Objective: To assess donor morbidity, recipient outcome, and changing trends during the past decade in donor nephrectomy for living-donor kidney transplantation.

Design and Setting: Retrospective review at an academic tertiary care referral center.

Patients: We reviewed 201 consecutive living-donor kidney transplantations performed between January 1988 and June 1997.

Intervention: Donor nephrectomy and living-donor kidney transplantation.

Main Outcome Measures: Donor surgical complications, correlation of preoperative imaging of donor vascular anatomy and operative findings, and donor lengths of stay in the hospital were analyzed. Recipient delayed graft function and actuarial 1- and 5-year patient and graft survival rates were also analyzed.

Results: Major donor postoperative complications were bleeding (0.5%), pneumothorax requiring a chest tube (1%), wound infection (1%), and pneumonia (1%). Minor postoperative complications were asymptomatic pneumothorax resolving spontaneously (10%), urinary retention (6%), and urinary tract infection (0.5%). Preoperative imaging failed to detect small accessory renal arteries in 12% of donors. The mean donor length of stay in the hospital was 5.0 days but decreased from 6.2 to 4.0 days during the study. Twenty donors (10%) were unrelated (ie, spouse or friend). Three (1.5%) cases of delayed graft function occurred. Overall recipient patient survival at 1 and 5 years was 97% and 90%, and graft survival was 95% and 83%, with no difference between related and unrelated living donors.

Conclusions: Living-donor nephrectomy is associated with low surgical morbidity. Recent trends include shortened lengths of stay in the hospital, the use of computed tomographic angiography instead of digital subtraction angiography for preoperative imaging of donor vascular anatomy, and an expanded use of unrelated living donors.

Arch Surg. 1998;133:426-431

Advances in organ transplantation have resulted in a dramatic increase in the demand for donor organs and an ever-widening gap between the number of patients on transplantation waiting lists and the supply of cadaver organs. United Network for Organ Sharing Scientific Registry data indicate that although the number of patients on waiting lists for kidney transplants more than doubled from 13,943 to 31,045 between 1988 and 1996, the number of actual kidney transplantations performed from cadaver donors increased by only 13% from 7,208 to 8,163 during the same period. Consequently, living donors have assumed increasing importance in kidney transplantation, and indeed, from 1988 through 1996, the number of living kidney donors increased by 73% from 1,809 to 3,126 and now accounts for almost a third of all kidney transplantations performed in the United States.

With an increasing reliance on living kidney donors and preliminary reports of the application of minimally invasive surgical techniques for donor nephrectomy, an accurate assessment of donor morbidity with the conventional open approach is essential. In addition, advances in radiological imaging have led to changes in the preoperative assessment of potential living donors. We reviewed 201 consecutive living-donor kidney transplantations during the past decade at our institution (Beth Israel Deaconess Medical Center, Boston, Mass) to assess donor surgical morbidity, the results of preoperative imaging of donor renal artery anatomy, recipient outcome, and changing trends during this period.
PATIENTS AND METHODS

Between January 1, 1988, and June 30, 1997, we performed 539 kidney transplantations at our institution. Of these, 201 (36%) were from living donors and constitute the study group.

From January 1988 through January 1993, all prospective donors underwent preoperative digital subtraction angiography (DSA) through femoral artery puncture for the evaluation of renal artery anatomy. Beginning February 1, 1995, all donors underwent preoperative computed tomographic angiography (CTA) with the use of the spiral technique and the intravenous administration of a contrast medium. Because of a history of allergy to contrast media, 4 donors underwent magnetic resonance angiography (MRA) instead of CTA or DSA. The results of preoperative imaging studies were compared with intraoperative findings.

All donor nephrectomies were performed by 1 of 2 surgeons (D.S., A.I.S.) through a retroperitoneal flank incision with partial rib resection (11 or 12) according to well-established techniques. The left kidney was removed preferentially because of the longer renal vein unless multiple renal arteries or anomalous venous anatomy (eg, circumaortic left renal vein) was present on preoperative imaging studies, in which case the right kidney was used. If multiple renal arteries were present bilaterally, the left kidney was used.

