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Central Venous Pressure Monitoring in Living Donor Kidney Recipients does not affect Immediate Graft Function: a propensity score analysis.

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Abstract

Background.—During kidney transplantation, intraoperative fluid management can affect post-transplant graft function. It is unclear whether or not central venous pressure (CVP) monitoring is required to guide fluid therapy during kidney transplantation.

Methods.—We compared post-transplant graft function in recipients of living donor kidney transplants between August 2006 and March 2009 based on the use or absence of intraoperative CVP monitoring. Graft function, assessed using the creatinine reduction ratio on postoperative day 2 (CCR2), was evaluated by multivariable linear regression analysis and in a propensity-matched cohort.

Results.—Two-hundred and ninety patients were included in the analysis. Central venous pressure was monitored in 84 patients. (29%) There was no difference in post-transplant graft function, as measured by CCR2, between patients with- and without CVP monitoring in both unadjusted and multivariable adjusted analysis. There were also no statistically significant differences in CCR2, delayed graft function, or 3-month renal function between those monitored with CVP, and those without, in the propensity-matched cohort.

Conclusions.—In this single center analysis, immediate post-transplant renal function was not associated with the use of intraoperative CVP monitoring.

Keywords

Kidney Transplantation; Central Venous Pressure; Anesthesia; Living Donor Kidney Transplantation

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Authorship:

Le.B., C.N., and J.F. designed the study; Le.B. and C.N. obtained Institutional Review Board approval; D.A., Le.B. and J.F. collected data; E.W. and J.F. performed the statistical analysis; D.A., C.N., G.R., Ly.B. and E.W. prepared the manuscript.

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Introduction

Delayed graft function (DGF) after kidney transplantation is associated with decreased long term graft survival, increased risk of infection and health care associated cost.[1–3] Previoulsy identified risk factors for DGF include donor age and creatinine, cold ischemia time, donation after cardiac death, and recipient body mass index. Several definitions for DGF are used clinically: DGF can be defined either based on the need for hemodialysis within the first 7 days after transplant, or by the change in post-operative creatinine clearance.[3]

Intraoperative fluid management during kidney transplantation could influence the incidence of DGF when extreme intravascular volume states are reached in the perioperative period. It is unproven whether or not central venous pressure (CVP) monitoring is necessary to adequately guide fluid therapy during living donor kidney transplantation. Early studies demonstrated an association between increased central venous and pulmonary artery pressures and improved postoperative graft function.[4–6] Conversely, some report restrictive hydration regimes yield similar outcomes.[7]

Central venous pressure monitoring requires the placement of a central venous catheter. Central venous catheters are associated with a risk of vascular injury, thrombosis, line infection, mechanical complications and increased cost.[8,9] Currently, there is no consensus on whether CVP monitoring is required for routine kidney transplantation.

The aim of this study was to compare intraoperative patient management and post-transplant graft function, as defined by the creatinine reduction ratio on post-transplant day 2 (CCR2)[10], an early surrogate of delayed graft function, in living donor kidney transplant recipients with and without perioperative CVP measurement.

Patients and Methods

All patients undergoing living donor kidney transplantation at the University of California, San Francisco (UCSF) Medical Center between August 2006 and March 2009, with donor kidney procurement also performed at UCSF, were included in the study. Patients undergoing transplantation after March 2009 were not included because central line placement was no longer part of the revised perioperative protocol.

Exclusion criteria were recipient age below 18 years and concomitant surgery such as removal of polycystic kidneys or combined liver- and kidney transplantation. The study was approved by the institutional review board of the University of California, San Francisco.

Graft Recovery and Surgical Technique

Donor and recipient surgery were performed simultaneously in two adjacent operating rooms to minimize cold ischemia time. All donor and recipient surgeries were performed locally at UCSF Medical Center. All organs were recovered via our standardized laparoscopic donor nephrectomy procedure, from ASA class I or II living donors. Intraoperative management of living kidney donors follows strict guidelines and follows a standard protocol at our institution.[11] All grafts were flushed with preservation solution (University of Wisconsin, DuPont Pharmaceuticals, Wilmington, DE) and stored on ice until

implantation. In the recipient, the arterial and venous anastomoses were performed in an end-to-side fashion to the external iliac artery and vein via a retroperitoneal approach, unless recipient anatomy required a modified approach. Cold ischemia time was less than 60 minutes in all cases during the study period.

