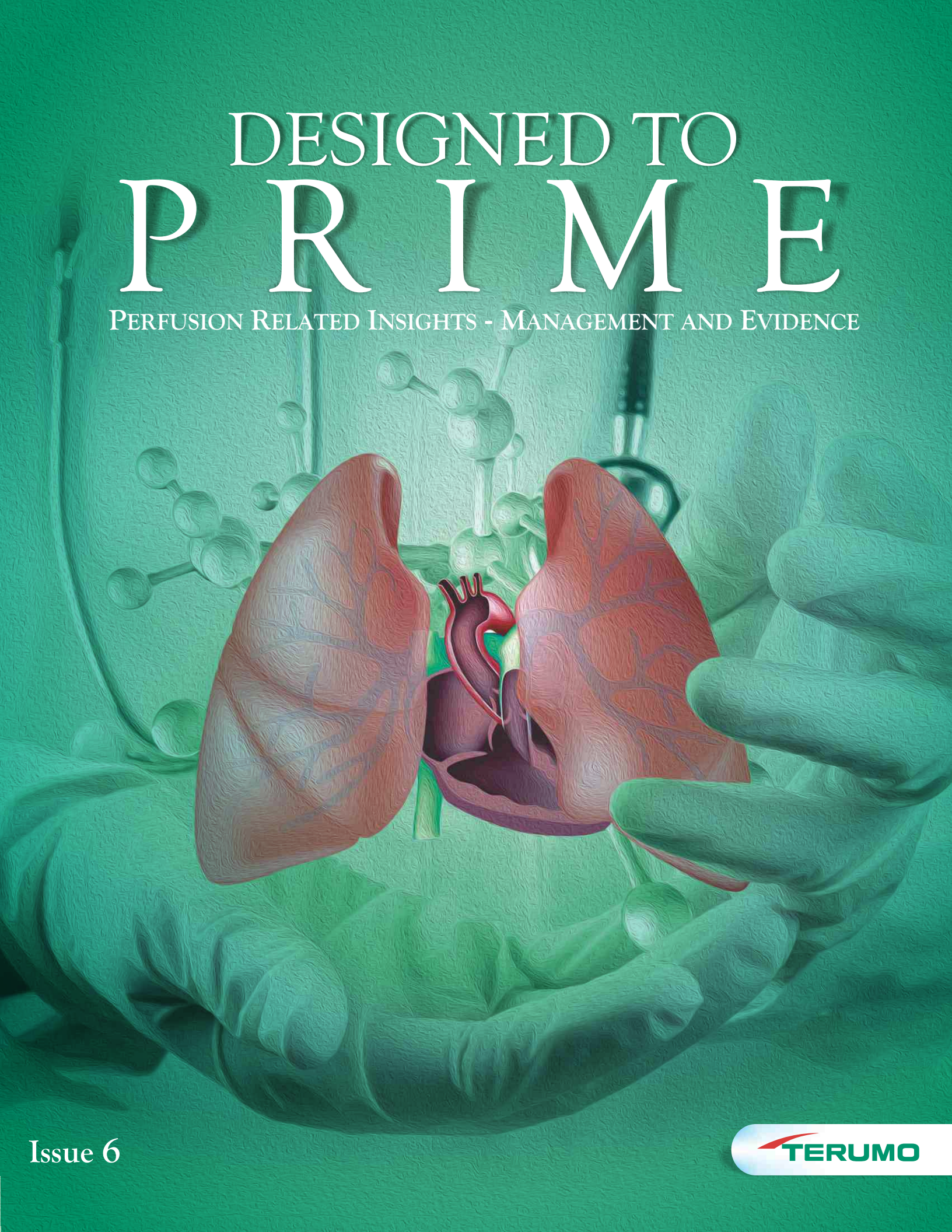
# DESIGNED TO PRIME

## Perfusion Related Insights - Management and Evidence



Issue 6

TERUMO

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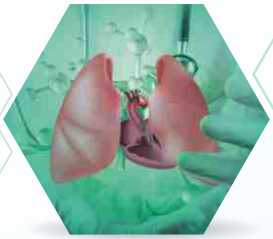
*PRIME Newsletter* invites new authors for contribution to the perfusion community. If you are interested in volunteering your time writing an article, topic of your expertise and willing to share your knowledge with our readers, we certainly encourage you to do so. We invite everyone interested in joining our team to contact us at the email given below. Any amount of time that you can volunteer in adding to our quality of publication will be greatly appreciated. Thank you for your interest in PRIME Newsletter. What are you waiting for?

E-mail- rahul_sharma@terumo.co.jp



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# Editorial Letter

Dear Readers,

First published in 2015 and now in its sixth issue, PRIME — 'Perfusion Related Insights - Management and Evidence' — is a quarterly scientific newsletter that offers current reviews, guidelines, and specialist experiences with regard to perfusion strategies. With the help of our editorial board, each issue is meticulously updated to reflect the latest advances in cardiac perfusion.

In this sixth issue, we are happy to present five articles under the section “Review Articles.” The first article examines the role of hemolysis in increasing systemic and pulmonary vascular resistances after prolonged cardiopulmonary bypass. The second article assesses the benefits of hemofilter and beating heart surgery in attenuating inflammatory response to cardiopulmonary bypass. On the other hand, the third article addresses the question whether femoral cannulation is a safe vascular access option for cardiopulmonary bypass. Comparison between on-pump and off-pump coronary artery bypass graft techniques in high-risk patients is presented in the fourth article. The final article determines the frequency of regional cerebral oxygen desaturation during cardiopulmonary bypass and the effectiveness of an intervention algorithm in managing the same.

