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The impact of intraoperative fluid management during laparoscopic donor nephrectomy on donor and recipient outcomes

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Abstract

Background: Intraoperative fluid management during laparoscopic donor nephrectomy (LDN) may have a significant effect on donor and recipient outcomes. We sought to quantify variability in fluid management and investigate its impact on donor and recipient outcomes.

Methods: A retrospective review of patients who underwent LDN from July 2011 to January 2016 with paired kidney recipients at a single center was performed. Patients were divided into tertiles of intraoperative fluid management (standard, high, and aggressive). Donor and recipient demographics, intraoperative data, and postoperative outcomes were analyzed.

Results: Overall, 413 paired kidney donors and recipients were identified. Intraoperative fluid management (mL/h) was highly variable with no correlation to donor weight (kg) ($R = 0.017$). The aggressive fluid management group had significantly lower recipient creatinine levels on postoperative day 1. However, no significant differences were noted in creatinine levels out to 6 months between groups. No significant differences were noted in recipient postoperative complications, graft loss, and death. There was a significant increase ($P < 0.01$) in the number of total donor complications in the aggressive fluid management group.

Conclusions: Aggressive fluid management during LDN does not improve recipient outcomes and may worsen donor outcomes compared to standard fluid management.

KEYWORDS

fluid directed management, fluid status, intraoperative fluid management, laparoscopic donor nephrectomy, recipient outcomes

1 | INTRODUCTION

Approximately 6000 living donor kidney transplantations are performed annually in the United States, comprising roughly 35% of the total volume of kidney transplantation. Laparoscopic donor nephrectomy (LDN) has become the preferred method for graft procurement due to decreased procedure-related donor morbidity, shorter hospital stay, and faster return to work.[1,2] This has effectively doubled the donor kidney pool.[3] Additionally, short- and long-term graft function and survival have not been shown to

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differ significantly between recipients of the open and laparoscopic approaches.[4]

Despite the safety and benefits of LDN, there is no consensus regarding the intraoperative fluid management required to optimize donor and recipient outcomes.[5] While studies have shown that volume expansion with fluid administration can attenuate the adverse effects of pneumoperitoneum on renal hemodynamics,[6,7] current research is inconclusive in characterizing the impact of pneumoperitoneum or volume expansion on early graft function.[4,8,9] In addition, much of the literature is outdated and based on animal models.[7,9-12] Furthermore, aggressive fluid management has been associated with adverse effects, including an increased risk of ileus, cardiopulmonary complications, and impaired wound healing.[13,14] Despite this, many providers have held the view that fluid resuscitation during LDN may improve recipient outcomes. Thus, contemporary research investigating larger patient populations is necessary to reach a consensus for both improved donor safety and recipient outcomes.

In this study, we sought to explore the relationship between intraoperative fluid management during LDN and outcomes in donors and recipients. We hypothesized that intraoperative fluid management is highly variable, and that aggressive fluid management does not improve clinical outcomes compared to standard or high fluid management strategies.

2 | METHODS

2.1 | Ethical Considerations

The protocol was reviewed by the University of Michigan Institutional Review Board (IRB) and was approved prior to initiation of the retrospective review. The requirement for written-informed consent was waived by the IRB.

2.2 | Hospital Setting

The University of Michigan is a 1000-bed tertiary care university hospital located in Ann Arbor, Michigan that provides inpatient and outpatient surgical care for patients in Michigan and several neighboring states. It is a high-volume surgical center with a total of 66 operating rooms where over 16 000 operations are performed each year.

2.3 | Study Population

A retrospective review of patients undergoing LDN, as well as adult recipients that underwent paired kidney transplantation, was performed at the center between July 2011 and January 2016.

