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Laparoscopic Procurement of Single Versus Multiple Artery Kidney Allografts: Is Long-Term Graft Survival Affected?

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Abstract

Background—Living donor kidneys with multiple arteries (MA) are increasingly procured laparoscopically for transplant.

Methods—We compare long-term graft function and survival of kidneys with single arteries (SA) and MA over a 10-year period.

Results—There were a total of 218 grafts with SA and 60 grafts with MA. The MA group had longer operative and ischemic times than SA group. There was a small increase in ureteral complication (8.3% vs. 2.3% $P=0.06$) and a significantly higher incidence of rejection (23.3% vs. 10.1%, $P=0.01$) in MA group than in SA group. Graft function was lower in MA group than SA group. The 5-year graft survival by Kaplan Meier analysis was better in SA group than in MA group ($P=0.023$). The estimated graft survivals at 1, 3, and 5 year were 94.4%, 90.6%, and 86% for SA group and 89.6%, 83.2%, and 71.8% for MA group. There was a higher percentage of graft loss from chronic allograft nephropathy in MA group than in SA group (16.7% vs. 5.5%, $P=0.01$). The presence of MA (vs. SA) was an independent risk for acute rejection (OR 3.60, 95% CI 1.59–8.14, $P=0.002$) and for graft loss (HR 2.31, 95% CI 1.05–5.09, $P=0.038$).

Conclusion—Laparoscopic procurement of living donor kidneys with SA may be associated with a lower risk of rejection, better function, and superior long-term survival when compared with kidneys with MA.

Keywords

Living donor; Laparoscopic nephrectomy; Kidney transplant; Multiple arteries; Graft survival

Laparoscopic nephrectomy in a human living donor was first performed in 1995 (1). It has become the standard of care in many transplant centers. Living donor kidneys with multiple arteries (MA) are also routinely procured laparoscopically. Anatomical issues related to the

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liver and longer length of the left renal vein have made left donor nephrectomy preferred even in the presence of MA (2,3). Compared with procuring kidneys with a single artery (SA), the presence of MA may lead to longer operative times for more complicated dissection. Ischemic times are also longer because kidneys with MA require back table arterial reconstruction and a more complex implantation. Higher incidences of vascular, ureteral, and other complications have been reported (4–7). However, short-term outcome of the use of SA versus MA kidneys appear to be similar in the previous reports (8–13). Long-term graft function and survival have not been well compared between living donor kidney transplants with SA versus MA.

In this study, we examine our 10-year experience in laparoscopically procured living donor kidney transplants with SA versus MA. Surgical complications, medical events, long-term graft function, and survival are compared.

PATIENTS AND METHODS

Study Population

We reviewed all donor/recipient pairs who underwent living donor kidney transplants from laparoscopically procured kidneys from January 1998 to December 2007. All patients had at least 1 year follow-up after transplant by the end of 2008. This study was approved by our Institutional Review Board. Operative records were examined to determine whether the procured kidneys had SA or MA.

Surgical Technique

All living donors underwent a hand-assisted laparoscopic donor nephrectomy. Dissection was performed using the Ligasure device (Valley Lab, Boulder, CO). Vessels were stapled and divided using the Autosuture laparoscopic stapler (Covidiene Healthcare, Mansfield, MA). Kidneys were flushed and preserved with University of Wisconsin solution before 2002 and with Histadine-Tryptophan-Ketoglutarate solution after 2002.

Medical Therapy

Triple immunosuppression regimen of steroids, tacrolimus, and mycophenolic acid was used. High-risk patients defined as prior transplant recipient, six antigen mismatches or panel-reactive antibody (PRA) more than 20% received basiliximab induction therapy. Standard antifungal, antibacterial, and cytomegalovirus prophylaxis were administered per protocol. Acute rejection was confirmed by kidney biopsy, and the severity was graded according to the Banff criteria.

Statistical Analysis

Outcome measures included (1) surgical complications and medical events, (2) quality of graft function as assessed by estimated glomerular filtration rate (eGFR) using the MDRD equation, (3) graft survival over 5 years. Statistical analyses were performed using SAS version 9.1.3 software (Cary, NC). Chi-square test was used for count data and *t* test for continuous measures. Multivariable logistic regression analysis with a stepwise variable selection was used for examining risk factors. Product-limit estimates of survival curves were generated by the Kaplan-Meier method. A *P* value of less than or equal to 0.05 was considered significant.