The "Expert Experiences" section covers two interesting topics by the experts — the advantages of using beating heart continuous coronary perfusion for closure of atrial septal defect and the role of extracorporeal membrane oxygenation in post-pulmonary thromboendarterectomy procedure.

The “Guidelines” section focuses on “checklists” from the American Society of Extracorporeal Technology Standards and Guidelines in Individuals with Perfusion Practice (2013), while the “Latest News” section reports on the effect of adding blood to prime in reducing inflammatory response to neonatal cardiopulmonary bypass and the impact of circulating non-hematological cells during cardiopulmonary bypass on coagulation cascade.

We trust and hope that perfusionists will find our selection of articles useful and engaging. We value your feedback, suggestions, and comments, as they motivate us to work better on the future issues of PRIME.

**Dr. Sandeep Arora**
Director Medical and Clinical Affairs
Terumo India Pvt. Ltd.

**Mr. Rahul Sharma**
Manager Clinical Excellence
Terumo India Pvt. Ltd.
rahul_sharma@terumo.co.jp

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# Role of Hemolysis in Pulmonary and Systemic Vascular Resistances post Cardiopulmonary Bypass

## Introduction

Cardiopulmonary bypass (CPB) procedure is commonly used while performing heart surgery with cardiocirculatory arrest. Prolonged CPB is associated with increased hemolysis, with consequent higher plasma oxy haemoglobin (oxy Hb) levels and vascular nitric oxide (NO) depletion. Nitric oxide produced by vascular endothelium causes vascular smooth muscle relaxation. Earlier studies have shown that pulmonary and systemic vasoconstriction were associated with reduced bioavailability of NO secondary to higher plasma oxy Hb levels. Rezoagli *et al.* evaluated the effect of prolonged CPB (≥ 140 minutes) on hemolysis and resultant systemic and pulmonary vasoconstriction in a prospective cohort study (N = 50).

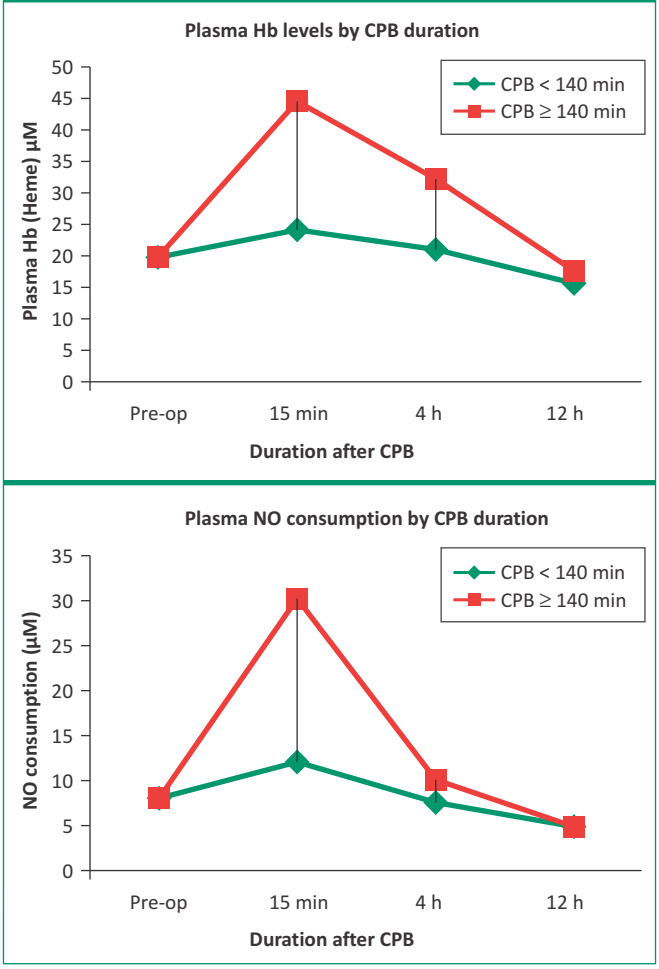
## Methods

Plasma Hb and plasma NO consumption were assessed before elective cardiac surgery and after CPB. Systemic and pulmonary hemodynamics were measured post CPB at regular intervals — 15 minutes, 4 hours, and 12 hours. The effects of CPB duration [shorter (< 140 minutes) vs. longer (≥ 140 minutes) CPB] on these parameters were evaluated.

## Results

Plasma Hb and NO consumption as well as systemic and pulmonary vascular resistances were highest at 15 minutes post CPB and reduced gradually in the following 12 hours (Figure 1). These parameters were higher in patients, who required prolonged CPB. The reductions in systemic and pulmonary vascular resistances (15 minutes to 4 hours) following prolonged CPB independently correlated with the fall in plasma NO consumption.

