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Article type : Research Report

Handling Section Editor (where applicable): Dr Chandra Ramamoorthy

Intraoperative hemodynamic factors predicting early postoperative renal function in pediatric kidney transplantation

Predictive factors of postoperative renal function in kidney transplantation in children

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/pan.13201](https://doi.org/10.1111/pan.13201)

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- a. What is already known: optimizing both cardiac output and blood pressure is important for graft perfusion during kidney transplantation
- b. What this article adds: we propose optimal mean arterial pressure values resulting in better early renal function after pediatric kidney transplantation
- c. Implications for translation: blood pressure should be adapted to recipient weight and transplant organ.

Abstract:

Background: The anesthetic management of kidney transplantation in children remains somewhat empirical. The goal of the present study was to investigate intraoperative hemodynamic factors affecting post-transplantation kidney function.

Material and Methods: We performed a retrospective analysis of data from patients undergoing kidney transplantation in our Pediatric Teaching Hospital from 2000 to 2014. Data collected included: donor and recipient demographic data, recipient comorbidities, fluids administered intraoperatively, and intraoperative blood pressure and central venous pressure. The main outcome of the study was the creatinine clearance at day 1 corrected to a body surface area of 1.73 m². Analysis was performed using Classification Tree Analysis with 10-fold cross validation.

Results: One hundred and two patients were included. The following predictors of increased postoperative creatinine clearance at day 1 were identified: decreasing recipient weight, mean blood pressure-to-weight ratio 10 minutes after reperfusion, reduced cold ischemia duration and increased intraoperative albumin infusion. Increased creatinine clearance was observed when mean blood pressure-to-weight ratio 10 minutes after reperfusion ≥ 4.3 in patients weighing 13 to 21 kg and ≥ 2.5 in those ≥ 22 kg. Overall the model explained 64% (and at cross validation 60%) of creatinine clearance variability at day 1.

Conclusion: Intraoperative hemodynamics during kidney transplantation should be optimized in order to increase mean blood pressure according to values indicated by our analyses. Cold ischemia duration should be shortened as far as possible.

Word count: 229

Keywords: renal function, kidney, transplantation, children

Introduction

Renal transplantation is the optimal treatment for end-stage renal failure in adults and children (1, 2). However, developed countries face organ shortages due to increased kidney transplantation rates with a trend to earlier transplantation, organ donation refusal by donors or donors' families, and the inadequacy of procured organs (immunological incompatibility, infectious contra-indication, etc.). As an illustration, recent data from the French Transplantation Agency (Agence de la Biomedicine) found the ratio of potential recipients for each organ has progressed from 4.1 in 2010 to 4.7 in 2015.

Given these considerations, pediatric recipient transplantation with adult donor kidneys is common, particularly so in living donor transplantations (3). The intraoperative management of adult donor pediatric recipient transplantations is delicate, especially for smaller recipients. Surgery is technically challenging due to vessel size miss-match at anastomoses, and the donor organ and recipient patient have potentially divergent hemodynamic requirements (4, 5). This has been clearly described by Salvatierra and colleagues (6) who reported that the cardiac output of infants receiving adult organs increased by approximatively two fold after kidney transplantation.

There are currently no clear recommendations on hemodynamic targets during pediatric kidney transplantation and most anesthesiologists rely on empiric targets or adult reference values when managing pediatric kidney transplantation (7-9). We therefore undertook the present study in order to determine factors affecting creatinine clearance at day one after pediatric kidney transplantation with special focus on intraoperative hemodynamic values during transplantation.

Material and Methods

This study was approved by the Robert-Debre Hospital Institutional Review Board (CEEERB #2016/249). All parents gave oral and written consent to allow research upon previously recorded clinical data. Data were retrospectively extracted from medical files, and the trial was non-interventional.

Patient inclusion and exclusion

Data were collected from an electronic medical records system on all patients less than 18 years of age when operated upon for pediatric kidney transplantation in our institution from 2000 to 2014. Exclusion criteria were: insufficient intraoperative or postoperative data.