RESULTS

We identified 278 donor-recipient pairs who underwent living donor kidney transplants during this 10-year period. There were 218 allografts with SA (78.4%) and 60 with MA (21.6%). The median follow-up was 5.2 (range, 1.2–11) years in SA group and 4.9 (range, 1–10.9) years in MA group. Table 1 summarizes both donor and recipient demographic characteristics. There

was no significant difference in any of these variables. Left kidneys were usually selected if they had one or two arteries. When left kidneys had three arteries and right kidneys only had one artery, then right kidneys were used. In the cases when both kidneys had MA, then left kidneys were selected. A total of seven kidneys were right sided, and all of them had SA. Six kidneys in MA group had three arteries. The MA group had their arteries reconstructed by syndactylizing the vessels to form a single lumen for anastomosis (21 patients), suturing smaller vessels to the side of the dominant vessel (19 patients), performing two separate arterial anastomoses (14 patients), or a combination of the above (six patients) for three arteries. No accessory artery was ligated. Ureteral stents were placed per recipient surgeon decision during the operation, and they were usually removed at 5 to 6 weeks.

Surgical Complications

Table 2 summarizes the surgical and medical events, renal function, graft loss, and patient death during this study period. Donors in the MA group required significantly longer operative hours than those in SA group for laparoscopic nephrectomy (1.9 ± 0.6 vs. 1.7 ± 0.5 , $P=0.03$), but the blood loss was similar. Three donors (all in SA group) had an intraoperative complication of venous bleeding requiring partial open conversion by extension of the hand port incision to gain hemostasis. Both cold ischemic time (CIT) and warm ischemic time (WIT) of grafts were significantly higher in MA group when compared with SA group (53.6 ± 18.8 min vs. 47.1 ± 16.9 min, 28.6 ± 6.8 min vs. 26.5 ± 4.9 min, respectively, $P=0.01$). The WIT was the anastomotic time only. The warm ischemia before flushing the kidney was not included, and it was usually less than 1 min with the majority of kidneys. Recipient complications were considered to be clinically significant when further intervention had been performed, and they were classified as vascular (bleeding/hematoma/thrombosis/stenosis), ureteral (stricture/leak), and others (lymphocele/ wound dehiscence/infection). There was a trend towards more ureteral complication in MA group (8.3% vs. 2.3%, $P=0.06$).

Medical Events and Graft Function

A similar percentage of patients in MA group (17%) received basiliximab induction when compared with SA group (16%). The 12-hr trough levels of tacrolimus, daily doses of mycophenolic acid and prednisone were similar between the two groups (data not shown). The MA group had significantly higher cumulative incidence of acute rejection than the SA group (23.3% vs. 10.1%, $P=0.01$) during this study period. A subgroup analysis showed no difference in the rejection rate by the different surgical techniques for arterial anastomosis in MA group (26.3% for end to the side anastomosis, 21.4% for separate arterial anastomoses, and 19% for syndactylization, $P=0.78$). Multivariable logistic regression analysis was used to examine the risk factors for acute rejection. The risk factors included recipient age, ethnicity, re-transplant, donor genetic relationship, donor operation time, CIT, WIT, peak PRA, human leukocyte antigen mismatch, MA, induction therapy, delayed graft function (DGF), as well as vascular, ureteral, or other complications. A stepwise variable selection was then conducted, and MA, DGF, and black ethnicity were found as the independent risk factors for acute rejection ($P<0.05$, Table 3). During the first postoperative year (at 6 and 12 months), graft function as reflected by eGFR was lower in the MA group than in the SA group ($P=0.01$ and 0.03). These differences became less significant at 2 and 3 years ($P=0.08$ and 0.05) and were similar by 4 years post-transplant (Table 2). The calculation of renal function was censored for graft loss.

Graft Survival and Patient Death

Figure 1 shows long-term graft survival by Kaplan-Meier analysis. The MA group had a significantly worse graft survival than the SA group over 5 years (log-rank $P=0.023$). Kaplan Meier estimated graft survivals at 1, 3, and 5 years were 94.4%, 90.6%, and 86% for the SA group and 89.6%, 83.2%, and 71.8% for the MA group. The overall graft survival at 1, 3, and

