ISSUE 18

PRIME CENTRE OF EXCELLENCE
PERFUSION RELATED INSIGHTS - MANAGEMENT AND EVIDENCE

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Perfusion-Related Insights – Management and Evidence

TERUMO

Editorial Letter

It is with immense pleasure that we present 18th issue of PRIME Newsletter — "Perfusion-Related Insights– Management and Evidence" — a quarterly scientific newsletter that includes review articles, meta-analysis, recently published recommendations, expert opinion and practice pearls on cardiopulmonary bypass (CPB) and perfusion strategies.

The current issue brings to you an interesting article and guidance recommendations, starting with the first section 'Speciality Insights', which sheds light on normoxic management of CPB and its significance in diminishing myocardial oxidative stress in patients undergoing coronary artery bypass grafting.

The second section 'Success Stories' discusses the use of cost-effective modified conventional CPB circuit in one case study and the role of fresh-frozen plasma transfusion in FXII deficient patient in another case study.

The next section 'Basic Facts' demonstrates the management of post-CPB coagulopathy by point-of-care testing. The first article of section four 'Practice Pearls' evaluates the cognitive, technical and motion analysis of a basic CPB task to differentiate between experts and trainees. The second article analyzes the cognitive workload during man-machine interaction in a socio-technically complex naturalistic setting.

The fifth section 'Journal Talk' is comprised of two articles. The first one describes different anticoagulation monitoring system during CPB, while the second study indicates beneficial role of intraoperative extracorporeal membrane oxygenation support in pediatric patients.

The sixth section 'Expert Opinion' presents outcome in patients of Jehovah's Witness faith, who refuses blood transfusion during CPB due to religious reasons. Under the seventh and last section 'News Corner', angiotensin-II is highlighted as an excellent therapeutic option for treating vasoplegic syndrome in patients undergoing cardiac surgery.

We hope this newsletter enriches your knowledge with the current practices and research updates in the field of cardiopulmonary bypass and perfusion.

Kindly let us know your comments and suggestions to help us improvise based on your feedback.

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PRIME Newsletter invites new authors for their contribution to the perfusion community. If you are interested in volunteering your time writing an article or a topic of your expertise and willingness to share your knowledge with our readers, we certainly encourage you to do so. We invite everyone interested in joining our team, and you can 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?

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NORMOXIC MANAGEMENT OF CARDIOPULMONARY BYPASS: A BETTER ALTERNATIVE TO REDUCE MYOCARDIAL OXIDATIVE STRESS

Introduction

Use of hyperoxic cardiopulmonary bypass (CPB) is associated with ischemia-reperfusion and/or hypoxemia-reoxygenation injury. Patient who are undergoing coronary artery bypass grafting (CABG) witnesses chronic myocardial ischemia during aortic cross clamping. The risk of myocardial ischemia-reperfusion injury increases during revascularization and restoration of myocardial blood flow. The current study aimed to apply normoxic CPB and analyze its effects in comparison to hyperoxic CPB, by measuring total oxidant status (TOS) and total antioxidant status (TAS).

Methodology

- This is a single-center, single-blind, parallel group randomized controlled trial (November 2017 and April 2018) that randomized patients into normoxia or treatment group and hyperoxia or control group in 1:1 ratio.
- Before intubation, all patients were pre-oxygenated with 100% oxygen (O_2) and then anesthetized with a combination of fentanyl, midazolam, propofol and rocuronium.
- A fraction of inspired oxygen (FiO_2) of 35% and 70% was used in normoxia and hyperoxia group respectively.
- 35% and 45% FiO_2 was used during hypothermic bypass and rewarming in normoxia group.
- The hyperoxia group received 50% and 70% oxygen during hypothermic bypass and rewarming respectively.
- Prior to CPB and after reperfusion, coronary sinus blood sample was collected to measure the myocardial total oxidant and antioxidant status.
- Primary endpoint of this study was myocardial total oxidant status, while secondary endpoints were myocardial total antioxidant status, length of intensive care unit (ICU) and hospital stay.

Results

- A total of 48 patients were included (40 males, 8 females) of which 22 (58 ± 9.07 years) received normoxic management and 26 received hyperoxic CPB (60.1 ± 9.1).
- Myocardial TOS was significantly reduced ($p < 0.05$) in the normoxia group. But, no significant difference was found in TAS and length of ICU and hospital stay (Table 1).

Parameters	Normoxia	Hyperoxia
Pre-operative		
Diabetes mellitus, n (%)	11 (50)	10 (40)
Hypertension, n (%)	9 (40.9)	10 (38.5)

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COPD, n (%)	2 (9.1)	1 (3.8)
Hyperlipidemia, n (%)	13 (61.9)	15 (60)
Carotid artery disease, n (%)	4 (18.2)	4 (15.4)
TOS (μmol H_2O_2 Eq/L), median (IQR)	18.5 (13.9-25.7)	20.06 (13.5-28.2)
TAS (μmol H_2O_2 Eq/L)	1.8 ± 0.21	1.7 ± 0.22
CPB duration (min)	85.18 ± 21.19	99.81 ± 32.12
Cross clamping duration (min)	50.45 ± 13.9	56.38 ± 20.6
Post-operative		
TOS 4 minutes after removal of aortic cross clamp (μmol H_2O_2 Eq/L), median (IQR)	49.5 (40.8-68.1)	66.9 (55.8-87.8)
TAS 4 minutes after removal of aortic cross clamp (μmol H_2O_2 Eq/L)	1.6 ± 0.21	1.5 ± 0.17
ICU length of stay (days), median (IQR)	1 (1-1.25)	1 (1-1.25)
Hospital length of stay (days), median (IQR)	6 (6-8)	6.5 (6-7)
Inotropic support, n (%)	3 (13.6)	8 (30.8)
Mortality, n (%)	1 (4.5)	1 (3.8)
Prolonged ICU stay (> 48 hours), n (%)	3 (13.6)	5 (19.2)
Prolonged hospital stay (≥ 10 days), n (%)	3 (13.6)	5 (19.2)
Acute kidney injury, n (%)	3 (13.6)	9 (34.6)
Stroke, n (%)	0	0
Prolonged mechanical ventilation (> 24 hours), n (%)	1 (4.5)	3 (11.5)
Pleural effusions, n (%)	1 (4.5)	3 (11.5)
Pneumonia, n (%)	3 (13.6)	2 (7.7)
Deep sternal wound infections, n (%)	1 (4.5)	1 (3.8)
Atrial fibrillation, n (%)	5 (22.7)	8 (30.8)
Low cardiac output syndrome, n (%)	0	2 (7.7)

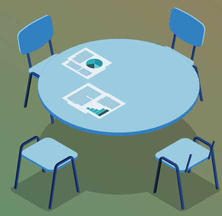
Table 1: Pre and post-operative clinical variables and complications in normoxic and hyperoxic groups

Conclusion

- Use of normoxic CPB can lead to low level of myocardial oxidative stress in comparison to hyperoxic CPB in adult patients undergoing elective CABG.
- Although mortality, ICU and hospital stay did not show any difference between the groups, but utilization of normoxic CPB approach can serve as a successful treatment without any event of hypoxemia.

Reference

Topcu AC, Bolukcu A, Ozeren K, Kavasoglu T, Kayacioglu I. Normoxic management of cardiopulmonary bypass reduces myocardial oxidative stress in adult patients undergoing coronary artery bypass graft surgery. Perfusion. 2021 Apr;36(3):261-8.



FORMATION OF CLOSED ECMO CIRCUIT BY MODIFICATION IN THE STANDARD CPB CIRCUIT

Introduction

Cardiopulmonary bypass (CPB) allows a bloodless field required during a cardiac surgery and its circuit involves a number of components such as cannulas, roller pumps, oxygenator, reservoir, etc. ECMO i.e. extracorporeal membrane oxygenation, on the other hand, is a system providing extracorporeal support similar to CPB. However, unlike CPB that provides short-term support for few hours, ECMO provides support for a comparatively longer period, varying from days to weeks. Recently, doctors were able to save a 16 year old female with post cardiotomy shock by modifying the standard CPB circuit into a cost-effective closed ECMO with the help of a roller pump.