Anesthetic management

Patients were pre-medicated with oral hydroxyzine (2 mg.kg^{-1}), a first generation antihistamine with strong anxiolytic properties that is commonly used in France. Anesthesia was performed according to local protocols with standard monitoring. All inductions used either inhaled sevoflurane, propofol ($3 \text{ to } 5 \text{ mg.kg}^{-1}$) or thiopental ($3 \text{ to } 5 \text{ mg.kg}^{-1}$), followed by atracurium (0.5 mg.kg^{-1}) or suxamethonium (2 mg.kg^{-1}) for muscle relaxation. After tracheal intubation a sufentanil bolus of $0.2 \text{ } \mu\text{g.kg}^{-1}$ was administered. Hypnosis was maintained using sevoflurane ($0.8 \text{ to } 1$ age-adjusted minimum alveolar concentration) in a $50\% \text{ O}_2\text{-Air}$ mixture. Ventilation was pressure controlled with an end-expiratory pressure of $5 \text{ cmH}_2\text{O}$, and inspiratory pressures titrated maintain end tidal CO_2 measurements between $4 - 4.7 \text{ KPa}$ ($30 - 35 \text{ mmHg}$). Analgesia was administered as $0.1 \text{ } \mu\text{g.kg}^{-1}$ sufentanil boluses. Patients were actively warmed from admission to theatre until exit in order to maintain core temperature above 36°C . At the end of the surgery all patients were transferred intubated and mechanically ventilated to the Intensive Care Unit (ICU) and sedated for overnight ventilation.

Intraoperative hemodynamics and intravenous fluids

Radial arterial and supra-diaphragmatic central venous pressure monitoring were employed in all patients, in addition to routine monitoring - heart rate (HR), oxygen saturation (SpO_2TC) and capnography (ETCO_2). Esophageal Doppler was used from 2006 onwards. An intraoperative crystalloid maintenance solution containing glucose 1 mmol.l^{-1} , 4 g.l^{-1} of NaCl and no potassium was administered at a rate of $10 \text{ ml.kg}^{-1}.\text{h}^{-1}$. Additional vascular filling employed normal saline solution 10 ml.kg^{-1} boluses over 10 minutes repeated as needed. At the beginning of warm ischemia, the crystalloid rate was increased to $20 \text{ ml.kg}^{-1}.\text{h}^{-1}$ and a bolus of 20 ml.kg^{-1} of albumin 5% was administered over 10 minutes followed by 10 ml.kg^{-1} every 10 minutes until reperfusion (10). Dopamine was titrated from 5 to $20 \text{ } \mu\text{g.kg}^{-1}.\text{mn}^{-1}$ and $2 \text{ } \mu\text{g.kg}^{-1}$ ephedrine boluses were administered during reperfusion to maintain the following hemodynamic endpoints: mean blood pressure (MBP) $\geq 70 \text{ mmHg}$, central venous pressure (CVP) $\geq 14 \text{ mmHg}$ during and after reperfusion, and Indexed Stroke Volume within 10% of its maximum value during the entire intraoperative period, where

esophageal Doppler was used. The blood pressure goal was adjusted where required following surgical opinion of kidney turgidity. Finally, because of the risk of hypovolemia, neither diuretics nor mannitol were used during the intraoperative period. Perioperative management – anesthetic and intensive care protocols and surgical technique - was unchanged during the study period.

Data collected

Data were collected regarding donors, recipients and intraoperative and postoperative conditions. Data previously described as influencing postoperative graft function were selected (1, 4, 6, 7, 10-13). The following donor characteristics were recorded: age, weight, living or cadaveric donor, donor-to-recipient weight ratio and the presence or absence of donor continuously infused vasoactive drug therapy during organ procurement. Donor blood pressures were not recorded because this data was lacking from most patient records. Recorded recipient characteristics included: presence or absence of pre-transplantation dialysis (hemodialysis or peritoneal), pre-transplantation plasma creatinine and hemoglobin, and the presence or absence of heart failure, pulmonary hypertension and systemic hypertension. The following intraoperative data were recorded: administered volumes of crystalloid and albumin, blood product transfusions, cold and warm implantation ischemia times (the latter defined as the time from removal from ice to reperfusion), use of esophageal Doppler, and hemodynamic values, namely: systolic blood pressure (SBP), MBP, HR and CVP before induction of anesthesia, 10 minutes after intubation, at reperfusion and 10 minutes post reperfusion. MBP to weight ratio was also calculated at reperfusion and 10 minutes post reperfusion to assess target pressure variability when adjusted for patients' weight. Although pulse pressure is considered a marker of kidney perfusion, it was not included in analysis as it is not commonly reported as a hemodynamic target during kidney transplantation. Collected postoperative data consisted of the presence or absence of secondary surgical intervention and the causes of such interventions, postoperative hemoglobin and creatinine at ICU admission, hemodynamic at admission to ICU, vasoactive drug use during the first postoperative day, serum creatinine 24 hours post reperfusion and the requirement for renal support during the first 5 days. Creatinine clearance at day 1 was then calculated according to Schwartz formulae and expressed as $\text{ml} \cdot \text{min}^{-1} \cdot 1.73\text{m}^{-2}$ to correct for patient size (14, 15).