Figure 1: Plasma Hb and NO consumption in patients undergoing CPB

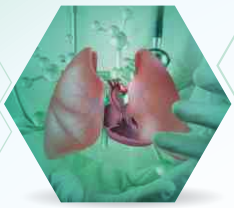



**Abbreviations:** CPB, cardiopulmonary bypass; Hb, hemoglobin; NO, nitric oxide.

**CONCLUSION**

Extended CPB procedure was associated with higher plasma NO consumption and Hb levels as well as increased systemic and pulmonary vascular resistances. The fall in plasma NO consumption at 4 hours post CPB was an independent predictor of consequent fall in systemic and pulmonary vascular resistances.

**Source:** Rezoagli E, Ichinose F, Strelow S, Roy N, Shelton K, Matsumine R, *et al.* Pulmonary and systemic vascular resistances after cardiopulmonary bypass: Role of hemolysis. *J Cardiothorac Vasc Anesth.* 2016 Jun 8. pii:S1053–0770(16)30181–1.





# Is Inflammatory Response to Cardiopulmonary Bypass Attenuated by Beating Heart Surgery or Hemofiltration

## Introduction

Cardiopulmonary bypass (CPB) procedure can induce inflammatory response ranging from subclinical organ dysfunction to serious multi-organ failure. The benefits of off-pump surgery and hemofilter can be assessed by inflammatory markers (cytokines), such as interleukin-10 (IL-10), interleukin-6 (IL-6), and transforming growth factor beta -1 (TGF- β1). Radhakrishnan *et al.* evaluated the effect of hemofiltration and off-pump surgery on the inflammatory response to CPB.

## Methods

Participants were divided into three groups — those undergoing coronary artery bypass graft (CABG) with CPB using hemofilter (N = 20); CABG with CPB (N=20); and off-pump CABG (OPCAB) procedure (N = 20). Inflammatory response was determined by measuring cytokine levels from venous samples at 0 hour, at completion (2–4 hours), and after surgery at 12, 24, and 72 hours.

## Results

The OPCAB group had significantly lower plasma IL-10 levels at 2–4 hours ($P < 0.05$), while the CPB with hemofilter group and the OPCAB group recorded considerably less IL-10 levels at 24 and 72 hours ($P < 0.05$). Furthermore, the OPCAB group had significantly lower IL-6 levels at 2–4 hours than the CABG group ($P < 0.05$).

> **Beating heart surgery was associated with attenuated inflammatory response in the immediate postoperative period. Both beating heart surgery and hemofiltration had an advantage of reduced inflammatory response at 24 and 72 hours post surgery.**

**CONCLUSION**

Off-pump CABG was associated with attenuated inflammatory response in the immediate post-operative period as indicated by low IL-10 and IL-6 levels. Both OPCAB and hemofilter usage in the CPB circuit had the advantage of reduced inflammatory response at 24 and 72 hours following surgery as evidenced by low IL-10 levels.

**Source:** Radhakrishnan K , Gamel AE, Jacobson G, Burton D, Cursons R. Does beating heart surgery or hemofiltration attenuate inflammatory response to cardiopulmonary bypass. *Heart, Lung* and *Circulation.* 2016 Aug;25(8):e89.

# Femoral Cannulation as a Safe Vascular Access Option for Cardiopulmonary Bypass in Minimally Invasive Cardiac Surgery

## Introduction

During cardiopulmonary bypass (CPB) procedure, femoral cannulation has become an important access option, particularly while performing minimally invasive cardiac surgery (MICS) or other complex surgeries. Contrary views, however, suggest that significant overall and site-specific morbidity is associated with femoral cannulation, as against the conventional aortoatrial cannulation. In a retrospective, observational cohort study, Saadat *et al.* assessed the efficacy and safety of femoral cannulation.

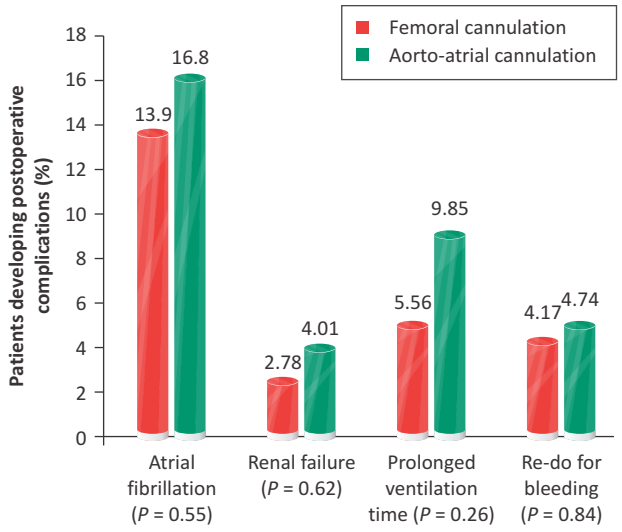
## Technique

The common femoral vein and artery are exposed through a groin incision. A guide wire is passed into the femoral artery using the Seldinger technique and advanced toward the descending thoracic aorta. With the aid of a transesophageal echocardiography (TEE) probe, the guide wire is positioned within the aortic lumen, and the cannula is advanced over it till the tip of the cannula reaches the iliac artery. By adopting the Seldinger technique, venous cannulation is established with a 25 Medtronic cannula, and its tip is advanced to the right atrial level. The TEE probe helps to ascertain the position of the cannula and the presence of blood flow after establishing CPB.

## Methods

Data from a single hospital's database pertaining to cardiac surgery over a period of 1 year were analyzed. Out of the 346 cardiac surgeries evaluated, aortoatrial cannulation was utilized in 274 (79.2%) procedures, while femoral cannulation was used in 72 (20.8%) surgeries; the majority of which were MICS [62/72 (86.1%)].