Both donor and recipient parameters were collected, including age, gender, donor-recipient relationship, and operative time. Additional donor demographics and perioperative characteristics included weight, body mass index (BMI), volume and rate of intraoperative fluid administration, estimated blood loss (EBL), and urine output. Postoperative donor outcomes included donor length of stay (LOS), and need to receive diuretic therapy, either furosemide or mannitol. Additionally, recipient data were retrieved, including warm ischemia time (time between organ removal from ice to implantation), cold ischemia time (time on ice), and immunosuppression regimens. All recipients were ABO compatible and had a negative crossmatch (T and B cell). Postoperative complications, serial creatinine levels, and glomerular filtration rate (GFR) were also recorded. GFR was calculated using the Modification of Diet in Renal Disease (MDRD) equation from serum creatinine, age, sex, and race.[15] Graft and recipient survival were also compared.

After the data were retrieved, the relationship between rate (mL/h) of intraoperative fluid administration and donor weight (kg) was assessed. LDN patients were then divided into tertiles based on the type of intraoperative fluid management strategy (mL/kg/h) after adjusting for weight and time. Tertiles were chosen to fully assess fluid management strategies which reflected standard, high, and aggressive intraoperative fluid administration. Donor and recipient demographics, intraoperative data, and postoperative complications and outcomes were compared among groups.

2.4 | Intraoperative Care (LDN and Kidney Transplantation)

All LDN patients underwent similar intraoperative care as previously described.[16] Prior to arrival for surgery, LDN patients were asked to consume 10 oz. of a preoperative carbohydrate drink. No preoperative hydration protocols were performed. Following anesthetic induction, LDN patients underwent ultrasound-guided bilateral transversus abdominus plane (TAP) block. Prior to incision, specific fluid goals were discussed between anesthesia and surgical staff. In general, LDN patients were administered between 3-5 L of lactated Ringer's (LR) solution intraoperatively. A mean arterial pressure of 55 mm Hg or greater was targeted. Additional intravenous fluids were administered to achieve this goal based on anesthesiologist discretion and surgeon preference in concordance with EBL and renal vein compression or emptiness. Colloids were not routinely used, but may have been administered in patients with significant bleeding not requiring transfusion. None of the patients had invasive blood pressure monitoring. For kidney transplant recipients, 2-4 L of LR was administered intraoperatively. Additional intravenous fluids were administered based on anesthesiologist discretion and surgeon preference.

2.5 | Operative Technique (LDN)

All patients underwent left LDN according to the original method previously described.[17] Briefly, the donor was placed in the right lateral decubitus position. A short-periumbilical incision was made to expose the fascia in order to facilitate wound protector placement as a designated hand-port. Pneumoperitoneum was created facilitating 12-15 mm Hg of insufflation. Two additional ports were placed in the left subcostal

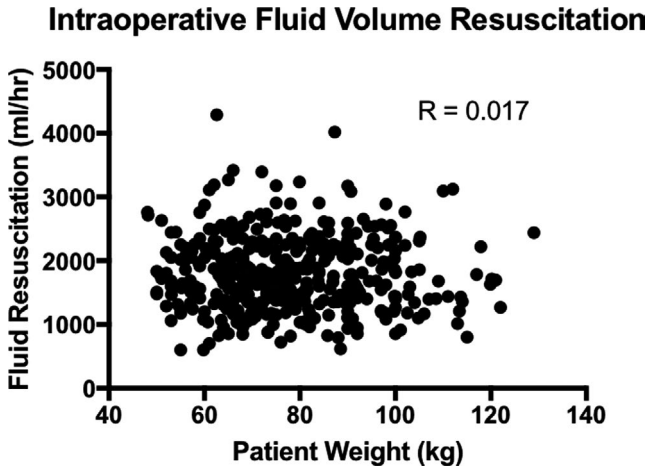

FIGURE 1 Variability of Intraoperative Fluid Resuscitation. Intraoperative fluid resuscitation (mL/kg) with high variability with no correlation to donor weight (kg) (R = 0.017)

region and mid-abdomen to facilitate dissection. The left colon, spleen, and the tail of pancreas were mobilized medially. The splenorenal ligament was identified, and Gerota's fascia was mobilized from the spleen. The renal vein and artery, the adrenal vein, and the ureter were dissected and mobilized from their superior and lateral attachments. Lumbar veins were carefully identified and divided as needed. The distal ureter was then secured with clips and divided, and the renal artery was stapled at its root with a vascular staple load. This was repeated with the renal vein. The kidney was then removed through the hand-assist port and immediately placed on ice and flushed with histidine-tryptophan-ketoglutarate (HTK) solution.

