Increased Transplantation of Kidneys With Multiple Renal Arteries in the Laparoscopic Live Donor Nephrectomy Era

Surgical Technique and Surgical and Nonsurgical Donor and Recipient Outcomes

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Background: For anatomical and technical reasons, many transplant centers restrict laparoscopic live donor nephrectomy (in contrast with open live donor nephrectomy) to left kidneys.

Hypothesis: This change in surgical practice increases procurement and transplantation rates of live donor kidneys with multiple renal arteries (RAs), without affecting donor and recipient outcomes.

Design and Setting: Retrospective review at an academic tertiary care referral center comparing laparoscopically procured single- vs multiple-RA kidney grafts (April 1997 to October 2000).

Patients: Seventy-nine consecutive left laparoscopic live kidney donors and 78 transplant recipients.

Main Outcome Measures: Donor and recipient complications and postoperative length of stay; cold and warm ischemia time; operating time; short-term and long-term graft function; and survival.

Results: We noted multiple RAs in 21 (27%) of all kidneys. The proportion of donors with 1 or more perioperative complications was 19% in the single-RA group vs 10% in the multiple-RA group (P was not significant). For the recipients, we noted no significant differences between groups with respect to surgical complications, quality of early and late graft function, rejection rates, graft losses (all immunologic), and graft survival. Cold and warm ischemia time and length of stay were similar for donors and recipients in both groups. Median operating times were significantly longer for the multiple-RA vs single-RA group (difference, 41 minutes for donors and 45 minutes for recipients; P<.02).

Conclusions: While the introduction of laparoscopic live donor nephrectomy has significantly increased the number of grafts with multiple RAs (compared with historical open controls), this change in practice is safe for both donors and recipients from a patient outcome-based perspective. However, from an economic perspective, the longer operating time associated with multiple-RA grafts provides strong added rationale for optimization of surgical instruments and techniques to make right-sided laparoscopic nephrectomy a routine intervention.

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PATIENTS AND METHODS

PATIENTS

Between April 1, 1997, and October 31, 2000, laparoscopic left-sided nephrectomy was offered to 81 prospective live kidney donors at the University of California Davis Medical Center, Sacramento. They were informed about their renal vascular anatomy, the nature of the new laparoscopic technique, and the lack of long-term follow-up data. All donors were given the option to undergo open nephrectomy if so desired. Two donors (both with 2 RAs on the left side and 1 on the right side) elected to undergo open right-sided nephrectomy because they wanted to minimize the potentially higher risk for vascular complications in their respective recipients.

The patient population of this retrospective study thus includes 79 consecutive laparoscopic live donors (mean donor age, 41.9 years; 52% male, 48% female) and their 78 recipients (mean recipient age, 41.9 years; 8% pediatric; 51% male, 49% female; 11% retransplants; 77% were receiving dialysis at transplantation). Of these 79 transplants, 49 (62%) were from living related donors, and 30 (38%) were from living unrelated donors. Median follow-up was 771 days (range, 85-1373 days). The primary renal diseases of the recipients are listed in Table 1.

PREOPERATIVE DONOR EVALUATION

During the preoperative donor evaluation, medical, surgical, and psychosocial suitability for live donation was assessed. Detailed informed consent was obtained. Imaging studies for delineation of renal and retroperitoneal anatomy included either 3-dimensional computed tomography scanning or angiography combined with conventional renal arteriography, or magnetic resonance angiography. All donor-recipient pairs were T-cell crossmatch and ABO blood type compatible.

PRESENT LAPAROSCOPIC NEPHRECTOMY AND ARTERIAL RECONSTRUCTION TECHNIQUE

The hand-assisted laparoscopic technique was not used. At the beginning of the operation, a Foley catheter was inserted, and the donor was placed in a right-lateral decubitus position on the operating table. The kidney rest was elevated and the table was flexed to maximize exposure of the left flank. The patient was secured in place with a deflatable beanbag and adhesive tape. Appropriate additional padding for the legs, arms, and axilla was applied. Throughout the operation, fluids were liberally administered to maintain the donor’s urine output at 2 at least mL/kg per hour. Furosemide and mannitol were administered intravenously at the discretion of the surgeon prior to division of the RA(s).

The abdominal cavity was insufflated with carbon dioxide using a Veress needle inserted at the transition between the middle and medial third of a line between the umbilicus and the patient’s left anterior superior iliac spine (paramedian position) (Figure 1). After appropriate insufflation (maximal pressure, 15 mm Hg), a laparoscopic port was placed through the Veress needle site and a 30° laparoscopic camera was inserted into the abdomen. Under direct vision, 2 additional ports were placed along the left paramedian line: 1 subcostally, and 1 approximately halfway between the 2 ports already in place (Figure 1). The camera was then placed into the subcostal port for the remainder of the operation. The entire p erirenal laparoscopic dissection was done with an ultrasonic dissector. First, the left side of the colon, including the splenic flexure, was mobilized. The splenorenal ligament was divided, allowing the spleen to fall back into the upper abdomen. Next, Gerota’s fascia was incised on the anterior upper surface of the kidney, away from the renal pelvis and hilar vascular structures, and the upper pole of the kidney was partially mobilized.

Prior to continuing the dissection, an additional port was inserted subcostally in the left posterior axillary line. The hook retractor, which was then inserted through this port, allowed retraction of the kidney laterally, gently stretching the RA and renal vein. The lateral retraction of the upper kidney pole also facilitated identification of accessory upper polar RAs, which were often found in a more anterior plane than the main artery. The renal vein was then identified, and the gonadal and adrenal veins were dissected, clip-ligated, and divided. Next, the main RA was identified at its aortic takeoff and freed from all periarterial, ganglionic, and lymphatic tissue.