Intraoperative Recipient Management

Per our institutional kidney transplant anesthetic protocol, general anesthesia was induced with propofol, cisatracurium, small doses of fentanyl and esmolol titrated to effect. Anesthesia was maintained with desflurane or sevoflurane, and fentanyl. Intraoperative muscles relaxation was maintained with cisatracurium. There are no dedicated anesthesiologists for kidney transplantation at our institution. The decision about whether or not to place a central line for CVP monitoring was left to the discretion of the anesthesiologist and surgeon. Blood pressure monitoring was at the discretion of the anesthesiologist and in the vast majority monitored non-invasively. All patients received antibiotic prophylaxis against skin flora prior to incision, and immunosuppressive induction according to our standard protocol. During completion of the vascular anastomoses, 100 mg furosemide and 12.5 g of mannitol were infused over 30 minutes in all patients.

Recipient Characteristics and Perioperative Variables

The following data were extracted from the patients electronic health record and electronic anesthesia chart: patient age and sex, ethnicity, body mass index (BMI), American Society of Anesthesiologists physical status (ASA) classification, year of surgery, prevalence of hypertension and/or coronary artery disease, left ventricular ejection fraction, preoperative dialysis, case duration (time the patient spent in the operating room), attending transplant surgeon, intraoperative fluid administration and estimated blood loss. Serum creatinine and glomerular filtration rate (GRF, MDRD Formula[12]) were recorded on postoperative day 1, 2 and after 3 months.

The primary outcome was the creatinine reduction ratio on postoperative day 2 (CCR2), calculated as follows: [(Cr day 1 - Cr day 2) * 100 / Cr day 1].[10] The incidence of delayed graft function requiring HD (defined as the neeed for HD during the first 7 days after transplantation), rejection, and length of hospital stay were recorded. If a patient was receiving HD during the first 7 days after transplantation, the CRR2 was entered as “0”.

CVP monitoring was defined as the continuous monitoring and registration of a CVP via central venous access. For patients undergoing CVP monitoring the mean intraoperative CVP was documented. Patients who did not receive continuous monitoring of CVP served as controls.

Missing data: All effort was made to recover missing data from the electronic medical record. Height was not documented for thirteen patients in the dataset; the gender-specific median height for males was substituted and BMI was calculated based on the patient’s recorded weight. If a weight was not recorded (2 patients), the gender-specific median weight was used. Serum creatinine measurement at 3 months was not available for 18 patients; the creatininine measurement closest to 3 months was substituted (range: 0.5–6

months, median 2 months). Three patients were missing crystalloid administration volume; value was replaced with the median (3000 mL). Estimated blood loss was not recorded in 11 patients; the median blood loss (100 mL) was therefore assumed in these cases. Finally, warm ischemia time was unavailable for 3 patients in the CVP group and 21 in the control group; these values were not imputed since the variable was not used in multivariable modeling.

Statistical Analysis

All analyses were conducted in Stata 14.2 (StataCorp, College Station, TX). A p-value of 0.05 was considered to indicate statistical significance.

Chi-squared tests for categorical data, two-sided t-tests for normally-distributed variables, and Wilcoxon rank-sum tests for non-normal data were used to compare characteristics of those who received CVP monitoring versus those who did not.

The primary analysis was a multivariable linear regression model for CRR2 with adjustment for the variables noted above. Adjustment variables were defined *a priori* without regard to statistical significance in univariate comparisons. Because we had no *a priori* hypotheses regarding interactions in the model, interactions with the primary variable of interest (i.e., CVP) were empirically tested; no statistically significant interactions were found.

