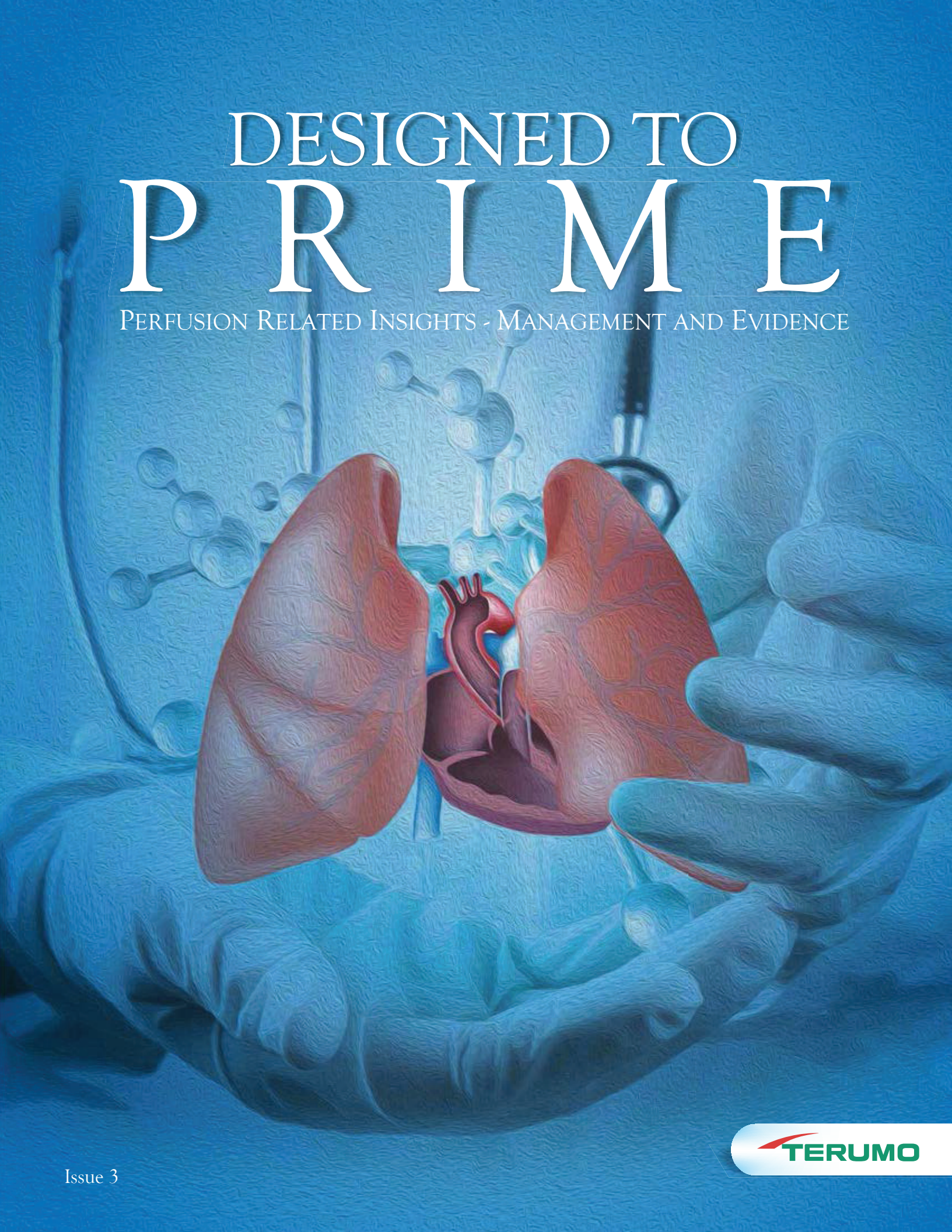
DESIGNED TO PRIME

Perfusion Related Insights - Management and Evidence



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Issue 3

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Editorial Letter

Dear Readers,

We are pleased to present the third issue of PRIME to you.

PRIME – '**P**erfusion **R**elated **I**nsights - **M**anagement and **E**vidence' – is a scientific newsletter published every quarter with the help of our editorial board members, and includes latest reviews, guidelines and expert experiences in relation to perfusion strategies.