Finally, the ureter was dissected with a no-touch technique. The dissection was started in a plane medial to the gonadal vein. We did not insist on visualizing the ureter at this point, as the periureteral fatty tissue in the infrapolar perirenal area was left intact to minimize the potential for ureteral devascularization. Dissection was carried further down to the point at which the left ureter crosses the left common iliac artery. Here, the ureter was visualized and its future distal transection point identified. Next the posterior surface of the kidney was also dissected free, leaving the kidney only attached to the RA(s), renal vein, and ureter.

The donor was then rotated back into the supine position, and a transverse, approximately 6 cm long incision of the skin and anterior rectus sheath (centered on the midline) was made suprapubically at, or inferior to, the pubic hairline (Pfannenstiel incision) (Figure 1). The midline was split longitudinally (lateral retraction of the left and right rectus muscles), and a purse-string suture was placed into the peritoneum. A laparoscopic specimen retrieval bag device was then inserted into the peritoneal cavity through the center of the purse-string suture. The purse-string suture was tied around the retrieval bag device, and the abdomen was reinsufflated. The patient was rotated back into the right lateral decubitus position, and 70 U/kg (bolus) of intravenous heparin sodium was administered. If necessary, the retrieval bag device could be used to retract the colon and small bowel medially to enhance exposure of the renal hilar region. Next, the ureter was transected distally after clipping the distal portion remaining with the donor. At that point, the quality of diuresis could be

striction of laparoscopic nephrectomy to left kidneys at many transplant centers is not surprising.

This constitutes a major shift in practice in comparison with historical open donor nephrectomy series (in which right kidney utilization rates ranged from 17%-31%).16-18 The most common indication for right-sided nephrectomy in the open series was the presence of unilateral (left-sided) multiple RAs with a contralat-

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observed directly, and additional fluids and diuretics were given as needed.

Next, the RA was transected after applying a laparoscopic linear noncutting stapler (Multifire ENDO TA 30 2.5; United States Surgical Corporation, Norwalk, Conn) as close as possible to its aortic takeoff. This phase of the operation was considerably facilitated by the hook retractor placed in the posterior axillary line, which allowed placement of the vascular stapler as near as possible to the aorta and inferior vena cava, respectively, by gently stretching the vascular pedicle, thus maximizing graft vessel length. If multiple RAs were present, they were handled as follows: (1) if they were close to the main RA aortic takeoff, they were included into the stapler and stapled at once with the main RA (single-stapler application); or (2) if they were too distant from the main RA, they were stapled or clipped separately. Intravenous protamine sulfate was then given to reverse the effect of heparin. The stapler was reloaded and applied to the renal vein, which was then also transected. The kidney was placed into the laparoscopic retrieval bag and extracted through the suprapubic Pfannenstiel incision. The kidney was flushed immediately after extraction (with Ringer’s lactate solution or Euro-Collins solution at 4°C) and preserved on ice until implantation. The Pfannenstiel incision was closed, and the operative site was inspected for hemostasis after abdominal reinsufflation. All port sites larger than 5 mm in diameter were closed under direct vision from within the abdominal cavity with an interrupted fascial suture.

The backtable ex vivo kidney preparation was performed either in the donor or recipient operating room. Arterial or venous extension grafts were not used. Ex vivo surgical management of kidney grafts with multiple RAs included any of following techniques: (1) end-side reimplantation of a smaller accessory artery into the main RA; (2) side-side anastomosis of 2 or 3 RAs of approximately equal caliber (“pants technique”); or (3) ligation of small, usually upper polar, accessory arteries, particularly if they supplied less than 5% to 10% of the renal parenchyma. All microsurgical arterial reconstructions were done using surgical loupes (magnification ×2.5).

RECIPIENT OPERATION

The graft was usually placed extraperitoneally into the right or left iliac fossa. Ureteral drainage was reestablished with an extravesical single- or multiple-stitch technique. Ureteral stents were not routinely used. Furosemide and mannitol were given intravenously before graft reperfusion. Perioperative central venous pressures were routinely monitored via a central venous catheter.

POSTOPERATIVE RECIPIENT MANAGEMENT

Intravenous diuretics were administered according to urine output. Platelet aggregation inhibitors and anticoagulating agents were not routinely given. The immunosuppressive protocol included a calcineurin inhibitor (tacrolimus or cyclosporin A), mycophenolate mofetil, and a prednisone taper. Recipients considered to be at higher immunologic risk (eg, retransplant recipients) also received an interleukin 2 receptor antibody (basiliximab or daclizumab) perioperatively. For recipients with delayed graft function, administration of the calcineurin inhibitor was postponed until return of adequate graft function, and a 7- to 10-day induction course of monoclonal antilymphocyte antibody (muromonab-CD3) or polyclonal antilymphocyte globulin was administered.

Rejection episodes (all biopsy proven) were treated by intravenous steroid pulse therapy or an oral prednisone taper. Histologically severe and all steroid-resistant rejections were treated with a 5- to 7-day course of polyclonal antilymphocyte globulin.

Graft biopsy specimens were obtained whenever rejection was clinically suspected (usually based on abnormal or otherwise unexplained laboratory parameters, deterioration on renogram, or development of graft tenderness).

Dialysis was performed as needed in the postoperative period, according to the patient’s clinical status and laboratory parameters. Delayed graft function was defined as the need for at least 1 dialysis session during the first 7 days after transplantation.