5 years was 93.7%, 88.2%, and 81.6%, respectively. The graft survival was also analyzed according to the different arterial anastomotic techniques in the MA group (Fig. 2), and no statistical difference was found (log-rank $P=0.237$). The causes of graft loss and patient death are summarized in Table 2. There was a higher percentage of graft loss in the MA group (31.7%) than in the SA group (15.1%) ($P=0.01$). Chronic allograft nephropathy (CAN) was the predominant cause of graft loss in the MA group (16.7%) when compared with the SA group (5.5%, $P=0.01$). Death with a functioning graft was the second most common cause and contributed equally to graft loss in both groups, which was followed by rejection, recurrent glomerular nephropathy, vascular thrombosis, and infections. The risk factors for graft loss were examined by Cox's proportional hazard regression analysis and significant factors were further analyzed by a stepwise variable selection model. MA, DGF, acute rejection, and vascular complications were found as the independent risk factors for graft loss ($P<0.05$, Table 4).

DISCUSSION

The advent of laparoscopic nephrectomy has extended to the procurement of living donor kidneys with MA. Autopsy reports suggest that the incidence of kidneys with MA is between 18% and 30% (14). Deceased donor kidneys with MA are routinely used for transplantation, and their long-term outcomes are reportedly not different from SA grafts (15). However, the renal arteries from deceased donors are longer and are frequently attached to an aortic patch, which makes reconstruction technically easier. In living donor kidneys with MA, there is an increased risk of injury from more extensive dissection during the laparoscopic nephrectomy. The requirement for complicated vascular reconstruction and more difficult anastomosis at the time of implantation impose additional ischemic injury and subsequent reperfusion injury. In addition, the small accessory arteries of grafts with MA might be ligated or thrombosed. Consequently, a higher rate of surgical and medical complications has been reported after transplant with MA grafts (4–7). Other reports suggested no difference in their outcome between MA and SA grafts (8–13). We hypothesize that these perioperative injuries may collectively lead to a reduced function and lower long-term survival in the transplanted kidneys with MA than the kidneys with SA.

In this study, 21.6% of our living donor kidneys had MA. The MA group required a significantly longer operation hours during their procurement (1.9 ± 0.6 vs. 1.7 ± 0.5 , $P=0.03$). Both CIT and WIT of grafts with MA were also longer than for the grafts with SA (53.6 ± 18.8 vs. 47.1 ± 16.9 min, 28.6 ± 6.8 vs. 26.5 ± 4.9 min, respectively, $P=0.01$). These are consistent with the other reports (3,5,8–10). All laparoscopic nephrectomies were performed by one of our two donor surgeons (DS/AP). There were no significant differences in operative/ischemia times, complications or graft loss between the two surgeons. There was a trend toward more ureteral complications in the MA group, although this was not significant. Carter et al. (5) reported a 17% incidence of ureteral complications among kidneys that had reimplanted accessory arteries. We did not observe a difference in the rate of vascular complications, especially thrombosis. But these reflect only large vessel thromboses. It is possible that small accessory arteries in MA group could be thrombosed after transplant, and these might not have been recognized by routine ultrasound imaging. Any thromboses of these small accessory vessels could decrease graft function and survival. Thromboses of lower polar arteries may also explain the higher ureteral complications in our MA group. A subanalysis noticed a higher incidence of surgical complications in the pediatric recipients (<12 years old). But the small number of pediatrics in MA group precluded a meaningful comparison.

We found that the cumulative incidence of biopsy-confirmed acute rejection was significantly higher in the MA group than the SA group. None of the previous studies reported a difference in rejection rate. The majority of rejection episodes were successfully reversed. There were

five graft losses in SA group (2.3%) and three graft losses in MA group (5%) from severe rejection (either vascular rejection or antibody mediated rejection). The rejection rate was not affected by the surgical techniques used for arterial anastomoses in the MA group. There were no significant differences in the “immunological factors” including recipient races, genetic relationship, retransplantation, peak PRA, or human leukocyte antigen mismatch between the two groups. Multivariable logistic regression analysis indicated that MA was an independent risk factor for acute rejection with an odds ratio of 3.6, which is similar to the well-known risk factors of black ethnicity and DGF. We postulate that the greater extent of perioperative injuries to the MA kidneys might predispose them to rejection. The measurable parameters, such as prolonged donor operation time, increased CIT and WIT, may not truly reflect the total injury of MA grafts. It is impossible to measure the mechanical injury during the more complicated donor dissection, vascular reconstruction, and anastomoses for MA grafts.

