Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 09, 2023

Original research article

The efficacy of PPV in predicting intraoperative volume status based on early allograft function in adult ESRD patients undergoing living related renal transplantation surgeries: Correlation of intraoperative central venous pressure (CVP) and pulse pressure variation (PPV)

[1]Dr. Tara Nandan A, [2]Dr. N.V. Vinoth Kumar, [3]Dr. Amar Nandhakumar, [4]Dr. N. Selvarajan

[1]Assistant Professor, Department of Anesthesia, Kodagu Institute of Medical Sciences, Madikeri, Karnataka, India

[2]Assistant Professor, Department of Anesthesia, JSS medical College and Hospital, Mysuru, Karnataka, India

[3]Consultant, Kovai Medical Centre and Hospital, Avinashi Road, Coimbatore, Karnataka, India

[4]Director, Critical Care Services, Coimbatore, Karnataka, India

Corresponding Author:
Dr. Tara Nandan A

Abstract

Traditionally, intraoperative volume status is assessed by monitoring central venous pressure (CVP) and it is recommended to maintain a CVP of 10-15 mmHg during renal transplantation surgeries to optimize the graft function. Various parameters have been used in the past to guide fluid therapy. Static measurements namely central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP) have been used in the past to guide fluid therapy. Based on the sample size of 32, we recruited 35 patients for our study. Of these, study was conducted in 32 patients as arterial line could not be secured for 3 patients before induction even after multiple attempts. All patients underwent preoperative hemodialysis prior to transplant surgery. After adequate fasting, all patients received preoperative antibiotics, steroids and anti-thymocyte immunoglobulin. Peripheral venous and radial arterial lines were established. In this study no correlation was found between PPV and CVP except significant negative correlation at the time of clamp release (p<0.05). There were no clinical signs of hypervolemia and fluid overload in the study group, as well as airway pressures were normal denoting optimal intrathoracic pressures. Postoperative period showed positive fluid balance with adequate urine output. All patients showed improved renal function tests till 5 days postop.

Keywords: PPV, CVP, Intraoperative volume

Introduction

Renal transplantation is a process where the previously diseased kidneys are replaced by new donor kidneys. The need for renal transplantation arises when there is end stage renal disease due to glomerulonephritis, chronic interstitial nephritis or obstruction, and hereditary or cystic disease. End stage renal disease is the last stage of chronic kidney disease (CKD) when the functioning capacity of the kidneys are 10-15% of their normal capacity and renal replacement therapy is necessary for survival. The mainstay of therapy at this stage is hemodialysis or peritoneal dialysis. Of these patients only a minority undergo renal transplantation after exhaustive evaluation. Majority of transplantations are living related donor transplants rather than deceased donor transplantation. Also chronic dialysis treatment for end stage renal disease has been found to be more expensive than renal transplantation.

Transplantation is preferred over dialysis for patients with end-stage renal failure because of its lower overall morbidity and mortality [1]. It is often possible to anticipate early graft function based on intra operative perfusion characteristics of the allograft and urine output [2, 3, 4].

Patients with chronic renal failure have a narrow margin of safety with IV hydration and may oscillate between hypovolemia and hypervolemia [5]. The anaesthesiologist must carefully adjust intravascular volume and arterial blood pressure to effectively perfuse the graft after vascular anastomosis [6].

Delayed return of renal function is usually associated with a 20% to 40% decrease in graft survival [7]. Awidson *et al.* [7] in a study found that 1-year graft survival decreased from 75% with immediate urine output to only 49% when onset of diuresis was delayed greater than 12 hours. This suggests that anaesthesiologist should assess and aggressively expand the intra vascular volume to promote early diuresis during anaesthesia for kidney transplantation.

Traditionally, intraoperative volume status is assessed by monitoring central venous pressure (CVP) and

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 09, 2023

it is recommended to maintain a CVP of 10-15 mmHg during renal transplantation surgeries to optimize the graft function [8]. Various parameters have been used in the past to guide fluid therapy. Static measurements namely central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP) have been used in the past to guide fluid therapy. CVP and PCWP are not fully reliable with wide variations in intrathoracic pressures. They act as a poor estimate of preload, as preload depends on ventricular volumes and the likelihood that CVP can accurately predict fluid responsiveness was found to be 56% [9]. To overcome the limitations of these static indices, dynamic indices have been devised and used. These indices are based on the response of the circulatory system to a controlled preload variation by specific maneuvers redistributing blood volume (e.g.: mechanical ventilation, leg raising). Dynamic indices such as pulse pressure variation (PPV), stroke volume variation have been shown to be more reliable than CVP in predicting fluid responsiveness [10]. Among these, pulse pressure variation has been shown to have a high sensitivity and specificity.
In view of the above context, we planned to evaluate that an easily established monitoring like PPV can effectively guide fluid therapy in renal transplant recipient patients and thus replace CVP.