2.6 | Operative Technique (Kidney Transplantation)

Recipients were placed on the operating room table in supine position. A curvilinear right iliac fossa incision was made and carried down through the external and internal oblique muscles exposing the retroperitoneum. A fixed retractor was placed to expose the iliac vessels. The external iliac vein was clamped, and a venotomy was created. After flushing the vein with heparinized saline, the donor renal vein was anastomosed to the recipient iliac vein in an end-to-side fashion. After clamping the external iliac artery, an arteriotomy was created and the artery irrigated with heparinized saline. The donor renal artery was then anastomosed to the recipient iliac artery in an end-to-side fashion. Finally, an external ureteroneocystostomy was performed using either the Lich technique or single U-stitch technique.

2.7 | Postoperative Care (LDN and Kidney Transplant Recipients)

Postoperatively, LDN patients were involved in an enhanced recovery protocol.[15] They were considered ready for discharge when their pain was controlled on oral medications and they were tolerating oral intake. Follow-up was scheduled with the surgical team 2-3 weeks after the operation.

For the first 24 hours postoperatively, kidney transplant recipients underwent standardized urine replacement with 0.9% normal saline. When able to tolerate oral intake, they were instructed to drink 2 L/d of liquids. Kidney transplant recipients were deemed ready for discharge when they were tolerating oral intake, were able to take and manage their immunosuppressive medications, and had an improving renal function. Transplant immunosuppression involved primarily mycophenolate mofetil, tacrolimus, and steroids. Patient was seen by the transplant nephrology team serially for evaluation of renal function.

2.8 | Endpoints

Primary endpoints involved postoperative short-and long-term creatinine levels and complications for both donors and recipients.

2.9 | Statistical Analyses

All analyses in this study were performed using GraphPad Prism version 6.00 (GraphPad Software; San Diego CA). Correlation testing was performed using Pearson's correlation formula with R-generation. One-way analysis of variance (ANOVA) for continuous variables was performed between groups. Chi-square testing was used to evaluate categorical variables between groups. Data are expressed as mean ± standard deviation (SD) unless specified otherwise. A P value < 0.05 was considered statistically significant.

3 | RESULTS

Overall, 413 patients who underwent LDN and their respective paired kidney transplant recipients were identified. In the LDN cohort, intraoperative fluid management (mL/h) was highly variable with no correlation to donor weight (kg) (R = 0.017) (Figure 1).

Laparoscopic donor nephrectomy patients and their paired kidney recipients were divided into tertiles based on donor intraoperative standard (n = 138), high (n = 138), and aggressive (n = 137) fluid management rates (mL/kg/h). Following tertile division according to these intraoperative fluid management strategies, total volume of intraoperative fluid administration (mL: standard, 3618 ± 1006; high, 4624 ± 1124; aggressive, 5454 ± 1550; P < 0.001) and intraoperative fluid administration rates (mL/kg/h: standard, 14.8 ± 2.9; high, 23.1 ± 2.2; aggressive, 34.4 ± 7.3; P < 0.001) were significantly different among groups (Table 1).