Case report

A girl of age 16 years, with low financial background was diagnosed with situs solitus, D-transposition of great arteries, large subaortic ventricular septal defect (VSD) with inlet extension and severe valvular pulmonary stenosis after a thorough cardiac evaluation. The girl was suffering from the complex cyanotic congenital heart disease since she was 5 years old. After the doctors discovered her to be NYHA class III patient, her biventricular repair operation in the form of Rastelli operation was conducted using the right ventricular-pulmonary artery conduit. The operation required multiple runs of CPB, cardioplegic arrest along with revision of VSD patch and aggressive conal muscle resection. A mild left ventricular outflow tract (LVOT) gradient (15 mmHg peak gradient) with no residual VSD and good biventricular function was observed. The total CPB time and aortic cross clamp (ACC) time was kept as 421 minutes and 166 minutes, respectively. In order to cut down the adverse outcomes of the surgery, it was required to lengthen the CPB as well as ACC times.

The patient with open chest and high inotropic support was then shifted to intensive care unit (ICU), where she began to develop symptoms of low cardiac output. The lactate levels started to rise and post-operative echocardiography revealed severe biventricular hypertrophy with biventricular dysfunction. Even after increasing her inotropes, her condition deteriorated and she sustained cardiac arrest approximately after 16 hours post-surgery. The patient was revived within 10 minutes with the help of aggressive cardiopulmonary resuscitation. However, her condition remained critical and hemodynamically unstable.

The surgeons then decided to modify the conventional CPB circuit and its oxygenator (Affinity, Medtronic, USA) as a short-term mechanical circulatory support. In this, the venous reservoir was bypassed using a 3 /8 "Y" connector in the venous line and was connected to its outlet using another 3/8 "Y" connector with additional short length of 3/8 tubing as shown in Figure 1. The circuit was primed and the venous reservoir inlet and outlet line were clamped together to form a closed circuit. The patient was then cannulated centrally with aortic and right atrial cannulation and the modified ECMO was initiated by venting left ventricle using the vent catheter and connecting to the venous line. The cardiac index of 2.5–3.0 l/min was maintained in the patient by supporting her with 75–100 ml/kg/minutes of flows.

Interestingly, after using the modified ECMO circuit, the patient showed marked improvement and started to show good cardiac ejection as well as hemodynamics. After 30 hours of observation, the patient was weaned of the circuit. Her chest was closed on 5th post-operative day and was discharged on the 14th post-operative day. The patient was followed up after 2 years and was doing well.

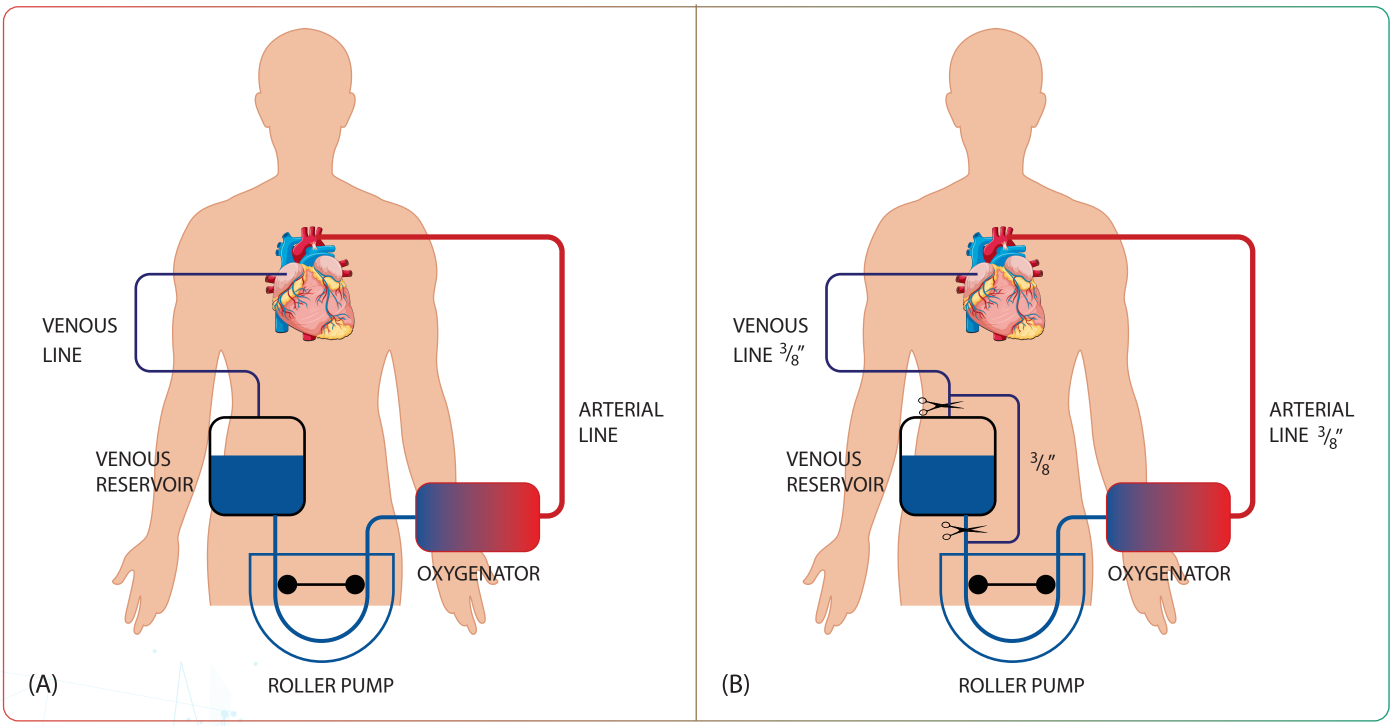


Figure 1: (A) Conventional CPB circuit and (B) modified ECMO circuit

Conclusion

- The modified conventional CPB circuit to form ECMO closed circuit can be used in situations where the conventional ECMO circuit is unavailable or is unaffordable.
- It can prove to be a cost-effective method to stabilize the patients suffering from critical heart disease.
- In cases of post-cardiotomy cardiogenic shock, the ECMO closed circuit can be safely used to provide mechanical support for short duration of 48-72 hours. However, it is advised to initiate the ECMO in less than 30 minutes of cardiac arrest to achieve the best possible outcomes of the surgery.

Reference

George B, Kandaswamy M, Jaganathan U, Kandaswamy S, Raju V. Extension of cardiopulmonary bypass outside the operating room as a short-term bridge to recovery "the poor man's ECMO". Indian Journal of Thoracic and Cardiovascular Surgery. 2021 Jan;37(1):108-11.

SIGNIFICANCE OF FRESH-FROZEN PLASMA TRANSFUSION IN FXII DEFICIENT PATIENT UNDERGOING CARDIOPULMONARY BYPASS

Introduction

Liver synthesizes and secretes coagulation factor XII (FXII) that initiates the intrinsic coagulation cascade by activating factor XI (FXI) during any injury. In vivo coagulation is more dependent on FXI, hence, deficiency or absence of FXII is not associated with clinical bleeding, though it is diagnosed incidentally during pre-operative assessment such as, prolonged activated partial thromboplastin time (aPTT) and activated clotting time (ACT). A study on stepwise approach to perioperative management of a child with FXII deficiency, undergoing cardiopulmonary bypass (CPB) is reported here.

