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Relation between Stroke Volume Variation and Central Venous Pressure in Fluid Management for Pediatric Patients Undergoing Living Donor Renal Transplantation

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Abstract

Background: Renal transplantation is a therapy option for people suffering from end-stage renal disease who are currently receiving hemodialysis. This study aimed to examine the effectiveness of stroke volume variation (SVV) in predicting fluid responsiveness (FR) and compare it to central venous pressure (CVP) in the setting of goal-directed fluid management during live donor pediatric renal transplantation.

Methods: This research was conducted on a cohort of 15 patients, ranging in age from 2 to 18 years old, of both sexes. These patients had American Society of Anesthesiologists (ASA) physical status class II or III and were diagnosed with end stage renal illness. They were undergoing surgery for living donor kidney transplantation. Electric cardiometry (EC) is performed on all patients.

Results: No significant correlation between CVP and SVV, the presence of weak positive correlation between CVP and Stroke Volume Index (SVI), the presence of weak positive correlation between CVP and thoracic fluid content (TFC) and no significant correlation between CVP trending value and each of SVV, SVI and TFC trending values. SVV, SVI and TFC were not able to diagnose CVP>15 cmH₂O.

Conclusion: SVV is useful in predicting hypovolemia but not hypervolemia in living donor pediatric renal transplantation patients. CVP is still crucial to guide the fluid therapy however other parameters are needed to be involved with CVP to more precise fluid management in pediatric renal transplantation patients.

Keywords: Pediatric; Renal Transplantation; Central venous pressure; Cardiometry; Stroke volume variation.

Introduction:

For almost two decades, kidney transplantation has been acknowledged as the most effective treatment for children suffering from end-stage renal illness ^[1]. The enhanced treatment of young patients and advancements in immunosuppressive medication have led to improved renal allograft and patient survival rates. Consequently, there has been a decrease in both the incidence and severity of acute rejection ^[1]. These type of patients with high risk of perioperative metabolic, cardiovascular and respiratory complications; require good anesthetic choice and perioperative management and monitoring ^[2].

Ensuring sufficient renal blood flow of the transplanted graft by optimizing intravascular volume is crucial in recipient procedures, particularly when there is a significant difference in body size between an adult donor's kidney and tiny pediatric patients. In successful situations, variations in central venous pressure (CVP) levels, ranging from 2 to 18mmHg, have been observed when adopting a specific CVP goal to provide sufficient graft perfusion. However, in some pediatric instances, excessive fluid supplementation exacerbates pulmonary edema and extends the need for ventilator support^[3]. That's why, continuous assessment of cardiac output (CO) is essential for monitoring in these patients to track rapid changes in hemodynamic variables ^[4].

Electric cardiometry (EC) is a continuous non-invasive method for measuring CO and other important hemodynamic variables. EC estimates cardiac parameters by measuring changes in thoracic electrical bio-impedance during the cardiac cycle ^[5]. When the chest fluid content is

increased the thoracic baseline bio-impedance is expected to decrease, and vice versa. The device estimates CO, stroke volume (SV), cardiac index (CI), systemic vascular resistance, heart rate variability and thoracic fluid content (TFC) [6-8].

Fluid responsiveness (FR) refers to the left ventricle's capacity to enhance its SV when fluid is administered. Both CVP and pulmonary artery occlusion pressure (PAOP) were shown to have little predictive value for FR in both patients who were breathing spontaneously and those who were mechanically ventilated. However, SV variability (SVV), a dynamic metric that indicates the state of intravascular fluid, has been identified as a reliable predictor of FR in patients undergoing brain surgery, general surgery, septic shock, and heart surgery. Typically, fluid challenge techniques include the injection of a concentrated amount of fluid and the subsequent measurement of its impact on SV or CO. Fluid responders are those who exhibit a 15% augmentation in SV or CO after a fluid challenge [9-11].

This study aimed to examine the effectiveness of SVV in predicting FR and compare it to CVP in the context of goal-directed fluid management during live donor pediatric renal transplantation.