Reflecting the nonrandomized nature of CVP placement, a prespecified sensitivity analysis using propensity matching was performed. On the basis of a logistic regression equation predicting the likelihood of CVP monitoring, we generated a matched weighted cohort with replacement, where all patients who underwent CVP monitoring were matched within a caliper distance of 0.05, at a ratio of 1:2, with control patients who did not receive CVP monitoring. Patients in the control group could be used more than once in this matching schema. After confirming appropriate covariate and propensity score overlap between the matched weighted groups, univariate statistics were used to compare the groups and their postoperative outcomes.

Results

Between August, 2006 and March, 2009, 320 living donor kidney transplants were performed in adults over the age of 18. Thirty patients underwent concomitant surgical procedures and were excluded, leaving 290 patients in the analysis. Eight transplant surgeons performed all surgeries. Central venous pressure was monitored in 84 patients (29.0%). Patient demographics and baseline characteristics for the unadjusted cohort are given in Table 1. Intraoperative parameters such as operating time, ischemia time and volume administered and estimated blood loss are shown in Table 2.

In the unadjusted analysis, patients who underwent CVP monitoring were more likely to have had their operation early in the study period, to be on preoperative HD, to have a longer case duration, and to have a longer hospital length of stay. There was no difference in unadjusted CRR2 or the incidence of DGF (Table 2). The rate of patients requiring HD in

the first 7 days was 4.9% (n=10) in the control group, and 4.8% (n=4) in the patients with CVP monitoring, not statistically different.

Multivariable linear regression demonstrated a significantly lower adjusted CRR2 in male patients (-6.2% [-10.6% to -1.9%], p=0.005), and a higher CRR2 in those receiving peritoneal dialysis (+10.3% [+3.6% to +16.9%], p=0.003). CVP monitoring did not significantly impact CRR2 (+2.5% [-2.1% to +7.2%]; p=0.59). There were no statistically significant associations with surgeon, age, black race, ASA physical status, CAD, HTN, ejection fraction, BMI, intraoperative fluid administration, and whether the operation was not the recipient's first kidney transplant.

The propensity matched sample consisted of the 84 patients who underwent CVP monitoring and 93 patients, matched with replacement to CVP patients at a ratio of 2:1, in the control group. Baseline characteristics were well-matched in the weighted cohort (Table 1). There was no difference in case duration, CCR2, incidence of DGF or hospital length of stay between the two groups (Table 2).

Discussion

In this single center analysis, there was no association between the use of CVP monitoring and immediate post-transplant renal function in recipients of living donor kidney transplants, in multivariable adjusted modeling of CRR2 and a propensity-matched cohort.

We used the CCR2 to compare post-transplant graft function between the two patient groups. The sensitivity of CCR2 to predict graft failure at 1 year is 100%.[3] A scaled outcome parameter allowed a more precise comparison of post-transplant kidney function between the two groups than the binary outcome of DGF.

There is no consensus whether CVP monitoring is beneficial and whether it should be considered as the standard of perioperative care in kidney transplant recipients.[4,5] Aggressive hydration guided by CVP monitoring has been deemed essential for successful graft function and outcome.[13] In a previous study of 155 deceased donor graft recipients, a low CVP at the end of surgery and a restrictive fluid strategy were identified as risk factors for DGF.[6] The mean amount of fluid administered in that study was 2161 ± 727 mL in patients with- and 2401 ± 792 mL in patients without DGF, respectively. In our study, the amount of fluid administered intraoperatively did not differ in between patients with and without CVP measurement. Interestingly, in the previously mentioned study[6], both groups received less fluid than the patients in our study, where a median of 3L was administered regardless of CVP monitoring.

There is evidence that a CVP target of 5 mmHg prior to- and 15 mmHg during the graft warm ischemia time may improve diuresis and increase hemodynamic stability compared to a constant infusion rate.[13] Although both groups in that study received the same amount of fluids, patients whose fluid balance was managed by CVP received more than twice the amount of fluid during the warm ischemia phase (2320 ± 658 mL and 840 ± 316 mL, respectively). The total amount of fluid administered in that study (mean approximately 3000 mL) was comparable to our study (mean 3300 mL). Our findings are in line with

recommendations from de Gasperi[7] that aggressive hydration might not be beneficial during kidney transplantation.

