Practice Variation in the Immediate Post-Operative Care of Pediatric Kidney Transplantation: A National Survey

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Abbreviations: (in alphabetical order)
CVP central venous pressure
PALISI Pediatric Acute Lung Injury and Sepsis Investigators
PICU pediatric intensive care unit

***Abstract**

Introduction: Advances in organ allocation, surgical technique, immunosuppression and long-term follow-up have led to a significant improvement in kidney transplant outcomes. While there are clear recommendations for several aspects of kidney transplant management, there are no pediatric specific guidelines for immediate post-operative care. The aim of this survey is to examine practice variations in the immediate post-operative care of pediatric kidney transplant patients.

Methods: We surveyed medical directors of Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) affiliated pediatric intensive care units regarding center specific immediate post-operative management of pediatric kidney transplantation.

Results: The majority of PALISI centers admit patients to the pediatric intensive care unit post-operatively. 97% of the centers involve a pediatric nephrologist in immediate post-operative care. Most patients undergo invasive hemodynamic monitoring; 97% of centers monitor invasive arterial blood pressure and 88% monitor central venous pressure. Most centers monitor serum electrolytes every 4 to 6 hours. Wide variation exists regarding blood pressure goal, fluid replacement type, frequency of obtaining kidney ultrasound and use of prophylactic anticoagulation.

Conclusion: There is consistent practice across PALISI centers in regards to many aspects of immediate post-operative management of pediatric kidney transplantation. However, variation still exists in some management aspects that warrant further discussions to reach a national consensus.

***Research Highlights**

- Pediatric kidney recipients are invasively monitored in post-operative period
- Wide variation exists regarding blood pressure goals and fluid replacement types
- The frequency of obtaining kidney ultrasounds post-operatively is not consistent
- Further discussions to reach a national consensus are warranted

Introduction:

End-stage renal disease affects 5 to 10 children per million per year and is associated with an increased mortality risk by 30-fold compared with the general pediatric population [1].

While the first kidney transplant was performed successfully in 1954, the field of pediatric transplantation lagged behind by 20 years. Major improvements in surgical approach and post-surgical care led to great strides in short-term and long-term outcomes. The drivers behind these improvements are related to advances in organ allocation, surgical technique, immunosuppression and long-term follow up [2-4]. The development of pediatric trial groups served as an important milestone that enhanced progress in all these areas and resulted in dramatic improvements. Remarkably, young children now have the best long-term graft survival among all age groups. As outcomes have improved, the patient population has become increasingly complex, including more children who have multiple congenital anomalies. In the United States, approximately 800 kidney transplants are performed per year in children under the age of 18 years, representing about 5% of all kidney transplants performed nationally (Figure 1) [5].

Pediatric kidney transplantation is generally performed in specialized centers due to complex technical, metabolic, immunologic, and physiologic factors. The transplant team usually is a multidisciplinary team comprising transplant surgeons, pediatric intensivists, pediatric nephrologists, and pediatric urologists alongside psychologists, renal transplant and dialysis nurses, social workers, pharmacists, and nutritionists.

There are clear recommendations for several management aspects of pediatric kidney transplantation, including induction and maintenance immunosuppressive medication, monitoring for allograft kidney function, recurrence of kidney disease, and infectious complications [6, 7]. Since there are no specific guidelines for the immediate post-operative care of pediatric kidney transplant recipients, we hypothesized that there is tremendous practice variation in the immediate post-operative care of those patients in the United States.

Methods:

The study was approved by the institutional review board of Indiana University. A Redcap online survey regarding center specific immediate post-operative management of pediatric kidney transplant recipients was sent to 78 medical directors of the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) affiliated pediatric intensive care units. The survey included 21 questions. The first part aimed to collect data regarding the size and clinical team composition of each pediatric intensive care unit (PICU) followed by questions regarding various aspects of immediate post-operative management of pediatric kidney transplantation including disposition of patients post-operatively, invasive monitoring practice, laboratory and imaging protocols, fluid replacement type, and anticoagulation practice. The survey was initially sent in May 2014 and a follow-up reminder was sent in June 2014. The responses were summarized using descriptive statistics; median and interquartile ranges or number and percentages were used as appropriate. Centers were divided based on their annual transplant volume into low (<6), medium (6-12) and high volume (>12) centers [8]. The survey responses were further analyzed based on the center volume using Chi-Square/Fisher's Exact test and Kruskal-Wallis test.