In case of delayed graft function, a biopsy was obtained at 7 days after transplantation and then every 7 to 10 days until renal function was adequate, or until the diagnosis of a nonfunctioning graft was made and the patient returned to dialysis.

OPERATING TIME

Operating time for donors and recipients was calculated as time from incision to skin closure. Since the kidney backtable preparation (and arterial reconstruction when applicable) was done either in the donor or recipient operating room (usually after skin incision), the total operating time (donor operating time plus recipient operating time) was also calculated to assess the overall effect of single vs multiple RAs on overall operating room use.

Operating times of donors and recipients who underwent concomitantly major additional procedures (eg, bilateral native recipient nephrectomy) were excluded from this analysis.

STATISTICAL ANALYSES

Donor and recipient demographic variables and outcome parameters were compared between the single- vs multiple-RA groups. Categorical variables were analyzed using the chi² test, and, when applicable, the Fisher exact test. Continuous variables (all nonparametric) were analyzed using the Mann-Whitney U test. Graft loss was defined as the return to permanent dialysis or death. Rejection-free and graft survival rates were calculated according to the Kaplan-Meier method. Survival rates between the 2 study groups were compared with the Gehan-Wilcoxon test and the log-rank test. For all statistical tests, P<.05 was considered significant.

However, it is unknown whether a higher rate of grafts with more complex anatomy mitigates some of the previously discussed advantages of laparoscopic as opposed to open nephrectomy. For example, the poten-
tial risks for the donor (eg, longer operating time, higher incidence of bleeding and other intraoperative complications, and more frequent conversion to open nephrectomy) may be increased. Insufflation of the abdomen with carbon dioxide during the laparoscopic intervention has been shown to decrease renal blood flow. These adverse hemodynamic effects may be further compounded by the longer operating time that is potentially associated with the presence of multiple RAs. The resulting nonspecific injury may not only impair early function, but also engender increased allograft immunogenicity and poorer long-term outcomes for the recipients. Finally, early and late postoperative vascular and ureteral complications, as well as renovascular hypertension, have all been associated with kidney grafts supplied by multiple RAs.

The lack of substantial data supporting the safety and efficacy of this shift in surgical practice prompted us to review our own experience. Our laparoscopic live donor nephrectomy program was initiated in 1997. At that time, we made a programmatic decision to apply this new technique only to left kidneys. Laparoscopic nephrectomy was thus offered to all live donors qualifying for left kidney donation, irrespective of their left RA anatomy. Only donors with anatomical indications not pertaining to the number of RAs (eg, unilateral, right RA fibromuscular dysplasia or right kidney cysts) were advised to undergo open rightsided nephrectomy.

The aims of this study were (1) to analyze the incidence of multiple-RA grafts when using this algorithm, (2) to describe potential surgical implications for the donor and recipient operations, and (3) to study, according to RA anatomy, donor and recipient short-term and long-term outcomes. All left kidneys with single RAs that were procured laparoscopically during the same period served as controls.

**RESULTS**

**MULTIPLE-RA INCIDENCE**

We noted multiple RAs in 21 (27%) of the 79 laparoscopically procured left kidney grafts. Of these 21 grafts, 17 (81%) had 2, and 4 (19%) had 3 RAs. Donor demographics for the single- vs multiple-RA groups were not significantly different (Table 2).

The surgical management of multiple RAs is indicated in Table 3. The most commonly used technique was a side-side anastomosis (in 62% of all multiple-RA kidney grafts).

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**Table 1. Primary Renal Diseases of Recipients**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Primary Renal Disease (n = 78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes (types 1 and 2)</td>
<td>17</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>11</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>9</td>
</tr>
<tr>
<td>Focal sclerosing glomerulosclerosis</td>
<td>8</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>8</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>6</td>
</tr>
<tr>
<td>Renal aplasia/dysplasia</td>
<td>4</td>
</tr>
<tr>
<td>Chronic reflux/pyelonephritis</td>
<td>4</td>
</tr>
<tr>
<td>Unknown etiology</td>
<td>8</td>
</tr>
<tr>
<td>Other etiologies</td>
<td>16</td>
</tr>
</tbody>
</table>

**Table 2. Donor Demographics According to Renal Arterial Anatomy**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Single Renal Artery* (n = 58)</th>
<th>Multiple Renal Arteries* (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/F</td>
<td>48/52</td>
<td>62/38</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>74</td>
<td>80</td>
</tr>
<tr>
<td>Hispanic</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>African American</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Related/unrelated</td>
<td>60/40</td>
<td>67/33</td>
</tr>
<tr>
<td>Median age (range), y</td>
<td>42 (22-70)</td>
<td>39 (23-60)</td>
</tr>
</tbody>
</table>

*All data are percentages unless otherwise indicated. For all pairwise comparisons, P is not significant.

**Table 3. Surgical Management of Grafts With Multiple Renal Arteries**

<table>
<thead>
<tr>
<th>Graft Characteristic (N = 21)</th>
<th>No. of Multiple Renal Arteries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grafts with 2 renal arteries</td>
<td></td>
</tr>
<tr>
<td>(n = 17)</td>
<td></td>
</tr>
<tr>
<td>Side-side anastomosis</td>
<td>10</td>
</tr>
<tr>
<td>End-side anastomosis</td>
<td>3</td>
</tr>
<tr>
<td>Ligation of 1 artery</td>
<td>4</td>
</tr>
<tr>
<td>Grafts with 3 renal arteries</td>
<td></td>
</tr>
<tr>
<td>(n = 4)</td>
<td></td>
</tr>
<tr>
<td>Side-side anastomosis of all 3 arteries</td>
<td>2</td>
</tr>
<tr>
<td>(creation of single orifice)</td>
<td></td>
</tr>
<tr>
<td>Side-side combined with 1 end-side anastomosis</td>
<td>1</td>
</tr>
<tr>
<td>Ligation of 2 arteries</td>
<td>1</td>
</tr>
</tbody>
</table>