Perioperative antibiotic agents consisting of cefazolin sodium or vancomycin hydrochloride in patients allergic to penicillin were given for 24 hours. Postoperative analgesia consisted of local infiltration of the wound and intercostal nerves with 0.5% bupivacaine hydrochloride with epinephrine during wound closure and intravenous meperidine hydrochloride or morphine sulfate (patient-controlled analgesia) for about 48 hours. A few patients received epidural analgesia instead of patient-controlled analgesia. All donors underwent upright portable chest radiographs postoperatively to exclude a pneumothorax. For the purposes of this review, an “asymptomatic pneumothorax” was small (<10%), without associated respiratory symptoms, and resolved spontaneously. A “symptomatic pneumothorax” was larger (>10-15%), accompanied by respiratory symptoms or expanding on a follow-up chest x-ray film (or both), and required the insertion of a chest tube.

A clear liquid diet was routinely started on the morning of the first postoperative day and advanced as tolerated to a regular diet. All urinary catheters, which were inserted after the induction of anesthesia, were removed on the morning of the first postoperative day. If the patient did not urinate within 8 hours, a urinary catheter was reinserted and removed the following morning. Wounds were defined as infected if pus drained from the incision.

Maintenance immunosuppression in all recipients consisted initially of triple-drug therapy with cyclosporine, prednisone, and either azathioprine (before July 1995) or mycophenolate mofetil (beginning July 1995), as previously described. Before July 1995, recipients of zero or 1 haplotype-matched living-donor kidneys also received a 5- to 7-day course of induction therapy with either antithymocyte globulin (ATGAM, Pharmacia & Upjohn, Inc, Kalama-zoo, Mich) or muromonab-CD3 (Orthoclone OKT3, Ortho Biotech Inc, Raritan, NJ).

Recipient actuarial patient and graft survival rates were calculated using a Kaplan-Meier estimation and compared using a log-rank test (Statistical Package for the Social Sciences 6.1 for the Macintosh computer).

RESULTS

SURGICAL COMPLICATIONS

For the 201 kidney transplant recipients, 167 left donor nephrectomies and 34 right donor nephrectomies were performed. Postoperative surgical complications are summarized in the Table. There was 1 (0.5%) case of bleeding requiring blood transfusion and reexploration. No discrete bleeding vessels were found after the evacuation of clot and wound irrigation, and the patient subsequently made an uneventful recovery and was discharged on the third postoperative day. Two patients (1%) had a symptomatic pneumothorax requiring chest tube insertion. Both cases occurred early in this series (patients 7 and 27, respectively). There were 2 (1%) significant wound complications: a wound infection with subsequent dehiscence requiring secondary closure and a wound cellulitis with coagulase-negative staphylococcal bacteremia treated with the administration of intravenous antibiotics. An additional 12 (6%) patients were discharged with a short course of oral antibiotic therapy for “wound erythema” but without wound drainage, opening of the wound, or cultures positive for bacteria. In 2 (1%) patients, pneumonia developed postopera-tively, and 1 patient had a generalized seizure on the second postoperative day. The results of a neurological evaluation were normal, and the seizure was possibly due to alcohol withdrawal. In 1 additional patient, an incisional hernia requiring repair developed 15 months after the kidney transplantation.

Minor postoperative complications included asymptomatic pneumothorax (10%), transient urinary retention (10%) requiring reinsertion of a urinary catheter for an additional 24 hours, and urinary tract infection (0.5%).
There were 2 (1.7%) additional complications related to preoperative DSA. Anaphylaxis due to the administration of iodinated contrast medium developed in 1 patient, and a second patient had a syncopal episode following angiography and was hospitalized overnight for observation. Both subsequently proceeded with donation.

LENGTH OF STAY

There was a progressive decrease in the hospital length of stay (LOS) during the study. The overall LOS was 5.0 days (range, 2-13 days). Before January 1994 (the first 98 patients), however, donors were routinely admitted the day before the surgical procedure, and this is included in the overall LOS. Beginning January 1994, all donors (and recipients) were admitted the day of the procedure. Thus, although the mean LOS for the first 100 patients (including the 1 preoperative day) was 5.9 days, the mean LOS for the second 100 patients was 4.1 days (range, 2-6 days).