The early graft function at 6 and 12 months posttransplant was significantly lower in the MA group than SA group. This trend persisted for 3 years after transplant. As the calculation of eGFRs included the functional grafts only, loss of a functional benefit in the SA group after 3 years was likely due to the fact that only “better kidneys” in the MA group survived at 4 and 5 years after transplant. The long-term graft survival was significantly lower in the MA group than the SA group over 5 years. We further identified MA, DGF, acute rejection, and vascular complications as the risk factors for graft loss.

Different surgical techniques for arterial anastomosis may also affect the vascular complication and graft outcome. Among the three methods used in MA group, anastomosing the smaller artery to the side of the dominant artery or performing two separate arterial anastomoses theoretically could run the risk of graft artery stenosis and ischemic injury, which might lead to CAN and poor graft survival. Angiogram of renal arteries was not performed as a work-up of graft dysfunction in the majority of our patients. The routine image by Doppler ultrasound might not detect all arterial stenosis. There were only three cases of well-documented renal artery stenosis (two in SA group, one in MA group) that required angioplasty and stent placement. However, our subgroup analysis did not show any difference of graft survival among the three anastomotic techniques. This sub-analysis might be limited by the small sample size in MA group.

The majority of previous studies reporting graft function and survival were short-term, usually not more than 1 year (8–13). None of these has noted any difference in graft function or graft survival between MA and SA groups. In a recent report by Kok et al. (10), 47 laparoscopically procured living donor kidneys with MA were compared with 138 kidneys with SA. Despite significantly longer operative time and WIT in the MA group, the graft function as measured by serum creatinine at 1 year was not different from their SA group. To our knowledge, there was only one published article by Troppmann et al. (3) comparing long-term graft survival. This study had 21 grafts with MA and 58 with SA. There was no difference in median serum creatinine or graft survival for 3 years after transplant. Our study is the first large series that describes significant differences in both graft function and survival between the MA group and SA group. The presence of MA (vs. SA) was an independent risk for both acute rejection and graft loss. The difference in long-term graft survival was mainly due to the significantly different number of graft loss from CAN. Our data support the theory that these issues may all be related. More perioperative injury of MA grafts can cause a higher incidence of rejection and decrease graft function, which eventually lead to more graft losses from CAN and worse long-term graft survivals when compared with the SA grafts. In addition, any unrecognized thromboses/stenosis of small accessory vessels in MA group could also contribute to these inferior outcomes. We also analyzed the outcomes, including operative time, ischemia times, complications, and graft survival, between the first and second 5-year periods of this study.

We did not note any significant difference in any of these parameters. Therefore, the “learning curve” may not explain the different outcomes observed in this study.

This study is limited by its retrospective nature, single-center data, and relatively small sample size in the MA group. Current United Network for Organ Sharing (UNOS) data for 1, 3, and 5-year graft survivals for all living donor kidneys are 95%, 87%, and 79.7%, respectively (16). Our graft survivals of SA and MA groups seem to fall on either side of these values and our overall graft survival of both groups (93.7%, 88.2%, and 81.6%) are similar to the UNOS data. Both short- and long-term graft survivals of our MA group (89.6% at 1 year and 71.8% at 5 years) remain comparable with the UNOS data for deceased donor kidney transplants (90.4% at 1 year and 68.2% at 5 years) (17). We have not changed our policy of using the MA grafts. Both donor and recipient are well informed about the increased risk for rejection and for lower graft survival with MA kidneys than SA kidneys. We have not recommended any living donor with MA kidney to have an open nephrectomy rather than laparoscopic nephrectomy, because we have not performed any direct comparison in these two methods for MA kidneys. We are not aware of any such published comparison. Promoting open nephrectomy for MA kidneys may also reduce the rate of living donation. Clearly, this is an important issue that needs to be further studied.

In conclusion, the laparoscopic procurement of living donor kidneys with SA may be associated with a lower risk of rejection, better graft function, and superior long-term survival compared with the kidneys with MA.

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Patients at risk:

MA	60	54	48	44	39	34
SA	218	207	191	165	138	116

FIGURE 1.

Five-year graft survival by Kaplan-Meier analysis between SA and MA groups.

FIGURE 2.

Graft survival based on reconstruction techniques in the MA group. (A) Suturing smaller artery to side of dominant artery (N=18), (B) separate arterial anastomoses (N=14), and (C) syndactylization (N=21).