Figure 1: Post-operative complications in patients undergoing femoral vs. aortoatrial cannulation



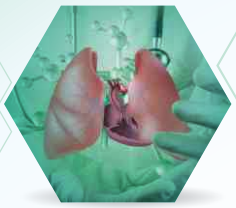

## Results

Stroke occurred in one case (1.39%) subsequent to femoral cannulation, particularly in a patient who underwent conventional sternotomy, as against six cases (2.19%) following aortoatrial cannulation ($P$ = 0.67). While comparing the postoperative complications (Figure 1), no significant difference was observed between the two groups. Operative mortality occurred in 5 cases (4 after MICS) following femoral cannulation (6.94%) and in 10 cases (3.65%) subsequent to aortoatrial cannulation ($P$ = 0.22).

**CONCLUSION**

Selective femoral cannulation is a safe alternative for CPB surgery, particularly while performing MICS. No significant difference was found between femoral and aortoatrial cannulation procedures in the overall mortality, local morbidity, or postoperative complication rates.

**Source:** Saadat S, Schultheis M, Azzolini A, Romero J, Dombrovskiy V, Odroniec K, et al. Femoral cannulation: A safe vascular access option for cardiopulmonary bypass in minimally invasive cardiac surgery. *Perfusion.* 2016 Mar;31(2):131–4.





# The PRAGUE-6 Trial – Off-Pump versus On-Pump Coronary Artery Bypass Grafting Surgery in High-Risk Patients

## Introduction

Off-pump coronary artery bypass graft (OPCAB) surgery is established as an alternative procedure to on-pump revascularization surgery. Previous randomized controlled trials involving low- or intermediate-risk patients showed no significant differences in mortality or postoperative complications between OPCAB and on-pump revascularization surgery. In the PRAGUE-6 trial, Hlavicka *et al.* compared the two procedures in high-risk patients.

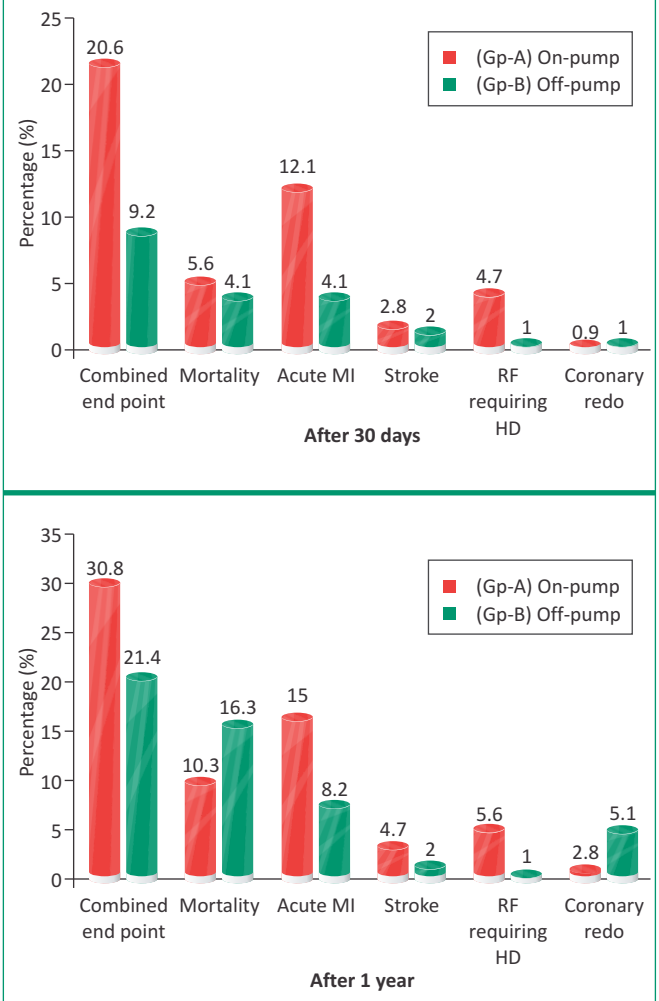
## Methods

In this prospective, single-center trial, high-risk patients (N = 206) with EuroSCORE ≥ 6, listed for isolated coronary surgery, were randomized to either group A undergoing on-pump revascularization (N = 108) or group B undergoing OPCAB (N = 98) procedure. Combined endpoint of all cause-mortality, myocardial infarction (MI), stroke, or kidney failure requiring new hemodialysis within the initial 30 days and 1 year following randomization was taken as the primary outcome. "Intention-to-treat" principle was used to analyze all data.

## Results

Early post-operative acute MI occurred in 12.1% of patients in group A, as against 4.1% in group B ($P$ = 0.048) and > 3 times higher in group A than in group B. Group A patients had considerably higher incidence of primary combined endpoint in the initial 30 days ($P$ = 0.028). However, no significant differences were noted in the primary endpoint at one year ($P$ = 0.117). In the initial 30 postoperative days, only one coronary re-intervention was reported in both groups. Primary endpoints at 30 days and after one year are shown in Figure 1.

Figure 1: Primary end points after 30 days and 1 year of randomization




**Abbreviation:** MI, myocardial infarction; RF, renal failure; HD, hemodialysis.

**CONCLUSION**

The OPCAB procedure performed in high-risk patients can considerably reduce the incidence of serious complications, especially global ischemia and MI, during the initial 30 postoperative days. However, no significant difference was reported in the incidence of complications after one year.