PREOPERATIVE RADIOLOGICAL IMAGING

To evaluate donor renal artery anatomy preoperatively, the first 122 patients underwent conventional angiography (DSA), and the subsequent 79 patients underwent either CTA (75 patients) or MRA (4 patients). Multiple renal arteries were found on preoperative imaging in 1 or both kidneys in 28% of donors: 9% had duplicated left renal arteries, 12% had duplicated right renal arteries, and 7% had bilateral duplicated renal arteries. One patient had 3 renal arteries bilaterally visualized preoperatively by DSA and underwent uneventful donor nephrectomy with subsequent successful transplantation to his brother.

We compared preoperative imaging with intraoperative findings. In patients who underwent preoperative DSA, an accessory renal artery was found intraoperatively in 14% of patients that was not visualized preoperatively. Of 75 patients who underwent preoperative CTA, 9 (12%) had an unexpected accessory renal artery found on the side of the donor nephrectomy. A missed accessory renal artery was noted in 1 of 4 patients who underwent MRA.

Of 26 kidneys with accessory renal arteries not visualized on preoperative imaging studies, 18 (69%) accessory arteries were thought by the recipient surgeon to be insignificant and were ligated. However, 8 (31%) were believed to be large enough or to supply enough renal parenchyma to require preservation. Of these 8 cases, both renal arteries were implanted separately in 7, and an end-to-side anastomosis between the accessory and main renal artery was performed in 1. A much higher percentage (7 of 16) of accessory renal arteries missed by DSA were thought to be significant and were preserved than those missed by either CTA (1 of 9) or MRA (0 of 4).

Although there was a high incidence of false-negative readings (ie, missed accessory renal arteries) regardless of imaging technique, no adverse sequelae occurred in either donor or recipient in these cases. There was no difference in surgical complications in donors with duplicated renal arteries, whether or not they were diagnosed preoperatively. In the only case of postoperative bleeding, the donor underwent a left nephrectomy with a single renal artery. Single renal arteries were present in each of the 3 cases of delayed graft function. Similarly, long-term graft survival was no different in patients with duplicated vs single renal arteries.

RECIPIENT OUTCOME

There were 3 (1.5%) cases of delayed graft function. In at least 1 of the cases, donor nephrectomy was unusually difficult because of dense perirenal adhesions. All 3 grafts subsequently recovered and are currently functioning 2½, 3, and 3½ years after transplantation, respectively.

Patient and graft survival rates are summarized in Figure 1 and Figure 2. Overall 1- and 5-year patient survival is 97% and 90%, and 1- and 5-year graft survival is 95% and 83%, respectively. Death with a functioning graft accounts for a relatively high proportion of graft losses in our series because of the high number of patients with diabetes mellitus receiving transplants at our institution, and if these patients are excluded, 1- and 5-year graft survival rates are 97% and 93%, respectively.

We performed 20 (10%) transplantations from living unrelated donors (10 spouses, 5 friends, and 5 in-laws or stepparents) during the study. The number of living–unrelated donor transplants has increased substantially during the past few years, and half of our living–unrelated donor transplantations were performed in the past 18 months.

Although the total number of cases is small, 1- and 5-year graft survival for living–unrelated donor transplantations was 93% and 83%, respectively. Figure 2 stratifies graft survival by donor type, ie, haplotype-identical living-related (ie, 2 haplotypes matched), non–haplotype-identical living-related (0 or 1 haplotype matched and more distant relatives such as cousins, uncles), and living–unrelated, and there is no significant difference in graft survival between living–unrelated and non–haplotype-identical living–related donor transplants.
COMMENT

With the incidence of end-stage renal disease in the United States increasing at a rate of more than 8% per year and the increasing disparity between cadaver donor supply and demand, there is increasing reliance on living-related donors for kidney transplantation. With the recent publication of United Network of Organ Sharing Registry data documenting comparable graft survival between living-unrelated and non–haplotype-identical living-related donor transplants, there has been a concomitant increase in the use of unrelated-living, especially spousal, donors as well. The major caveat in the use of any living donor for kidney transplantation remains the potential short- and long-term morbidity following donor nephrectomy in an otherwise healthy person.