Case history

- A 3 year old girl (body weight 14.7 kg) with sinus venous atrial septal defect and partial anomalous pulmonary venous return was admitted.
- A prolonged aPTT of > 200 seconds was discovered during pre-operative assessment that corrected to 34 seconds after mixing with normal plasma. Despite having normal fibrinogen level (2.2 g/L), prothrombin time (12 seconds), thrombin time (16 seconds), normal concentrations of coagulation factors VIII, IX, XI and von Willebrand factor, a low concentration of FXII (< 1%) was found that became 7% on repeated testing.
- A perioperative transfusion of fresh-frozen plasma (FFP) of 400 mL (~30 mL/kg) was planned to correct the ACT. However, to avoid volume overload and haemodilution, only half of the intended dose was transfused along with a standard dose of heparin (400 IU/kg).
- The child was transitioned to CPB. The CPB circuit was primed with 200 mL of FFP, 280 mL of packed RBCs, 1400 IU of heparin and 70 mL of Plasma-Lyte 148. The circuit was filtered to achieve a hematocrit of 28%, and balanced with sodium bicarbonate and calcium chloride.
- Total aortic cross clamp and CPB time was 13 and 25 minutes respectively that required no further heparin.
- ACT was performed at every time point using either low range cartridge (ACT-LR; dried preparation of celite, potato dextrin, stabilizers and buffers; heparin concentrations up to 2.5 IU/mL of blood) or high range cartridge (ACT-HR; dried preparation of silica, kaolin, phospholipid, stabilizers and buffers; heparin concentrations of 1-6 IU/mL of blood).
- There was no unusual bleeding or hemorrhage in the post-operative duration, though the 24 and 48 hours post-FFP FXII level was low. The patient was discharged on 4th day.
- Details of perioperative coagulation profile of the patient are presented in the Figure 2.

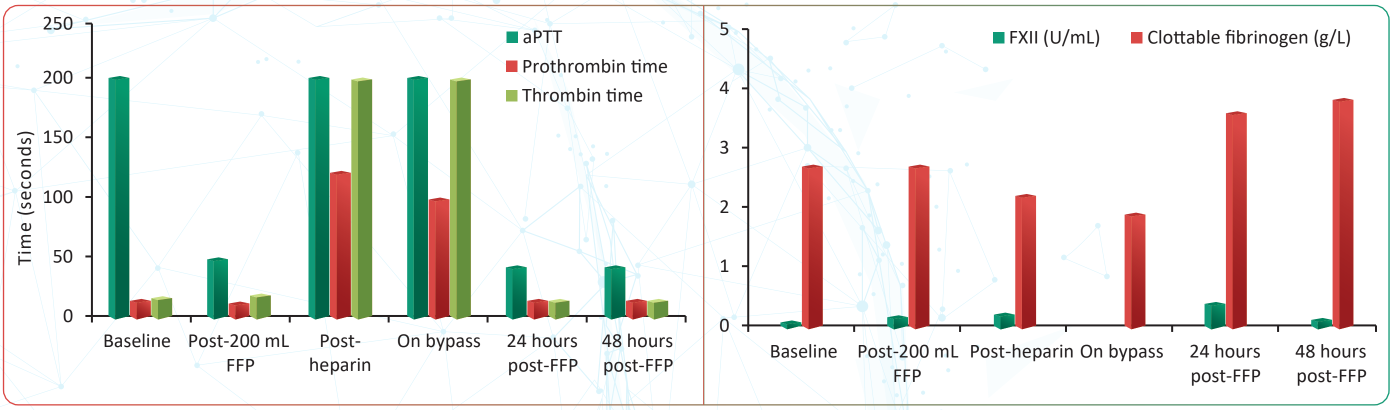


Figure 2: Coagulation profile at different time points during CPB

Conclusion

- Patients with FXII deficiency, who requires CPB, can be managed by perioperative transfusion of FFP.
- ACT-HR is recommended during FFP transfusion as it uses kaolin and silica.
- FFP transfusion is a simple and effective method with application of standard anaesthesia for safe CPB surgery in FXII deficiencient patients.

Reference

Shrimpton N, Patukale A, Rane M, Barbaro P, Alphonso N, Venugopal P. Cardiopulmonary bypass in a child with severe Factor XII deficiency. Perfusion. 2021 Mar 5:0267659121999305.

MANAGEMENT OF CARDIOPULMONARY BYPASS ASSOCIATED COAGULOPATHY

Introduction

Cardiopulmonary bypass (CPB) offers significant surgical advancements like oxygenation, carbon dioxide elimination, temperature management and systemic circulation and perfusion. But CPB is also associated with coagulopathy, characterized by excessive bleeding, blood transfusions and worse patient outcomes. The fluids that is used to prime the bypass circuit causes hemodilution along with activation of the extrinsic and intrinsic system, ultimately resulting in coagulopathy.

Management of post-CPB coagulopathy

> ***" Do as much as possible for the patient, and as little as possible to the patient." - Dr. Bemard lown, Nobel-prize winning physician and the developer of the cardioverter-defibrillator***

To manage coagulopathy after surgery, patient's baseline coagulation status along with correction of pre-operative anemia and coagulopathy must be evaluated. The modifiable and non-modifiable risk factors of pre-operative management are shown in Figure 3. All cardiac surgery is accountable for bleeding and all staffs involved with the surgery should understand that and have quick access to resuscitative medications and blood products. Table 2 presents coagulopathy management approaches during the surgery.

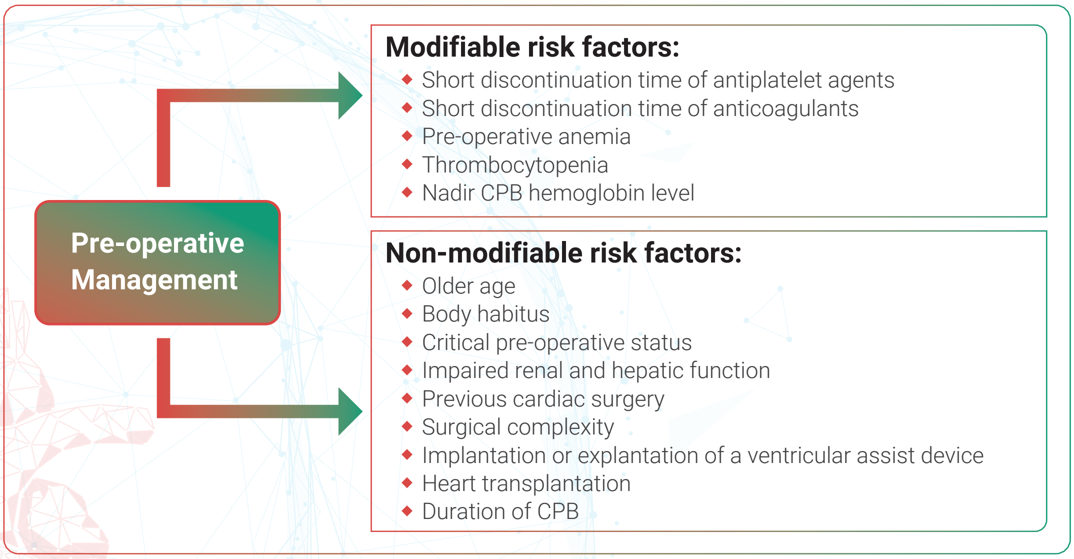


Figure 3: The modifiable and non-modifiable risk factors of pre-operative management of coagulopathy

Heparin Management and Protamine Reversal

- 300-400 IU/kg of IV unfractionated heparin prior to CPB
- Monitored with the activated clotting time (ACT) by
  - Hemachron
  - - i-STAT

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- ACT target of ≥ 480 seconds considered as adequate
- Protamine is given at the conclusion of bypass to neutralize heparin anticoagulation
- Heparin management system plus is used to calculate heparin dose-responsiveness curve for a target ACT

Adjuncts and Equipment

- Aprotinin and epsilon amino caproic acid
- Tranexamic acid inhibits plasminogen to plasmin conversion
- Red cell salvage minimizes allogeneic transfusions
- Sequestration allows the transfusion of autologous red cells, platelets and coagulation factors
- Retrograde autologous priming of CPB lines reduces hemodilution
- Autologous platelet-rich plasma transfusion to conserve blood

Testing

- Standard laboratory testing like Clauss method to measure plasma fibrinogen concentration
- Point-of-care testing or viscoelastic testing reduces transfusion requirements up to 50% and improves patient outcomes:
  - Thromboelastography (TEG)
  - Rotational thromboelastometry (ROTEM)
  - Quantra™ hemostasis analyzer measures clotting time, clot stiffness, platelet and fibrinogen contribution to clot stiffness and the effect of heparin
- Point-of-care platelet function testing or platelet function analyzer is a whole blood aperture closure assay

Fibrinogen Replacement

- Cryoprecipitate
- Fibrinogen concentrate (offers more advantages in terms of standardized fibrinogen dose delivery, storage, reconstitution and safety due to purification and pathogen reduction)

Others

- High ratio plasma and platelet to red cell transfusion reduces end organ dysfunction and mortality
- Awareness of surgical bleeding is necessary and each patient with bleeding event should be monitored carefully to prevent higher risk of adverse post-operative results
- Thrombin generation during CPB are associated with increased bleeding and must be monitored throughout
- Prothrombin complex concentrates and plasma is commonly used in coagulopathic surgical patients
- Recombinant activated factor VII and factor VIII inhibitor bypass activity (FEIBA) is effective for intractable bleeding in cardiac surgical patients
- Desmopressin improves platelet aggregation and reduces bleeding
- Direct oral anticoagulants

Table 2: Intra-operative management of post-CPB coagulopathy

Conclusion

- The hemostatic defects in patients having CPB can be multifactorial, management of which requires point-of-care testing.
- Management of coagulopathy in patients undergoing cardiac surgery is challenging, but the anesthesiologist, surgeon, and intensivist involved in the care of these patients should be well familiar with the process.
- Understanding of CPB associated coagulopathy facilitates appropriate management and can improve patient care and survival.

