativamente la morbilidad en la población de donantes. La Universidad de Miami/Centro de Trasplantes del Hospital Jackson Memorial ha realizado un gran número de nefrectomías del donante vivo, con un aumento de la utilización de la nefrectomía laparoscópica del donante vivo y en el presente artículo comunicamos nuestra experiencia acumulada.

MÉTODOS: Realizamos una revisión retrospectiva de todas las nefrectomías del donante vivo realizadas durante los últimos diez años, incluyendo las nefrectomías laparoscópicas. Se recogieron las complicaciones quirúrgicas, tanto menores como graves. También se registraron las conversiones de laparoscopia cirugía abierta. Se revisó el seguimiento, incluyendo las creatininas al año del trasplante en los grupos de nefrectomía abierta del donante y laparoscópica.

RESULTADOS: Se han realizado 413 nefrectomías del donante vivo durante diez años. De éstas, 257 fueron laparoscópicas y 156 abiertas. En dos casos, la nefrectomía laparoscópica fue convertida a abierta. Tres donantes necesitaron de intervención después de la nefrectomía. No hubo ninguna muerte perioratorio ni trombosis venosa profundas. Las complicaciones menores, incluyendo hernia, fiebre y diarrea por C. difficile fueron muy raras, siendo la más frecuente el dolor testicular en ocho casos.

CONCLUSIONES: Nuestra amplia experiencia en nefrectomía del donante vivo, con 413 casos a lo largo de diez años, ha sido muy favorable. El riesgo de complicaciones graves fue extremadamente bajo, con seis casos comunicados en esta serie. Las complicaciones menores también fueron raras. La nefrectomía del donante vivo es un método seguro y factible de aumentar el número de donantes para trasplante renal con mínima morbilidad.


INTRODUCTION

Living donor nephrectomy was first successfully completed between twins in 1954 (1). At that time, neither histocompatibility nor immunosuppression had been described and prior transplantation attempts resulted in rapid graft loss.

For patients with end stage renal disease (ESRD), transplantation offers significant advantages over chronic dialysis including decreased risk of death, decreased financial burden, and markedly improved quality of life (2, 3). Unfortunately the number of available donors falls far short of the number of patients awaiting transplant. For many years, the vast majority of transplants came from deceased donors. However, for the first time in 2001, the number of living donors surpassed the number of deceased donors (4). As a result, increasing attention has been paid to living donor nephrectomies, including techniques (5), perioperative care, and long-term follow up. The Miami Transplant Institute (MTI) at the University of Miami/Jackson Memorial Hospital is one of the highest volume kidney transplant centers in the USA. Approximately 28% of renal transplantation in Florida is performed at the MTI (6). Herein we report our experience with living donor transplantation over the last ten years.

MATERIALS, METHODS AND TECHNIQUES

Patients undergoing any form of living donor nephrectomy, including hand-assisted laparoscopic donor nephrectomy (LDN) and open donor nephrectomy (ODN), were identified over the past ten years. Retrospective chart review was performed to evaluate pre-, intra- and post-operative factors. Preoperative creatinine was recorded, as was the postoperative value. Perioperative complications were ascertained based on the chart review. Postoperatively, creatinine was measured in the donor cohort for at least one year. These values were noted, and a comparison was performed between LDN and ODN patients.

The ODN procedure was performed as previously described (7). Briefly, with the patient placed in a lateral decubitus position and the operating table maximally flexed, a skin incision was made from the tip of the 11th or the 12th rib anteriorly towards the umbilicus ending at the lateral border of the rectus abdominis. The length of the skin incision has been minimized recently to 10 – 15 cm, so-called a “mini-incision” ODN, and removal of the rib is not required in most of the cases. After dissection of the muscle layers, mechanical retractors are applied and peritoneum is retracted medially to enter retroperitoneal space. Subsequently, Gerota’s fascia is entered and the kidney is dissected from perinephric fat. Careful dissection of the renal hilum ensures intact renal vessels. To prevent arterial spasm and to preserve good blood flow to the kidney, topical papaverine and systemic mannitol are often used before extraction. The ureter is dissected and divided at the level of the iliac arteries. Following heparinization, vascular clamps are applied to the renal artery(ies) and vein(s), and then divided sequentially. The kidney is removed from the field and perfused using supplemented ice-cold
Ringer’s solution. Heparin is reversed by protamine and vascular stumps are oversewn using polypropylene continuous sutures. Then, the incision is closed in layers.