Statistical analysis

The primary outcome of this study was to determine factors affecting postoperative creatinine clearance at day 1. This early endpoint was preferred to kidney function at 6 months or at one year because it is less likely to be affected by immunological factors. In comparison to other early outcomes such as urine output or early dialysis in ICU, creatinine clearance appears the most appropriate. In acute tubular necrosis, for example, urine output may be preserved while creatinine clearance is reduced. Postoperative renal replacement therapy depends upon many factors including renal function, physician's judgment and the occurrence of complications such as volume overload. This factor was thus analyzed as the secondary outcome of this study.

Descriptive statistics used mean $\pm$ standard deviation and median [ranges] for continuous variables, given the possible non-normal distribution of some outcomes, and percentages for discrete variables. In order to determine predictors of postoperative creatinine clearance at day 1, classification tree analysis was used (16-19) - a methodology previously used by our team in other publications. Classification trees are built by nodes and optimized in order to homogenate the population according to the influence of entered parameters. Classification tree analysis relies on the dichotomization of the population according to predictive factors entered into the model. Each dichotomization (node) builds two child groups. The dichotomizing factor is chosen so as to produce the least variability of child nodes at each step. Consequently, child group variability is reduced at each successive node, and groups undergo further dichotomization following the same methodology. There is no limitation concerning the number of analyzed predictors; all data collected for the donor and the recipient (during the intraoperative period) were entered in analysis. In addition, classification tree analysis does not require variables to be normally distributed. The tree is easily interpreted by focusing on terminal nodes which constitute "groups". Going up in the tree, groups are defined according to the presence or absence of risk factors defined in tree ramification. The validity of the model was studied by calculating the percentage of variability explained by the model (derived from the misclassification risk of the classification tree analysis model) and tenfold model cross-validation. The latter process divides the study population into 10 random subgroups. The first tree is based on all cases except those in the first sub sample; the second tree is based on all of the cases except those in the second subsample, and so on. For each tree, misclassification risk is estimated by applying the tree to the subsample excluded in generating it. The overall misclassification risk is the average of the risks for all of the trees. Classification tree analysis results are displayed as a tree, with

each node containing the predictive factor, the number of patients within the node, the mean and standard deviation of postoperative day 1 creatinine clearance.

The secondary outcome was investigated by exploring the statistical association between postoperative renal replacement therapy in ICU using the same classification tree analysis factors as above, with the addition of creatinine clearance at day 1 as an explaining factor.

Correlation analysis was performed and comparisons were performed using the Mann & Whitney non-parametric test or χ^2 (or exact Fischer test) for continuous and discrete variables, respectively. Statistical analysis was performed using JMP 9.02 (JMP. SAS Institute Inc., Cary, NC, 1989-2011) and SPSS 20.0 software (IBM Company, Chicago, Illinois, USA).

Results

During the defined study period, 166 children underwent kidney transplantation. Sixty four patient charts were found to have incomplete data. As a result, 102 patients were included for analysis. Only two patients suffered acute arterial transplant thrombosis, and both were already excluded due to insufficient intraoperative data.

Donor descriptive statistics are displayed in table 1. Recipient characteristics, Preoperative and intraoperative data are displayed in table 2. Intraoperative hemodynamic data is graphically displayed in figure 1. Postoperative data are displayed in table 3. Intrafamilial living donor kidneys were transplanted in a quarter of patients (table 1) resulting in a low mean cold ischemia duration (table 2). Secondary intervention occurred without leaving the operating theatre in 10 cases because of vascular flow impairment observed with on-table Doppler examination. No re-interventions occurred during the first postoperative day.

Classification tree analysis found the following: Increased creatinine clearance at day 1 was associated with decreased weight, increased MBP to weight ratio at 10 minutes after reperfusion, decreasing cold ischemia duration and an increasing intraoperative albumin administration (figure 2, table 4).