Materials and Methods:

This research is a prospective cohort observational study conducted on a group of 15 patients, ranging in age from 2 to 18 years old, of both sexes. The patients included in the study had American Society of Anesthesiologists (ASA) physical status class II or III and were diagnosed with end stage renal disease. The purpose of the study was to observe and analyze the outcomes of living donor renal transplantation surgery in these individuals. The research was conducted in the Pediatric Specialized Hospital (Abou-Elreesh Hospital) in Cairo, Egypt, from March 2019 to March 2022, after clearance from the Ethical Committee of Cairo University Hospitals. The family of the patients were required to provide an informed written permission. Only Nine children were included in this study due to technical problem (2cases with pace on maker) and some political problems few allowed operations due to COVID-19 quarantine.

Exclusion criteria were patients with cardiomyopathy, patients with any type of arrhythmia as it interferes with the EC readings, significant valvular, congenital heart disease, moderate to severe pulmonary hypertension. mean PAP (Moderate = 41-55mmHg), (Severe = > 55mmHg) measured by ECHO, severe respiratory conditions (e.g.: Acute Bronchitis, Acute or severe Asthma, Bronchiectasis, Pneumoconiosis, acute or sever Pneumonia.), uncontrolled hypertension (HTN), hemoglobin (Hb) < 7gm/dl and patients who need intraoperative dopamine infusion.

All patients were subjected to: history taking, laboratory investigations [complete blood count (CBC), arterial blood gases, serum electrolytes, coagulation study and liver and kidney function tests], invasive blood pressure, pulse oximeter, side stream capnography, temperature probe, urinary catheter, CVP and EC, echocardiogram, and electrocardiogram (ECG).

Patients were advised to take their antihypertensive medications preoperatively. Prophylactic antibiotics, immunosuppressant, anti-acid, and antiemetic medications.

Sedative dose of IV midazolam (0.05-0.1mg/Kg) was given to all patients who need it. Anesthesia was induced by IV propofol (2mg/kg), fentanyl (2ug/kg), and Atracurium (0.5mg/kg). Smooth intubation with a cuffed endotracheal tube of appropriate size was done. Anesthesia was maintained with Isoflurane adjusted between 1% and 1.5% in oxygen and an Atracurium infusion at 0.5mg/kg/h.

EC was applied to the patient to estimate his/her SV and other measured data. One lumen of the double lumen MAHURKAR™* or central venous catheter were connected to a pressure transducer and used for continuous CVP measurement or measured manually in all patients. The CVP was calibrated at the level of the right atrium (specifically, the 4th intercostal gap in the mid-axillary line) while the patient was in a supine position. Prior to transplantation, the

organ taken from the adult donor was preserved in ice and treated with a cold solution called histidine-tryptophan-ketoglutarate (HTK). It was then prepared on a workbench and transferred to the next operating room.

Lactated ringer solution was the standard fluid transfused during anesthesia; started at a rate of 1-3 ml/Kg/h following intubation. The CVP is measured continually and recorded at 10min intervals till the end of vascular anastomosis, additional 10ml/Kg boluses were given if CVP is < 15cmH₂O at any subsequent measurement. Furosemide in a dose of 2 mg/Kg was given IV to all patients with the beginning of vascular anastomosis. For patients who had preoperative or developed intraoperative anemia (Hb level <8g/dl or hematocrit <28%) or in case of acute blood loss >10% of the calculated patient circulatory volume, packed red blood cells were transfused accordingly. Postoperative pain was managed by IV paracetamol infusion (15mg/Kg) and pethidine (0.1mg/Kg) intramuscular injection and local anesthesia infiltration. After skin closure, inhalational anesthesia and the neuromuscular blocker infusion were discontinued, and then the residual block was reversed with neostigmine (0.05mg/kg) and atropine (0.02mg/kg) when the patient started to breathe spontaneously and regularly. Finally, extubation was done if the patient had stable hemodynamic parameters.