In this issue of PRIME, the 'Review Article' section talks about the controlled reoxygenation during cardiopulmonary bypass. The article says that controlled reoxygenation cardiopulmonary bypass is associated with reduced markers of organ damage, inflammation, stress and oxidative stress in the single ventricle patients undergoing cardiac surgery.

In the current issue, the first article from the 'Expert Experiences' section focuses on tiny circuit designed for neonates - a protocol shared by our experts. The second contribution is about extracorporeal membrane oxygenation (ECMO) for the left ventricle preparation in late presenting transposition of the great arteries with intact interventricular septum.

This is followed by the 'Guidelines' section, wherein we have included a clinical practice guideline on cardiopulmonary bypass, which primarily speaks about the temperature management during cardiopulmonary bypass.

Under the 'Latest News' section, we have integrated an interesting article about whether microplegia is really superior over standard blood cardioplegia. This article covers the results of a meta-analysis study.

We hope that perfusionists will find these articles interesting and helpful. We are looking forward to receive your valuable feedback, comments and suggestions to help us work better on our future issues.

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SECTION 1

REVIEW ARTICLE

Controlled reoxygenation during cardiopulmonary bypass decreases the markers of organ damage, inflammation, and oxidative stress in single-ventricle patients undergoing pediatric heart surgery

Objective

The current study was conducted to examine the effects of controlled reoxygenation cardiopulmonary bypass (CPB) on biomarkers of organ damage, stress, inflammation, and long-term functional outcomes in cyanotic patients with either a single- or double- ventricle undergoing open heart surgery.

Methods

Cyanotic patients were randomized to receive CPB using either standard oxygen levels or controlled reoxygenation. These patients were having either a single (n=32) or double (n=47) ventricle and were undergoing surgical correction. Measurement of the markers of cardiac injury, stress, inflammation, and cerebral and hepatic injury was done preoperatively, at 10 and 30 minutes after starting CPB, and at 10 minutes and 4 and 24 hours after CPB.

Results

In the single-ventricle group, controlled reoxygenation CPB significantly reduced (p<0.05) the markers of organ damage, stress, inflammation, and oxidative stress (Table 1). On the other hand, the markers of inflammation and cardiac injury were not changed by controlled reoxygenation CPB in the double-ventricle group.

Discussion

When starting CPB in cyanotic patients with a single-ventricle, controlled reoxygenation lowered the markers of organ injury, stress, and systemic inflammation in comparison with standard reoxygenation. However, it was observed that the protective efficacy of this intervention was markedly decreased in patients with double ventricle. The mechanism of action of controlled reoxygenation CPB in these cyanotic patients is considered to be the gradual reintroduction of oxygen into chronically hypoxic organs such as the heart. However, the key finding of this study was that controlled reoxygenation is only effective in lowering the markers of inflammation and cardiac injury in patients with a single-ventricle. Cyanosis in single-ventricle patients is observed to remain at a relatively constant level, rendering the heart (and other organs) chronically hypoxic. On the other hand, the degree of cyanosis observed in patients with double ventricle tends to be lower and fluctuating. Therefore, it is possible that single ventricle patients will sustain more reoxygenation injury while receiving standard (hyperoxic) CPB. A higher degree of organ reoxygenation injury in patients with a single-ventricle will trigger relatively more oxidative stress and inflammatory response.

Table 1: Comparison of markers in single ventricle patients after 24 hours of controlled reoxygenation and standard (Hyperoxic) oxygen levels

Markers	Controlled reoxygenation	Standard (Hyperoxic)
Troponine	1.26	2.26
8-Isoprostane	2.50	4.77
Interleukin	634.63	35.21
Interleukin	815.96	21.67

CONCLUSION

Controlled reoxygenation cardiopulmonary bypass was found to reduce the markers of organ damage, inflammation, stress, and oxidative stress in the single-ventricle patients undergoing cardiac surgery.

Source: Caputo M, Mokhtari A, Miceli A, Ghorbel MT, Angelini GD, Parry AJ, *et al*. Controlled reoxygenation during cardiopulmonary bypass decreases markers of organ damage, inflammation, and oxidative stress in single-ventricle patients undergoing pediatric heart surgery. *J Thorac Cardiovasc Surg*. 2014;148(3):792-801.e8; discussion 800-1.