Reference

Bartoszko J, Karkouti K. Managing the coagulopathy associated with cardiopulmonary bypass. Journal of Thrombosis and Haemostasis. 2021 Mar;19(3):617-32.

A HIGH-FIDELITY SIMULATION ENVIRONMENT TO EXAMINE MULTIMODAL CARDIOPULMONARY BYPASS SKILLS

Introduction

The aim of cardiothoracic surgical training is to provide competent and safe surgeons, though this idea is challenging as the current system lacks the methodology to measure an individual's cognitive and technical skills. Within a high-fidelity environment, evaluation of multimodal cardiopulmonary bypass (CPB) skills can differentiate between expert and trainee performance.

Methodology

- Signed informed consent was received from all participants, who were studied in an operating room equipped with an operating table and an overhead lighting.
- A perfused porcine beating heart with a blood substitute was provided in a silicone pericardial well. The simulator was controlled by laptop computer console that had a monitor to display hemodynamic indicators and trans-esophageal echocardiographic images.
- A trained physician assistant or the first assistant was provided to the participants along with an experienced scrub technician, who passed the instruments, such as, suture, cannulae and tubing.
- The participants required to manage blood pressure related to aortic cannulation and decannulation, and then place the patient on CPB, apply the aortic cross-clamp, and arrest the heart. The participants needed to perform standard aortic decannulation again.
- 10 cognitive points and 9 technical points for aortic cannulation/decannulation, 4 cognitive and 3 technical points for CPB, and 8 cognitive and 5 technical points for cross-clamp were assigned. The overall procedure was compared between experts and trainees.
- Physical movement as well as hand movements of the surgeon and the assistant was assessed by electromagnetic motion sensors attached to thumb, index and middle finger of each hand under the gloves.

Results

- Cognitive and technical aspects of expert and trainee during aortic cannulation/decannulation task, CPB task and cross-clamp task is presented in Figure 4.
- Combined cognitive and technical scores for all tasks ($n = 15$) showed significantly decreased cognitive score ($p < 0.05$), but non-significant technical score.
- Motion analysis demonstrated no significant differences in the motion metrics such as, idle time, path length, bimanual dexterity, smoothness and completion time between experts and trainees during aortic cannulation/decannulation and CPB task. Only during cross-clamp task a significantly increased ($p < 0.05$) path length was found in case of trainees, compared to experts.

- A significant difference ($p < 0.05$) in percentage of simultaneous hand movement (of both participant and assistant) was recorded between expert and trainee.

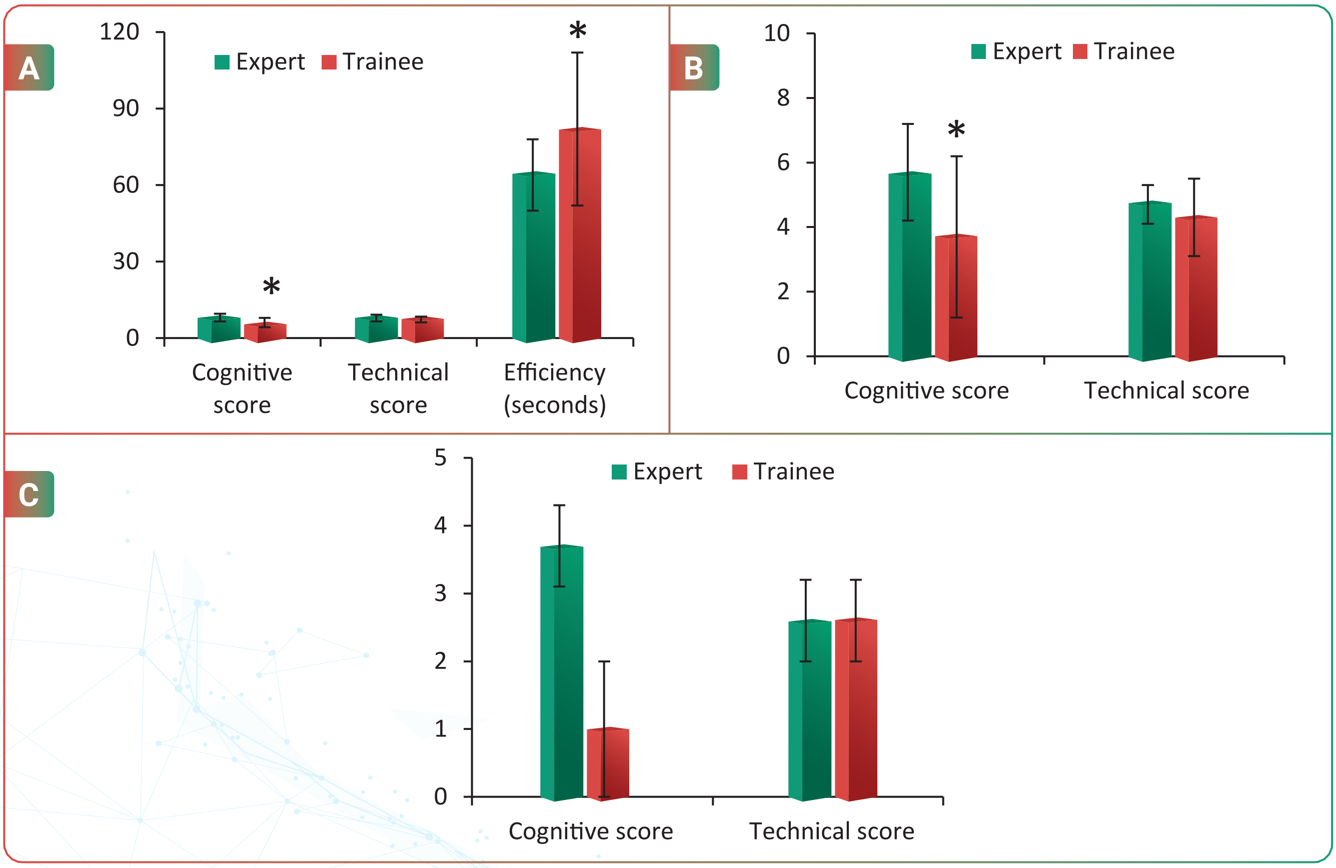


Figure 4: Comparison between expert and trainee during (A) Aortic cannulation/decannulation task, (B) CPB task and (C) Cross-clamp task. Data is presented as mean ± SD, *p < 0.05, n = 9 in aortic cannulation/ decannulation task, and n = 3 in both CPB and cross-clamp task

Conclusion

- A high-fidelity simulation environment can measure cognitive, technical and motion analysis of a basic CPB task.
- It is a valid system to differentiate between experts and trainees on the basis of their performance and efficiency.
- Although this system is not ready for "prime time" application but it still provides excellent implications for training and certification in cardiothoracic surgery.
- Future studies involving more trainees and experts to perform more complex tasks, problem solving and decision making can be conducted.

Reference

Hermsen JL, Mohamadipanah H, Yang S, Wise B, Fiedler A, DiMusto P, Pugh C. Multimodal cardiopulmonary bypass skills assessment within a high-fidelity simulation environment. The Annals of Thoracic Surgery. 2021 Aug 1;112(2):652-60.