Values predictive of increased creatinine clearance at day 1 were identified for two groups according to patient size: MBP to weight ratio at 10 minutes after reperfusion ≥ 4.3 (56 - 90 mmHg) in patients 13 to 21 kg and MBP to weight ratio at 10 minutes after reperfusion ≥ 2.5 (55 mmHg - 120 mmHg) in those ≥ 22 kg. Patients exhibiting values of MBP to weight ratio at 10 minutes after reperfusion greater than these defined vales were found to have a creatinine clearance statistically greater than other patients (median [ranges]: 185 [20 – 1500]

ml.mn-1.1.73m⁻² versus 39 [6 – 449] l.mn-1.1.73m⁻², $p < 0.001$, respectively; Area Under the Curve of Receiving Operator Characteristics : 0.8 [95% confidence interval : 0.73 – 0.90]). Finally, creatinine clearance was significantly correlated to MBP to weight ratio at 10 minutes after reperfusion (correlation coefficient = 0.64, $p < 0.001$) and age (correlation coefficient = -0.64, $p < 0.001$). Overall, the classification and regression tree analysis model explained 64% of creatinine clearance variability and at cross validation explained 60% of variability.

Postoperative renal replacement therapy in ICU was statistically associated with a creatinine clearance at day 1 $< 78 \text{ ml.mn}^{-1}.1.73\text{m}^{-2}$, a donor-to-recipient Weight ratio ≥ 3.5 and $\geq 189 \text{ ml.kg}^{-1}$ of intraoperative crystalloid (supplemental file 1). Overall, the classification and regression tree analysis model explained 33% of renal replacement therapy risk variability and 30% at cross validation.

Finally, there was no statistically significant difference in the main study outcome between patients requiring early re-intervention with those who did not (creatinine clearance at day 1: 102 [35 – 786] ml.mn⁻¹.1.73m⁻² versus 56 [6 – 1505] ml.mn⁻¹.1.73m⁻², $p = 0.08$, respectively). Nor were there differences in other factors potentially contributing to organ flow, namely: recipient weight (27 [14 – 51] kg versus 30 [10 – 71] kg, $p = 0.2$, respectively), albumin administration (19 [0 – 47] ml.kg⁻¹ versus 15 [1 – 68] ml.kg⁻¹, $p = 0.3$, respectively), cold ischemia duration (11 [2 – 26] hours versus 15 [1 – 28] hours, $p = 0.9$, respectively) and MBP-to-weight ratio at 10 minutes after reperfusion (2.3 [1.6 – 6.2] mmHg.kg⁻¹ versus 2.4 [1 – 7.5] mmHg.kg⁻¹, $p = 0.09$, respectively).

Discussion

In this pediatric population of patients undergoing pediatric kidney transplantation, predictors of an increased postoperative creatinine clearance at day 1 were: decreasing recipient weight, an increased MBP-to-recipient-weight ratio 10 minutes after reperfusion, a decreased cold ischemia duration and an increased amount of intraoperative colloids administered. Overall the model explained 64% of creatinine clearance variability at day 1 and 60% of this variability at cross validation.

The first important result of our study was the determination of optimal arterial blood pressure values (figure2, table 4). A strong correlation was found between postoperative creatinine clearance at day 1 and MBP 10 minutes after reperfusion. As stated above, graft perfusion relies on increased recipient cardiac output as described by Salvatierra *and coll.* (6). However, arterial blood pressure is also a major determinant of graft perfusion, as suggested

by many guidelines (7, 13). Our results defined optimal MBP in two patient subgroups according to weight. Although these ranges of mean blood pressure were high - and higher than physiological blood pressures for recipient age - they may well reflect optimal pressures for graft function. As such, they may be considered a valid clinical target for anesthesiologists trying to both avoid excessive afterload and to maintain cardiac output. Unfortunately, no comparison between recipient and donor mean blood pressures was possible due to lack of data. Concerning the choice of which agent to use to influence systemic blood pressure, a recent study performed in children undergoing pediatric kidney transplantation found that the use of dopamine delays renal function recovery (19). However, this potential negative effect of dopamine may well be counterbalanced by its effect on the cardiac output and renal perfusion. Colloids, including albumin, have been found to have no advantage over crystalloids in intensive care patients (20), yet were found to be predictive of day 1 creatinine clearance in our study. As such, intraoperative albumin (nodes 6 and 7: figure 2, table 4) employed to optimize perfusion pressure and cardiac output through the graft might be advantageous in the specific situation of kidney transplantation (21). Moreover, higher doses of intraoperative crystalloids were associated with an increased risk of postoperative renal replacement therapy. Both volume overload leading to respiratory complications and hyperchloremic acidosis associated with normal saline infusions could lead to renal replacement therapy in the context of increased crystalloid therapy (22). Finally, our predictive model for creatinine clearance at day 1 found that cold ischemia duration (nodes 2 and 3, nodes 8 and 9, nodes 6 and 7: figure 2, table 4) influenced early postoperative creatinine clearance. This is most likely to be the result of the reduced ischemic tubular necrosis (23).