TABLE 1

The donor and recipient characteristics between SA and MA groups (mean±SD)

	SA (n=218)	MA (n=60)	P
Donors			
Age (yr)	37.6±10.6	37.8±9.8	NS
Race			
White	139 (63.8%)	45 (75%)	NS
Black	65 (29.8%)	13 (21.7%)	
Others	14 (6.4%)	2 (3.3%)	
Genetically related	161 (73.9%)	42 (70%)	NS
Genetically unrelated	57 (26.1%)	18 (30%)	
Artery length (cm)	3.6±0.5	2.5±0.5 (main artery)	NS
Vein length (cm)	2.9±0.5	2.9±0.5	NS
Ureter length (cm)	9.9±1.6	10.2±1	NS
Recipients			
Age (yr)	37.8±18.4	41.8±18	NS
Children (≤12 yr)	24 (11%)	3 (5%)	NS
Race			
White	138 (63.3%)	42 (70%)	NS
Black	68 (31.2%)	15 (25%)	
Others	12 (5.5%)	3 (5%)	
First transplant	207 (95%)	58 (96.7%)	NS
Second transplant	11 (5%)	2 (3.3%)	
Causes of ESRD			
HTN	82 (37.6%)	24 (40%)	NS
DM	50 (23%)	13 (21.7%)	
GN	38 (17.4%)	10 (16.7%)	
PCKD	12 (5.5%)	3 (5%)	
Others	36 (16.5%)	10 (16.6%)	
Peak PRA (%)	10.2±22	12.3±25	NS
HLA mismatch	2.89±1.6	3.26±1.8	NS

SA, single artery; MA, multiple arteries; ESRD, end-stage renal disease; PRA, panel reactive antibody; HTN, hypertension; DM, diabetes mellitus; GN, glomerulonephritis; PCKD, polycystic kidney disease.

TABLE 2

Summary of the transplant events, graft function, graft loss, and patient death during this 10-yr study period (mean±SD)

	SA (n=218)	MA (n=60)	P
Events			
Donor operation time (hr)	1.7±0.5	1.9±0.6	0.03
Donor blood loss (mL)	98±104	90±68	NS
Warm ischemic time (min)	26.5±4.9	28.6±6.8	0.01
Cold ischemic time (min)	47.1±16.9	53.6±18.8	0.01
Vascular complications	9 (4.1%)	3 (5.0%)	NS
Ureteral complications	5 (2.3%)	5 (8.3%)	0.06
Other complications	12 (5.5%)	2 (3.3%)	NS
Delayed graft function	15 (6.8%)	5 (8.3%)	NS
Acute rejection	22 (10.1%)	14 (23.3%)	0.01
Graft function by eGFR (mL/min)			
6 mo	66±35	56±22	0.01
12 mo	63±25	54±24	0.03
2 yr	62±22	56±20	0.08
3 yr	61±20	52±17	0.05
4 yr	57±21	53±20	NS
5 yr	56±22	54±23	NS
Total graft loss	33 (15.1%)	19 (31.7%)	0.01
Causes of graft loss			
CAN	12 (5.5%)	10 (16.7%)	0.01
DWFG	9 (4.1%)	3 (5%)	
Rejection	5 (2.3%)	3 (5%)	
Recurrent GN	3 (1.4%)	1 (1.7%)	
Thrombosis	2 (1%)	1 (1.7%)	
Infection	2 (1%)	1 (1.7%)	
Total patient death	21 (9.6%)	8 (13.3%)	NS
Causes of death			
CVD	10 (4.6%)	4 (6.7%)	
Infection	6 (2.7%)	2 (3.3%)	
Others	5 (2.3%)	2 (3.3%)	

eGFR, estimated glomerular filtration rate; CAN, chronic allograft nephropathy; DWFG, death with a functioning graft; CVD, cardiovascular disease.

TABLE 3

The independent risk factors for acute rejection

	Odds ratio	P value	95% CI
Recipient race (black vs. non-black)	2.84	0.0089	1.30–6.22
MA (vs. SA)	3.60	0.0021	1.59–8.14
DGF (yes vs. no)	4.25	0.0052	1.54–11.73

SA, single artery; MA, multiple arteries; DGF, delayed graft function.

TABLE 4

The independent risk factors for graft loss

	Hazard ratio	P value	95% CI
MA (vs. SA)	2.31	0.0384	1.05–5.09
Acute rejection (yes vs. no)	7.23	0.0001	3.40–15.34
DGF (yes vs. no)	3.22	0.0095	1.33–7.80
Vascular complication (yes vs. no)	19.78	0.0001	8.45–46.34

SA, single artery; MA, multiple arteries; DGF, delayed graft function.