3.1 | Donor

Significant differences (P < 0.05) in several donor demographics and intraoperative data were noted among fluid management groups (Table 1). Significant differences were observed in donor age (years:

TABLE 1 Donor demographics, intraoperative data, and postoperative outcomes

	Normal (N = 138)	High (N = 138)	Aggressive (N = 137)	*P*-Value
Demographic data				
Age (y)	45.1 ± 12.4	40.3 ± 11.9	43.0 ± 11.7	<0.05
Sex (n, %)				
Male	70 (51%)	47 (35%)	30 (22%)	<0.001
Female	68 (49%)	91 (65%)	107 (78%)	
Race				
White	108 (78%)	105 (76%)	107 (78%)	0.89
Black	18 (13%)	11 (8%)	6 (4%)	
Asian	1 (1%)	2 (1%)	6 (4%)	
Other	11 (8%)	20 (15%)	18 (14%)	
Relationship to recipient				
Living related	69 (50%)	68 (49%)	62 (45%)	0.75
Living unrelated	55 (40%)	56 (41%)	60 (44%)	
Unknown	14 (10%)	14 (10%)	15 (11%)	
Weight (kg)	86.8 ± 15.9	78.6 ± 12.9	68.4 ± 12.7	<0.001
BMI (kg/m^2)	29.0 ± 4.2	27.5 ± 4.7	24.6 ± 4.2	<0.05
Intraoperative data				
Total fluid volume (mL)	3618 ± 1006	4624 ± 1124	5454 ± 1550	<0.001
Total fluid rate (mL/kg/h)	14.8 ± 2.9	23.1 ± 2.2	34.3 ± 7.3	<0.001
Estimated blood loss (mL)	73.3 ± 109.1	55.4 ± 80.7	101.3 ± 250.1	0.64
Urine output (mL)	468.8 ± 387.4	787.9 ± 626.6	984.4 ± 1089	<0.001
Urine output (mL/kg/h)	14.8 ± 3.0	23.1 ± 2.15	34.4 ± 7.3	<0.001
Operative time (min)	171.6 ± 28.5	154 ± 29.7	141.9 ± 31.3	<0.05
Patients receiving furosemide (n, %)	2 (1.4%)	13 (9.4%)	26 (19%)	<0.001
Patients receiving mannitol (n, %)	53 (38.4%)	49 (35.5%)	51 (37.2%)	0.88
Postoperative outcomes				
Length of stay (d)	1.72 ± 0.8	1.89 ± 0.9	1.91 ± 0.8	0.12

Data are expressed as mean ± SD or count (percentage).

standard, 45.1 ± 12.4; high, 40.3 ± 11.9; aggressive, 43.0 ± 11.7; $P < 0.05$), sex (male, %: standard, 51%; high, 35%; aggressive, 22%; $P < 0.001$), weight (kg: standard, 86.8 ± 15.9; high, 78.6 ± 12.9; aggressive, 68.4 ± 12.7; $P < 0.05$), and BMI (kg/m^2: standard, 29.0 ± 4.2; high, 27.5 ± 4.7; aggressive, 24.6 ± 4.2; $P < 0.05$). Donors who received aggressive fluid management were noted to have significantly higher rates of intraoperative urine output compared to those who received standard fluid management (urine output, mL/kg/h: standard, 14.8 ± 3.0; high, 23.1 ± 2.15; aggressive, 24.4 ± 7.3; $P < 0.001$). Operative time was noted to be significantly longer in the standard fluid management group compared to the high and aggressive fluid management groups (operative time, minutes: standard, 171 ± 28.5; high, 154 ± 29.7; aggressive, 141 ± 31.3; $P < 0.05$). A significantly higher number of patients received furosemide in the aggressive fluid

TABLE 2 Donor complications at 1 year following donor nephrectomy

	Standard (N = 138)	High (N = 138)	Aggressive (N = 137)	*P*-Value
Prolonged hospitalization (>7 d)	0 (0%)*	0 (0%)*	4 (2.9%)*	<0.05
Renal dysfunction	0 (0%)	1 (0.7%)	2 (1.5%)	0.37
Wound infection	0 (0%)	1 (0.7%)	4 (2.9%)	0.08
Incisional hernia	0 (0%)*	0 (0%)*	4 (2.9%)*	<0.05
Reoperation	0 (0%)	0 (0%)	1 (0.7%)	0.37
Total	0 (0%)*	2 (1.45%)*	15 (10.9%)*	<0.01

Data are expressed as count (percentage). Renal dysfunction defined as CrCl <50 cc/min.
*Designates $P < 0.05$ between normal and aggressive and high and aggressive groups.

management group compared to other groups (%: standard, 1.4%; high, 9.4%; aggressive, 19%; $P < 0.001$).