Results:

Thirty-five (45%) of PALISI centers responded to the survey. Thirty-three centers (94% of responding centers) have a pediatric kidney transplant program with median of 10 (IQR 6, 15) cases per year. Center characteristics are summarized in Table 1. Of the 33 centers that have a kidney transplant program 8 were low volume, 11 medium volume and 14 high volume.

Only 61% of centers have written protocols or guidelines to manage those patients and 73% have printed or electronic order sets for immediate post-operative care. The vast majority of centers (94%) routinely admit patients to the PICU post-operatively and involve a pediatric nephrologist and a pediatric intensivist in the immediate post-operative care (Figure 2). Most patients receive invasive monitoring; 97% of centers monitor invasive arterial blood pressure and 88% monitor

central venous pressure (CVP). In regards to arterial blood pressure goals, a large variation exists regarding blood pressure target: 15% of centers use pre-operative recipient's baseline blood pressure, 3% use 50th percentile for recipient's age, 24% use 90-95th percentile for recipient's age, 21% use normal blood pressure range for the donor and 37% have no set blood pressure goal.

Most centers monitor intake and output hourly and serum electrolytes every 4 to 6 hours, but there is a wide variation in the type of fluid used to replace urine output. 46% of centers use 0.45 to 0.75 normal saline for urine output replacement, 21% use 0.9 normal saline, and 30% choose fluid type based on serum and/or urine electrolytes. Based on our survey, we identified no agreement if and when urine electrolytes should be checked. 51% of centers perform an ultrasound of the kidney graft on day 1 post-operatively, 24% perform daily ultrasound for the first few days, and 24% perform ultrasound only if there is concern about graft function. Routine prophylactic anticoagulation is rarely used; only one center uses prophylactic anticoagulation routinely while 8 centers use prophylactic anticoagulation in patients with history of hypercoagulable state or history of thrombosis. There was no statistically significant difference regarding the immediate post-op management based on the center volume.

Discussion:

Despite the dramatic improvements of pediatric kidney transplant outcomes in the last two decades and the strong standardized approach regarding multiple aspects of long-term care for those children, clear guidelines for the immediate post-operative care are still lacking in the United States. Our survey shows that in most centers the immediate post-operative care for children after kidney transplantation occurs in PICU with multidisciplinary team involvement. The structure of the multidisciplinary transplant team varies; most centers include a pediatric nephrologist and a pediatric intensivist along with the kidney transplant surgeon.

Increasing evidence over the past two decades show significant advantages to standardization of medical care by implementing protocols, checklists, and care bundles [9]. These approaches not

only help clinicians adhere to best-practice guidelines but also have important positive impacts on patient outcomes and healthcare economics and may have additional benefits in advancing medical knowledge as well as improving staff and family satisfaction.

There is great variability regarding standardization of the immediate post-operative management: only 65-70% of the units have either written protocols or electronic order sets for the immediate post-operative care of pediatric kidney transplant recipients. In addition to general pediatric perioperative care, the specific fluid and electrolyte management in the first 24-48 hours after the kidney transplant procedure requires close attention, particularly for small children. All the surveyed centers agree that urinary output volume should be monitored and replaced at least hourly. Electrolytes such as potassium, magnesium, and phosphate are commonly lost in the setting of high urine output after kidney transplant and should be monitoring closely [10]. Serum sodium should be closely monitored and corrected. However, our survey showed that there is variation in the initial fluid type used to replace urine output.

Assessment of adequate hydration status during the first hours and days in kidney transplant patients is important. Dehydration can contribute to delayed graft function due to decreased renal perfusion; on the other hand, fluid overload can result in pulmonary edema and ascites [11]. Although the majority of the pediatric centers use central venous pressure (CVP) to monitor hydration status in the immediate post-operative period, there is no optimal goal of CVP identified in the literature and its impact on immediate and late graft function [12]. An indwelling bladder catheter can provide an accurate estimate of urine output as well as protect the fresh suture of the ureter on the bladder. On the other hand, it can be an additional source of infection. There is still controversy as to the most optimal post-operative day to remove the indwelling catheter [13].