The hand-assisted laparoscopic donor nephrectomy is initiated by induction of general anesthesia. The patient is then positioned at 30° in the right lateral decubitus position. The patient is placed in such a way that when the operating table is flexed and kidney rest elevated, the exposure to the left flank is greatest. The left kidney is used in all cases of laparoscopic donors due to the additional length of the renal vein. A periumbilical incision is created and subsequent pneumoperitoneum is created. Our preference is for 12-15 mmHg pressure to be utilized. Subsequently, trocars are placed. We initially place the 10 mm camera trocar and then visually place two to three further trocars. One is placed in the midaxillary line subcostally. Another is placed in middle of the line joining the umbilical trocar and the iliac crest. Occasionally, a 5mm assistant trocar is placed cranial to the third trocar for additional retraction and exposure assistance.

The incision starts on the peritoneal lining and is continued down over the line of Toldt to reflect the descending colon medially. Similarly the peritoneal incision is extended superiorly towards the crus of the diaphragm.

One major modification we use is the en-bloc mobilization of the spleen and pancreas with the colon during the laparoscopic nephrectomy. The mobilization of the spleen starts with the dissection of the posterior peritoneal attachment. The spleen is mobilized and used as a ‘handle’ to elevate the tail of the pancreas. Extreme care must be taken not to place undue traction on the spleen. It should be retracted in a medial direction which subsequently exposes both the splenic-diaphragmatic and splenorenal ligaments. These should be divided with electrocautery prior to continuing the dissection. The spleen should be bluntly dissected off Gerota’s fascia and the diaphragm early, to prevent a pneumothorax. The surgeon reflects the spleen and left colon towards the midline and at the same time incises the avascular fibro-fatty plane about 1cm. from the posterior aspect of the pancreatic capsule. This helps in ‘peeling’ the pancreas off the kidney. The following points are important: Visualize and preserve the splenic artery and vein using the spleen as a handle (as above). Avoid un-necessary traction on the spleen which can cause a tear in the capsule and bleeding. Avoid dissection into the body of the pancreas. Avoid injury to the gastric serosa while mobilizing the posterior aspect of the stomach. Identify and preserve the inferior mesenteric vein at the lower border of the pancreas. Adhere to the principle of en-bloc mobilization, rather than individual organ dissection. To that end, the spleen may remain attached to the greater curvature of the stomach by the left gastroepiploic and short gastric vessels. After the mobilization is completed, the kidney and the adrenal gland are exposed for the continuation of the dissection. The adrenal is separated from the kidney after ligation of the adrenal vessels. In order to prevent ureteral devascularization, the ureter is taken en-bloc with the gonadal vein and periureteral fat and tissue. Subsequently, the remainder of the procedure is continued in the traditional hand-assisted fashion (5), including division of the renal vessels after administration of heparin and reversal with protamine.

RESULTS

Over ten years, from 1998 to 2008, 413 live donor nephrectomies were performed. Of these, 156 were ODN and 257 were LDN. See Figure 1 for the operative trends comparing ODN to LDN. No perioperative mortalities were reported. Over the ten year period, six major complications were noted: there were two conversions from LDN to ODN. The conversion rate was 0.8%. Three patients required reoperation, and one patient required transfusion secondary to postoperative anemia but had no evidence of bleeding. The overall major complication rate was 1.4%.

In the cases of conversion from LDN to ODN, one was due to surgeon’s preference given adverse anatomy related to multiple renal arteries. The second was due to an adherent adrenal gland and instrument malfunction (vascular stapling was incomplete).
Of the three patients requiring reoperation, partial or complete small bowel obstruction was the indication in two, who both underwent laparoscopic surgical management of the obstruction. The third patient underwent reoperation for bleeding postoperatively—the Weck clip had come off the renal artery stump at the time of reoperation. All cases of reoperation were in patients who had originally undergone laparoscopic donor nephrectomy. The major complication rate was 0% in open donor nephrectomy and 1.4% in laparoscopic donor nephrectomy.