Methodology
Study design
Observational cross sectional study.

Study Population and Area
With the approval of the hospital ethical committee and after obtaining informed consent 32 patients undergoing living related renal transplant surgeries in Medical Center and Hospital were recruited for the study

Sample size calculation
The objective of this thesis is to evaluate the efficacy of intravascular volume assessment by PPV with CVP in renal transplant recipients. In this case, the effect size is primarily considered to estimate the sample size and the following parameters used to compute the sample size; alpha (95%), power (80%), effect size (90%) and standard deviation (1.32).

$$\mathrm{n} = \frac{\mathrm{A}\left(Z_\alpha + Z_\beta\right)^2}{\left(\frac{\mathrm{E}}{\mathrm{S}(\Delta)}\right)^2}$$

The estimated final sample size is 32

Study group
Based on the sample size of 32, we recruited 35 patients for our study. Of these, study was conducted in 32 patients as arterial line could not be secured for 3 patients before induction even after multiple attempts.

Inclusion criteria
We included adult patients with chronic renal failure who underwent living-related kidney transplantation surgery.

Exclusion criteria
- Patient refusal.
- Patients with severe left ventricular dysfunction.
- Cardiomyopathy with ejection fraction less than 50%.
- Patients with arrhythmias.
- Severe anemia (Hb less than 5g/dL).
- Bleeding diathesis.
- Previous transplant recipients.
- With surgical difficulty such as multiple renal vessels.
- Contraindications for central venous catheter placement.

Procedure and observation
All patients underwent preoperative hemodialysis prior to transplant surgery. After adequate fasting, all patients received preoperative antibiotics, steroids and antithymocyte immunoglobulin. Peripheral venous and radial arterial lines were established. Monitoring included pulse oximetry, capnography and electrocardiography. Anaesthesia was induced with propofol 1-2mg/kg, Fentanyl 1-2mcg/kg and maintained on isoflurane end tidal concentration at 0.9% (MAC 0.8) with air and oxygen. Muscle

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 09, 2023

relaxation achieved using atracurium 0.5mg/kg for endotracheal intubation and maintainence with an infusion titrated to 2 twitches on neuromuscular monitoring. Patients were mechanically ventilated with a minimum of 8ml/kg of tidal volume and appropriate respiratory rate to achieve an $ETCO_2$ between 30 and 35 mmHg.

Hemodynamic monitoring and management

Post induction, central line was placed. Baseline PPV measured using Philips Intellivue MP50 once mechanical ventilation was ascertained and the tidal volume was set at 8ml/Kg, in all patients. Simultaneously a baseline CVP was also measured. CVP and PPV monitored continuously in the intra operative period.

We maintained the CVP of 10-15 mmHg; and if PPV rises above 13% we aimed to assess fluid responsivenes. If the estimation of blood loss exceeded 500ml, colloid or blood was infused depending on the patient's hemoglobin with an aim to keep the hemoglobin around 9 gm/dl. Forced air warming was used to maintain temperature which was measured with a probe in the nasopharynx. If hypotension persisted despite normal CVP or PPV, this was treated with vasopressor injection ephedrine 5 mg boluses.

The total estimated blood loss was noted down at the end of surgery. Early allograft function was assessed in the intraoperative period. Urine output was constantly monitored.

Reversal of neuromuscular blockade was done with neostigmine and glycopyrrolate. Patients were extubated when fully awake. Post operatively patients were shifted to the intensive care unit and monitored for serum creatinine and fluid balance in the postoperative ward.

The post-operative follow up of the patient was done after the first 24 hours. Post-operative fluid management was managed as per protocol by the intensive care unit. Input and output, serum creatinine in the post-operative period were recorded from the records of the patients.

Early graft function was determined by following parameters:

- Turgidity score of the new kidney on unclamping of the renal artery.
- Time of onset of urine production on unclamping of the renal artery.
- Total urine output from unclamping of the renal vessels to the end of the surgery.
- Post-operative intake-output chart.
- Post-operative serum creatinine.