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Table 4. Perioperative Donor Morbidity and Length of Stay According to Renal Arterial Anatomy*

<table>
<thead>
<tr>
<th>Event</th>
<th>Single Renal Artery (n = 58)</th>
<th>Multiple Renal Arteries (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donors with ≥1 complication†</td>
<td>11 (19)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Renal vein injury</td>
<td>2‡ (3)</td>
<td>...</td>
</tr>
<tr>
<td>Renal artery injury (vascular stapler malfunction)</td>
<td>1‡ (2)</td>
<td>...</td>
</tr>
<tr>
<td>Bleeding from renal artery staple line*(stapler malfunction)</td>
<td>...</td>
<td>1‡ (5)</td>
</tr>
<tr>
<td>Splenic capsule tear</td>
<td>2‡ (3)</td>
<td>...</td>
</tr>
<tr>
<td>Relaparotomy for postoperative bleeding</td>
<td>1 (2)</td>
<td>...</td>
</tr>
<tr>
<td>Blood transfusion requirement</td>
<td>3 (5)</td>
<td>...</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>1 (2)</td>
<td>...</td>
</tr>
<tr>
<td>Relaparotomy for early small bowel obstruction</td>
<td>1 (2)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>2 (3)</td>
<td>...</td>
</tr>
<tr>
<td>Hospital readmission for constipation</td>
<td>1 (2)</td>
<td>...</td>
</tr>
<tr>
<td>Left anterior thigh parasthesia</td>
<td>1 (2)</td>
<td>...</td>
</tr>
<tr>
<td>Median postoperative length of stay (range), d</td>
<td>3 (2-7)</td>
<td>3 (2-5)</td>
</tr>
</tbody>
</table>

*All data are numbers (percentages). For all pairwise comparisons, P was not significant. Ellipses indicate not applicable. †Three donors had >1 complication. ‡Indicates a conversion to open nephrectomy.

DONOR OUTCOME

In all, 11 donors (19%) in the single-RA group vs 2 donors (10%) in the multiple-RA group experienced at least 1 complication (Table 4; P was not significant). The pressure-induced rhabdomyolysis in one donor resulted from extended operating time due to concomitant ipsilateral adrenalectomy; the transiently impaired postoperative renal function resolved without requiring dialysis. Both splenic capsule tears were treated successfully after conversion to open nephrectomy without splenectomy. The individual incidence of complications presented in Table 4 was not significantly different for the single- vs multiple-RA group.

In 6 (8%) of all donors, the laparoscopic operation was converted to open nephrectomy (5 patients in the single-RA group vs 1 patient in the multiple-RA group; P was not significant). The conversion indications are presented in Table 4.

Median postoperative length of stay was 3 days in both groups (Table 4; P was not significant). Perioperative donor mortality was 0%.

OPERATING AND KIDNEY GRAFT ISCHEMIA TIMES

The differences between warm ischemia times for both donors and recipients, and cold ischemia time, were not statistically significant when comparing the single- vs multiple-RA groups (Table 5).

Kidneys with multiple RAs were associated with significantly longer operating times for both donors (P < .002) and recipients (P < .009) when compared with single-RA grafts (Table 5). Accordingly, the median total operating time was also nearly 45 minutes longer for kidneys with multiple RAs (585 minutes for multiple vs 541 minutes for single RAs; P < .003) (Table 5).

RECIPIENT OUTCOME

Recipient demographics in both study groups did not differ significantly (Table 6). One recipient with a multiple-RA graft experienced early postoperative bleeding from the end-side reimplantation site, requiring surgical reexploration (Table 7). We noted no incidence of vascular graft thrombosis. In all, 3 ureteral complications (4%) occurred (all in the single-RA group; P was not significant): 1 immediate postoperative mechanical obstruction (technical complication), 1 early postoperative distal ureteral stenosis at 6 weeks, and 1 late, distal ureteral stenosis occurring 3.7 years posttransplantation as a result of chronic rejection. There were 2 lymphoceles in each study group (Table 7; P was not significant).

QUALITY OF EARLY GRAFT FUNCTION

We noted no significant differences in immediate postoperative urine output when comparing both study groups.

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Early (on days 1-6) and late (at 1, 3, and 6 months, and at 1, 2, and 3 years) median serum creatinine levels were not significantly different for single- vs multiple-RA grafts (Figure 2). We noted delayed graft function in only 4 recipients (7%) of single-RA kidneys; P was not significant. In 2 cases, the delayed function resulted from early recurrence of disease: in 1 case from early acute vascular rejection, and in 1 case, there was no discernible cause.

### GRAFT REJECTION AND SURVIVAL RATES

Differences between rejection rates at 6 months, overall rejection rates (Table 8), and rejection-free survival rates (Figure 3) were not statistically significant for the single- vs multiple-RA kidneys (Table 8); P was not significant. In 2 cases, the delayed function resulted from early recurrence of disease: in 1 case from early acute vascular rejection, and in 1 case, there was no discernible cause.