Minor complications were noted in 28 patients, for an overall rate of 6.7%. One patient each had the following: anemia not requiring transfusion (LDN), pneumothorax (ODN), chylous ascites (LDN), pancreatitis (LDN), and rhabdomyolysis (LDN). Two patients each had: cellulitis/wound infection (one LDN, one ODN), C. difficile diarrhea (one LDN, one ODN), incisional hernia (one LDN, one ODN), and pleural effusion (both ODN). Three patients had postoperative fever (two ODN, one LDN). Four patients required readmission for pain and ileus (all LDN). Finally, eight patients, all from the LDN cohort, complained of testicular pain postoperatively. When separated by technique, the rate of minor complications in ODN was 5.1% and for LDN was 7.8%. Table one represents all complications in the donor nephrectomy series at our institution.

Given that a large number of LDN were performed in addition to ODN, our analysis also included comparison of these two modalities. Preoperative creatinine in the LDN and ODN groups were 0.86 and 0.87 ng/dL respectively (p=0.82). At three weeks postoperatively, the creatinine values were 1.26 ng/dL (LDN) and 1.21 ng/dL (ODN) (p=0.23). At last follow up over 52 weeks postoperatively, there remained no significant difference in the recipient creatinine values between the ODN and LDN groups. See Figure 2 for representation of these values.

DISCUSSION

Living donor nephrectomy has a number of significant advantages over deceased donor transplantation. Primarily, the length of graft survival is significantly increased with living donor transplants as compared with deceased transplantation (8). As a result, costs incurred due to graft loss including reinitiation of dialysis, re-evaluation for transplant, and repeat transplantation are markedly reduced, resulting in significantly less expense in patients undergoing live donor transplantation compared to deceased donor transplant (9).

The first living donor nephrectomy was performed in 1954 between identical twins. Prior to this, experimental transplants uniformly failed due to biologic obstacles including, but not limited to, ABO, HLA, and cross-match incompatibility (10). Subsequent advances in the field greatly improved the survival of grafts in unrelated, particularly spousal, renal transplantation, with recent research on long-term graft survival showing particularly good results (11).

Given the improvement in recipient graft survival and long-term success in patients in end-stage renal disease, much attention has been turned to the kidney donor. For over thirty five years since the initial donor nephrectomy performed by Murray in 1954, renal donation has been performed using an open approach. Until the mid-1990s, there were minimal modifications of surgical technique in the open approach to live donor nephrectomy. A number of authors have reported their experience with mini-laparotomy incisions compared to flank incisions in this patient group (12-14). Most comparisons show minimal difference between approaches, with some groups reporting slightly improved pain scores and shorter length of stay in patients undergoing a mini-incision donor nephrectomy as compared with a traditional flank incision donor nephrectomy (14). Our open approach has been the orthodox flank approach with transition to the mini-incision. This approach has been very successful with minimal complications and morbidity to the patients. There have been two incisional hernias related to this approach, neither requiring reoperation or invasive treatment. This compares with other centers reporting from a 3.6% to 7% rate of incision hernia in open donor nephrectomy (15, 16).
perience with post-operative pain, initiation of diet, length of stay, and patient satisfaction has been excellent (data not presented) and similar to that presented by a number of other centers (17, 18).

The first laparoscopic nephrectomy performed in 1991 by Clayman, et al (19) initiated a significant shift in living donor nephrectomy technique. For the first time in the human, laparoscopic nephrectomy had been shown to be safe, well tolerated, with minimal additional morbidity related to the procedure. Subsequently, the laparoscopic nephrectomy was applied in a porcine donor nephrectomy model by Gill, et al (20). The success of this model provided the impetus for transition of these techniques in donor nephrectomy in the human. The initial report of human laparoscopic living donor nephrectomy, by Ratner, et al, in 1995, was a landmark moment in the field of

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donor nephrectomy (21). Subsequent modifications and initial comparisons confirmed this method as being safe, effective, and having no detrimental effect on graft survival (22-24).

Since these initial reports, a vast body of literature has accumulated that provides strong evidence of the feasibility of laparoscopic living donor nephrectomy. Much of the literature focuses on three aspects of LDN as compared to ODN: the intraoperative variables, postoperative differences, and long-term graft outcomes.