Since the inception of our program, and in the most recent 201 cases reviewed here, donor mortality has been 0%. Two separate reviews of transplantation centers in the United States and Canada reported a mortality of either 0.03% or 0.06%. Although not addressed in this review, others have reported the long-term medical risk of unilateral nephrectomy in an otherwise healthy person to be negligible.\textsuperscript{11-13}

The incidence of major postoperative surgical complications in our series was extremely low and consistent with other recent reports in the literature.\textsuperscript{3,14-16} An apparent difference is the incidence of pneumothorax requiring a chest tube, which was 7% in the series of D’Alessandro et al.\textsuperscript{14} Cosimi\textsuperscript{2} reported an incidence of 9% in his collective series, although whether all patients required chest tubes was not specified. Chest tubes for postoperative pneumothorax were required in only 1% of our patients, although radiographic evidence of an incidental or asymptomatic pneumothorax was found in an additional 10%. Whether this difference represents a lower threshold for the use of chest tube drainage elsewhere or differences in surgical technique is not clear. The risk of pneumothorax is obviated with a transabdominal approach, but splenic laceration or late bowel obstruction are uncommon but serious complications.\textsuperscript{16} A factor in our overall low complication rate may be that the performance of the donor operation has been limited to 2 surgeons at our institution.

Postoperative pain, especially with a flank approach with limited rib resection; hospital LOS; and return to full activity are major concerns of patients and families and major impetuses for the application of laparoscopic techniques for nephrectomy in a living donor. Cosimi\textsuperscript{2} reports a 3.2% incidence of “prolonged discomfort” from the nephrectomy wound. We have found adequate postoperative analgesia with the infiltration of bupivacaine with epinephrine during wound closure and patient-controlled analgesia with intravenous meperidine or morphine, with most patients converted to oral analgesic medication on postoperative day 2 or 3 and a mean LOS in the hospital of 4 days. Nausea and vomiting is a problem in a few patients and is usually controlled with antiemetic agents. Epidural analgesia may also be used with excellent results, but the incidence of postoperative ileus and urinary retention may be increased.

In the initial report of Ratner et al\textsuperscript{3} of the first 10 laparoscopic nephrectomies in live donors, patients had lower analgesic requirements, an earlier resumption of oral intake, shorter LOS, and earlier return to work, although comparison was with 20 historical controls from the previous 4-year period, during which these measurements were longer than more recent series of open donor nephrectomies, including this one. A follow-up report\textsuperscript{17} of their first 30 laparoscopic live-donor nephrectomies continued to document short donor LOS in the hospital (3.1 days) and earlier resumption of full activity and return to work; 2 (7%) patients, however, required postoperative transfusions, and 2 (7%) allografts were lost because of early thrombosis. Both were right kidneys, and thrombosis was presumably due to the difficulty in getting an adequate length of a short right renal vein laparoscopically.

In the only other major series of laparoscopic nephrectomies in live donors to date, Jacobs et al\textsuperscript{18} reported comparable graft function in recipients and shorter LOS in the hospital and return to work in donors compared with those in whom an open technique was used. In their first 65 patients, Jacobs et al\textsuperscript{18} reported delayed graft function in 3, transfusion requirements in 4, delayed ileus in 2, and splenic laceration requiring open splenorrhaphy in 1. Only left laparoscopic nephrectomies were performed to avoid possible problems with a short right renal vein. Both are initial experiences and likely exhibit the same learning curve that accompanies the introduction of any new surgical technique. Current data on this procedure are limited to these preliminary reports, and whether the more widespread application of this technique will result in extremely low morbidity as reported with the open technique remains to be determined.