**Source:** Hlavicka J, Straka Z, Jelinek S, Budera P, Vanek T, Maly M, *et al.* Off-pump versus on-pump coronary artery bypass grafting surgery in high-risk patients: PRAGUE-6 trial at 30 days and 1 year. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* 2016 Jun;160(2):263–70.

# Assessment of Regional Cerebral Oxygen Desaturation Frequency during Cardiopulmonary Bypass and Responsiveness to an Intervention Algorithm – A Multicenter Pilot Study

## Introduction

Regional cerebral oxygen saturation ($rSco_2$), which indicates adequacy of cerebral perfusion, is monitored using near-infrared spectroscopy (NIRS) during cardiac surgery, especially cardiopulmonary bypass (CPB) procedure. According to earlier studies, $rSco_2$ desaturation occurring during coronary artery bypass graft (CABG) is associated with the risk of postoperative cognitive dysfunction and stroke. In a multi-center pilot study, Subramanian *et al.* evaluated the frequency of $rSco_2$ desaturation occurring during cardiac surgery involving CPB; the efficacy of an intervention algorithm in reversing $rSco_2$ desaturation; and the accuracy of $rSco_2$ desaturations identified by clinicians as against those recorded by near-infrared spectroscopy (NIRS) monitor.

## Methods

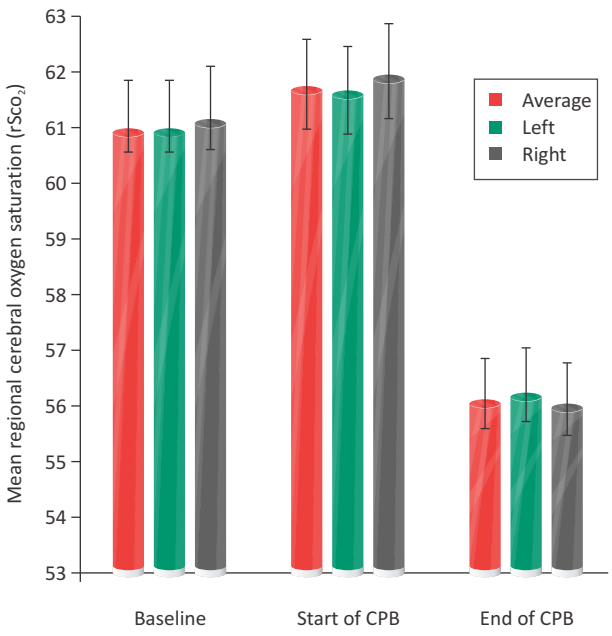
The study enrolled 235 patients undergoing CABG and/or valvular surgery at 8 study centers. During surgery, $rSco_2$ was monitored using NIRS. The extent and frequency of $rSco_2$ decrements of > 20% from baseline were recorded, and the effectiveness of treatment algorithm in resolving $rSco_2$ decrement was assessed. After surgery, data obtained from NIRS monitor were compared with the clinician-identified desaturation episodes.

## Results

No significant differences were found between the average $rSco_2$ values at baseline and during CPB. However, lower $rSco_2$ values were obtained at the end of CPB ($P < 0.001$) than those obtained at baseline and during CPB (Figure 1).

Episodes of $rSco_2$ desaturations were reported in 61% of patients during CPB. The area under the curve for the extent and duration of $rSco_2$ desaturations was 145.2 (384.8% x min). Clinicians identified only 89.5% (340 out of 380) of the total $rSco_2$ desaturation episodes. Treatment algorithm caused reversal of $rSco_2$ desaturations in the majority of the clinician-identified episodes (207 out of 340), while 115 episodes resolved with regular clinical care.

Figure 1: Regional cerebral oxygen saturation by time

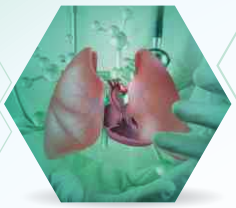



**Abbreviation:** CPB, cardiopulmonary bypass.

**CONCLUSION**

One or more $rSco_2$ desaturations occurred during CPB in 50–75% of patients, who underwent cardiac surgery. Clinicians failed to identify around 10% of these episodes. The treatment algorithm was effective in resolving the majority of clinically detected $rSco_2$ desaturation episodes.

**Source:** Subramanian B, Nyman C, Fritock M, Klinger RY, Sniecinski R, Roman P, *et al.* A multicenter pilot study assessing regional cerebral oxygen desaturation frequency during cardiopulmonary bypass and responsiveness to an intervention algorithm. *Anesth Analg.* 2016 Jun;122(6):1786–93.





# Beating Heart Continuous Coronary Perfusion for Atrial Septal Defect Closure

**Contributed by:** Dr. Vijaya Vivek Lanje, Clinical Perfusionist-Dept of CVTS, Suretech Hospital and Research Center Jamtha, Nagpur

Cardioplegia is the gold standard strategy for myocardial protection during cardiac surgery using cardiopulmonary bypass (CPB). However, cardioplegic approach subjects the heart to a period of mandatory ischemia, with consequent risk of reperfusion injury. Beating heart continuous coronary perfusion (BHCCP) technique is associated with better myocardial function and less myocardial edema.