Decreasing recipient weight was predictive for increasing postoperative creatinine clearance (node 1 to 9: figure 2, table 4). This explains the supramaximal postoperative creatinine clearance values recorded ($778 \pm 740 \text{ ml} \cdot \text{mn}^{-1} \cdot 1.73^{-2}$) in patients weighing less than 13 kg. This result is in accordance with previous studies that found that low weight recipients with pre-emptive kidney transplantation had better kidney function and longer graft survival when compared to older patients, (13, 24, 25). By contrast, increasing donor-to-recipient weight ratio was associated with an increased risk of postoperative renal replacement therapy. This result might indicate both surgical difficulty during transplantation in such recipients and the lower recipient systemic pressures and cardiac output when compared to donors, and correlates with the results of Salvatierra's study in low-weight patients (6).

Our results did not demonstrate CVP to be a predictor of early graft function. Indeed, adult studies inconsistently find CVP to predict post-transplantation graft function (11, 12).

This is not surprising given that CVP is a complex parameter depending on multiple factors: pericardial pressure, intrathoracic pressure, intra-abdominal pressure, vascular resistance, blood volume and cardiac function (26). Esophageal Doppler monitoring was similarly not found to be predictive of improved postoperative renal function – which may be due to substantial intraoperative crystalloid use (average 103 ml.kg⁻¹) across all patients.

Overall our model explained 64% of creatinine clearance variability, leaving 36% of this variability unexplained. Other potential factors that could come into play include immunological compatibility and surgical conditions – particularly graft quality. Tenfold cross-validation of the model reported a percentage of explained variability close to the overall result, indicating that the model is valid and stable even when randomly removing patients from the cohort. Postoperative dialysis in the ICU was more likely with reduced postoperative kidney function, donor-to-recipient weight mismatch and increased crystalloid administration. However, given the low percentage of explained variability of this secondary outcome (33%) other factors may be involved, and further research into this area is required.

Our study suffers some limitations. It is a retrospective study and as a consequence data may suffer from imprecision. Secondly, intraoperative monitoring varied between patients - particularly the use of esophageal Doppler. However, this is unlikely to have influenced our results given that this factor was not found predictive of postoperative CC. Finally, dopamine was the main agent drug used to maintain intraoperative MBP within target values. Although it is suspected to be nephrotoxic (27) and is associated with delayed recovery of renal function when used during pediatric kidney transplantation (28), dopamine was part of our protocol at the time of the study. Sixty four patients were not included because of lacking data – which might induce recruitment bias. Finally, Schwartz's formula was employed in the current study, potentially overestimating glomerular filtration in low body weights and underestimating it at high body weights (29, 30).

In conclusion, our results indicate that MBP targets at and after reperfusion should be optimized as follows: MBP-to-recipient-weight ratio 10 minutes after reperfusion ≥ 4.3 in patients 13 to 21 kg and MBP-to-recipient-weight ratio 10 minutes after reperfusion ≥ 2.5 in those ≥ 22 kg. The blood pressure values defined in this study may assist clinicians when setting hemodynamic goals during pediatric kidney transplantation. In addition, excessive intraoperative crystalloid administration should be avoided. Vascular filling and intraoperative systemic blood pressure must be managed using a combination of crystalloids, albumin and vasoactive agents. Finally, cold ischemia duration should be shortened as much

as possible. Further prospective randomized multicenter trials, examining these findings are mandatory to confirm these results.

ACKNOWLEDGEMENTS

Assistance with the study: None

Financial support and sponsorship: none.

Conflict of interest: authors declare no conflict of interest

Presentation: Presentations of preliminary data were performed during the national congress of the French Society of Anesthesiology and Intensive Care in Paris on September 2016.

The current study is dedicated to the Professor Yves NIVOCHE who improved, for more than 20 years, the intraoperative management of kidney transplantation in Robert Debre Hospital.