Significant differences ($P < 0.05$) were also noted in several postoperative donor outcomes among fluid management groups. Donor LOS was longer in the aggressive fluid management group (days; aggressive, 1.91 ± 0.8; standard, 1.72 ± 0.8), although this was not statistically significant ($P = 0.13$) (Table 1). However, there was a significant increase in the number of total postoperative complications in the aggressive fluid management group compared to other groups (total complications; standard, 0 [0%]; high, 2 [1.45%]; aggressive, 15 [10.9%]; $P < 0.01$) (Table 2). Specifically, the number of patients that had prolonged hospitalization (>7 days) and incisional hernia was significantly higher ($P < 0.05$) in the aggressive fluid management group compared to the standard fluid management group. No significant differences were observed in creatinine levels at baseline, 30 days, and 90 days following LDN between fluid management groups (Table 3).

3.2 | Recipient

No significant differences were noted in recipient demographics and intraoperative data, including warm and cold ischemia times (Table 4). No significant differences were noted in immunosuppression regimens between groups.

The aggressive fluid management group had a significantly lower average creatinine level on postoperative day 1 compared to other groups (Cr, postoperative day 1; standard, 3.68 ± 2.0; high, 3.74 ± 2.2; aggressive, 3.15 ± 1.9; $P < 0.05$) (Table 3). However, no significant differences were noted in subsequent creatinine levels at 30 days, 90 days, and 6 months following transplantation among groups. In addition, no significant differences were noted in recipient postoperative complications, including acute rejection and delayed graft function, graft loss, and recipient death at 1 and 2 years following transplantation (Tables 5 and 6).

4 | DISCUSSION

In this study, we sought to quantify the variability in intraoperative fluid management during LDN and investigate the effects of fluid management strategies on donor and recipient outcomes. Several key findings were noted. First, intraoperative fluid management was highly variable with no correlation to donor weight. Second, LDN patients in the aggressive fluid management group had significantly more total complications compared to other fluid management groups; there was also a trend toward a longer LOS for those who received aggressive fluid management. Third, donor patients who received aggressive fluid management had paired kidney recipients with a significantly decreased early creatinine level at postoperative day 1; however, no differences were observed in creatinine levels at any subsequent postoperative time points up to 6 months between groups. Lastly, no significant differences were noted in recipient complications, and graft and recipient survival among fluid management groups.

Within the last two decades, LDN has become the mainstay technique of living donor kidney transplantation. The laparoscopic approach, compared to open technique, has afforded decreased donor complications and postoperative pain, as well as a shorter hospital stay and quicker return to work.[1,2] A potential threat following the laparoscopic approach, however, is an increased theoretical risk to the donor kidney secondary to pneumoperitoneum. When an insufflation pressure of 12-15 mm Hg is achieved, pneumoperitoneum can be associated with a decrease in renal blood flow and subsequently worse renal function.[18] In the short term, this may affect early renal function following transplantation.[19] However, in the long-term, no differences in renal function have been noted between open donor nephrectomy (ODN) and LDN at 1 year following surgery.[20] Nevertheless, the clinical significance of these findings is largely to be determined.