EVALUATION OF COGNITIVE WORKLOAD IN THE PERFUSIONISTS DURING CARDIAC SURGERY

Introduction

Heart rate variability (HRV), a measure of slightest fluctuation between two consecutive heart rate (HR) intervals, is measured by electrocardiogram (ECG) and is used as an indicator of physical and psychological health. Depending on the analytic approach, the HRV components can be categorized into time-domain, frequency-domain and nonlinear measures. The time-domain measures such as the root mean square of the successive differences (RMSSD), percentage of normal-to-normal peaks differing by at least 50 ms (pNN50) and the frequency-domain measure log of the high frequency power band (HF log) are indicator of parasympathetic nervous system (PNS), higher value of which reflects fitness. The critical role of perfusionists during cardiac surgery is to maintain effective cardiopulmonary bypass (CPB) pump operation. Objective of this study was to investigate changes in HRV as a representation of the perfusionist's cognitive workload, who were performing the CPB pump during the cardiac surgery.

Methodology

Three Board-certified cardiac perfusionists (n = 23 cases) were included in this study. HRV was measured (RMSSD, HF log, index of the PNS activity or PNS index, pNN50, and average interval duration between consecutive R-peaks or mean RR), and self-reported cognitive workload was collected during isolated aortic valve replacement (AVR) or isolated coronary artery bypass graft (CABG) procedures from these study participants. Video and audio was recorded of the primary perfusionist, and chest strap was used to measure HR before going on bypass, while on bypass (pre-clamp, clamp and post-clamp) and after completion of bypass. Within each phase, the values from each 1 minute window was collected and averaged. Surgery task load index comprised of mental demand, physical demand, task complexity, distractions, and degree of difficulty dimensions was used to record self-reported cognitive workload. The operative settings of the operation room were maintained similar to real event like number of individuals present in the room, noise, ambient lighting and room temperature.

Results

- Surgery task load index showed prominent changes during the bypass phase than the pre or post-bypass phases of the surgery (Figure 5).
- RMSSD and PNS index demonstrated lowest HRV values during bypass indicating higher cognitive workload levels, while higher values during pre and post-bypass phases (Figure 6).
- HRV values were lowest during the pre-clamp phase that indicated lower PNS activity; whereas were highest during the clamp and post-clamp phases of bypass (Figure 6).

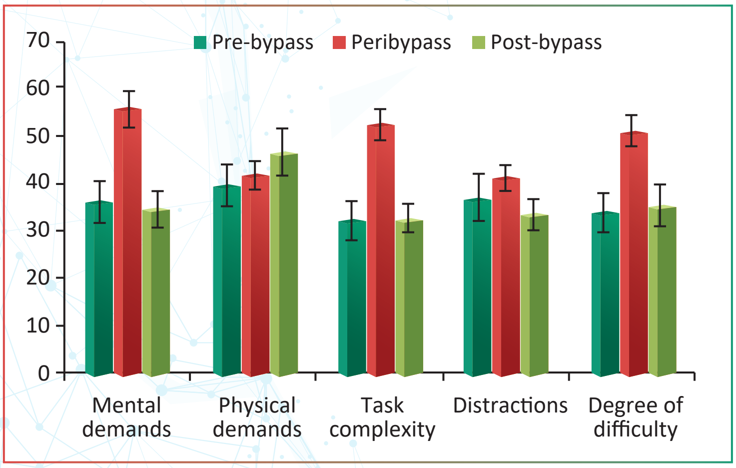


Figure 5: Surgery task load index during the three phases

- Cognitive workload was highest during the time between bypass initiation and aorta clamping.

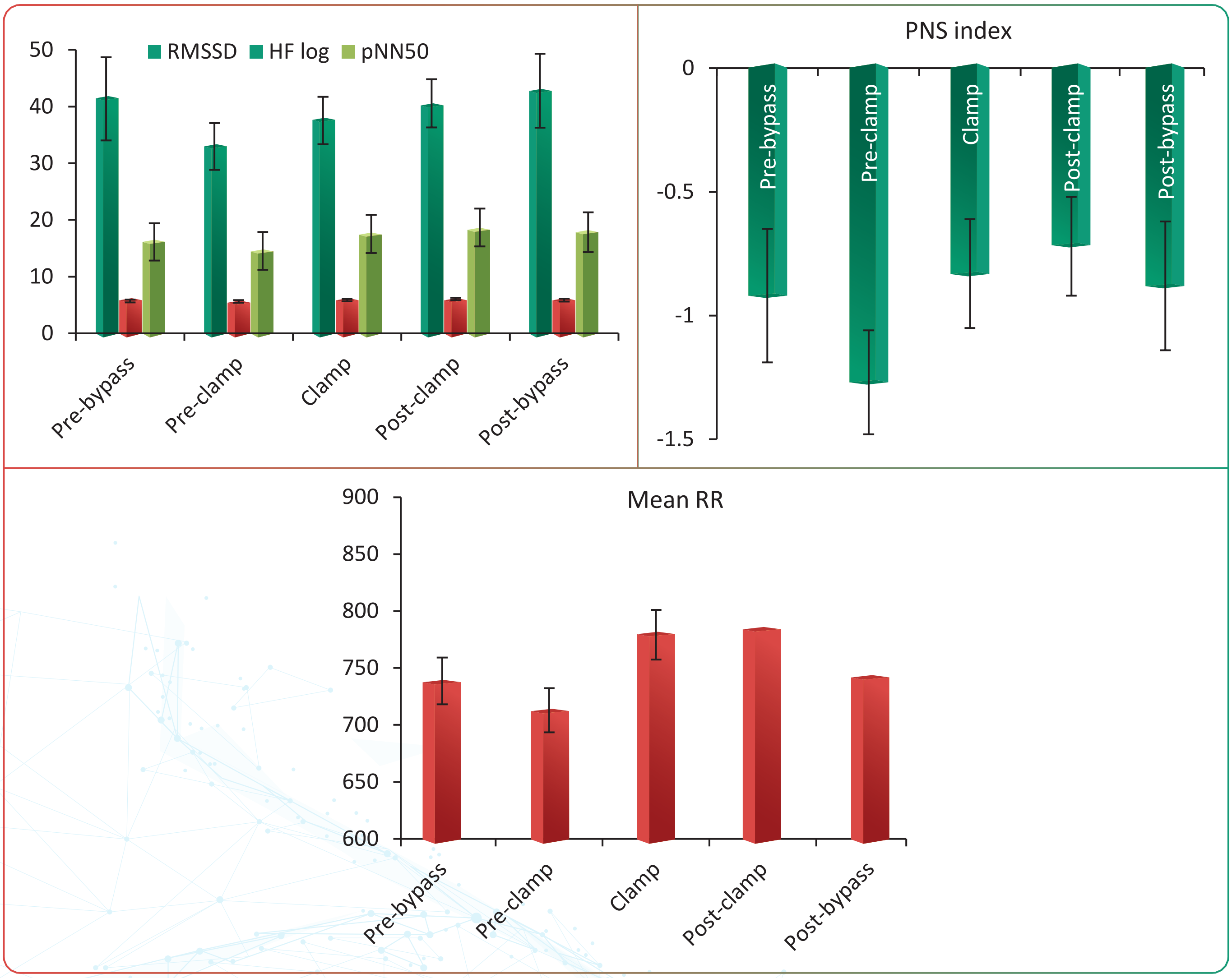


Figure 6: HRV components during the five phases

Conclusion

- The strength of HRV analysis is that it captures very tiny fluctuation in HR interval that marks the changes in stress during human-machine interaction.
- HRV analysis suggested a higher cognitive workload between initiation of bypass and placing the aortic cross clamp.
- The pre-clamp phase during CPB can be used as a target for cognitive support to manage workload levels during interaction between the perfusionist and the bypass machine.
- High cognitive overload is anticipated during perfusionist-CPB pump machine interaction as well as during perfusionist-surgeon and perfusionist-anesthesiologist interaction.
- Evaluation of cognitive workload of a perfusionist in a socio-technically complex naturalistic setting is helpful in reducing the operation room stress and to increase surgery efficiency.