References

1. Dharnidharka VR, Fiorina P, Harmon WE. Kidney transplantation in children. *N Engl J Med*. 2014 2014/08/07/;371(6):549-58.
2. Giessing M, Muller D, Winkelmann B, Roigas J, Loening SA. Kidney transplantation in children and adolescents. *Transplant Proc*. 2007 2007/09//;39(7):2197-201.
3. Perez-Bertolez S, Barrero R, Fijo J, Alonso V, Ojha D, Fernandez-Hurtado MA, et al. Outcomes of pediatric living donor kidney transplantation: A single-center experience. *Pediatr Transplant*. 2017 Jan 29.
4. Salvatierra O, Millan M, Concepcion W. Pediatric renal transplantation with considerations for successful outcomes. *Semin Pediatr Surg*. 2006 2006/08//;15(3):208-17.
5. Tydén G, Berg U, Bohlin AB, Sandberg J. Renal transplantation in children less than two years old. *Transplantation*. 1997 1997/02/27/;63(4):554-8.
6. Salvatierra O, Singh T, Shifrin R, Conley S, Alexander S, Tanney D, et al. Successful transplantation of adult-sized kidneys into infants requires maintenance of high aortic blood flow. *Transplantation*. 1998 1998/10/15/;66(7):819-23.

7. Beebe DS, Belani KG, Mergens P, Liao JC, So SK, Najarian JS, et al. Anesthetic management of infants receiving an adult kidney transplant. *Anesth Analg*. 1991 1991/12//;73(6):725-30.
8. Lemmens HJM. Kidney transplantation: recent developments and recommendations for anesthetic management. *Anesthesiol Clin North America*. 2004 2004/12//;22(4):651-62.
9. Schmid S, Jungwirth B. Anaesthesia for renal transplant surgery: an update. *Eur J Anaesthesiol*. 2012 2012/12//;29(12):552-8.
10. Othman MM, Ismael AZ, Hammouda GE. The impact of timing of maximal crystalloid hydration on early graft function during kidney transplantation. *Anesth Analg*. 2010 2010/05/01//;110(5):1440-6.
11. Bacchi G, Buscaroli A, Fusari M, Neri L, Cappuccilli ML, Carretta E, et al. The influence of intraoperative central venous pressure on delayed graft function in renal transplantation: a single-center experience. *Transplant Proc*. 2010 2010/11//;42(9):3387-91.
12. Campos L, Parada B, Furriel F, Castelo D, Moreira P, Mota A. Do intraoperative hemodynamic factors of the recipient influence renal graft function? *Transplant Proc*. 2012 2012/08//Jul- undefined;44(6):1800-3.
13. de Haro Jorge I, García-Aparicio L, Vila-Santandreu A, Martín Solé O, Musquera M, Peri L, et al. [Kidney transplantation in children weighing 11 kg or less]. *Cir Pediatr*. 2014 2014/07//;27(3):131-4.
14. Schwartz GJ, Gauthier B. A simple estimate of glomerular filtration rate in adolescent boys. *J Pediatr*. 1985 Mar;106(3):522-6.
15. Schwartz GJ, Feld LG, Feld LG, Langford DJ, Langford DJ. A simple estimate of glomerular filtration rate in full-term infants during the first year of life. 19840709 DCOM- 19840709(0022-3476 (Print)).
16. Lemon SC, Roy J, Clark MA, Friedmann PD, Rakowski W. Classification and regression tree analysis in public health: methodological review and comparison with logistic regression. *Ann Behav Med*. 2003 Dec;26(3):172-81.
17. Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, et al. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technol Assess*. 2004 Sep;8(36):iii-iv, ix-xi, 1-158.
18. Loh WY. Classification and regression trees. *Wiley Interdisciplinary Reviews: Data Mining and Knowledge Discovery*. [10.1002/widm.8]. 2011;1(1):14-23.
19. Marshall RJ. The use of classification and regression trees in clinical epidemiology. *Journal of Clinical Epidemiology*. [16/S0895-4356(00)00344-9]. 2001;54(6):603-9.