Results

Table 1: Baseline data

		Count	%
Age	Mean ± SD (Median)	38.75±10.38 (38)	
Weight	Mean ± SD (Median)	64.84 ± 14.55 (61.07)	
Gender	Female	4	12.5%
	Male	28	87.5%
ASA Grade	3	28	87.5%
	4	4	12.5%
CVP Site	L IJV	6	18.8%
	R IJV	22	68.8%
	R Subclavian	4	12.5%
ART Site	L Brachial	2	6.2%
	L Radial	2	6.2%
	R Radial	26	81.2%
	R Ulnar	2	6.2%
Induction	Supine	32	100.0%
After clamp release	Head Down	24	75.0%
	Supine	8	25.0%

Table 2: CVP

CVP	Mean	SD	Median	P value
0 Min	8.94	2.65	9	
30 Min	10.25	3.20	10	0.001*
60 Min	12.25	2.86	13	<0.001*
90 Min	13.06	3.72	13	<0.001*
120 Min	13.44	3.46	13	<0.001*
150 Min	12.56	2.73	13	<0.001*
180 Min	13.69	3.81	15	<0.001*
Clamp release	13.31	2.89	14	<0.001*

Paired Samples Test

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 09, 2023

Table 3: Correlation between CVP & PPV

Correlation between CVP & PPV	Pearson Correlation (r)	P value
0 Min	-0.409*	0.02*
30 Min	-0.152	0.407
60 Min	-0.391*	0.027*
90 Min	-0.376*	0.034*
120 Min	-0.059	0.750
150 Min	-0.290	0.108
180 Min	-0.091	0.622
Clamp release	-0.638**	<0.001*

Table 4: Correlation between MAP & PPV

Correlation between MAP & PPV	Pearson Correlation (r)	P value
0 Min	0.005	0.977
30 Min	-0.225	0.216
60 Min	-0.312	0.082
90 Min	-0.349*	0.05*
120 Min	-0.364*	0.04*
150 Min	-0.598**	<0.001*
180 Min	-0.596**	<0.001*
Clamp release	-0.687**	<0.001*

Table 5: Correlation between CPV & MAP

Correlation between CPV & MAP	Pearson Correlation (r)	P value
0 Min	-0.017	0.926
30 Min	0.316	0.078
60 Min	-0.246	0.175
90 Min	0.124	0.500
120 Min	0.330	0.065
150 Min	0.537**	0.002*
180 Min	0.353*	0.047*
Clamp release	0.421*	0.017*

Table 6: Correlation between PPV & IVF

Correlation between PPV & IVF	Pearson Correlation (r)	P value
0 Min	-0.117	0.524
30 Min	-0.166	0.363
60 Min	-0.561**	0.001*
90 Min	-0.462**	0.008*
120 Min	-0.305	0.090
150 Min	-0.206	0.259
180 Min	-0.376*	0.034*

Table 7: CVP, MAP, PPV v/s Head Position

At Clamp release	Head position				P value
	Supine		Head down		
	Mean	SD	Mean	SD	
CVP	13.75	4.37	13.17	2.32	0.629
MAP	102.00	8.38	97.58	17.21	0.493
PPV	3.50	0.93	4.67	2.26	0.169

Independent Samples Test

Table 8: U/O intraop

	Mean	SD	Median	P value
U/O intraop	437.19	292.20	358	
u/o1	9572.19	2415.81	9510	<0.001*
u/o2	7615.19	1765.01	8050	<0.001*
u/o3	6206.69	1557.82	6190	<0.001*
u/o4	4690.75	1776.49	4050	<0.001*
u/o5	3179.06	949.39	2875	<0.001*

Paired Samples Test

Table 9: S. creatinine preop

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 09, 2023

	Mean	SD	Median	P value
S. creatinine preop	9.19	2.79	9.5	
S. creatinine 1	3.72	1.72	3.6	<0.001*
S. creatinine 2	2.19	1.26	2.1	<0.001*
S. creatinine 3	1.71	1.18	1.7	<0.001*
S. creatinine 4	1.45	1.13	1.3	<0.001*
S. creatinine 5	1.29	.94	1.0	<0.001*

Paired Samples Test

Discussion

Patients with ESRD present special challenges to both intensivists and anaesthetists. Large volume of fluids may be needed intra-operatively to compensate for the preoperative dialysis in addition to replacing intra-operative blood loss.

Fluid requirement is difficult to assess owing to the occult blood loss under the drapes, irrigating fluids, and unreliability of commonly used indices like urine output due to the use of osmotic diuretics. Hence, the anaesthetist has to rely on hemodynamic parameters to guide fluid management and maintain normovolemia in these patients.