Reference

Kennedy-Metz LR, Dias RD, Srey R, Rance GC, Conboy HM, Haime ME, Quin JA, Yule SJ, Zenati MA. Analysis of Dynamic Changes in Cognitive Workload During Cardiac Surgery Perfusionists' Interactions With the Cardiopulmonary Bypass Pump. Human factors. 2021 Aug;63(5):757-71.

THE OPTIMAL ANTICOAGULATION MONITORING SYSTEM DURING CARDIOPULMONARY BYPASS

Introduction

An inexpensive, widely available measurement of heparin anticoagulation during cardiopulmonary bypass (CPB) is activated clotting time (ACT). There are variations regarding ACT time as according to international surveys many Institutions use ACT value 400-500 seconds, whereas, some cardiac centers use < 400 or > 500 seconds. This variation persists due to use of different technologies, CPB circuits and coagulation activators along with temperature, fluctuating coagulation factor level and platelet count.

Different approaches for monitoring heparin concentration during CPB

- Two cartridge-based analyzers, Hemochron and i-STAT was used during elective cardiac surgery and found lower correlation between the devices. This study concluded that ACT for CPB must be determined specifically for each individual device. Inside a small capillary, the Hemochron device exerts a forward and backward oscillation that identifies the fluctuation in the blood sample flow rate. The oscillation rate slows down due to clot formation, indicating the end of the test. The i-STAT on the other hand uses an electrical sensor to detect the rise in specific split product, mimicking the reaction of fibrinogen with thrombin, where endpoint is detection of conversed thrombin substrate.
- These two devices are affected by various factors like coagulation factors, hypothermia, low platelet count or impaired platelet function that likely results in ACT differences. Some studies reported higher ACT by Hemochron device, while some found higher i-STAT ACT values.
- Another study used a method of patient's blood mixed with celite in a glass tube and inverted every 30 seconds that further mixed by placing it on a rocker and by keeping a 40 watt light bulb on. A stopwatch started at the beginning of the procedure and stopped once first clot was formed. This method provided anticoagulation during CPB within 300-600 seconds and an ACT of 480 seconds.
- An alternative to ACT device is heparin-protamine titration system or heparin monitoring systems that lowers post-operative bleeding risk and transfusion requirements. It monitors the real heparin activity rather than the common ACT device. However, it is also based on ACT measurements and can have likely limitations of conventional ACT devices.
- Other assays include rotational thromboelastometry (ROTEM) that detects residual heparin activity after protamine reversal and thromboelastography (TEG), which is activated by kaolin and tissue factor. But these tests have their own limitations as the usefulness of ROTEM in CPB is not investigated adequately and kaolin and tissue factors lower the sensitivity of TEG for heparin activity.
- The anti-Xa assay is considered as an only alternative to ACT during CPB as it measures heparin concentrations properly but it too has limitations. The use of anti-Xa requires trained lab personnel and its use is also poorly investigated.

Conclusion

- ACT is proved to be the commonest and preferable monitoring system of heparin activity during CPB. The internationally suggested ACT values can be used, with a prediction of ACT of 400-500 seconds when using a heparin bolus of 300-400 U/kg.
- At this moment switching from ACT to anti-Xa monitoring is not suggested in cardiac surgery with CPB.

Reference

Bolliger D, Maurer M, Tanaka KA. Toward Optimal Anticoagulation Monitoring During Cardiopulmonary Bypass: It Is Still A Tough "ACT". Journal of Cardiothoracic and Vascular Anesthesia. 2020 Nov 1;34(11):2928-30.

EXTRACORPOREAL MEMBRANE OXYGENATION AS A SAFE ALTERNATIVE OF CARDIOPULMONARY BYPASS IN PEDIATRIC LUNG TRANSPLANTATION

Introduction

Cardiopulmonary bypass (CPB) is often responsible for adverse post-operative outcomes like increased bleeding, acute pulmonary injury and early allograft dysfunction may be due use of heparin, activation of inflammatory cascades and coagulation pathways. Therefore, another alternative during lung transplantation is use of intraoperative extracorporeal membrane oxygenation (ECMO). CPB uses an open reservoir and cardiotomy suction, whereas, a closed and miniaturized circuit is used in ECMO that provides support to patients who cannot be wean. ECMO returns patients' blood directly into a centrifugal pump head and re-oxygenating blood is delivered to the patient without using extra heparin. This also results in lower systemic inflammatory response along with decreased postoperative mechanical circulatory requirements, reduced bleeding and length of hospitalization, fewer transfusion requirements, re-operations and lower rates of primary graft dysfunction. However, data regarding rate of mortality in ECMO users, especially in pediatric patients are limited.

Methodology

A single-center retrospective analysis of patients (< 18 years) undergoing lung transplantation (divided into CPB or ECMO cohorts) was done. 30 days, 6 months and 1 year follow-up outcomes of pre-operative or baseline, procedural and post-operative data were compared between two cohorts. Details of CPB and ECMO technique are given in Figure 7.

Results

- Cystic fibrosis was the prime reason for lung transplantation in 61.5% and 54.5% patients using CPB and ECMO respectively.
- There was no significant difference in measured pre-operative variables between two groups.
- During intra-operative period a significant difference was found in terms of median sternotomy (84.6 vs. 50%), bypass time (164 vs.186.5 minutes), fresh-frozen plasma (FFP) (8.9 vs. 16.6 mL/kg) and platelets (4.2 vs. 8 mL/kg) between ECMO and CPB groups.
- When re-transplantation was excluded, patients on ECMO showed lower intra-operative packed red blood cell values (12.6 vs. 28.2 mL/kg).

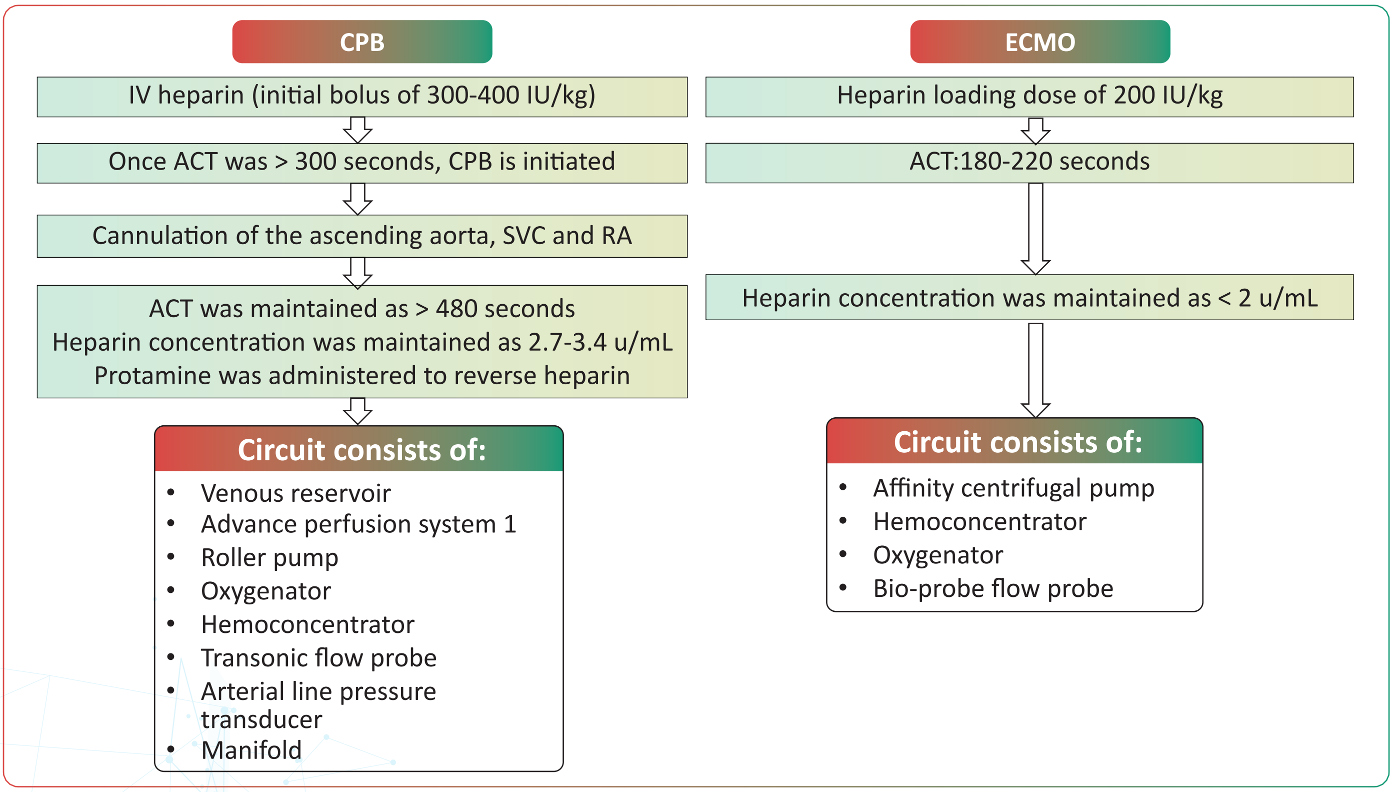


Figure 7: Details of CPB and ECMO techniques. SVC= Superior vena cava, RA= Right atrium, ACT= Activated clotting time