The great majority of surveyed centers monitor blood pressure invasively, but there is a wide variation in blood pressure goals between centers. Normal to high-normal blood pressure targets may be warranted to provide adequate perfusion to the graft in the first 24-48 hours of immediate

post-operative care. If fluid boluses are not enough to reach blood pressure and central venous pressure goals, adding a vasoactive agent such as dopamine would be appropriate in this setting. At the same time, there is not enough pediatric or adult evidence to support that routine use of low dose dopamine improves graft survival [14]. Arterial hypertension is frequently observed during this immediate post-operative period which may be related to liberal fluid management, use of immunosuppressive drugs (e.g., calcineurin inhibitors), use of systemic corticosteroids, and to post-operative pain [15].

Vascular thrombosis of transplanted kidneys is a significant cause of pediatric graft loss [16]. Renal Doppler ultrasound can be utilized in cases of unexplained decreases in the urinary output or worsening arterial hypertension to rule out vascular thrombosis, but the benefit of using routine ultrasound in the immediate post-operative period is not well studied in pediatric population

The rate of vascular thrombosis in kidney transplant recipients ranges from 2% to 12% internationally and about 7% in the United States [17, 18]. Young recipient age, history of thrombosis, and history of hypercoagulability are risk factors for graft vascular thrombosis. Our survey showed some centers use anticoagulation only if the kidney transplant recipient has a history of hypercoagulable state or history of thrombosis. The effect of using this strategy on the incidence of thrombosis and graft survival in the pediatric population is yet to be studied.

Our study has several limitations that can affect the generalizability of the results. The survey did not include other centers that may perform pediatric kidney transplantation who are not part of the PALISI network and only half of the PALISI centers responded to our survey. Our data are based on self-reports from medical directors and we do not have secondary validation of the accuracy of that information provided. In addition, while intensivists try to normalize hemodynamic parameters and electrolyte balance by invasive and frequent laboratory monitoring, there are not enough studies in the pediatric population to indicate what are the optimal targets for each of these metrics

for different recipient age, donor age and source of the kidney and if achieving these goals affect the short or long-term graft function.

Conclusion:

There is consistent practice across PALISI centers in the immediate post-operative management of pediatric kidney recipients in regard to PICU admission, hemodynamic monitoring, and the degree of laboratory testing. However, practice variation still exists in some management aspects, including blood pressure goals, type of fluid replacement used, and use of renal Doppler and prophylactic anticoagulation. This study may be useful as a framework to establish multidisciplinary consensus guidelines regarding the immediate post-operative care for pediatric kidney transplantation and promote collaboration for prospective studies in this area.

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Table

Table 1. Demographics of Responding Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Centers (N=35)*	
Number of PICU beds	24 (20, 35.5)
Number of intensivists in the group	10 (9, 15)
Have Transplant Intensive Care Unit	2 (5.7%)
Have 24 hour in-house PICU attending coverage	22 (62.9%)
Have kidney transplant program	33 (94.3%)
Number of kidney transplant per year	10 (6, 15)
*Data presented as median (25^{th}, 75^{th} IQR) or as number (%)	