Case 1: Extracorporeal membrane oxygenation for left ventricle preparation in late presenting transposition of the great arteries with intact interventricular septum

Bijender Pal Singh Bali, Sonam Sisodia, Vishal Singh, Arun. R, Ashutosh Marwah, Rajesh Sharma

Background

Due to left ventricle (LV) regression and inability to support the systemic circulation, patients having dextro-transposition of great arteries and intact ventricular septum (d-TGA/IVS) and presenting beyond the first few weeks of life are considered to be high-risk patients for an arterial switch operation (ASO).

Objectives

To review the experience of extracorporeal membrane oxygenation (ECMO) for LV preparation beyond the neonatal period, in neonates presenting with TGA IVS with regressed LV function.

Methods

Records of patients who underwent ASO for TGA-IVS with regressed LV and who required ECMO support postoperatively were used to perform a retrospective study.

Results

During the study period, 15 patients required ECMO support subsequent to primary ASO for TGA-IVS with regressed LV. Of the 13 patients who were weaned off ECMO, 8 survived till discharge. Five patients died during the hospital stay. The mean LV ejection fraction at discharge was 40%. All hospital survivors were doing well at mean follow-up duration of 36 months (range 3 months–5 years).

Discussion

In the present study, 13 out of 15 infants were weaned off ECMO with improved LV dimensions and function, suggesting that despite borderline or regressed LV configuration, the systemic ventricle performed better after being supported on ECMO.

In this series, integrated ECMO-CPB circuit was used in 9 patients based upon echocardiographic features suggestive of LV regression.

The advantages of an integrated ECMO-CPB circuit are:

- Early initiation prevents end organ damage
- Surgical asepsis

In this study, it was observed that the duration of ECMO and a late age of presentation i.e., older children seem to have significant effect on the overall outcome. The children who failed weaning were older than 6 months of age (p=0.04). Prolonged ECMO duration of more than 90 hours, i.e., the mean ECMO duration in the study, was likely to have higher possibilities of co-morbid factors and have an effect on the overall outcome.

Infections (sepsis) and bleeding were the noted complications. Infection is considered to be a major issue in this initial experience, resulting in prolonged intensive care unit and hospital stay. Specific alterations to different points of entry of infection should be addressed, which may improve the end outcome significantly.

CONCLUSION

- ASO can be performed in children up to 6 months of age with regressed LV to achieve good results
- The LV can be retrained and its function may be retrieved by LV assist–ECMO as required, which facilitates single stage anatomic correction with acceptable results for patients presenting late for surgery
- The need for extracorporeal mechanical support as a rescue option and the risks involved may act as limiting factors for the adoption of this strategic approach

Case 2: Tiny circuit design for neonates (<5 kg) with the help of pole mounting arm - Our protocol

P. Mathavan, Chief Perfusionist - Dept. of CTVS, JIPMER, Puducherry

Materials

Standard bypass materials for neonatal cardiac surgery include Sarns APS-I heart–lung machine, a Terumo Baby-Rx or Maquet Neonatal Oxygenator, a Maquet ultrafilter (BC20 plus) and a 3/16 -1/4-inch circuit.

Composition of PRIME

The whole circuit priming volume is 360 ml, which consists of plasmalyte-A, heparin, mannitol, sodium bicarbonate, albumin, and packed red cells.

Priming method

The circuit is primed with heparinized Plasmalyte-A solution, and de-aired and replaced with blood by chasing technique. Then mild gas flow is turned on, and after a minute, arterial blood gas (ABG) sample is taken to see the electrolytes. Hemofilter is used to filter the prime in order to avoid hyperkalemia, inflammatory mediators in stored blood and extra volume. After 5 minutes, ABG is checked and corrections are made if needed. Finally, albumin and drugs are added.

Discussion

The ratio of the priming volume to the patient blood volume can be decreased by reducing the total volume of the extracorporeal circuit. Various studies have shown that a lower surface area with a reduction in the priming volume possesses a strong influence on the requirement of platelets and fresh frozen plasma in the postoperative period. Other studies have shown reduced hemodilution by retrograde autologous priming, which displaces a part of the crystalloid prime from the circuit and by experimental use of vacuum-assisted venous drainage, where the venous reservoir can be positioned at the same height as that of the patient; and therefore, it is important to considerably reduce tubing lengths. Due to the difficulty in obtaining fresh donor blood for such patients, packed red blood cell transfusions containing citrate-phosphate-dextrose (CPD) are used. The CPD, increased lactate and potassium levels in the stored blood can contribute a significant metabolite and electrolyte load to the patient showing rapid changes in osmolal concentrations. If the ratio of prime to the patient volume is high, these factors are considered to be of major importance in determining the metabolic responses in cardiac surgery. Ridley *et al*. showed that the continuous washing by ultrafiltration and the use of a balanced replacement solution can lower these effects and produce a more physiological priming solution. But, the ideal situation is to maximally reduce the priming volume at the beginning of bypass in order to eliminate the requirement of blood transfusion. The other important reason behind reducing the surface area of the circuit is to reduce the exposure of these patients to the plasticizer present in the tubing used for the circuit.