- No difference was found in mortality (1 in 13 ECMO patients and 4 in 22 CPB patients) between two groups at any given time points. Details of these patients are given in Table 3.
- No significant difference was noted in overall hospital stay, post-operative length of stay, inotrope requirements, total intubation time, oxygen support and chest tube days between the groups.
- Total time on ECMO was lower than the total time on CPB support.

Group	Survival days	Age	Cause of death
CPB	0	15	Uncontrolled bleeding, ventricular fibrillation
CPB	86	15	Hypertrophic cardiomyopathy with probable cardiac arrhythmia
CPB	246	6	Chronic respiratory failure
CPB	340	10	Sepsis
CPB	350	1	Pulmonary hemorrhage
ECMO	223	10	Acute diffuse bronchopneumonia

Table 3: Details of post-operative mortality

Conclusion

- Intra-operative ECMO support in pediatric patients during lung transplantation seems to reduce transfusion requirements (predominantly of packed RBCs) in comparison to CPB.
- As no significant variations were found in mortality, surgical times, hospital stay, post-operative inotrope support, oxygen requirements, the ECMO can be used as safe alternative of CPB.

Reference

Parikh AN, Merritt TC, Carvajal HG, Shepard MS, Canter MW, Abarbanell AM, Eghtesady P, Nath DS. A comparison of cardiopulmonary bypass versus extracorporeal membrane oxygenation: Does intraoperative circulatory support strategy affect outcomes in pediatric lung transplantation?. Clinical Transplantation. 2021 Mar 13:e14289.

A RETROSPECTIVE COHORT STUDY ON CARDIOPULMONARY BYPASS MANAGEMENT AND ACUTE KIDNEY INJURY

Introduction

Patients sometimes tend to refuse blood transfusion during cardiac surgery due to religious grounds, especially people of Jehovah's Witness (JW) faith. However, use of blood substitutes like perfluorocarbons and hemoglobin-based oxygen carriers is somewhat acceptable in this faith with proper right to informed consent. The current study performed a meta-analysis of 6 studies to compare results of modifiable cardiopulmonary bypass (CPB) relating to acute kidney injury (AKI) in JWs (USA: 0.6%, Canada and Australia/New Zealand: 0.3%, Britain: 0.2%) and matched-control population.

Methodology

The Australian and New Zealand Collaborative Perfusion Registry (ANZCPR) is used to collect the data. 118 patients, who have refused blood transfusion, were included in the study. The primary endpoint AKI was defined as serum creatinine criteria of the modified RIFLE (renal Risk, Injury, Failure, Loss of renal function and End-stage renal disease) classification. Secondary endpoints were 4 hour post-operative blood loss, mechanical ventilation time, length of post-operative stay, use of intra-aortic balloon pump, return to the operating theatre, myocardial infarction, stroke, a new requirement for dialysis, new renal insufficiency (serum creatinine > 0.2 mmol/L, greater than pre-operative value and requirement for post-operative dialysis/haemofiltration), combined morbidity (incidence of post-operative ventilation > 48 hours) and in-hospital mortality. The two groups were compared on the basis of CPB interventions and post-operative outcomes.

Results

- 49% of patients accepted transfusion, with red cell transfusion rates of 41%.
- Those who refused transfusion, received cell salvage (70% over the entire period, 67% during early and 72% during late time periods) and hemofiltration (8%) along with more frequently administration of tranexamic acid.
- The volume of retrograde autologous priming (RAP) from the CPB circuit was not different in patients refusing or accepting transfusion during overall or during the early or late periods.
- There was no in-groups difference in modifiable CPB factors (mean arterial pressure, oxygen delivery or DO_2i, retrograde autologous prime, circuit prime volume). However, the DO_2i was increased over time in both groups.
- AKI was lower in patients, who have refused to receive transfusion (8%), compared to their counterpart (22%).
- Lower post-operative blood loss along with shorter post-operative length of stay was recorded in patients refusing transfusion.
- Morbidity and mortality was similar in both groups.
- Patient's pre-operative, intra-operative and post-operative data are presented in Figure 8 & 9.
- Table 4 has shown intra-operative procedures used in patients accepting and refusing transfusion.

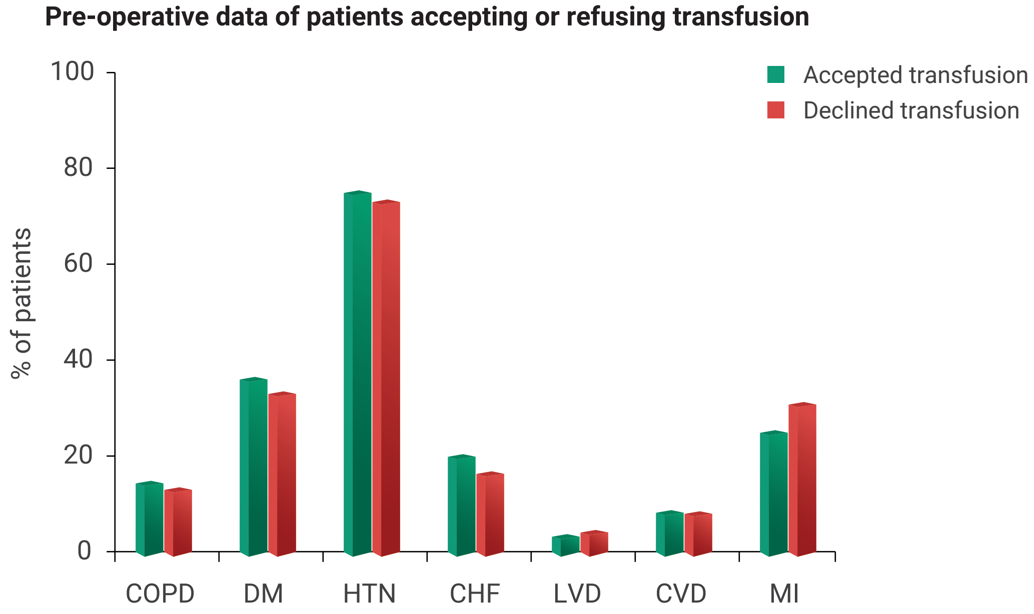


Figure 8: Pre-operative data of patients accepting or declining blood transfusion. COPD= Chronic obstructive pulmonary disease, DM= Diabetes mellitus, HTN= Hypertension, CHF= Congestive heart failure, LVD= Left ventricular dysfunction, CVD= Cerebrovascular disease, MI= Myocardial infarction