Computed tomographic angiography has replaced conventional angiography for the preoperative evaluation of donor vascular anatomy in many centers. It is less invasive with fewer complications; less expensive; gives renal parenchymal, ureteral, and venous anatomy; and it may also be used to provide functional data.\textsuperscript{19} Al-
though angiography has been the criterion standard for the evaluation of living renal donors, the incidence at our center of “missed” accessory renal arteries between CTA and DSA is comparable. Moreover, although the number was small, fewer accessory renal arteries missed by CTA were significant and required reimplantation compared with those missed by DSA. Although recipient outcome was no different regardless of imaging technique or the presence of multiple renal arteries, accurate preoperative imaging is critical in uncovering unsuspected renal disease and defining anatomy to choose which kidney is the safer to remove. Our experience with MRA is limited. It shares many of the advantages of CTA, but whether it proves to be as accurate remains to be determined.19

Although we performed our first living-unrelated (spousal) donor transplantation in 1987, we began actively encouraging this donor source following the landmark article by Terasaki et al7 in 1995. In the past 2 years in this series, 15% of our living donors were unrelated, and overall graft survival is comparable to non–haplotype- identical living donors as reported by Terasaki et al8 for this series, 15% of our living donors were unrelated, and overall graft survival is comparable to non–haplotype- identical living donors as reported by Terasaki et al8 in 1995. In the past 2 years

Living-donor nephrectomy is associated with an extremely low morbidity. Recent trends in the past decade at our center include shortened LOS in the hospital, the replacement of conventional angiography with CTA or MRA for preoperative donor evaluation, and the expanded use of unrelated living donors. Whether newer approaches such as laparoscopic nephrectomy can be performed as safely awaits more widespread application of this technique.


Mary Ann Simpson, PhD, and Douglas Hale, MD, assisted with data retrieval and statistical analysis.

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DISCUSSION

Francis L. Delmonico, MD, Boston, Mass: This report presents an excellent series consistently well done by radiographic assessment of donor vessel anatomy, operative technique, and immediate postoperative care. I wish to focus my remarks on 2 important aspects of Dr Shaffer’s presentation—(1) the safety of living kidney donation and (2) the substantial increase we have observed in living-unrelated kidney donation. The Deaconess series presents an operative mortality of 0%, and we certainly commend them for that; however, several deaths have been reported worldwide. In the Deaconess series, no instances of postdonation renal failure occurred; however, renal failure has been reported to develop in about a dozen patients many years after living kidney donation. On the basis of a mortality rate, albeit extremely rare, and the observation that some donors have gone on to have renal failure, prominent transplantation physicians such as Thomas Starzl, MD, have at one time expressed strong opposition to living organ donation. In my view, Dr Shaffer’s report is a weighty refutation of Starzl’s position.

However, if I have one concern about Dr Shaffer’s report, it is the absence of long-term follow-up for his 201-patient series. Have there been any instances of the long-term development of renal failure in the Deaconess kidney donors? And, perhaps a larger question, what is the responsibility of the transplantation community for follow-up on living renal do-
nors, perhaps at least 1 year following donation, to be aware of their continued well-being? Regarding the virtual explosion in the use of not only living-related but especially living-unrelated donors (10% of Dr Shaffer’s series are living-unrelated donors), the New England Organ Bank data were recently presented by Richard Luskin, MD, the executive director of the New England Organ Bank, at the End-Stage Renal Disease Network meeting. The first of these overviews reveals the rapid increase especially in unrelated donors. This shows the proportion of kidney donors in New England from 1988, which is the beginning of Dr Shaffer’s series, until 1996, and it reveals cadaver donors, then living-related donors, and then a marked increase in unrelated donors. The percentage has increased to 11% from a period in which no unrelated donors were used. Now the feedback we got at that meeting was that it’s a rapid explosion and that although most of these are derived from spouses, some of them are coming from “friends.” Thus, there is a challenge to the transplantation community about worldwide abuse, specifically in the Third World countries. What assurances do you have in the preoperative evaluation of these donors that the hazard of compensation is avoided?

The use of living-unrelated donors exposes a fallacy of the current allocation system of renal allografts. The necessity of HLA matching to achieve long-term success is clearly disputed by Dr Shaffer’s data and national data as well. Many are now concluding that the outcome of living-unrelated renal transplantation emphasizes that the ischemic period of preservation is the most consequential element of not only immediate but long-term success. So what is your perspective about that aspect of your now using unrelated-living donors?