Patient assessment

When a 10ml/Kg bolus was given a CVP reading was recorded after infusing 1.5ml/Kg of the 10ml/Kg bolus and another CVP reading was recorded 1min after the whole 10ml/Kg bolus has been transfused. SV, and SVV were obtained from the EC records. Stroke index (SI), CO, cardiac index (CI), systemic vascular resistance, systemic vascular resistance index and Index of contractility (ICON), total amount of given fluid and its nature and any hypotensive episode ($\leq 20\%$ reduction of pre-induction systolic blood pressure reading) started from beginning of vascular anastomosis and ended by discontinuation of anesthesia, number of fluid boluses, kidney turgidity, P/F ratio (pO₂/FiO₂ ratio), arterial blood samples were obtained with 2-mL syringes containing heparin from a radial arterial catheter, transported in iced water and analyzed with ABL System 777 blood gas analyser, TFC, chest X-rays, total amount of urine volume, serum creatinine was obtained and recorded as a preoperative value (post-dialysis) as a baseline value, and every day for five days after surgery, any intraoperative complication and length of ICU stay, postoperative non- function of the graft, occurrence of graft rejection, need of surgical re-exploration, need of postoperative dialysis and fate of patients (discharge or death) were also recorded in all patients.

The primary outcome was the correlation between delta (the difference between two consecutive readings) CVP and SVV. The secondary outcomes were correlation between absolute and delta SVV, Stroke Volume Index (SVI) and TFC values in relation to absolute and delta CVP value, to validate SVV in prediction of CVP reading in fluid non-responder patients, to outline the possibility of SVV to replace CVP for goal directed fluid therapy during renal transplantation and to find a cut-off value of SVV corresponding to CVP reading of 15cm H₂O.

Sample Size Calculation:

We calculated the number of patients in this study group according to previous studies to be 13 patients. We added 2 more patients to the total number to avoid dumping in data. There were no deaths in our group study; all patients gave full data in the perioperative period except one child, who developed postoperative pulmonary congestion and sever edema under the skin that the cardiometry device signals were too weak to give any reading. Only 14 patients had given full data reading in this study group.

Statistical analysis

The statistical analysis was conducted using SPSS v26 software (IBM Inc., Chicago, IL, USA). The quantitative variables were expressed as the mean and standard deviation (SD). The qualitative factors were shown as frequency and percentage (%). The Spearman correlation

coefficients were used to evaluate the substantial association between two quantitative measures within the same group.

Results:

The mean age was 10 ± 3 years. Regarding sex distribution showed increased incidence along male children patients receiving pediatric renal transplantation 60% than female children 40%. The anthropometric measure is lower than the normally accepted range for their age groups in Egypt due to growth retardation in children with CRF. **Table 1**

Our research shows that the cold ischemia period, which is estimated from the beginning of the venous anastomosis to the removal of the clamps after the completion of the arterial anastomosis, is much longer than what was previously reported in other studies. In explanation of such prolonged mean cold ischemia time in our results, there were two donors in our study that have surgical anatomical difficulties (double renal arteries) meanwhile the estimated cold ischemia time of kidneys of other donors was much shorter. **Table 2**

$\text{PaO}_2/\text{FiO}_2$ ratio increased intraoperative up to 413 then increased after decamping up to 444 but decreased postoperative to 425. But all values don't show acute lung injury ($\text{PaO}_2/\text{FiO}_2 < 300$) at any stage of perioperative period. Urine output Intraoperative were 1656ml (due to delayed adaptation of renal tubular function and it's the first sign of progressive recovery of kidney function) but decreased after one day to 38ml then increased after 2 and 3 days to 44ml. Decrease of creatinine level gradually in postoperative period denote significant improvement in graft function. **Figure 1**

There was no significant correlation between CVP and SVV. There was weak positive correlation between CVP in each of SVI and TFC. However, there was no significant correlation between CVP trending value and each of SVV, SVI and TFC trending values. **Table 3**

The SVV, SVI and TFC were not able to diagnose $\text{CVP} > 15 \text{ cmH}_2\text{O}$. **Table 4**

Table 1: The anthropometric measurements and demographic information of the individuals that were examined

		N= 9
Age (years)		10 ± 3
Sex	Male	5 (60%)
	Female	4 (40%)
Weight (Kg)		25 ± 9
Height (m)		131 ± 21
Hb (gm/dL)		12 ± 2

Data are presented as mean \pm SD or frequency (%). Hb: hemoglobin, CRF: Chronic renal failure.