Anaesthesiologists mostly manage intraoperative fluid therapy by approximation and in some situations predictors of cardiac preload like CVP are used to guide fluid management. The CVP is used based on the assumption that it reflects the right ventricular end diastolic volume and hence it is an indicator of LV preload. However in critically ill patients there are changes in the LV and RV compliance, venous tone and intra-thoracic pressures. In those situations CVP has been proven to be poorly reflective of the fluid responsiveness. However, by convention it is still used as a guide to fluid management. Pestel *et al*., showed in an experimental pig model that CVP did not change till more than 30% of estimated blood volume was removed. Hence using CVP to guide the fluid management especially intra-operatively where there is acute blood loss or major fluid shifts may be erroneous.

The modern approach is goal-directed therapy (GDT) for fluid management, where interventions are performed specifically to attain a meaningful clinical variable. Here management of fluids using stroke volume variation(SVV) as a guide is an extremely well-validated approach to reduce morbidity. Three recent prospective, randomized, controlled trials have suggested that optimization of respiratory variation may have the potential to improve outcomes and despite the evidence pointing to use of goal directed fluid therapy, it has not been actively used by anesthetists.

In patients undergoing high risk abdominal surgery, less invasive methods like stroke volume variation (SVV), PPV are being used increasingly to guide fluid management and have been shown to be more useful than CVP. PPV has been shown to be reflective of intravascular volume like systolic pressure variation (SPV) in neurosurgical patients. The PPV derived from Philips Intellivue MP50 system has been shown to be reliable. The threshold value of PPV was found to be 13% in a study done comparing delta PPV and delta down and this was used as the cut off value. There are limited studies using PPV in renal transplant recipients. Also, the effect of fluid management and hemodynamic stability based on PPV as well as tissue perfusion in comparison to CVP guided treatment has not been studied.

This observational study was done to determine whether there is correlation between intraoperative central venous pressure (CVP) and pulse pressure variation (PPV) and to determine the efficacy of PPV in predicting intraoperative volume status based on early allograft function in adult ESRD patients undergoing living related renal transplantation surgeries.

In this study, patients were ASA grade 3 and 4, as all were in ESRD. Hamilton *et al*. [11] in their study concluded that use of a preemptive strategy of hemodynamic monitoring and coupled therapy reduces surgical mortality and morbidity. Hence perioperative hemodynamic optimization with PPV has the ability to improve postoperative outcome in these high-risk surgical patients.

In this study p value >0.05 between of PPV in supine and head down position and statistically not significant. Hence the drawback of CVP being unreliable in positions other than supine and lateral can be overcome by the use of PPV.

In this study CVP was maintained between 8-14 mm Hg. Thomsen H S, *et al*. [12] studied influence of normal central venous pressure on onset of function in renal allografts. They recommended a central venous pressure above 4 mm Hg during the perioperative and early postoperative period as guidance for fluid replacement. Mahmoud M. Othman, M D, *et al*. [13] in their study on the impact of timing of maximal crystalloid hydration on early graft function during kidney transplantation and found that hydration directed toward maintaining a given CVP during kidney transplantation produced a more stable hemodynamic profile and promoted diuresis.

In this study mean arterial pressure(MAP) was maintained throughout above 95 and above 98 at the time of clamp release. Navpreet Kaur Aulakh *et al*. [14] in their study derived that a CVP around 12 mm Hg and mean MAP >95 mm Hg with good perioperative fluid hydration is associated with good early graft function.

In this study intraoperative HR, and temperature were meticulously monitored and maintained.

Intraoperative PPV was recorded and the threshold value of 13% used as cut off value for fluid

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 09, 2023

administration. Throughout the surgery PPV was maintained below 10% in this study.
Onset of urine output after reperfusion was less than 10 min except in one patient which was 30 min and the consistency of the transplanted kidney after declamping of the renal vessels was soft in only one patient. But serum creatinine values showed a pre op mean 9.19 to fifth postoperative day mean of 1.29 and urine output during intraoperative and postoperative period showed adequate graft function in all the study group patients.
In this study no correlation was found between PPV and CVP except significant negative correlation at the time of clamp release. One study concluded that as an indicator of cardiac preload, PPV has a negative linear correlation with initial distribution of volume of glucose in patients after anesthesia induction. It does not correlate well with CVP in the normal range. It implies that an individual PPV, not CVP, is equivalent to initial distribution of volume of glucose in assessing volume status after induction. Priesman S *et al.* [15] in their study in patients undergoing CABG derived that functional haemodynamic parameters i.e. PPV are superior to static indicators of cardiac preload i.e. CVP in predicting the response to fluid administration.
Navpreet Kaur Aulakh *et al.* [14] in their study concluded that a mean map >95 mm Hg with good perioperative fluid hydration is associated with good early graft function. In this study MAP was maintained greater than 95mmHg and all patients had good early graft function.
No significant intraoperative blood loss occurred in the study group, hence no colloids or blood products were infused. None of the study patients required re-exploration due to bleeding or graft rejection.
There were no clinical signs of hypervolemia and fluid overload in the study group, also airway pressures were normal denoting optimal intra thoracic pressures.
Postoperative period showed positive fluid balance with adequate urine output. All patients showed improved renal function tests till 5 days postop.
From this study it can be concluded that PPV can effectively augment CVP as an index to guide fluid therapy. The complications associated with central line insertion like pneumothorax, haemothorax, misplacement of line and catheter related blood stream infections can be avoided. Since patients undergoing renal transplant surgeries are monitored using invasive arterial line, the additional cost of a central line can also be avoided.