## Objective and design

Beating heart technique is aimed at avoiding ischemic reperfusion injury and minimizing aortic cross-clamp (X-CL) time with the aid of antegrade continuous coronary perfusion (ACCP). This prospective study (N = 52) assessed the outcome of closure of all types of atrial septal defects (ASD) using ACCP of an empty beating heart without systemic hypothermia.

## Technique

After establishing the diagnosis with color-flow Doppler and 2-dimensional echocardiography, location, size, and type of ASD as well as associated anomalies, if any, were determined. Median sternotomy with conventional CPB (bicaval cannulation with ascending aorta cannulation) was performed in all cases. Antegrade cardioplegic needle was inserted into the ascending aorta to facilitate ACCP and de-airing on completion. The aorta was cross clamped with backup perfusion flow. Aortic root was perfused with normothermic oxygenated blood (4–5 mL/kg/min) throughout the surgery, and the root pressure was maintained at 110–120 mmHg. Ischemic changes on the ECG, perfusion pressure, aortic root pressure, saturation, temperature, and urine output were monitored throughout the procedure. Both caval loop snug down before right atriotomy. Operative field was kept bloodless by placing a cardiotomy sucker in the coronary sinus ostium. Entire procedure was performed without cardioplegia. De-airing and right atrial closure were carried out in the usual fashion.

## Outcomes

All patients tolerated the surgery well and were extubated within 4 hours after surgery. None of them needed ionotropic support or vasodilatation. No ECG changes occurred during or after surgery. No patient required ICU stay for more than 24 hours. Post-operative echocardiography revealed normal left ventricular function and no residual shunt across the interatrial septum. Early postoperative arrhythmias were absent in patients who underwent perfused beating-heart surgery, as against those who were operated under cardioplegic arrest.

## Advantages of beating heart procedure

Once the aortic X-CL is released after surgery, myocardium is exposed to extremes of ischemia and reperfusion, which may result in arrhythmia, myocardial stunning, low cardiac output, and perioperative myocardial infarction. Keeping the heart beating results in less myocardial edema and better myocardial function. Other benefits of beating-heart ASD repair include immediate ability to evaluate the severity of co-existing mitral or tricuspid valvular insufficiency and detect iatrogenic conduction injuries.

**CONCLUSION**

Beating-heart ASD closure is safe and effective than the conventional techniques. It can also be used for other non-coronary procedures, including valve repairs and replacements.

# Role of Extracorporeal Membrane Oxygenation in Pulmonary Thromboendarterectomy Surgeries – A Retrospective Analysis

**Contributed by:** Lakshmi Gopinadh, P.V.S. Prakash, Sunil Mekala, Dr. Devi Prasad Shetty, Dr. Binoy Chattuparambil, Dr. Julius Punnen, Dr. Patel Ebrahim. Narayana Health, Bangalore.

Extracorporeal membrane oxygenation (ECMO) is a rescue therapy that supports patients with life-threatening respiratory or cardiac dysfunction, when conventional therapies fail. During ECMO, blood is continuously circulated extracorporeally via a blood pump, passed through a membrane oxygenator to facilitate oxygenation and carbon dioxide elimination, and then returned to the patient. This process allows time for the heart and lungs to rest, recover, and heal. In this analysis, the authors discuss the importance of ECMO as a life support in patients, who underwent pulmonary thromboendarterectomy (PTE).

## Discussion

Pulmonary embolism (PE), the third most common cause of cardiovascular death, results from the blockage of pulmonary arteries and their branches by blood clots secondary to deep vein thrombosis of the legs. Patients with PE will be presenting with thromboembolic pulmonary artery hypertension, cardiac arrest, right heart failure, low cardiac output, hypotension, ventilation perfusion (V/Q) mismatch, and hypoxia.

Pulmonary thromboendarterectomy is a complex surgical procedure to extract existing thrombus from the pulmonary arteries and their branches using cardiopulmonary bypass (CPB) under deep hypothermic circulatory arrest (DHCA). This procedure relieves pulmonary artery hypertension by reducing V/Q ratio, alleviating right ventricular (RV) dysfunction, limiting the retrograde extension of the obstructive thrombus, and protecting against arteriopathological changes in the pulmonary vessels that remain patent. After PTE, ECMO is required due to persisting pulmonary artery pressure, inability to wean off CPB, RV dysfunction, pulmonary hemorrhage, reperfusion lung injury, and pulmonary edema with poor gas exchange.

## Process

Extracorporeal membrane oxygenation was initiated either immediately after surgery or on the first post-operative day. Patients were put on veno-arterial (V-A) ECMO, which takes over the functions of both heart and lungs by preventing the vicious cycle of hypoxic vasoconstriction. Patients were put on veno-venous (V-V) ECMO to support gas exchange without causing further lung damage. Conversion of V-V to V-A ECMO was done when hemodynamic compromise occurs while on V-V ECMO. Most of the patients received central cannulation, while a few received peripheral cannulation. Blood gas investigations, anticoagulation profile, venous pressures, and pre- and post-membrane pressures were monitored. Weaning took place in stages by evaluating different parameters. After sustained stability for more than two hours, cannulas were removed.