20. Human albumin solution for resuscitation and volume expansion in critically ill patients. *Cochrane Database Syst Rev*. 2011 Oct 05(10):CD001208.
21. Schnuelle P, Johannes van der Woude F. Perioperative fluid management in renal transplantation: a narrative review of the literature. *Transpl Int*. 2006 2006/12//;19(12):947-59.
22. Toyonaga Y, Kikura M. Hyperchloremic acidosis is associated with acute kidney injury after abdominal surgery. *Nephrology (Carlton)*. 2016 Jun 16.
23. Sarwal MM, Cecka JM, Millan MT, Salvatierra O. Adult-size kidneys without acute tubular necrosis provide exceedingly superior long-term graft outcomes for infants and small children: a single center and UNOS analysis. *United Network for Organ Sharing. Transplantation*. 2000 2000/12/27//;70(12):1728-36.
24. Haberal M, Karakayali H, Sevmis S, Akbulut S, Colak T, Baskin E, et al. Preemptive living donor renal transplantation: a single-center experience. *Transplant Proc*. 2009 2009/09//;41(7):2764-7.
25. Hardy BE, Shah T, Cicciarella J, Lemley KV, Hutchinson IV, Cho YW. Kidney transplantation in children and adolescents: an analysis of United Network for Organ Sharing Database. *Transplant Proc*. 2009 2009/06//;41(5):1533-5.
26. Sondergaard S, Parkin G, Aneman A. Central venous pressure: we need to bring clinical use into physiological context. *Acta Anaesthesiol Scand*. 2015 2015/05//;59(5):552-60.
27. Kellum JA, M Decker J. Use of dopamine in acute renal failure: a meta-analysis. *Crit Care Med*. 2001 2001/08//;29(8):1526-31.
28. Taylor K, Kim WT, Maharramova M, Figueroa V, Ramesh S, Lorenzo A. Intraoperative management and early postoperative outcomes of pediatric renal transplants. *Paediatr Anaesth*. 2016 2016/10//;26(10):987-91.
29. Safaei-Asl A, Enshaei M, Heydarzadeh A, Maleknejad S. Correlation between cystatin C-based formulas, Schwartz formula and urinary creatinine clearance for glomerular filtration rate estimation in children with kidney disease. *J Renal Inj Prev*. 2016;5(3):157-61.
30. Filler G, Melk A, Marks SD. Practice recommendations for the monitoring of renal function in pediatric non-renal organ transplant recipients. *Pediatr Transplant*. 2016 May;20(3):352-63.

Legend Figures

Figure 1: intraoperative values of systolic blood pressure (SBP), mean blood pressure (MBP) and central venous pressure (CVP), expressed as mmHg. Data are displayed as median (horizontal bar) and ranges (boxes).

Figure 2: Classification tree analysis. Each box displays the number of patients in the node (subgroup of patients) and mean and SD (standard deviation) values of creatinine clearance at day 1. MBP/W10: mean blood pressure-to-weight ratio 10 minutes after reperfusion; C I: cold ischemia.

Table 1: Donor descriptive characteristics (N = 102). IFT: intrafamilial transplantation.

Factor	Mean $\pm$ sd / Median [ranges] OR N(%)
Age (years)	20 $\pm$ 12 / 15 [5 – 48]
Weight (kg)	56 $\pm$ 21 / 56 [18 – 96]
Vasoactive therapy during procurement	44 (43.1 %)
IFT / Cadaveric	27 (26.5 %) / 75 (73.5 %)
Donor/ Recipient weight ratio	2 $\pm$ 1.4 / 1.6 [0.5 - 6.2]

Table 2: Recipient descriptive characteristics (N = 102 patients). BMI: body mass index, CVP: central venous pressure, Hb: hemoglobin, MBP: mean blood pressure.

