

Role of Urinary PO₂ Analysis during Conventional versus Conventional and Modified Ultrafiltration Techniques in Adult Cardiac Surgery

Abstract

Background: Medullary hypoxia is the initial critical event for kidney injury during cardiopulmonary bypass, and therefore urinary PO₂ with its potential of detecting medullary oxygenation for its management. Therefore, we tested the role of urinary PO₂ in predicting kidney injury in those undergoing conventional versus combined (conventional and modified) ultrafiltration during cardiac surgery in adults. **Methodology:** We prospectively evaluated 32 adults between 18 and 65 years of age undergoing elective on-pump cardiac surgery with ejection fraction >35% by conventional (group C) versus combined ultrafiltration (group CM). Urine samples were analyzed for PO₂ after induction, 30 min, 3 h, and 6 h post filtration along with blood urea and serum creatinine after induction, at 6 h, 24 h, and 48 h post filtration. Demographic variables, cardiopulmonary bypass duration, flow rates, inotropic score, ventilation duration, diuretic use, and intensive care unit (ICU) stay were assessed between two groups. **Results:** Both the groups (16 in each group) had comparable urinary PO₂ after induction ($P = 0.387$) with significant decrease in group C at 30 min, 3 h, and 6 h post filtration ($P < 0.05$). There was a statistically significant increase in serum creatinine (mg/dL) at 48 h in group C compared with group CM (1.57 vs. 1.25, respectively; $P \leq 0.05$). There was an increased diuretic usage and length of ICU stay in group C. **Conclusion:** Combined ultrafiltration technique had renoprotective effect in cardiac surgery analyzed by urinary PO₂ levels.

Keywords: *Cardiopulmonary bypass, ultrafiltration, urinary PO₂*

Introduction

Cardiopulmonary bypass (CPB) is a nonphysiological procedure associated with immune responses and hemodilution that disrupt the function of organs (on-pump syndrome).^[1] Perioperative hemofiltration is one of the treatment modalities to prevent this syndrome.^[2] Conventional ultrafiltration (CUF) has limitations in terms of the retraction of the fluids from the patient's body, while modified ultrafiltration (MUF) is performed independent of the volume of the CPB circuit.^[3] MUF is an effective tool in reducing inflammatory mediators that cause organ dysfunction and undesirable hemodynamic changes.^[4] It is more effective in removing excess fluid and provides more effective hemoconcentration than CUF.

Hypoxia in the renal medulla is the hallmark of acute kidney injury (AKI) following CPB due to inflammatory

mediators and urinary PO₂ is an index of medullary oxygenation.^[5] Even mild AKI after CPB is associated with >4-fold increase in risk of in-hospital death.^[6] Biomarkers that are available now offer limited prediction of AKI during surgery when interventions still are feasible.^[7] Therefore, we compared conventional versus combined (conventional and modified) ultrafiltration techniques to determine its efficacy in renoprotection using urinary PO₂ levels.

Methodology

Study design

In this prospective study, urinary PO₂ levels were compared in patients undergoing conventional (group C) versus combined ultrafiltration (group CM) during CPB. Elective patients who fulfilled the study criteria were recruited following informed consent. Inclusion criteria were age between 18 and 65 years, elective on-pump cardiac surgery, and EF >35%. Exclusion criteria were preexisting renal disease, serum

Vijitha Burra,
Sunil PK¹,
Praveen NB,
Nagaraja PS,
Naveen G Singh,
Manjunatha N²,
Vikram
Somashekhar
Basappanavar³

Departments of Anaesthesiology, ¹Cardiovascular and Thoracic Surgery and ²Cardiac Anaesthesiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Jayanagar, Bengaluru, Karnataka, India, ³Department of Anesthesiology, Pediatric Cardiac Anesthesiologist, Al Jalila Childrens Hospital, Dubai, UAE

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Address for correspondence:

*Dr. Sunil PK,
Department of Cardiovascular and Thoracic Surgery,
Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru - 560 069, Karnataka, India.
E-mail: docnag10@gmail.com*

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creatinine >1.5 mg/dL, surgery within 72 h of coronary angiogram, uncontrolled hypertension, use of nephrotoxic agents, and emergency surgery.

Objective

To evaluate the effect of conventional versus combined (conventional and modified) ultrafiltration on urine oxygen tension (PO₂) and determine its efficacy in reducing the length of intensive care unit (ICU) stay in patients undergoing cardiac surgery.