**Comment**

The rapidly increasing laparoscopic kidney donation rates have been accompanied by an equally significant shift in surgical practice—many centers performing this operation are restricting it to left kidneys. Accordingly, a review of the published experience demonstrates a very inconsistent laparoscopic surgical approach to the prospective live kidney donor. Several large centers have reported that they perform only left-sided nephrectomies laparoscopically. Only one other major program recently published their experience with laparoscopic procurement of right kidneys (in 7.5% of their donors). However, they proceeded with open division of the right renal vein following a laparoscopic dissection. This semi-
laparoscopic approach may preclude the right kidney donors from experiencing some of the advantages associated with a truly minimally invasive operation. Finally, Arenas et al\textsuperscript{10} recently indicated a 47% proportion of right kidneys in a relatively small series of 15 laparoscopic nephrectomies, but without providing details on surgical technique and donor complications. The underlying rationale for this overall overwhelming preference of the left kidney by laparoscopic surgeons is the anatomically longer left renal vein, coupled with the inability to obtain as long a length of the renal vein with the laparoscopic as with the open technique.

This limitation to the left side has significant consequences for the arterial anatomy of living donor kidneys available for implantation. In the literature, an incidence of 18% to 30% of unilateral multiple RAs was described.\textsuperscript{16,23,25,31} The incidence of bilateral multiple RAs ranges from only 2% to 15%,\textsuperscript{16,23,31} Having the ability to choose between the left and right kidney (to avoid unilateral multiple RAs, for example) has led to right kidney procurement rates of as high as 31% in open donor nephrectomy series.\textsuperscript{10-18} We hypothesized therefore, that forgoing the option of choice between the right or left kidney would lead to higher utilization rates of kidneys with multiple RAs, unless one were to limit laparoscopic nephrectomy only to kidneys with normal anatomy— precluding, thereby, as many as 30% of all donors from benefiting from a procedure with less morbidity.

The presently available literature contains little information on the incidence of multiple RAs in laparoscopically procured grafts. Consistent with the findings of anatomical studies, Kuo et al\textsuperscript{12} reported a 30% incidence of left kidneys with multiple RAs in their laparoscopic experience. Sasaki et al\textsuperscript{11} noted that 19% of kidneys had multiple RAs in their laparoscopic experience, despite taking a relatively conservative approach (ie, a low threshold for open nephrectomy, exclusion of left kidneys with more than 2 arteries from laparoscopic nephrectomy) when preoperatively detecting anatomical arterial variants. This compares with a 15% to 18% incidence of multiple-RA grafts from living donors using the open technique (procurement of either right or left kidneys).\textsuperscript{22,25} The drastically changed approach to kidneys with multiple RAs in the laparoscopic live donor nephrectomy era is probably best epitomized by the statement of Ratner et al\textsuperscript{17} that “... multiple left renal arteries are less problematic than a right kidney.”

But even compared with open left-sided nephrectomy only, laparoscopic procurement of the same kidneys would still yield a higher rate of multiple-RA grafts. Since the laparoscopic staplers are introduced from a distance, and at an angle to the RA and renal vein (compared with an openly applied vascular clamp), not all potentially available vascular length may be obtained. While curved open clamps are available, all laparoscopic stapler tips are straight. This does not allow for placement of the laparoscopic staplers as close to the aorta and inferior vena cava as an open clamp would. Moreover, the width of the vascular stapler is greater than the width of a conventional vascular clamp. This will lead, in cases in which the RA has a single aortic orifice but an early bifurcation, to multiple RAs with the laparoscopic operation, while open nephrectomy would still yield a graft with a single RA.

Consistent with our hypothesis, our 27% rate of kidney grafts with multiple RAs is considerably higher than those of historical experiences with open nephrectomy.\textsuperscript{22,25} This high rate of multiple-RA grafts may theoretically exert an adverse effect on outcome. Previous authors\textsuperscript{23-26} have associated multiple RAs with several posttransplant complications. Therefore, during the initial 2 decades of clinical renal transplantation, such anatomy was even considered to be a transplant contraindication.\textsuperscript{25} Vascular complications that have been described for multiple-RA grafts include graft thrombosis, RA stenosis, and an increased risk for renovascular hypertension.\textsuperscript{23,27} With regard to the ureter, Loughlin et al\textsuperscript{24} described a higher incidence of early ureteral necrosis and renal pelvicaliceal fistulas with multiple RAs.\textsuperscript{24} Premature atherosclerotic occlusion of small, accessory, lower polar arteries may hypothetically lead to late, ischemic, distal ureteral strictures. But importantly, the longer, technically more challenging procurement operation of kidneys with multiple RAs may also expose the donor to added risk for complications, such as bleeding and the need for blood transfusion, or may mandate a higher rate of conversion to open nephrectomy. A more difficult donor operation may also result in more graft injury (eg, longer pneumoperitoneum time with reduction of intrinsic renal blood flow and more mechanical trauma to the kidney).\textsuperscript{19} The postimplantation recovery from this injury may in turn result in more inflammation, increased graft immunogenicity, more rejection episodes, and premature graft loss.\textsuperscript{21}

Unfortunately, no detailed data addressing potential safety concerns for laparoscopic donors of multiple-RA kidneys have been published. In our analysis, we noted no significant perioperative morbidity differences for postoperative donors of single- vs multiple-RA grafts. Rates of conversion to open nephrectomy, intraoperative and postoperative complications, as well as length of stay, were not significantly different. Our data indicate that procurement of kidneys with multiple RAs can be accomplished safely and does not impose an

Figure 4. Kidney graft survival. $P=.70$ using the Gehan-Wilcoxon test; $P=.62$ using the log-rank test.
additional socioeconomic burden on the donor by lengthening hospital stay.