Controversy exists regarding fluid management and the optimal fluid balance in the perioperative period. Numerous intraoperative fluid management strategies, including restrictive and liberal, have been proposed. However, both have their benefits and risks. Liberal intraoperative fluid management may lead to poor wound healing, postoperative ileus, as well as fluid overload contributing to heart and pulmonary failure.[13,14,21] Restrictive fluid management, however, may result in hypovolemia, inadequate organ perfusion, and postoperative symptoms including nausea and vomiting.[21,22] Similarly, there are various propositions regarding the benefits of these strategies. Some studies demonstrate benefit from liberal fluid resuscitation intraoperatively, [22,23] while others demonstrate no

TABLE 3 Creatinine levels before and after surgery

	Standard (N = 138)	High (N = 138)	Aggressive (N = 137)	*P*-Value
Donor				
Cr, Preop	1.19 (0.27)	1.18 (0.25)	1.15 (0.24)	0.40
GFR, Preop	64.5 (14.8)	61.9 (13.1)	63.1 (15.4)	0.56
Cr, 30 d	1.20 (0.30)	1.21 (0.22)	1.16 (0.24)	0.40
Cr, 90 d	1.19 (0.25)	1.18 (0.23)	1.17 (0.24)	0.50
Recipient				
Cr, Postop Day 1	3.68 (2.0)*	3.74 (2.2)*	3.15 (1.9)*	<0.05
Cr, 30 d	1.46 (0.50)	1.49 (0.63)	1.47 (0.60)	0.89
Cr, 90 d	1.43 (0.60)	1.35 (0.38)	1.38 (0.43)	0.40
Cr, 6 Mo	1.41 (0.65)	1.34 (0.37)	1.37 (0.42)	0.37

Creatinine (Cr) listed as mg/dL. Glomerular function rates (GFR) listed as mL/min/1.73 m^2. Data are expressed as mean ± SD or count (percentage).
*Designates $P < 0.05$ between normal and aggressive and high and aggressive groups.

TABLE 4 Recipient demographics, intraoperative data, and immunosuppression

	Normal (N = 138)	High (N = 138)	Aggressive (N = 137)	*P*-Value
Demographics				
Age (y)	45.1 ± 12.4	40.3 ± 11.9	43.0 ± 11.7	0.06
Intraoperative Data				
Warm ischemia time (min)	33.6 ± 10.2	31.8 ± 8.2	33.0 ± 11.6	0.43
Cold ischemia time (min)	124.4 ± 70.8	128.7 ± 64	130.3 ± 71.5	0.63
Immunosuppression				
Tacrolimus	138 (100%)	135 (97.8%)	135 (98.5%)	0.22
Mycophenolate mofetil	123 (89.1%)	127 (92%)	130 (94.7%)	0.31
mycophenolate sodium	19 (13.7%)	22 (15.9%)	24 (17.5%)	0.71
Cyclosporine	1 (0.7%)	0 (0%)	0 (0%)	0.37
Everolimus	4 (2.9%)	5 (3.6%)	8 (5.8%)	0.45

Data are expressed as mean ± SD or count (percentage). Warm ischemia time defined as time from organ removal from ice to implantation.

difference in outcomes.[25] However, optimal fluid management strategies in the perioperative period remain a matter of investigation.

Only a few studies have been conducted to determine the optimal fluid management strategies in patients undergoing both LDN and ODN. Initial studies focused on attenuating the effects of pneumoperitoneum on renal blood flow, creatinine, and urine output using crystalloid and colloid resuscitation. Mertens zur Borg et al randomized patients undergoing LDN to three fluid management strategies: (a) crystalloids administered overnight, at induction, and before pneumoperitoneum; (b) crystalloids administered overnight and a colloid bolus at induction and before pneumoperitoneum; and (c) aggressive crystalloid infusion during the operation.[26] Preoperative crystalloids with colloid administration demonstrated higher donor stroke volume and increased urine output during LDN compared to those receiving aggressive intraoperative crystalloid infusions.[26] However, follow-up studies comparing preoperative crystalloids with colloid administration at the onset of induction and during pneumoperitoneum demonstrated similar hemodynamics, urine output, creatinine, graft survival, and recipient survival between LDN and ODN patients.[27]