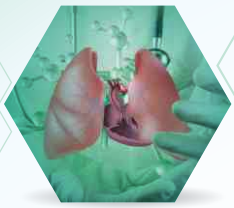
## Outcomes

The findings from this study show that 48.6% (37 out of 76) patients were successfully weaned off from ECMO (V-A ECMO – 71; V-V ECMO – 5). The average time on ECMO support was 7 days.

**CONCLUSION**

Extracorporeal membrane oxygenation is a lifesaving tool in patients with high pulmonary artery pressure, pulmonary hemorrhage, pulmonary reperfusion injury, and right ventricular failure. The post-PTE survival percentage is 48.6 in our center. Early ECMO placement has a significant role as rescue therapy in the post-PTE patients.

**Source: 1.** Berman M, Tsui S, Vuylsteke A, Snell A, Colah S, Latimer R, *et al*. Successful extracorporeal membrane oxygenation support after pulmonary thromboendarterectomy. *Ann Thorac Surg.* 2008 Oct;86(4):1261–7. **2.** Thistlethwaite PA, Madani MM, Kemp AD, Hartley M, Auger WR, Jamieson SW. Venovenous extracorporeal life support after pulmonary endarterectomy: Indications, techniques, and outcomes. *Ann Thorac Surg.* 2006 Dec;82(6):2139–45. **3.** Guttendorf J, Boujoukos AJ, Ren D, Rosenzweig MQ, Hravnak M. Discharge outcome in adults treated with extracorporeal membrane oxygenation. *Am J Crit Care.* 2014 Sep;23(5):365–77.





# The American Society of ExtraCorporeal Technology Standards and Guidelines in Individuals with Perfusion Practice (2013)

## Standard and guidelines for checklists

A checklist shall be used by the perfusionist for every cardiopulmonary bypass (CPB) procedure.

The patients' permanent medical record shall have the checklist included in it.

Checklists should be used in a read-verify approach by the perfusionist, where important steps that ought to have been performed are confirmed. Checklists should be completed by two people, one being the primary perfusionist in charge of operating the heart-lung machine through the intra-operative period.

A checklist should be used by the perfusionist during the whole perioperative period, including set-up, prior to bypass, initial onset of bypass, before termination of bypass, after bypass, and/or any return to bypass.

A checklist should be used by the perfusionist for other additional perfusion services, such as intra-aortic balloon pump, cell salvage, and extracorporeal membrane oxygenation.

**Source:** Baker RA, Bronson SL, Dickinson TA, Fitzgerald DC, Likosky DS, Mellas NB, *et al;* International Consortium for Evidence-Based Perfusion for the American Society of ExtraCorporeal Technology. Report from AmSECT's International Consortium for Evidence-Based Perfusion: American Society of Extracorporeal Technology Standards and Guidelines for Perfusion Practice: 2013. *J Extra Corpor Technol.* 2013 Sep;45(3):156–66.



# Time of Addition of Blood to Prime Impacts the Inflammatory Response to Neonatal Cardiopulmonary Bypass

Cardiopulmonary bypass (CPB) in neonates is associated with complications resulting from systemic inflammation, and this can contribute to the morbidity occurring after neonatal cardiac surgery from acute lung injury, capillary leak syndrome, coagulopathy, systemic inflammatory response syndrome, and multi-organ failure. Higher susceptibility of neonates to systemic inflammation post CPB is attributed to the necessity for priming the CPB circuit with blood. These complications can be reduced by using asanguinous prime; however, this can lead to significant hemodilution in neonates, involving addition of blood. Available evidence indicates that hemodilution in neonates undergoing CPB can adversely affect short- and long-term postoperative periods with regard to surrogate inflammatory markers as well as psychomotor development. Schmidt *et al.* evaluated whether adding blood after establishing CPB modifies the inflammatory response in comparison with blood prime.

## Blood prime versus asanguinous prime

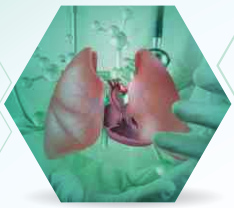
Neonatal swine (N = 19) were randomized into a control group exposed to blood prime and three experimental groups receiving asanguinous prime but exposed to blood at different time points — after CPB but before cooling, at the end of cooling, and at the end of re-warming. All the animals were placed on central bypass for a total time of two hours. Though hematocrit levels varied between groups throughout CPB, the final values were similar in all groups.

Despite spending time with lower hematocrit values, higher lactate levels were not reported at the end of CPB in the groups that received asanguinous prime, when compared to the blood prime group. Groups receiving asanguinous prime produced less tumor necrosis factor - α (TNF-α) than the blood prime group ($P$ = 0.023). The asanguinous prime group with blood added on CPB had less TNF-α and interleukin 10 (IL10) production. The group that received blood while cool, released less TNF-α and IL10 than the group that received blood while warm. In addition, less edema was reported in the asanguinous prime group than the blood prime group, with the least weight gain reported in the group that received blood at the end of cooling ($P$ = 0.011).

**CONCLUSION**

Outcome of this study indicates that using asanguinous prime cooled to deep hypothermia for neonatal CPB is a practical approach, and adding blood later reduces the inflammatory response.

**Source:** Schmidt BS, Jordan JE, Lane MR, DiPasquale VM, Graf LP, Ootaki Y, *et al.* Timing of adding blood to prime affects inflammatory response to neonatal cardiopulmonary bypass. *Cardiol Young.* 2016 Jul; 8:1–8.