Table Center Volume

Center Responds Based on Center Yearly Pediatric Kidney Transplant Volume*

Variable	High Volume N=14	Medium Volume N=11	Low Volume N=8	*p*-value
Total number of PICU beds	34 (24, 44)	26 (20, 40)	17 (11, 25)	0.013
Number of intensivists in PICU group	15 (10, 19)	10 (9, 16)	10 (9, 13)	0.11
Have a separate transplant ICU	1 (7.1%)	1 (9.1%)	0 (0%)	1.0
Have 24 hour in-house PICU attending coverage	8 (57.1%)	8 (72.7%)	5 (62.5%)	0.9
Majority of your kidney transplant recipients being admitted to PICU post-operatively	12 (85.7%)	11 (100%)	8 (100%)	0.5
Pediatric nephrologists involved in immediate post-operative care of kidney transplant recipients	13 (92.9%)	11 (100%)	11 (100%)	1.0
For kidney transplant immediate post-operative management your PICU has				
• Informal unit policy	1 (7.1%)	1 (9.1%)	3 (37.5%)	0.17
• Written protocol guidelines	10 (71.4%)	6 (54.6%)	4 (50.0%)	0.6
• Preprinted or electronic order-set	11 (78.6%)	9 (81.8%)	4 (50.0%)	0.37
• None of the Above	1 (7.1%)	0 (0%)	0 (0%)	1.0
What invasive monitoring do you use for kidney transplant recipients in immediate post-operative period				
• Invasive blood pressure monitoring	13 (92.9%)	11 (100%)	8 (100%)	1.0
• Central venous pressure	11 (78.6%)	10 (90.9%)	8 (100%)	0.43
What is the blood pressure goal for kidney transplant recipients in immediate post-operative period?				
• Pre-operative recipient's baseline	4 (28.6%)	1 (9.1%)	0 (0%)	0.43
• 50th % for recipient's age	1 (7.1%)	0 (0%)	0 (0%)	
• 90-95th % for recipient's age	2 (14.3%)	4 (36.4%)	2 (25.0%)	
• 50th % for donor's age	4 (28.6%)	2 (18.2%)	1 (12.5%)	
• No set goal	3 (21.4%)	4 (36.4%)	5 (62.5%)	
How often do you monitor intake and output for kidney transplant recipients?				
• Hourly	13 (92.9%)	11 (100%)	8 (100%)	1.0
• Every 2 hours	1 (7.1%)	0 (0%)	0 (0%)	
How often do you check SERUM electrolytes in kidney transplant recipients in the immediate postoperative course (first 12-24 hours):				

• Every 2 hours	2 (14.3%)	1 (9.1%)	0 (0%)	0.44
• Every 3 hours	0 (0%)	1 (9.1%)	0 (0%)	
• Every 4 hours	4 (28.6%)	6 (54.5%)	5 (62.5%)	
• Every 6 hours	8 (57.1%)	3 (27.3%)	3 (37.5%)	
Do you check URINE electrolytes in kidney transplant recipients in the immediate post-operative course (first 12-24 hours):				
• No	4 (28.6%)	5 (45.4%)	5 (62.5%)	0.4
• Yes, routinely	4 (28.6%)	3 (27.3%)	0 (0%)	
• Yes, only if urine output is excessive or serum electrolytes are changing rapidly	6 (42.9%)	3 (27.3%)	3 (37.5%)	
Which fluid do you usually use to replace urine output:				
• 0.45 to 0.75 normal saline	8 (57.1%)	3 (27.3%)	4 (50.0%)	0.41
• Normal saline or Ringer's lactate	3 (21.4%)	2 (18.2%)	2 (25.0%)	
• It depends on serum and/or urine electrolytes	2 (14.3%)	6 (54.5%)	2 (25.0%)	
• Others	1 (7.1%)	0 (0%)	0 (0%)	
How often do you do a kidney ultrasound in the immediate post-operative period?				
• Routinely, only day 1 post-operatively	10 (71.4%)	4 (36.4%)	3 (37.5%)	0.14
• Routinely, daily for first few days	2 (14.3%)	2 (18.2%)	4 (50.0%)	
• Only as needed if there is concern about graft	2 (14.3%)	5 (45.4%)	1 (12.5%)	
Do you routinely use prophylactic anticoagulation for renal transplant recipients?				
• No	9 (64.3%)	8 (72.7%)	6 (75.0%)	1.0
• Yes	1 (7.1%)	0 (0%)	0 (0%)	
• Only if they have history of hypercoagulable state or thrombosis	4 (28.6%)	3 (27.3%)	2 (25.0%)	

PICU: pediatric intensive care unit
*Data presented as median (25th, 75th IQR) or as number (%)

Figure legends:

Figure 1. Trends of yearly pediatric solid organ and kidney transplantation in the United States from 1988 to 2014. Data retrieved from United Network for Organ Sharing (UNOS) website in August 2016

Figure 2. Practice variation in immediate post-operative care of pediatric kidney transplant recipients in PALISI centers that responded to survey and have kidney transplant program (N=33).