Central line insertions are associated with well known complications.[9,14,15] The incidence of serious complications such as pneumothorax, haemothorax and arterial puncture has been reported at 3.1% in a cohort of 487 catheter insertions.[9] Central lines might not be removed promptly after transplantation, and this can put the patient at risk of catheter related blood stream infections and venous thromboembolic events.[15] Furthermore in the kidney transplant population, central venous stenosis is a complication of long-term venous access such as hemodialysis catheters.[16] Avoiding central line placement during kidney transplantation could avoid difficulties associated with line placement in patients with central venous stenosis and also prevent the risk of developing subsequent central venous stenosis. Time needed for placement of central venous catheters can prolong operating room time and associated cost. In our study, intraoperative time was significantly higher in the unmatched CVP cohort, but this difference did not reach statistical significance after propensity-matching.

There are several limitations to this work, which should be considered when interpreting our findings. Due to its retrospective nature, the study cannot account for all variables that may have influenced CVP line placement or eventual outcome. Furthermore, some data values could not be recovered from the clinical chart and were imputed based on clinical characteristics. This is a single-center study, where a high volume of living donor renal transplants are performed annually; results may not apply to institutions where living donor renal transplants are performed less frequently. Also, the study is limited to living donor transplants; it is unknown whether our findings can be applied to recipients of deceased donor transplants. Living donor kidney recpients were used to reduce the influence of donor related variables which are known to influence graft function, such as deceased donor age, hypertension and prolonged cold ischemia times, as these variables increase the risk of DGF irrespective of recipient volume state.[17]

Despite its limitations, we believe this study provides important information for transplant providers reviewing or establishing perioperative kidney transplant protocols. Propensity score matching can not replace randomization, but it allows to control for other potentially cofounding variables in our cohort. Our data suggest that central line placement can be safely omitted during living donation renal transplantation unless there are other indications such as extremely poor vascular access, or the need for vasopressor therapy.

At our institution, central line placement was performed only for other reasons of clinical necessity (e.g., anticipated vasopressor administration, inadequate peripheral intravenous access) for both living- and deceased-donor kidney transplants after 2009. In the two years following the study period (March 2009 – March 2011), CCR2 after living donor kidney transplantation was similar to graft function reported in this study. (40 ± 20%, unpublished data)

In conclusion, there was no difference in perioperative fluid management between the two groups. There was no association between postoperative kidney function, as measured by the

CCR2, after living donor kidney transplantation between patients with and without intraoperative CVP monitoring. Our experience suggests that adequate fluid resuscitation during living donor kidney transplantation can be provided without CVP monitoring.

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Abbreviations:

ASA	American Society of Anesthesiologists physical status classification
BMI	body mass index
CCR2	creatinine reduction ratio on post-transplant day 2
CVP	central venous pressure
DGF	delayed graft function
HD	hemodialysis
MDRD GRF	Serum creatinine and glomerular filtration rate
UCSF	University of California, San Francisco

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Table 1:

Patient demographics and comorbidities

			Full cohort			Propensity-matched weighted cohort		
			Control	**CVP**	**P value**	**Control**	**CVP**	**P value**
			n=206 (71.0%)	**n=84 (29.0%)**		**n=93**	**n=84**	
Demographics								
Age (years)			47.0 ± 13.3	49.8 ± 13.4	0.10	50.0 ± 14.3	49.8 ± 13.4	0.93
BMI (kg/m^2)			27.0 ± 4.8	26.0 ± 4.3	0.086	25.6 ± 4.8	26.0 ± 4.3	0.60
Male sex			126 (61.2%)	47 (56.0%)	0.41	55.4%	56.0%	0.95
Black race			19 (9.2%)	8 (9.5%)	0.94	12.5%	9.5%	0.57
Year		2006	24 (11.7%)	17 (20.2%)		12.5%	20.2%	
		2007	76 (36.9%)	39 (46.4%)	**0.024**	38.7%	46.4%	0.27
		2008	78 (37.9%)	23 (27.4%)		41.1%	27.4%	
		2009	28 (13.6%)	5 (6.0%)		7.7%	6.0%	
Comorbidities								
ASA physical status		2	31 (15.1%)	7 (8.3%)		6.0%	8.3%	
		3	168 (81.6%)	70 (83.3%)	0.079	85.7%	83.3%	0.84
		4	7 (3.4%)	7 (8.3%)		8.3%	8.3%	
Hypertension			184 (89.3%)	73 (86.9%)	0.56	87.5%	86.9%	0.92
Coronary artery disease			36 (17.5%)	21 (25.0%)	0.14	19.6%	25%	0.47
Left ventricular extraction fraction (%)			65 [60–65]	65 [60–65]	0.49	63 [57–65]	65 [60–65]	0.75
Retransplant			20 (9.7%)	12 (14.3%)	0.26	6.0%	14.3%	0.070
Preoperative dialysis status		None	62 (30.1%)	10 (11.9%)		13.7%	11.9%	
		Peritoneal	34 (16.5%)	8 (9.5%)	**<0.001**	8.9%	9.5%	0.93
		Hemodialysis	110 (53.4%)	66 (78.6%)		77.4%	78.6%	