Table 2: Cold ischemia time and others

		N=9
Cold ischemia time		51 ± 22
Baseline HR (bpm)		106 ± 21
Baseline MAP (mmHg)		87 ± 12
Baseline CVP (cmH_2O)		5 ± 5
Total intraoperative fluid	Crystalloids (mL)	2275 ± 848
	Blood (mL)	275 ± 358
Length of stay (days)		7 ± 7.14

Data are presented as mean ± SD. HR: heart rate, MAP: mean arterial pressure, CVP: central venous pressure.

Table 3: Correlation between absolute and delta SVV, SVI and trending TFC values in relation to absolute and trending CVP value

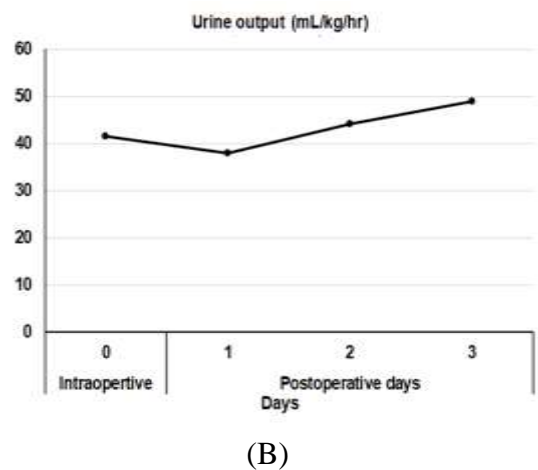
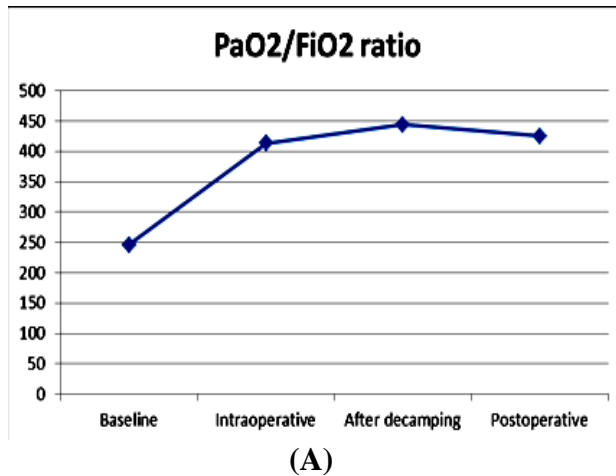
	r- CI 90%	P
SVV	0.16 (-0.03 – 0.35)	0.104
Delta SVV	0.07 (-0.13 – 0.26)	0.505
SVI	0.27 (0.08 – 0.44)	0.005*
Delta SVI	0.02 (-0.18 – 0.22)	0.822
TFC	0.21 (0.02 – 0.38)	0.034*
Delta TFC	0.04 (-0.16 – 0.24)	0.678

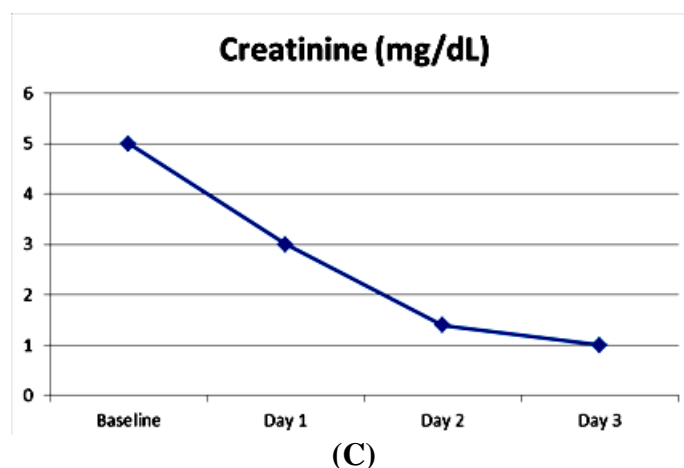
r= correlation coefficient, CI=confidence interval, *significant p value <0.05, SVV: Stroke volume variation, CVP: Central venous pressure, SVI: Stroke Volume Index, TFC: Thoracic fluid content.