Conclusion

Pulse pressure variation can be used as a reliable index to guide fluid management in renal transplant surgeries in supine position. Pulse pressure variation monitoring may lead to better intraoperative and postoperative hemodynamic stability. Pulse pressure variation can replace CVP guided fluid therapy, avoid complications associated with central lines and reduce additional cost. Further large scale studies are warranted to confirm these findings.

References

1. Bilchick KC, Wise RA. Paradoxical physical findings described by Kussmaul: Pulsus paradoxus and Kussmaul's sign. Lancet. 2002;359:1940-2.
2. Rick JJ, Burke SS. Respirator paradox. South Med J. 1978;71:1376-8.
3. Michard F, Chemla D, Richard C, Wysocki M, Pinsky MR, Lecarpentier Y, *et al*. Clinical use of respiratory changes in arterial pulse pressure to monitor the hemodynamic effects of PEEP. Am J Respir Crit Care Med. 1999;159:935-9.
4. Connors Jr, AF Speroff T, Dawson NV, Thomas C, Harrell Jr, FE Wagner D, *et al*. The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT Investigators. JAMA. 1996;276:889-97.
5. Polanczyk CA, Rohde LE, Goldman L, Cook EF, Thomas EJ, Marcantonio ER, *et al*.: Right heart catheterization and cardiac complications in patient undergoing non cardiac surgery: An observational study. JAMA. 2001;286:309-14.
6. Sandham JD, Hull RD, Brant RF, Knox L, Pineo GF, Doig CJ, *et al*. Canadian Critical Care Clinical Trials Group: A randomized, controlled trial of the use of pulmonary artery catheters in high-risk surgical patients. N Engl. J Med. 2003;348:5-14.
7. Richard C, Warszawski J, Anguel N, Deye N, Combes A, Barnoud D, *et al*. Early use of the pulmonary artery catheter and outcomes in patients with shock and acute respiratory distress syndrome. JAMA. 2003;290:2713-20.
8. Michard F, Teboul JL. Predicting fluid responsiveness: A critical analysis of the evidence. Chest. 2002;121:2000-8.
9. Bendjelid K, Romand JA. Fluid responsiveness in mechanically ventilated patients: A review of indices used in intensive care. Intensive Care Med. 2003;29:352-60.
10. Kumar A, Anel R, Bunnell E, Habet K, Zanotti S, Marshall S, *et al*. Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. Crit. Care Med. 2004;32:691-9.
11. Hamilton MA, Cecconi M, Rhodes A. A systematic review and meta-analysis on the use of

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 09, 2023

preemptive hemodynamic intervention to improve postoperative outcomes in moderate and high-risk surgical patients. Anesth Analg. 2011;112:1392-402.

12. Mathis MR, Schechtman SA, Engoren MC, Shanks AM, Thompson A, Kheterpal S, *et al*. Arterial pressure variation in elective non-cardiac surgery: Identifying reference distributions and modifying factors. Anesthesiology. 2017;126:249.
13. Othman MM, Ismael AZ, Hammouda GE. The impact of timing of maximal crystalloid hydration on early graft function during kidney transplantation. Anesth Analg. 2010;110:1440-6.
14. Navpreet Kaur Aulakh, Kamakshi Garg, Abhishek Bose, Baldev Singh Aulakh, Harmandeep Singh Chahal, Gurmehar Singh Aulakh. Influence of hemodynamics and intra-operative hydration on biochemical outcome of renal transplant recipients. J Anaesthesiol Clin Pharmacol. 2015 Apr-Jun;31(2):174-9.
15. Preisman S, Kogan S, Berkenstadt H, Perel A. Predicting fluid responsiveness in patients undergoing cardiac surgery: functional haemodynamic parameters including the Respiratory Systolic Variation Test and static preload indicators. Br J Anaesth. 2005 Dec;95(6):746-55.