# Fresh Findings in Cardiac Surgery Procedures – Circulating Non-Hematological Cells during Cardiopulmonary Bypass

Inflammatory and coagulative disorders occurring after cardiopulmonary bypass (CPB) are attributed to several factors. Features of CPB technique, including heparinization, hemodilution, pump trauma, hypothermia, and interaction with air and synthetic components can alter the pathophysiology and composition of blood during CPB. In addition, lipid and air microembolism may be caused by surgical maneuvers. These factors are considered to be responsible for activation of inflammatory and coagulative mediators, and arterial and capillary dilation post CPB. Santise *et al.* examined the presence of non-hematological cells introduced into the circulation during CPB and their effect on coagulation cascade.

## Origin of cells

Peripheral arterial blood samples were collected from 20 consecutive subjects undergoing on-pump coronary artery bypass graft (CABG) procedure. The presence and nature of cells were assessed using CELLSEARCH (immunomagnetic enrichment and sample staining procedures of circulating epithelial cells) test, immunofluorescence, and immunocytochemistry to evaluate the expression of calretinin and cytokeratin. Samples obtained by suction of blood from the operative field had 258.5 cells (mean 263.85 ± 57.5), while the remaining samples were negative ($P$ < 0.00001). Mesothelial origin of these cells was confirmed by immunological tests.

## Impact on coagulation

The ROTEM (thromboelastography) assay was used to assess the impact of circulating non-hematological cells on blood coagulation. Blood samples containing mesothelial cells when subjected to ROTEM assay demonstrated prolonged clotting time, longer clot formation time, highest clot firmness time, and lesser alfa angle amplitude (Table 1), when compared to controls.

Figure 1: The ROTEM assay results of pericardial lavage versus control

| Parameters | Pericardial lavage | Control | *P* values |
|---|---|---|---|
| **Clotting time** | 53.4 ± 8.2 sec | 48.3 ± 8.9 sec | 0.05 |
| **Alfa angle amplitude** | 66.7 ± 9.1° | 71.1 ± 5.1° | 0.04 |
| **Clot formation time** | 137.1 ± 31.5 sec | 111.9 ± 25.2 sec | 0.009 |
| **Clot firmness time** | 59.0 ± 5.4 sec | 61.9 ± 4.6 sec | 0.004 |

**CONCLUSION**

During CPB, the presence of non-hematological cells with a mesothelial immunephenotype in the blood stream modifies coagulation assays *in vitro*, and they could play a role in microembolization phenomena and alterations in coagulation.

**References :** Santise G, Marinaro C, Maselli D, Dominici C, Di Vito A, Donato G, *et al.* Circulating non-haematological cells during cardiopulmonary bypass: New findings in cardiac surgery procedures. *Perfusion.* 2016 Oct;31(7):584–92.

## SELF ASSESSMENT

SECTION 5

**1. Two-stage venous cannulation refers to _____.**

a. Cannulation of superior and inferior venae cavae one after the other ☐
b. Insertion of one venous cannula with drainage holes in the superior and inferior venae cavae ☐
c. Insertion of separate venous cannulae into the superior and inferior venae cavae ☐
d. Insertion of one venous cannula with drainage holes in the right atrium and inferior vena cava ☐

**2. Vacuum-assisted venous return, which decreases the need for hemodilution and the use of blood, is accomplished by application of negative pressure to the venous reservoir. The pressure, thus, applied is approximately _____.**

a. -70 to -80 cm of water ☐
b. -40 to -60 cm of water ☐
c. -90 to -100 cm of water ☐
d. -20 to -30 cm of water ☐

**3. During complete cardiopulmonary bypass, unforeseen electrical activity of the heart is managed by _____.**

a. Administering additional muscle relaxant by the anesthesiologist ☐
b. Squeezing excess blood out of the heart by hand ☐
c. Administering additional cardioplegic solution by the perfusionist ☐
d. Repositioning retrograde arterial cannula by the surgeon ☐
e. Administering shock to the heart at 200 J ☐

**4. In patients who have severe atherosclerosis of the ascending aorta, the risk of stroke after cardiopulmonary bypass can be reduced by _____.**

a. Visualization of the aortic lumen by using transesophageal echocardiography ☐
b. Adopting bilateral proximal carotid compression while surgically manipulating aorta ☐
c. Using β-adrenergic blockers or electrical fibrillation for myocardial protection ☐
d. Considering alternative cannulation sites and techniques ☐
e. All of the above ☐

**5. All patients who are undergoing hypothermic cardiopulmonary bypass must be screened for cold-agglutinins.**

a. True ☐ b. False ☐

**6. Unexpected increase in cardiopulmonary bypass arterial line pressure associated with a simultaneous fall in systemic pressure and/or a decrease in venous drainage indicates _____.**

a. Venous air embolism ☐
b. Acute aortic dissection ☐
c. Acute myocardial infarction ☐
d. None of the above ☐

**7. Retrograde cerebral perfusion is an effective treatment option when significant air is believed to have entered the cerebral circulation.**

a. False ☐ b. True ☐

**8. What is the device used for performing hemodialysis during cardiopulmonary bypass in patients with renal failure?**

a. Cell saver ☐
b. Roller pump ☐
c. Oxygenator ☐
d. Hemoconcentrator ☐

Answers: 1–D; 2–B; 3–C; 4–E; 5–A; 6–B; 7–B; 8–D.

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