For the recipient, overall intraoperative and early postoperative complication rates were not significantly different either. The only vascular complication specifically attributable to a multiple-RA kidney was postoperative bleeding from an arterial reconstruction site in 1 patient. This very low vascular complication rate was achieved using standard microvascular reconstruction techniques and without using any autologous vein patches or extension grafts, as suggested by others previously.22 We believe that these more complex reconstruction techniques may not be necessary for the vast majority of all laparoscopically procured multiple-RA grafts. Instead, one can rely on reconstruction techniques that have been proven safe, both short-term and long-term, in a large open donor nephrectomy series.22,27 There was only one ureter complication that was possibly due to surgical compromise of its blood supply: a distal stricture at 6 weeks posttransplant that occurred in a patient with a single RA. Kuo et al12 also failed to detect a difference in ureteral complications for single- vs multiple-RA kidneys, although their overall ureteral complication rate (11%) was somewhat higher than ours. Albeit not statistically significant, it is interesting to note that the lymphocele incidence was 3 times higher in the multiple-RA group than in the single-RA group. A higher incidence of postoperative lymphoceles inherent to laparoscopically procured kidneys was recently suggested by Burrows et al.31 The causes for this are unclear; however, one might speculate that this finding may be due to less efficient sealing and ligation of renal hilar lymphatics by the ultrasonic dissectors often used in the closed technique. This hypothesis could also provide an explanation for our results. The even more careful dissection and preparation of renal hilar structures in kidneys with multiple (vs single) RAs may leave more graft lymphatics patent, resulting in a higher rate of lymphoceles. But a larger number of transplants will be necessary to confirm or refute this hypothesis. Quality of early graft function, as measured by urine production and serum creatinine levels, was not significantly different between the 2 study groups. Long-term quality of function, rejection, and graft loss rates, as well as graft survival were also similar. These findings are consistent with the more limited data on function of kidneys with multiple (vs single) RAs that were recently published by another center.12 One limitation of this part of the analysis is the relatively short follow-up time. With overall graft survival rates exceeding 90% at 3 years, subtle differences in early graft injury leading possibly to impaired immunologic outcome (the injury-inflammation-immune recognition triangle proposed by Halloran et al20) may be difficult to detect, especially since warm and cold ischemia times were similar for both study groups. Only a longer follow-up on a larger number of transplants may answer this question.

Importantly, we noted a significant difference in operating time: kidneys with multiple RAs were associated with longer operating room time for both donors and recipients. One of the limitations of this retrospective study is that this finding cannot be further interpreted in detail from the available data. Only a prospective (currently ongoing) data collection will allow us to differentiate clearly whether these differences result only from an intrinsically longer operating time for donors and recipients, or, at least in part, from the time necessary for additional backtable work (ie, for the vascular reconstruction), which adds variably to either donor or recipient operating time in our institutional practice. In any event, the higher charges that will result from the longer overall operating room time are an important factor, as laparoscopic (in comparison with open) nephrectomy has been associated with higher initial expenditures, which were thought to result mainly from the use of disposable laparoscopic instruments. Hence, a recent comparison of hospital charges between laparoscopic vs open kidney donors (including a 48- to 72-hour postoperative stay) by Kuo et al34 showed only a 10% difference in favor of the laparoscopic group. Adding costly operating room and anesthesia time to this equation may decrease the economic attractiveness of renal transplantation from laparoscopic live donors, and may further postpone the “break-even” point (time required before transplant cost is recovered by saving the cost of dialysis).35

Although there is thus no apparent major surgical or immunological detriment resulting from the current practice favoring left-sided laparoscopic nephrectomy, development and standardization of laparoscopic techniques for right kidney procurement are much needed. Such techniques would also allow surgeons to routinely offer laparoscopic nephrectomy to donors who have indications other than RA multiplicity to undergo right-sided nephrectomy (eg, right-sided cysts with differential kidney function shifted in favor of the left kidney; unilateral, right-sided fibromuscular dysplasia). Although the initial experience with transplantation of laparoscopically procured right kidneys was fraught by a high renal vein thrombosis rate, further analysis of the report by Ratner et al35 shows that 2 of the 3 thrombosed kidneys had major venous anatomical abnormalities, and that 1 kidney thrombosed due to extension of a peripheral venous thrombus into the renal vein of the graft. Taking this more detailed analysis into account, we propose that, based on evidence in the literature and from our experience, laparoscopic procurement and transplantation of right kidneys can be accomplished safely, provided that certain precautions are taken. In the donor, an optimal stapler insertion angle (ie, an appropriately placed port) for the stapling of the right renal vein at the vena cava is crucial. It would also be of importance to stretch the right renal vein maximally (by retracting the kidney laterally) prior to transection to maximize available vessel length. Use of a laparoscopic linear noncutting stapler (applying a single row of staples) instead of a laparoscopic linear cutting stapler (applying a double row of staples and cutting in between) further maximizes available graft vessel length. Moreover, the development of a slightly curved vascular stapler of minimal width by the laparoscopic instrument industry would be highly desirable. Application of these strategies in the donor would require a semi-openly placed vascular clamp only in exceptional cases. The subcostal incision that was proposed for this purpose may indeed obviate some of the advantages of the laparoscopic technique with respect to perioperative morbidity and donor.
recovery. In the recipient, the risk for renal vein thrombosis may be minimized by right-sided implantation, as left-sided implantation has been associated in multivariate analyses with higher thrombosis rates not only for kidneys, but also for pancreata (in the latter grafts, the portal vein is usually even shorter than the right renal vein).22,26 The higher vascular complication rates after left-sided implantation may also be due to the more posterior localization of the left common and external iliac veins, allowing for less spatial flexibility. Spatial flexibility for optimal vessel alignment can be enhanced by fully mobilizing the common and external iliac veins, as previously described,26 by ligating and dividing all internal iliac branches. This maneuver also allows the surgeon to transpose the iliac vein lateral to the right common and external iliac artery if mandated by a very short right renal vein. If major venous anomalies (eg, duplicated renal veins) are noted on preoperative imaging studies in donors of right kidneys, an open right nephrectomy should be planned from the beginning. Lastly, if any unexpected vascular anomalies or variations are encountered during laparoscopic right nephrectomy, a lower threshold for conversion to open nephrectomy than contralaterally should be employed. As a consequence of the results of the present study and using the surgical strategies discussed above, we have recently begun to proceed with a right-sided, fully laparoscopic nephrectomy when indicated.