Table 4: The ability of SVV, SVI and TFC to diagnose CVP 15 cm H₂O

	AUC (95%)	P
SVV	0.57 (0.47 – 0.67)	0.228
SVI	0.58 (0.48 – 0.67)	0.155
TFC	0.54 (0.44 – 0.64)	0.482

AUC= Area under the Curve, CI 95% = confidence interval, *significant p value <0.05, SVV: Stroke volume variation, CVP: Central venous pressure, SVI: Stroke Volume Index, TFC: Thoracic fluid content.





(C)
Figure 1: (A) PaO₂/FiO₂ ratio, (B) Urine output and (C) Creatinine (mg/dL) among intraoperative and post 1, 2 and 3 days

Discussion

Renal transplantation is an effective therapy option for individuals with end-stage renal disease who are receiving hemodialysis, with favorable results ^[13].

The measurement of CVP provides information on the pressure in the right atrium, which might affect the outflow of blood from the transplanted kidney. It also serves as an indirect measure of the amount of blood filling the heart before it is pumped out. ^[12] EC is a continuous non-invasive method for measuring CO and other important hemodynamic variables. The device estimates CO, SV, CI, systemic vascular resistance, HR variability and TFC ^[13].

Our results revealed that the cold ischemia time was 51 ± 22 ; the base line vital signs including baseline HR, baseline mean arterial pressure (MAP) and baseline CVP were 106 ± 21 ; 87 ± 12 and 5 ± 5 respectively. The total amount of fluid given including crystalloids and blood were 2275 ± 848 and 275 ± 358 respectively. The length of hospital stays for our study group was 7 ± 7.14 .

Previous studies revealed the presence of negative effects of longer cold ischemia time on outcomes after living donor kidney transplantation. Our result's cold ischemia time is longer than reported elsewhere (51 ± 22) that could lead to deleterious outcomes. One study by Gill et al. ^[14] It was discovered that cold ischemia periods of 16 hours or less did not result in the loss of allografts due to any reason. In contrast, a prior investigation conducted by Krishnan et al. ^[17] demonstrated that each hour of cold ischemia duration was linked to an escalating likelihood of delayed graft function. This is because prolonged cold ischemia times contribute, in part, to the development of ischemia reperfusion injuries through pathophysiological mechanisms. In our result we used balanced crystalloid instead of normal saline. A study by Gonzalez-Castro et al. ^[15] indicated that the use of normal saline could lead to problems such as acidosis, hyperkalemia, hyper-chloroemia and acute kidney injury and administering balanced crystalloids including potassium during the preoperative phase of kidney transplantation may be considered a safe practice.

Our results indicated that PaO₂/FiO₂ ratio increased intraoperatively up to 413 then increased after decamping up to 444 but decreased postoperatively to 425. Previous studies indicated that intraoperative volume overload can easily cause pulmonary edema due to the presence of diastolic cardiac dysfunction that is common in renal failure patients ^[16].

Our results indicated that the intraoperative urine output was 1656 ml/hr but decreased after one day to 38 ml/hr then increased after 2 and 3 days to 44ml/hr. Urine-based assessments may be used to assess renal function. Adequate urine production in the first phases after kidney transplantation is seen as an indication of effective restoration of blood flow following the surgical connection of blood vessels^[17]. A previous study by Khosroshah et al. ^[18] indicated that

the mean urine outputs were about 420ml/hr, 230ml/hr, and 145 ml/hr at 24 and 48 hours and 1 month post renal transplantation.