Studies have also compared intraoperative fluid management strategies during LDN alone. In a prospective study with retrospective augmentation, Bergman et al assessed patients receiving high fluid rates (>10 mL/kg/h) and fluid-restricted rates (<10 mL/kg/h) during LDN.[8] Although LDN patients subjected to intraoperative fluid-restriction had lower intraoperative urine output, no significant differences were observed in recipient postoperative creatinine up to 12 months, delayed graft function, or acute rejection between

TABLE 5 Recipient postoperative complications at 1 year following transplant

	Low (N = 138)	Medium (N = 138)	High (N = 137)	*P*-Value
Cancer	0 (0)	1 (0.7%)	2 (1.5%)	0.36
Diabetes mellitus	5 (3.6%)	9 (6.5%)	7 (5.1%)	0.54
Bacterial infection	18 (13%)	15 (10.1%)	16 (11.7%)	0.85
Viral Infection				
BK infection	9 (6.5%)	6 (4.3%)	16 (11.7%)	0.07
Other	3 (2.1%)	6 (4.3%)	7 (5.1%)	0.42
Major cardiac event	6 (4.3%)	3 (2.2%)	2 (1.5%)	0.29
Transfusion	7 (5.1%)	5 (3.6%)	12 (8.8%)	0.17
Acute rejection	20 (14.5%)	26 (18.8%)	19 (13.9%)	0.47
Delayed graft function	2 (1.5%)	1 (1.5%)	1 (1.5%)	0.99
Ureteral leak	1 (0.7%)	0 (0%)	0 (0%)	0.63
Ureteral stricture	1 (0.7%)	1 (0.7%)	1 (0.7%)	0.99
Vascular thrombosis	1 (0.7%)	1 (0.7%)	0 (0%)	0.63
Wound infection/ dehiscence	2 (1.5%)	0 (0%)	0 (0%)	0.15
Total	86 (62.3%)	84 (61%)	83 (60%)	0.83

Data are expressed as mean ± SD or count (percentage).

TABLE 6 Graft loss and recipient death

	Standard (N = 138)	High (N = 138)	Aggressive (N = 137)	*P*-Value
Graft loss	7 (5.1%)	12 (8.7%)	12 (8.8%)	0.39
1-year graft loss	3 (2.2%)	2 (1.5%)	3 (2.2%)	0.87
2-year graft loss	3 (2.2%)	3 (2.2%)	5 (3.6%)	0.69
Recipient death	3 (2.2%)	3 (2.2%)	2 (1.5%)	0.87
1-year recipient death	3 (2.2%)	1 (0.7%)	2 (1.5%)	0.60
2-year recipient death	3 (2.2%)	3 (2.2%)	2 (1.5%)	0.88

Data are expressed as count (percentage).

groups.[8] Although prospective, the study had several limitations including a limited number of patients per group (<30 patients). Our study, however, is the largest study (>130 patients per group) evaluating fluid management strategies during LDN and their impact on donor and recipient outcomes.

To fully assess different fluid management strategies, we chose to divide our LDN cohort into three groups, which allowed assessment of three fluid management strategies including standard, high, and aggressive fluid administration. These terms were decided after consultation and data interpretation with our expert anesthesiology colleagues. The findings of this study demonstrate that aggressive fluid management during LDN does not improve recipient outcomes compared to standard intraoperative fluid management. Although early differences in creatinine levels were observed at postoperative day 1, no significant differences were observed at subsequent time points up to 6 months. This is consistent with other studies.[8,26,27] Furthermore, no significant differences were observed in recipient postoperative complications, graft loss, and death among fluid management groups. However, we did observe several potential adverse events that can be associated with aggressive intraoperative fluid management during LDN. The aggressive fluid management group had a significantly higher number of total complications in donor patients, including prolonged hospitalization (>7 days) secondary to cardiopulmonary issues and incisional hernia, compared to other fluid management groups. We suspect that the increased edema and incisional tension from aggressive fluid management may be responsible for the increased rate of hernia. Although not statistically different, there was also a trend toward prolonged LOS in the aggressive fluid management group.