Finally, our experience with the 2 donors who declined laparoscopic left-sided nephrectomy of multiple-RA kidneys out of concern for their recipient (opting for right open nephrectomy instead) also underscores the degree of autonomy that live donation grants to patients. We believe that, particularly in this setting, donor involvement in the decision-making process (within medically reasonable limits) is extremely important and that this approach ultimately further contributes to the high postdonation satisfaction scores that were recently reported.

In summary, while introduction of laparoscopic nephrectomy has significantly increased the number of grafts with multiple RAs, from a patient outcome–based perspective, this changed practice is safe for both donor and recipient. Short-term and long-term graft functioning are comparable, without evidence for functional or immunologic sequelae, and in spite of the longer operating time noted for multiple-RA grafts. Longer follow-up is necessary to assess potential late ureteral and vascular complications (eg, ureteral stricture, RA stenosis). However, from an economic perspective, the longer operating time associated with multiple-RA grafts that are more frequently encountered when exclusively procuring left kidneys provides strong added rationale for optimization of surgical instruments and techniques to make right-sided laparoscopic nephrectomy a routine intervention.

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REFERENCES


Peter G. Stock, MD, San Francisco, Calif: I appreciate the opportunity to review this very impressive series. During the initial experiences with laparoscopic living-donor nephrectomy, there was a great deal of concern in terms of the safety and efficacy of this procedure. The initial skepticism was related to the obvious inherent technical difficulties in removing a kidney with minimal trauma and minimal ischemic times so that it could be safely transplanted. This skepticism was fueled by the fact that the procedure was initially performed in several East Coast institutions with a high degree of local competition. There is no question that advertising the capability to perform laparoscopic donor procedures greatly increases the number of referrals for living-donor renal transplants. Fortunately, as this paper elegantly demonstrates, this procedure has proven to be a safe and effective procedure. Of further importance, laparoscopic kidney donation has increased the number of willing living donors that should not be trivialized, with the average wait time for cadaveric kidney transplants now approximating 5 years in the state of California.

Multiple papers have now confirmed that compared with open nephrectomy, laparoscopic nephrectomy is associated with a shorter length of hospital stay, decreased pain, and faster return to work. This paper explores the safety and efficacy for extending the inclusion criteria for laparoscopic donation to include left kidneys with multiple arteries. My comments and questions relate principally to the safety issues in the donor, but also to the outcome of the donor kidneys with multiple arteries procured using the laparoscopic approach.

Since the donor safety issues are of paramount concern, my first question relates to the mean operating time for procuring kidneys with multiple arteries. The mean operating time that you reported of 345 minutes is presumably double that of the open procedure. I would like to inquire whether the issues of hospital stay, pain control, and time to return to work were analyzed for this group of laparoscopic donors as compared with donors with single arteries. Considering a different donor safety issue, I wanted to ask you if your institution has a policy of procuring right kidneys in women who intend on having subsequent pregnancies. Because of the increased frequency of obstruction of the right ureter during pregnancy, several transplant surgeons favor right donor nephrectomy in this category of living donors if all other factors are equal.

In your paper, you report that either conventional renal arteriography or a magnetic resonance angiography (MRA) were used to evaluate the blood supply to the kidney. Since MRA also affords the ability to visualize the renal veins, do you prefer to utilize this technique? Although your paper focuses on kidneys with multiple arteries, is there any situation with multiple renal veins where you would favor using the right kidney if it had simpler venous anatomy, particularly in light of the fact that the original losses really related to venous problems rather than arterial problems.

In your discussion, you point out that the arterial length with the laparoscopic approach is shorter than that with the open approach, and this has led to an increased incidence of multiple arteries following procurement. At UCSF we have switched over to utilizing a locking clip instead of the stapler on the artery, and have found this very useful in providing extra length. An additional benefit of the locking clip is that verification of adequate application can be made prior to division of the artery. Furthermore, when a particularly short vessel is anticipated, the recipient surgeon mobilizes the iliac vein to a superficial position by ligating the hypogastric vein to facilitate positioning of the transplanted organ. When you get an inferior pole artery, have you considered an anastomosis to the inferior epigastric artery as an alternative to the techniques that you have discussed in your paper?

Recent data suggest that the small arteries in transplanted organs are beginning to demonstrate signs of atherosclerosis as early as 18 months following the transplant. For this reason, I would like to ask what type of antiplatelet regimens are being utilized in the recipients of kidneys with small multiple arteries. It may be too early to ask the question of the incidence of hypertension.

Finally, I would like to congratulate the authors for a very impressive series with a technically challenging procedure. Based on these results, are there plans to extend the inclusion criteria for laparoscopic donation to the right kidney in the immediate future? If so, what technical modifications will be necessary to make this equally safe and effective?

Quan-Yang Duh, MD, San Francisco: I want to congratulate the authors for a very good series and honest report of their data. I want to comment on the technical aspect of this operation. We have performed 50 cases of laparoscopic donor nephrectomy at UCSF, initially started by Dr. Freise and me, and now our transplant surgeons do it by themselves.