A recent study has shown that leaching of the plasticizer from the circuit causes increased concentration in the blood at a linear rate dependent on the surface area of the circuit, as 40% of the tubing composition by weight can be attributed to these plasticizers. As per Karle *et al.,* The incorporation of an arterial filter in the circuit is controversial for pediatric surgery, and its use in this system increases the prime by 40 ml.

CONCLUSION

- Significant reduction of the priming volume and donor blood transfusion requirements can be obtained with the positioning of the main arterial pump head on a pole mounting arm
- The development of the new equipment and the selection of disposables used for neonatal extracorporeal circulation play an important role in reducing the priming volume of the circuit
- Especially in neonatal/pediatric patients, the reduction in the requirement of donor blood transfusion and the risks associated with the exposure of foreign material are considered to be important

GUIDELINES

SECTION 3

The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: Clinical Practice Guidelines for Cardiopulmonary Bypass - Temperature Management During Cardiopulmonary Bypass.

Optimal site for temperature measurement

It is recommended that the oxygenator arterial outlet blood temperature should be used as a surrogate for cerebral temperature measurement during cardiopulmonary bypass.

For accurate monitoring of cerebral perfusate temperature during warming, it is recommended to assume that the oxygenator arterial outlet blood temperature underestimates cerebral perfusate temperature.

Pulmonary artery catheter or nasopharyngeal temperature recording is considered to be reasonable for weaning and immediate post-bypass temperature measurement.

Avoidance of hyperthermia

It is recommended for surgical teams to limit arterial outlet blood temperature to <37°C in order to avoid cerebral hyperthermia.

Source: Engelman R, Baker RA, Likosky DS, Grigore A, Dickinson TA, Shore-Lesserson L, *et al*. The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: Clinical practice guidelines for cardiopulmonary bypass-Temperature management during cardiopulmonary bypass. *Ann Thorac Surg*. 2015;100(2):748-57.

LATEST NEWS

SECTION 4

Is microplegia really superior to standard blood cardioplegia? The results from a meta-analysis

Introduction

Microplegia is associated with all the advantages of blood cardioplegia without the potential disadvantages of hemodilution (such as myocardial edema). A systematic review and meta-analysis were performed to compare microplegia and standard blood cardioplegia for the cardioprotective effects in patients undergoing coronary artery bypass grafting (CABG).

Data were analyzed from MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL).

Discussion

Five studies, involving 296 patients, were included out of 77 retrieved citations. It was observed that the microplegia group used less volume of cardioplegia in comparison with the standard blood cardioplegia group. No statistical differences were observed in the incidence of low output syndrome (RR, 0.95, 95% CI: 0.55 to 1.62), spontaneous return to sinus rhythm (RR, 1.64, 95% CI: 0.61 to 4.41) and perioperative myocardial infarction (RR, 0.62, 95% CI: 0.19 to 2.08).

Conclusion

Microplegia was related to less volume of cardioplegia, whereas the incidences of spontaneous return to sinus rhythm and perioperative myocardial infarction were similar. Still large controlled randomized trials are required to confirm this.

Source: Gong B, Ji B, Sun Y, Wang G, Liu J, Zheng Z. Is microplegia really superior to standard blood cardioplegia? The results from a meta-analysis. *Perfusion*. 2015;30(5):375-82.

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[1] Kocakulak M, et al. Investigation of Blood Compatibility of PMEA Coated Extracorporeal Circuits. Journal of Bioactive and Compatible Polymers. 2002; 17:343-356.

[2] Vang S, et al. Clinical Evaluation of Poly(2-methoxyethylacrylate) in Primary Coronary Artery Bypass Grafting. JECT. 2005; 37:23-31.

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