Finally, you speculate about laparoscopic nephrectomy. This is an element of your series that should not be overlooked. In each instance that you and your associates set out to perform living-donor nephrectomy, you accomplished this successfully. But we have received word in unreported observations that there are now failures of the laparoscopic nephrectomy approach to retrieve the kidney and that the proponents of this method have abandoned doing so on the right side because of the complex anatomy of a short renal vein. Thus, your series seems to be a substantial refutation of the laparoscopic nephrectomy approach when you contrast your results with that complication. Perhaps I could get a comment about that.

**David Hull, MD, Hartford, Conn:** Over the years, as noted, a disproportionate number of people have been waiting for transplantation. This allowed the ethics in the discussion of whether to use unrelated live donors to go by the wayside because the need for transplantsations outstripped the donor population. So I would like to know about the ethics and where it went.

I have reviewed the information with laparoscopic nephrectomy and reviewed the Hopkins group and participated in a learning project there, went to the laboratory at Hartford, and have been involved in 2 donor nephrectomies using laparoscopic surgery. These were complicated because I had a Harrington rod insertion long ago, and the donor operation was difficult, although the kidney transplantation went well in the recipient and the donor recovered quickly. In the second patient, the procedure was a success. On the fourth postoperative day, however, a bowel perforation developed in this 63-year-old donor. My understanding of the laparoscopic procedure is that it is easy to perform once the technology is perfected, as with any new technology. Hopkins and the University of Maryland are now approaching laparoscopic nephrectomy in perhaps more than 200 live donors, and the results are good. What I have learned from this is that patients will donate kidneys more readily and more willingly, therefore increasing the potential donor pool from the use of laparoscopic methods. This is a real finding, and one would argue that length of stay and pain are significant concerns. A midline infraumbilical incision of 7.5 to 8 cm cannot be compared with a much larger flank incision, sometimes with rib resection. The laparoscopic procedure has a lot of benefits and will probably come to use more commonly in the future.

What are the upper and lower age limits of the donors from your population? Some donors in Massachusetts were in their 80s at the time of live donation.

**Dr Shaffer:** For Dr Delmonico, it is obviously troublesome that some deaths have occurred and some cases of renal failure worldwide have been reported following living-donor nephrectomies. This is a tremendous concern. This is an operation in which there should be 0% mortality and 0% morbidity. We and investigators at other centers are striving to achieve that. Specifically, though, we have had no instances of renal failure that we know of, but clearly this study does not give long-term follow-up. There have been excellent long-term follow-up studies from other centers; for example, the University of Minnesota and Sweden report no long-term adverse sequelae in renal function following living-donor nephrectomy. There may be a slight incidence of proteinuria, but no progressive decline in renal function.

As to compensation and the other ethical and social issues that Dr Delmonico brings up, it is difficult to answer these in this forum. In our living-related donor program, we have long had a policy whereby a physician not affiliated with the transplantation program evaluates and clears a patient medically. A social worker also evaluates each donor. If there are any unresolved psychological issues, a psychiatrist or psychologist will see the patient. In fact, for living-unrelated donors, we have made it a policy to have a separate committee that consists initially of a social worker and a nurse discuss the desire of the person to donate a kidney, and again, based on what they find, appropriate referral to a psychiatrist for screening before transplantation is made.

With regard to the comments on laparoscopic nephrectomies, I have no experience with it, but it is clear that there is a learning curve as with any new surgical technique and that there have been early problems in the Hopkins series. Of their first 30 kidneys, thrombosis developed in 2. The incidence of delayed graft function was close to 5%, but as they gain more experience, these complications have diminished. Learning from the Hopkins series, the workers at the University of Maryland have apparently avoided using right kidneys completely and only use the left kidney. The controls (open technique) in both the Hopkins and Maryland series have longer lengths of stay than our series. With any new technique, there is a substantial learning curve. Those groups have really pioneered this technique. Whether it will provide significant long-term advantages remains to be determined.