Figure 1

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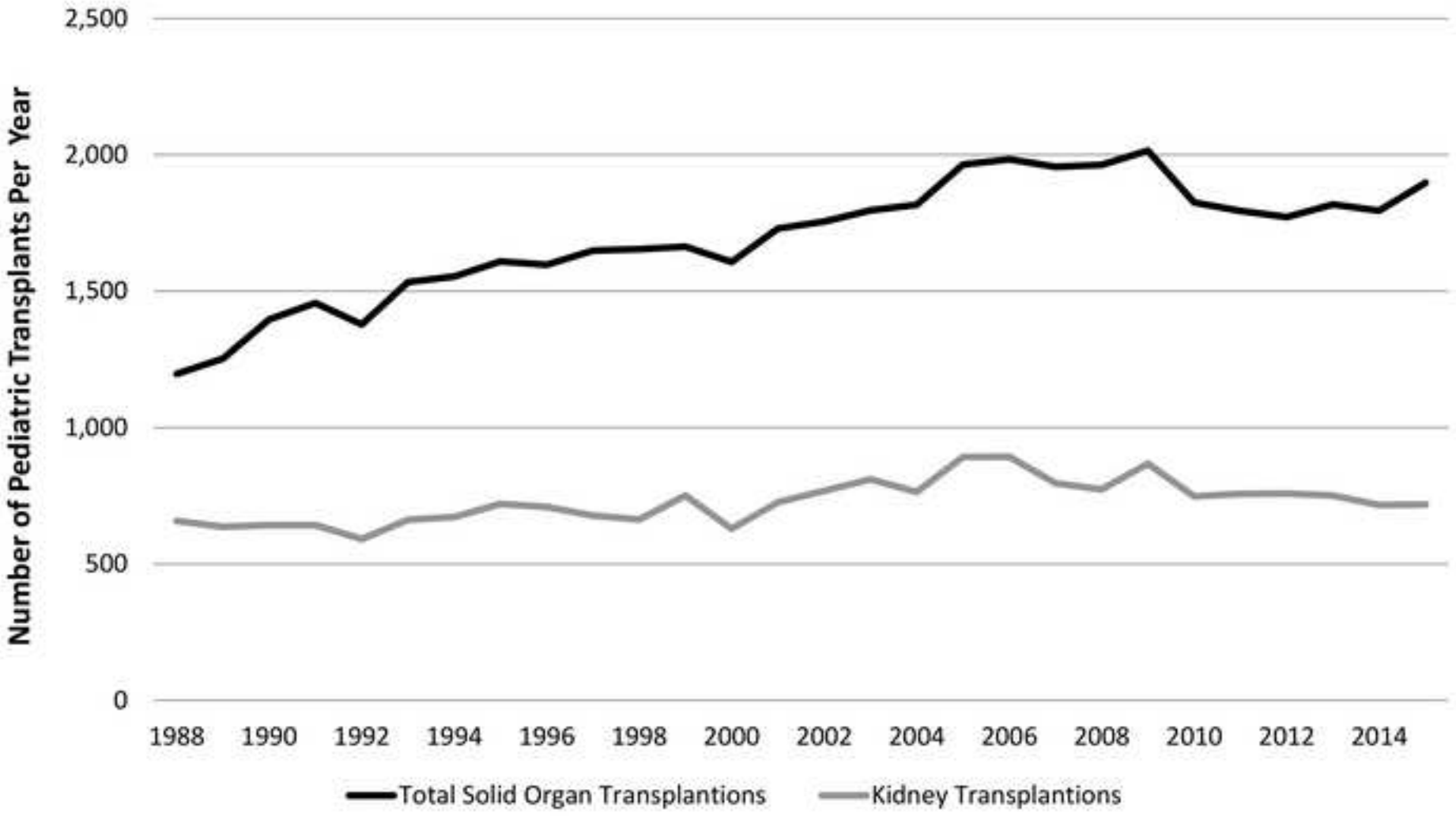

Figure 2

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