CVP: group of patients undergoing central venous pressure monitoring; BMI, body mass index

Data are given as mean ± standard deviation, n (%), %, or median [IQR];

Percentage for the propensity-matched weighted cohort is given as weighted %

kg/m^2, kilograms per square meter;

Table 2:

Intraoperative factors and postoperative outcomes

		Full cohort			Propensity-matched weighted cohort		
		Control	CVP	P value	Control	CVP	P value
		n=206 (71.0%)	n=84 (29.0%)		n=93	n=84	
Intraoperative factors							
Surgeon	1	21 (10.2%)	5 (6.0%)	0.087	6.0%	6.0%	0.97
	2	27 (13.1%)	9 (10.7%)		8.3%	10.7%	
	3	19 (9.2%)	11 (13.1%)		9.5%	13.1%	
	4	41 (19.9%)	11 (13.1%)		19.1%	13.1%	
	5	22 (10.7%)	14 (16.7%)		16.1%	16.7%	
	6	18 (8.7%)	7 (8.3%)		7.7%	8.3%	
	7	27 (13.1%)	5 (6.0%)		4.8%	6.0%	
	8	31 (15.1%)	22 (26.2%)		28.6%	26.2%	
Duration (minutes)		227 [202–254]	241 [224–281]	**0.001**	231 [203–272]	241 [224–281]	0.063
Warm ischemia time (minutes)		27.3 ± 7.3	28.1 ± 8.1	0.39	27.5 ± 8.1	28.1 ± 7.9	0.67
CVP (mmHg)		NA	11.4 ± 4.3		NA	11.4 ± 4.3	
Total fluids (L)		3.25 ± 0.87	3.29 ± 1.10	0.76	3.30 ± 1.08	3.29 ± 1.10	0.95
Total fluids per kilogram body weight per hour of operative time (mL)		11.5 ± 4.0	11.0 ± 3.8	0.33	11.9 ± 3.8	11.0 ± 3.6	0.16
Estimated blood loss (mL)		100 [100–150]	100 [100–150]	0.73	100 [100–150]	100 [100–150]	0.70
Outcomes							
Hospital length of stay (days)		4 [4–5]	5 [4–6]	**<0.001**	4 [4–5]	5 [4–6]	0.094
Creatinine reduction ratio on postoperative day 2 (%)		34.9 ±18.2	36.8 ±17.9	0.43	34.5 ± 18.4	36.8 ± 17.9	0.51
Delayed graft function requiring dialysis		10 (4.9%)	4 (4.8%)		6.5%	4.8%	
Acute rejection		15 (7.3%)	6 (7.1%)	0.97	4.8%	7.1%	0.49
MDRD GFR at 3 months (mL/min)		55.3 [47.0–67.5]	57.2 [48.0–72.2]	0.36	58.7 [46.0–67.9]	57.2 [48.0–72.2]	0.40

CVP: group of patients undergoing central venous pressure monitoring;

Data are given as mean ± standard deviation, n (%), %, or median [IQR];

Percentage for the propensity-matched weighted cohort is given as weighted %.

mmHg, millimeters of mercury; L, liters; mL, milliliters; mL/min, milliliters per minute