Anesthesia

A standardized protocol was followed for induction and maintenance of anesthesia. Each patient revealed continuous perioperative monitoring of central venous, systemic arterial pressures, SPO₂, electrocardiogram, nasopharyngeal temperature, and urine output.

CPB management, filtration techniques

A standard adult extracorporeal tubing set was used incorporating a 40- μ m arterial line filter in conjunction with a Trillium Affinity NT Hollow Fiber Oxygenator. The circuit was primed with 1500 mL of Ringer's lactate, 50 mL of 20% mannitol, 50 mL of sodium bicarbonate, and 7000 IU of sodium heparin. An S3 roller pump (Stöckert Instrumente GmbH, Munich, Germany) controlled nonpulsatile flow that was maintained at or above 2.5 L/min/m². Myocardial protection was provided by intermittent antegrade or retrograde cardioplegia. The cardioplegic mixture consisted of St. Thomas or del Nido solution. Diastolic cardiac arrest was induced with 20 mL/kg of cardioplegic infusion supplemented at 20-min intervals by further doses of 10 mL/kg. The mean perfusion pressure was titrated between 50 and 70 mmHg with a combination of phenylephrine and sevoflurane. Alpha-stat management of acid-base status was used during CPB. Blood PO₂ was maintained between 200 and 300 mmHg. Hematocrit was adjusted between 25% and 30%, and patients were randomized to conventional (group C) versus conventional plus MUF (group CM). Hemofiltration was done using Nipro hemofilter (Nipro medical systems, India) in both the groups.

Methods for measurement of urinary PO₂ (partial oxygen pressure)

Owing to technical limitation and availability of instruments, we have used blood gas analyzer (Cobas b 221, Roche diagnostic, India) for the measurement of urine PO₂. Urine sample was taken with a needle directly from Foley's catheter in a 2-cc new plain syringe. First, urine samples were taken after induction (baseline), 30 min, 3 h, and 6 h post filtration.

Assessment of renal function

Changes in renal function were assessed by measuring blood urea and serum creatinine preoperatively, at 6, 24,

and 48 h post filtration. Urine output was also measured at 3, 6, and 12 h post filtration. Demographic variables and perioperative characteristics were also collected. Inotropic score, CPB duration, CPB flow rates, ventilation duration, and ICU stay were also noted.

Statistical analysis

It was carried out using SPSS software, version 16.0 (SPSS, Inc., USA). Chi-square test and independent sample *t*-test were used to compare categorical and continuous variables, respectively. Data were presented as mean \pm standard deviation or proportion as appropriate. The "*P*"-value less than 0.05 was considered to be significant.

Results

In all, 32 adults undergoing elective on-pump cardiac surgery with comparable demographic characteristics between the two groups (*P* > 0.05) with mean age (group CM = 36.19 \pm 18.98 vs. group C = 42.93 \pm 4.37) are summarized in Table 1.

Table 1: Demographic data

	Group CM (n=16), mean \pm SD	Group C (n=16), mean \pm SD	<i>P</i>
Age	36.19 \pm 18.98	42.93 \pm 4.37	0.176
Sex, <i>n</i> (%)			0.157
Female	10 (62.5%)	6 (37.5%)	
Male	6 (37.5%)	10 (62.5%)	
Weight	52.81 \pm 20.46	54.06 \pm 4.94	0.814
Height	155.81 \pm 19.12	156.31 \pm 7.55	0.923
BSA	1.50 \pm 0.44	1.51 \pm 0.42	0.453

SD: Standard deviation; BSA: Body surface area

Table 2: Preoperative and intraoperative findings

	Group CM, mean \pm SD	Group C, mean \pm SD	<i>P</i>
Preop urea	33.68 \pm 9.68	29.62 \pm 9.39	0.238
Preop creatinine	0.44 \pm 0.12	0.46 \pm 0.17	0.120
CPB time	185.0 \pm 74.21	172.37 \pm 56.14	0.591
CPB flows	4.15 \pm 0.99	4.15 \pm 0.12	0.980
Cardioplegia			
del Nido	14 (56)	11 (44)	0.200
St. Thomas	2 (28.6)	5 (71.4)	

SD: Standard deviation; CPB: Cardiopulmonary bypass

Table 3: Urine PO₂ at different time points

	Group CM, mean \pm SD	Group C, mean \pm SD	<i>P</i>
After induction	160.56 \pm 15.315	164.37 \pm 8.51	0.387
30 min post filtration	162.00 \pm 13.08	151.68 \pm 10.26	0.019
3 h post filtration	163.43 \pm 10.65	142.56 \pm 10.31	<0.001
6 h post filtration	158.81 \pm 11.10	141.12 \pm 10.29	<0.001

SD: Standard deviation

Preoperative serum creatinine, CPB time, CPB flows, and type of cardioplegia (del Nido, St. Thomas) were comparable between the two groups as mentioned in Table 2.