Our results indicated that intraoperative creatinine level was 5mg/dL but decreased postoperatively after one day to 3mg/dL then decreased after 2 days to 1.4mg/dL and finally decreased after 3 days to 1mg/dL. A previous study by Bia ^[19] indicated that after renal transplant, Kidney function gradually improved, reaching its lowest level with a blood creatinine of 1.7mg/dl after 6 weeks.

Our results indicated no significant correlation between CVP and SVV, the presence of weak positive correlation between CVP and SVI, the presence of weak positive correlation between CVP and TFC and no significant correlation between CVP trending value and each of SVV, SVI and TFC trending values. A study by Othman et al. ^[20] Research has shown that a treatment method that focuses on maintaining a low CVP before clamping the donor kidney, and then maintaining a high CVP until unclamping the renal artery after connecting it, leads to better results and increased urine production following kidney transplantation compared to using a constant infusion rate. A recent study by Kaur et al. ^[21] It has been shown that conventional pressure-based and static indicators such as CVP, pulmonary capillary wedge pressure, and MAP are inadequate in accurately reflecting the current volume status in high-risk surgical patients.

As an option, a "mini fluid challenge" has been suggested. However, small amounts of fluid can only cause small changes in SV and CO. Because of this, this test needs a very accurate way to measure CO ^[22]. A recent study by Eriksen et al. ^[23] Examined the impact of HFVT compared to IGDT on early GFR in a pig model of renal transplantation and discovered data indicating that the IGDT group had a less prominent inflammatory response. Our results indicated that few patients respond dramatically to mini bolus with noticed increase in CVP with some clinical effect on the lung of patient some crepitation appear clinically, but no significant change in pO_2/FiO_2 ratio intraoperative, may be border line function of the heart, which need larger sample to select those patient, and more significant tool to select non responder as we detected them only by CVP on table by following the method of mini bolus followed by full bolus only. In contrary, a previous study by Mahmoud et al. ^[24] indicated that the SVV, SVI and TFC were not able to diagnose $CVP > 15 \text{ cmH}_2\text{O}$ ($CVP > 11.03 \text{ mmHg}$).

Clinicians prioritize adjusting hemodynamic factors to enhance graft perfusion following kidney transplantation due to the observed correlation between graft function quickly after reperfusion and long-term graft survival^[10].

Many factors were indicated to cause delayed graft function such as $MAP < 70 \text{ mmHg}$ at the time of reperfusion; low volume repletion ($CVP < 8 \text{ mmHg}$) and an intraoperative MAP of $< 93 \text{ mmHg}$ together with volume overload ($CVP = 11 \text{ mmHg}$) may be a risk factor for postoperative graft dysfunction ^[25]. In pediatric renal transplantation, a study by Urquijo et al. ^[26] It was shown that children aged 5 and younger should have a CVP maintained between 15-20mmHg, whilst older children may accept CVP levels of 12-14mmHg. A recent study by Kinoshita et al. ^[27] revealed that providing volume repletion and vasopressors as needed to maintain $SAP \geq 150 \text{ mm Hg}$ and $CVP \geq 15 \text{ cmH}_2\text{O}$ ($\geq 12 \text{ mmHg}$) at the time of reperfusion and thereafter is crucial to improve outcomes in living donor renal transplantation.

Limitations were A limited sample was used in the study. The research took place in only one location. To gain a better understanding of how pediatric kidney transplant patients with end-stage renal disease, impaired cardiovascular physiology, and reduced hemodynamic autoregulation can benefit from dynamic analyses of flow parameters for optimal fluid management, we suggest conducting prospective comparative clinical studies.

Conclusions:

SVV is useful in predicting hypovolemia but not hypervolemia in living donor pediatric renal transplantation patients. CVP is still crucial to guide the fluid therapy in this population, especially AKS. However, other parameters are needed to be involved with CVP to more precise fluid management in pediatric renal transplantation patients.

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