We also had some unexpected significant differences among donor demographics and intraoperative characteristics. Significant differences were noted in age and gender among fluid management groups. The standard fluid management group was significantly older than the high fluid management group; however, no significant difference in age was noted when compared with the aggressive fluid management group. Male predominance was also noted in the

standard fluid management group. However, we do not believe that this significantly affected the outcomes of our study. In addition, we noted higher donor weight (kg), BMI, and operative time in our standard fluid management group compared to the aggressive fluid management group. The increased weight and BMI likely translated into longer operative times for the standard fluid management group due to operative complexities.

Overall, the findings of this study highlight that, contrary to prior belief, aggressive fluid management during LDN does not appear to impact outcomes in transplant recipients. As aggressive fluid management can be potentially deleterious to the donor and may generate problems, as shown in this study, attaining normal fluid status during LDN appears to be a beneficial prospect. Patient-tailored resuscitation may be the ideal approach, and future prospective, randomized control trials studies are required to further confirm these recommendations. Although we did not use these in our study, noninvasive methods like esophageal Doppler and inflatable finger cuffs are available and may help achieve a patient-tailored resuscitative approach perioperatively. Further studies are required to generate data to support their use.

This study has several limitations. First, this is a retrospective review, which may limit its clinical translation. However, these findings prompt future work in providing safe and effective care of healthy donors. This will require prospective studies and randomized trials to better assess the role of donor intraoperative fluid management on clinical outcomes. Second, this study has several confounding factors, as several significant differences were found among donor groups. Although we do not feel this significantly affects our conclusions, it may affect postoperative outcomes. Third, some aspects of clinical data, including both donor and recipient data (immunosuppressive induction agents, pre- and postoperative fluid status, postoperative pain levels, etc), were difficult to obtain via chart review and are not included. Fourth, fluid management strategies were divided into tertiles, including "standard," "high," and "aggressive" fluid management groups, after consultation with anesthesiology colleagues; this was based on the historic context that higher fluid management strategies may improve recipient outcomes. However, we recognize that standard fluid management in this study may be higher than typical intraoperative fluid management for other operative cases and this is clearly a limitation. Fifth, patients in the donor cohort had mean estimated GFRs <70 mL/min in all three groups. We suspect this was secondary to the MDRD underestimating the GFR, which can occur by up to 29% in healthy individuals.[28] Our institution has an acceptable GFR minimum of 60 mL/min. Although these donor GFRs were lower than expected, there were no significant differences in GFR among groups. However, this may affect the generalizability of our results. Sixth, although creatinine is an important marker of renal function, we recognize that there are superior markers of acute renal function and ischemia, including neutrophil gelatinase-associated lipocalin (NGAL); however, evaluating these markers was beyond the scope of this study. Seventh, fluid management strategies from this data set were based on the historic context that aggressive fluid management may improve recipient outcomes; although we were unable to assess restrictive fluid management strategies in this study, we plan to assess it in future studies. Eighth, this study is limited to a single institution; future work will involve prospective studies across multiple institutions with inclusion of larger patient cohorts to determine optimal fluid resuscitation during LDN.

5 | CONCLUSIONS

In conclusion, fluid management strategies during LDN remain highly variable and may have significant effects on donor and recipient outcomes. Although aggressive fluid management during LDN may decrease early creatinine levels in recipients, it does not appear to have any significant effects on long-term creatinine levels, postoperative complications, or graft survival. However, aggressive fluid management may increase the risk for postoperative complications and prolong hospitalization for donor patients following LDN. Further work is required to help construct guidelines to help further optimize fluid management during LDN.

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CONFLICT OF INTEREST

None.

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