Most authors report a statistically significant difference in operative length when ODN is compared to LDN. The vast majority of sources report that ODN is generally performed more quickly than LDN (18, 25, 26). A number of authors have reported increased complications in the LDN cohorts as compared to ODN patients (24-26). However, these reports should be taken in the context of the learning curve of the laparoscopic technique compared to the open. In fact, Jacobs et al., reported that over the course of three years of their experience with LDN, both the operative time and rate of complications decreased significantly. Blood loss during these cases has also been compared with minimal differences noted. Most sources agree that the laparoscopic approach has less blood loss (18), however, the potential for massive blood loss is greater in these cases given the (rare) risk of equipment malfunction including staple misfires and clip failures.

Postoperatively, patients undergoing LDN appear to have a number of advantages over those who underwent ODN. Almost all sources agree that the average postoperative analgesic requirements are markedly reduced in patients after the laparoscopic surgery as compared to the open approach (23, 24, 27, 28). Initiation of diet, overall length of hospital stay, and return to full activity are also significantly improved in LDN patients compared to those undergoing ODN (23, 28).

Finally, and of maximal importance, there appears to be no significant difference in graft function in recipients from donors undergoing either LDN or ODN (23, 30, 31). All of these authors reported that there were no differences in early postoperative creatinine levels and long-term creatinine between the groups. Given the slightly reduced warm ischemia and operative time, some authors have suggested improved early graft function but such reports have not shown statistically significant results.

Our experience has been similar to these published reports in all regards. We have had no intraoperative or postoperative deaths or deep venous thrombi. The conversion rate of less than 1% compares favorably with other reports of 1% to 6.3% (25, 26, 29). We have not reported operative times, however our experience mirrors that of other groups concerning open and laparoscopic techniques. Three patients required reoperation in our experience. Two had partial or complete small bowel obstruction requiring exploration and surgical management. One patient underwent reoperation for intraabdominal bleeding. At the time of exploration, the Weck laparoscopic clip came off the renal artery stump. As a result of this complication, our technique has been modified to include penetrating stapling devices as recommended by numerous organizations and we have noted no further complications.

The minor complication rate of 6.7% was also similar to that reported by other centers. Two patients presented with cellulitis and wound infection requiring antibiotics and evaluation of the wound. The fascial layers were noted to be intact and these patients did not require operative management. Four patients required readmission- for pain and prolonged ileus. None of these patients needed invasive treatments. Interestingly, the most common minor complication noted was testicular pain in eight patients. This appears to be a frequently seen complication, reported previously by other centers (32, 33).

The etiology is unknown, however hypotheses include injury to sensory nerves supplying the testicle during the ureteral dissection or possibly transection of the spermatic cord. Ligation of the gonadal vessels may also contribute to this finding in donor males. In all reported cases, the pain improved spontaneously and without any intervention.

Our transition to a mini-incision from the orthoadox flank incision is also notable. The incisional size is minimally different from the laparoscopic hand port site with improved pain and cosmesis for the patient in our observations. We have noted no complications related to this transition. The proportion of LDN and ODN has been steadily changing over time (see Table I). At the initiation of the donor program, almost all of the cases were done using the open technique. Since then there has been a steady rise in the number of laparoscopic procedures and most recently almost 75% of all the donor surgeries were performed with this technique. All were left sided donors. We do not anticipate this trend reversing in the near future. The graft function as measured by post-operative creatinine has not been statistically different between the LDN and ODN groups at any time point measurement postoperatively.
CONCLUSIONS

Living donor nephrectomy has revolutionized renal transplantation and, by extension, end stage renal disease. Treatment of ESRD via transplantation has multiple advantages to the recipient and the number of patients receiving renal transplantation has increased significantly. Techniques for living donor nephrectomy have been greatly refined since the initial donor nephrectomy in the 1950s. Currently, fewer open donor nephrectomies are being performed, instead replaced by a greater number of laparoscopic donor nephrectomies. The advantages to the donor are numerous, including improved cosmesis, shorter length of stay and less pain. Our experience in living donor nephrectomy has mirrored these shifts in technique. Currently, almost three quarters of all donor nephrectomies are performed laparoscopically. The complication rate is minimal and long-term graft outcome is excellent.

REFERENCES AND RECOMMENDED READINGS
(*of special interest, **of outstanding interest)


25. Oyen O, Andersen M, Mathisen L et al. Lapa-