I have a comment about the vascular clip. We had one conversion to open operation because the GIA stapler did not work properly. We then changed to a TA stapler, then to the locking clips. The nice thing about the locking clip is that you can see whether it is working or not before you cut the artery. In addition, it gives you a few millimeters extra on the artery.

My second comment is regarding the learning curve. It wasn’t clear from the presentation whether complications have tended to occur in the earlier patients. Early on in our experience, we have tended to avoid multiple vessels and patients with obesity or prior operations. But in centers with more experience, obesity, prior operations, and multiple vessels are no longer contraindications. I think this is related to the learning curve. I don’t think one should conclude from this report that it is a good idea to start with difficult patients. It is still a good idea to start with simple cases, and then as one develops the expertise, go on to the potentially more complicated ones.

Where in the learning curve did these complications, especially the one that required conversion, occur?

Alan H. S. Cheung, MD, Honolulu, Hawaii: I would also like to add my congratulations to the UC Davis team for their excellent series. I have 2 technical questions for them. With their
longer operating time in the double or triple renal artery patients. I wonder if they could speculate whether the hand-assisted technique would be useful in these more challenging patients. The second question has to do with the type of perfusion solution that they use. I didn’t hear them mentioning that in their talk. What exact perfusion solution was used for these patients?

R. Hirose, MD, San Francisco: I would also like to add my congratulations for this excellent series. I have 2 questions that are related to some of the issues that Dr Stock brought up. The authors mention that they now use MRA as their preferred technique of imaging the donors. I am wondering if there was any incidence of missed extranumery arteries when using MRA. My second question relates to generalization of the issues that Dr Stock brought up about doing right nephrectomies. I would like to know, what are the criteria, if any, at your center of doing right-donor open nephrectomy? For example, if you had 4 arteries on the left and 1 on the right, would that be an indication? What are the indications, or have you done any open right-donor nephrectomies in this era of laparoscopic donor nephrectomy?

Dr Wolfe: I would like to thank all of the discussants for their comments and questions. We certainly agree with Dr Stock that patient safety is of paramount importance.

More than one discussant has asked about the operating time that is somewhat prolonged among the patients with multiple renal arteries. The fact is that in the process of performing a laparoscopic dissection, the identification of the specific location of vessels must be done more slowly and cautiously than can be done in an open case because the risk of injuring a vessel as you come upon it seems to be greater in laparoscopic dissections in general. As a result, when we knew in advance that there were multiple renal vessels, we proceeded more cautiously with the dissection in order to identify these vessels before they were injured. Furthermore, there is operating time for the backtable where the reconstruction of the vessels for transplant anastomosis is done. The operating time has diminished as experience has been gained and we became more facile with identification of these vessels in the retroperitoneal fat.

The length of stay was similar for both groups. An observation that was made by those of us who devoted much of our effort to the laparoscopic surgical development in the last 10 years has been that the duration of an operation is not a determinant of the extent of injury that the patient experiences, the length of time required to recover from the operation, or pain control and other measures of injury. The fact that it takes somewhat longer to do a laparoscopic operation has not proven to be a determinant of the extent of injury that the patient experiences as a result of the operative procedure.

We do not have a policy regarding avoidance of left-sided nephrectomy in females who may go on to childbearing. Currently we prefer the MRA imaging. It was not immediately available when this series began. We did in fact have one case in which a duplicate vena cava and 2 additional renal veins were not identified by the 3D-CT-angiography and renal arteriography. This patient required conversion to open nephrectomy for prompt hemostasis and repair.

The question was asked: Do we have a protocol for using the right kidney? The answer is yes if there is a contraindication to use of the left kidney. We also had 2 patients who declined to undergo left laparoscopic nephrectomy when told that we were uncertain whether the multiple renal arteries may represent a risk of complications to the recipient. These donors chose to minimize risk to the recipients and underwent a right open nephrectomy. Recently, we have done a right laparoscopic donor nephrectomy.

The stapling device that we use now is the endoscopic TA-30 in which only one row of staples is placed and then the vessel is cut with scissors following removal of the stapler and renal vessel length is preserved.

The GIA stapler places 2 parallel rows of staples and cuts between. Both of the stapler malfunctions occurred with a reticulating version of the GIA stapling device. This complication has not occurred using the TA, which is a simpler device and saves distance on the donor vein because you do not have a row of staples on the kidney side, which would then have to be removed on the backtable.

We have not used locking clips but recognize that the advantage of not having a separate row of staples on the kidney side is real. We do not have an antiplatelet protocol for the recipients.

There is a learning curve with this operative procedure as there has been with other complex laparoscopic procedures that have been undertaken. We benefited substantially by visiting 2 established programs and learning from them what they had learned regarding technical tricks. We presumably had less of a learning curve as a result.

We now dissect the spleen and colon away from their lateral attachments together, allowing them to fall medially. All but one conversion did occur in the first 50 cases. Our program began, as did many other successful programs, with a laparoscopic surgeon and a transplant surgeon combining forces and experience, operating together for the first 15 to 20 cases in order to maximize the skills of both surgeons.

We have not used the hand-assisted device. The incision necessary to extract the kidney is approximately one half the size of the incision necessary for me to get my hand in. The goal is to minimize the incision size and trauma to the patient, and if you can do that without the hand-assisted, then we feel that that is preferable.

Do we have criteria for using the right kidney? Yes. For example, if there is an impairment to the right kidney such as a cyst that would reduce the functioning parenchyma, then the donor should give up the right kidney and keep his or her normal left kidney.