Urinary PO₂ was comparable between the two groups post induction ($P = 0.387$) with statistically significant difference at 30 min, 3 h, and 6 h post filtration with $P < 0.05$ as shown in Table 3. At 3 h, 6 h, and 12 h post filtration, there was no statistically significant change in urine output between those groups with $P = 0.57$, $P = 0.291$, and $P = 0.293$ respectively as shown in Table 4. Changes between two groups with reference to urinary PO₂ were represented in Figure 1. There was a statistically significant increase in serum creatinine at 48 h (group CM vs. group C = 1.25 ± 0.14 vs. 1.57 ± 0.16 , $P < 0.001$) as

Table 4: Urine output at different time points

	Group CM, mean±SD	Group C, mean±SD	P
Intraop	2015.62±855.91	1319.06±301.07	0.005
At 3 h	138.75±56.58	130.00±22.80	0.570
At 6 h	288.75±108.00	255.94±56.81	0.291
At 12 h	579.37±207.66	519.68±80.98	0.293

SD: Standard deviation

Table 5: Serum creatinine at different time points

Serum creatinine	Group CM, mean±SD	Group C, mean±SD	P
At 6 h	0.82±0.19	1.00±0.29	0.042
At 24 h	1.18±0.27	1.26±0.24	0.405
At 48 h	1.25±0.14	1.57±0.16	<0.001

SD: Standard deviation

Table 6: Other variables

	Group CM, mean±SD	Group C, mean±SD	P
Inotropic score	9.64±4.73	12.87±4.70	0.062
Ventilation time	181.56±69.17	190.62±49.89	0.674
Diuretics	4 (22.2%)	14 (77.8%)	<0.001
ICU stay	3.25±1.43	5.00±1.21	0.001

SD: Standard deviation; ICU: Intensive care unit

shown in Table 5. In Figure 2, the comparison of serum creatinine between two groups were shown at various time points. Intraoperatively, there was a significant change in urine output with $P = 0.005$ between the two groups.

Postoperatively, there was a significant increase in use of diuretics ($P < 0.001$) and ICU stay in group C ($P = 0.001$) as shown in Table 6.

Discussion

Advances in CPB and perfusion techniques have been accomplished over the last 50 years in open heart surgery.^[1] CPB increases the blood levels of immune mediators leading to a systemic inflammatory response syndrome.^[7] This syndrome is associated with reduced systemic vascular resistance, demanding vasoconstriction, fluid replacement therapy, and elevated cardiac output.^[8,9] Increased capillary permeability, weight gain, and inflammatory mediators will complicate postsurgical recovery and organ function.^[10]

Ultrafiltration can mitigate adverse effects of CPB by removing inflammatory mediators and free water. There are two different techniques of ultrafiltration: CUF and MUF.^[11,12] CUF is performed during CPB, with limitations in terms of retraction of the fluids from the patient during surgery. Therefore, there is a need for MUF that is performed at the end of CPB being independent of volume of the CPB circuit.^[13] Due to technical differences in time of these two techniques, more liquid can usually be retracted through MUF than CUF.^[14] The technique of MUF was developed at the Great Ormond Street in London, in 1991, by Naik *et al.*^[14,15] MUF is more effective in removing excess fluid from patients than CUF and can reduce systemic inflammatory response syndrome and improve clinical outcomes.^[16,17]

The renal medulla is one the first affected tissues from decreased perfusion during CPB, and therefore AKI is common after cardiac surgery.^[18] In severe AKI, 1%–2% of patients require renal replacement therapy after surgery with mortality exceeding 35%.^[19] There are no validated methods to assess the risk of AKI intraoperatively. Urinary