Factor	Mean $\pm$ sd / median [ranges] OR N (%)
Age (years)	10.2 $\pm$ 5.3 / 11.5 [1 – 19]
Weight (kg)	32 $\pm$ 17 / 33 [10 – 66]
BMI	11.7 $\pm$ 3.7 / 12 [6 – 20]
Pre-transplantation Hemodialysis	85 (83 %)
Pre-transplantation Peritoneal Dialysis	16 (15.7 %)
Duration of dialysis (months)	15 $\pm$ 17 / 11 [0 – 67]
Pre-transplantation Hypertension	52 (51 %)
Left ventricular ejection fraction < 60 %	4 (3.9 %)
Left ventricular hypertrophy	41 (40.2 %)
Pre-transplantation Hb (g/dl)	12 $\pm$ 1.4 / 11.8 [8.2 – 14.7]
Pre-transplantation creatinine (μ mol/l)	440 $\pm$ 200 / 440 [86 – 1076]
Monitoring CVP	102 (100 %)
Monitoring Esophageal Doppler	57 (57.9 %)
Intraoperative crystalloids (ml/kg)	103 $\pm$ 61 / 95 [25 – 341]
Intraoperative albumin (ml/kg)	16 $\pm$ 14 / 14 [0 – 61]
Intraoperative red cell transfusion	22 (21.6 %)
Intraoperative fresh-frozen plasma transfusion	3 (2.9 %)
Intraoperative platelets transfusion	1 (1 %)
Intraoperative nephrectomy	31 (30.3 %)
Re-intervention for vascular flow impairment	10 (9.8 %)
Continuous vasoactive therapy after reperfusion	54 (52.9 %)
Duration of anesthesia (minutes)	363 $\pm$ 104 / 360 [180 – 900]
Duration of surgery (minutes)	255 $\pm$ 96 / 240 [120 – 780]
Duration of cold ischemia (hours)	16.6 $\pm$ 7 / 15 [1 – 28]
Duration of hot ischemia (minutes)	48 $\pm$ 15 / 45 [20 – 88]
MBP/weight at reperfusion (mmHg/kg)	3 $\pm$ 1.6 / 2.1 [0.9 – 9]
MBP/weight 10 minutes after reperfusion (mmHg/kg)	3 $\pm$ 1.6 / 2.3 [1 – 7.5]

Table 3: Postoperative hemodynamic data and renal function in the intensive care unit. SBP: systolic blood pressure, MBP: mean blood pressure, CVP: central venous pressure, Hb: haemoglobin, ICU: intensive care unit.

Factors	Mean $\pm$ sd / median [ranges] OR N(%)
SBP at admission to ICU (mmHg)	122 $\pm$ 26 / 120 [44 – 180]
MBP at admission ICU (mmHg)	86 $\pm$ 28 / 90 [25 – 160]
HR admission to ICU (bpm)	120 $\pm$ 27 118 [75 – 180]
CVP at admission to ICU (mmHg)	17 $\pm$ 3 / 17 [12 – 25]
Hb at admission to ICU (mg.dl ⁻¹)	9.6 $\pm$ 1.7 / 9.8 [4.7 – 13,6]
Creatinine at admission to ICU (μ M)	413 $\pm$ 169 / 384 [49 – 1049]
Creatinine at day 1 (μ M)	230 $\pm$ 197 / 172 [17 – 1089]
Creatinine clearance at day 1 (ml.mn ⁻¹ . m ⁻²)	71 $\pm$ 84 / 35 [5 – 469]
Creatinine clearance at day 1 (ml.mn ⁻¹ .1.73 m ⁻²)	168 $\pm$ 267 / 63 [6 – 1505]
Percentage of normal creatinine at day 1	142 $\pm$ 225 / 51 [6 – 1319]
Percentage use of vasoactive drugs at day 1	32 (31.4 %)
Dialysis in ICU	15 (14.7 %)

Table 4: Classification tree analysis of factors predictive of creatinine clearance at day 1 following pediatric kidney transplantation. MBP/W10: mean blood pressure-to-weight ratio 10 minutes after reperfusion.

Nodes	Weight (kg)	MBP/W10 (mmHg.kg ⁻¹)	Cold ischemia (hours)	Intraoperative Albumin (ml.kg ⁻¹)	Creatinine Clearance (ml.mn ⁻¹ .1.73 m ⁻²)
1	< 13				778 ± 740
2	13-21	≥ 4.3	< 14		526 ± 166
3	13-21	≥ 4.3	≥ 14		185 ± 132
4	13-21	< 4.3	< 14		228 ± 140
5	13-21	< 4.3	≥ 14		156 ± 119
6	≥ 22	≥ 2.5		≥ 14	132 ± 55
7	≥ 22	≥ 2.5		< 14	78 ± 63
8	≥ 22	< 2.5	< 4		77 ± 27
9	≥ 22	< 2.5	≥ 4		32 ± 23

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Title:

Intraoperative hemodynamic factors predicting early postoperative renal function in pediatric kidney transplantation

Date:

2017-09-01

Citation:

Michelet, D., Brasher, C., Marsac, L., Zanoun, N., Assefi, M., Elghoneimi, A., Dauger, S. & Dahmani, S. (2017). Intraoperative hemodynamic factors predicting early postoperative renal function in pediatric kidney transplantation. PEDIATRIC ANESTHESIA, 27 (9), pp.927-934. <https://doi.org/10.1111/pan.13201>.

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