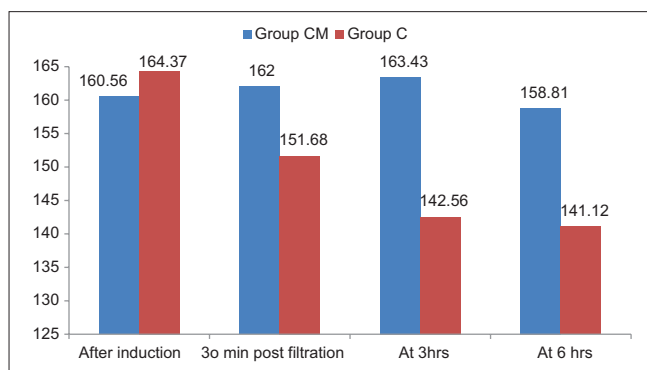


Figure 1: Urinary PO₂ at various time points

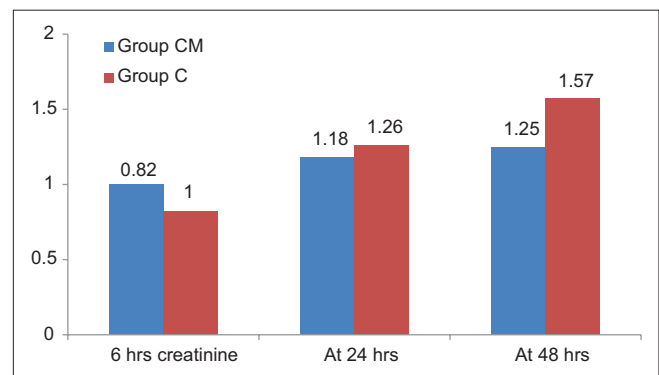


Figure 2: Serum creatinine at various time points

hypoxia capture combined effects of pre- and intraoperative factors that lead to medullary hypoxia during on-pump surgery. Partial pressure of the urine taken from the renal pelvis is related to the perfusion of renal medulla.^[20] The delay between medullary hypoxia and measurement of urinary hypoxia should be only minutes, and this biomarker has potential in management of high-risk patients and prevents AKI.^[21] Therefore, urinary PO₂ provides an index of medullary oxygenation.

Many authors studied the role of urinary PO₂ as a biomarker for AKI during cardiac surgery and identified fluctuations in oxygen tension in the urine correlating with incidence of AKI.^[21,22] Zhu *et al.* evaluated the role of urinary PO₂ as an intraoperative marker of AKI during cardiac surgery and found that patients with low urinary PO₂ for longer period had higher risk of developing AKI.^[22] Similarly, Cochrane *et al.* found urinary PO₂ to be a guide in management of perfusion and reduce kidney injury by optimization of pump flows and arterial pressure. In our study, we evaluated the role of urinary PO₂ analysis in assessing the kidney injury during conventional and combined ultrafiltration in cardiac surgery.

In this study, the authors studied the role of urinary PO₂ trend in patients undergoing conventional and combined (conventional plus modified) ultrafiltration during bypass. Although urinary PO₂ levels were comparable after induction between the two groups, they were significantly low in group C at 30 min, 3 h, and 6 h post filtration correlating with higher serum creatinine in group C. In our study, urinary PO₂ levels were progressively decreased correlating with the progressive increase in serum creatinine in group C. At 30 min post filtration, there was a significant decrease in urine PO₂ in group C ($P = 0.019$). Even at 3 h, despite comparable urine output between two groups, there was a fall in PO₂ in group C ($P < 0.001$). Similarly, at 6 h post filtration, there was a fall in urine PO₂ (group C vs. CM = 158.81 ± 11.10 vs. 141.12 ± 10.29 ; $P < 0.001$). At 48 h, there was a significant raise in creatinine in group C who had fall in urinary PO₂ as early as 30 min post filtration demonstrating parallel change. The rate of decline in PO₂ in group C is more than group CM which alarms the clinician very early regarding the kidney injury, which is being depicted at 48 h with rise in creatinine. Owing to higher serum creatinine in group C, patients had higher diuretic usage ($P < 0.001$) and greater length of ICU stay ($P = 0.001$).

Limitations

There is a technical limitation of the availability of instrument required for the accurate measurement of urinary PO₂; in view of this, we measured urine PO₂ from the urine sample directly collected from the Foley's catheter tubing. The study is also limited by its sample size for drawing better conclusions regarding the role of urinary PO₂ analysis.

Conclusion

Although this study had limitations, we can safely conclude that combined (conventional plus modified) ultrafiltration has better renoprotection with low incidence of kidney injury by urinary PO₂ analysis.

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Conflicts of interest

There are no conflicts of interest.

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