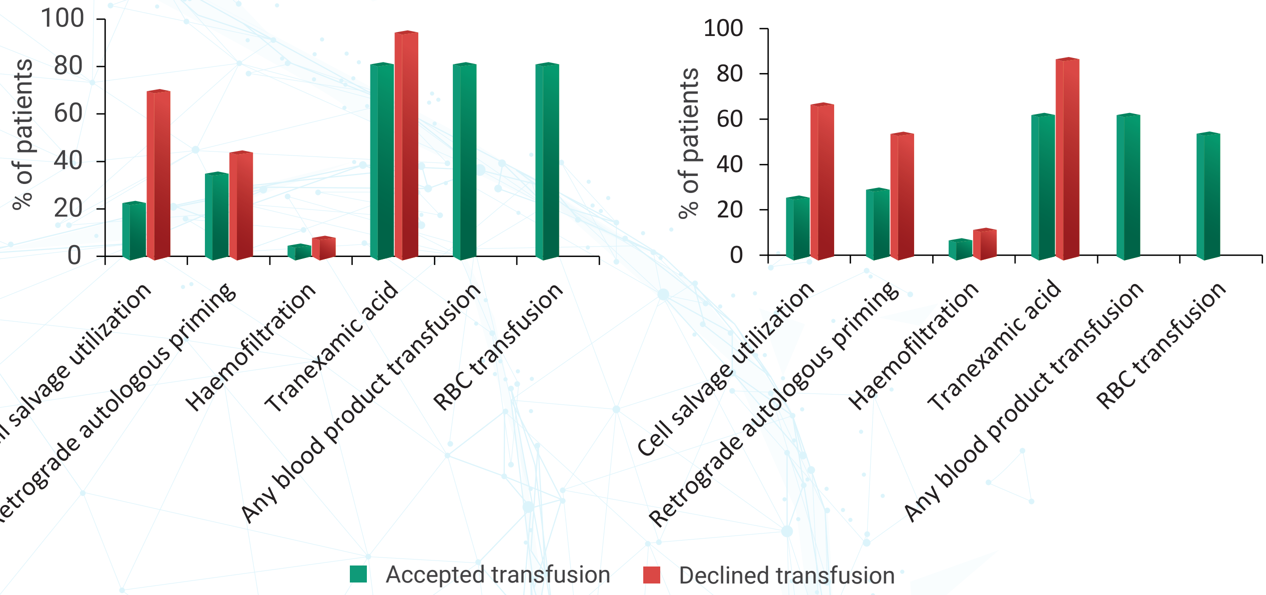


Figure 9: Intra-operative (left) and post-operative (right) data of patients accepting or declining blood transfusion

	Accepted transfusion	Declined transfusion
Coronary bypass graft	47%	50%
Mitral valve replacement	7%	7%
Aortic valve replacement	18%	14%
Other	14%	14%
Aortic valve replacement + coronary graft	11%	10%
Mitral valve replacement + coronary graft	3%	4%

Table 4: Intra-operative procedures used in patients accepting and declining transfusion

Conclusion

- This study provides data on modifiable factors of CPB from a large registry (ANZCPR) in cardiac surgery patients refusing transfusion.
- A significantly lower incidence of AKI was evident in JW patients, who have refused blood product transfusion with no difference in morbidity or mortality.
- The hospital stay and post-operative blood loss was reduced with ineffective mortality rate in these patients.
- The intra-operative management in these patients allows optimization of patient outcomes.

Reference

Willcox TW, Newland RF, Baker RA. Cardiopulmonary bypass management and acute kidney injury in 118 Jehovah's Witness patients: a retrospective propensity-matched multicentre cohort from 30,942 patients. Perfusion. 2020 Nov;35(8):833-41.

News Corner

ANGIOTENSIN-II AS AN EFFECTIVE THERAPEUTIC OPTION FOR PATIENTS SUFFERING FROM VASOPLEGIC SYNDROME

Introduction

Angiotensin-II (converted from angiotensin-I by angiotensin converting enzyme) is used as vasopressor to treat vasoplegic syndrome in a patient, who underwent cardiopulmonary bypass (CPB).

Case study

- An 81 year old man with 16% left ventricular ejection fraction (LVEF) and co-morbidities like hypertension, obesity, chronic kidney disease, diabetes mellitus, atrial fibrillation and congestive heart failure was admitted and referred for four-vessel coronary artery bypass graft.
- Time for aortic cross clamp and CPB was 71 minutes and 107 minutes respectively.
- Pre- and post-operative parameters are presented in Table 5.
- During the case the patient was administered with norepinephrine (0.31 mg/kg/minutes) along with milrinone (0.5 mg/kg/minutes) and epinephrine (0.03 mg/kg/minutes) to treat post-CPB vasoplegic syndrome.
- Post-operation, vasopressin (0.06 units/min) was started along with norepinephrine (0.23 mg/kg/minutes).
- Angiotensin-II was started at 20 ng/kg/min that further titrated to 40 ng/kg/min. Its remarkable effects were visible as the norepinephrine dose was reduced by 33.3% within the first hour.

Before operation	After operation
MAP < 55 mm Hg	BP 59/33 mmHg
Hemoglobin 8.5 g/dL	MAP 42 mm Hg
LVEF 25%	Heart rate 90 beats per minute
	Cardiac index 2.4 L/min/m²
	SVR 496 dynes/s ·cm^{-5}
	Hemoglobin 9 g/dL
	Chest tube output 200 mL in first hour
	Chest tube output 70 mL in second hour

Table 5: Pre- and post-operative parameters of the patients

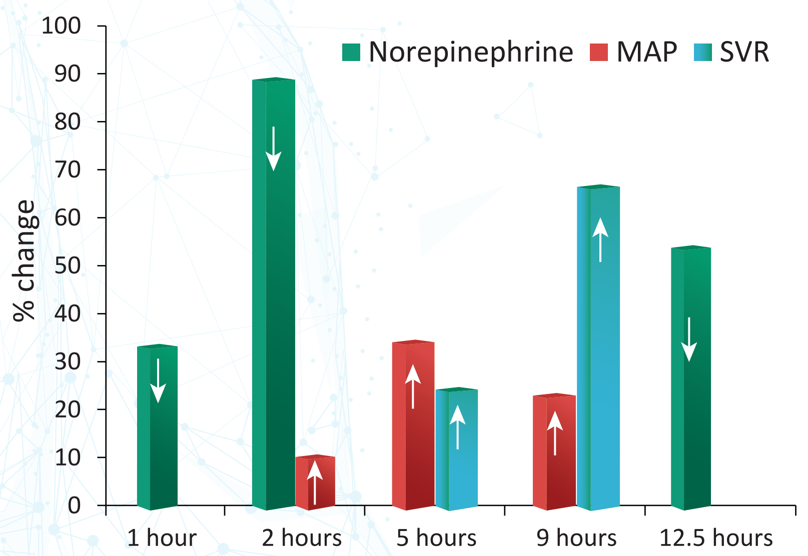


Figure 10: Percentage change in norepinephrine dose, MAP and SVR after use of angiotensin-II. ↓ is decrease in percentage, ↑ is increase in percentage

- Changes in norepinephrine dose, mean arterial pressure (MAP) and systemic vascular resistance (SVR) after angiotensin II administration is shown in Figure 10.

- After 20 hours of ICU admission, the patient was extubated and after 1.5 days of extubation, norepinephrine was discontinued.
- The patient was discharged after 12 days.

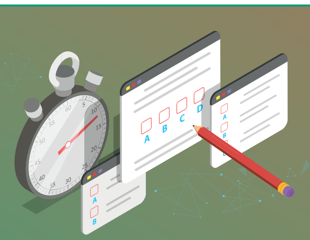
Conclusion

- Angiotensin-II is already used for Angiotensin-II in High Output Shock (ATHOS-3) study and proved to be beneficial for improvement of all-cause mortality in this previous study.
- Due to the patient's previous history of stage 3 chronic kidney disease and acute kidney failure, the prolonged intubation was avoided. This study first time used angiotensin-II in the treatment of vasoplegic syndrome, since its approval by the US-FDA, which showed beneficial role of the vasopressor, in terms of treatment success.
- Use of angiotensin-II is proved to be an excellent therapeutic option for treating vasoplegic syndrome in patients undergoing cardiac surgery.

Reference

Evans A, McCurdy MT, Weiner M, Zaku B, Chow JH. Use of angiotensin II for post cardiopulmonary bypass vasoplegic syndrome. The Annals of thoracic surgery. 2019 Jul 1;108(1):e5-7.

Interactive Capsule



Crossword

ACROSS

4. ______________ CPB is better than hyperoxic CPB as it decreases myocardial oxidative stress.

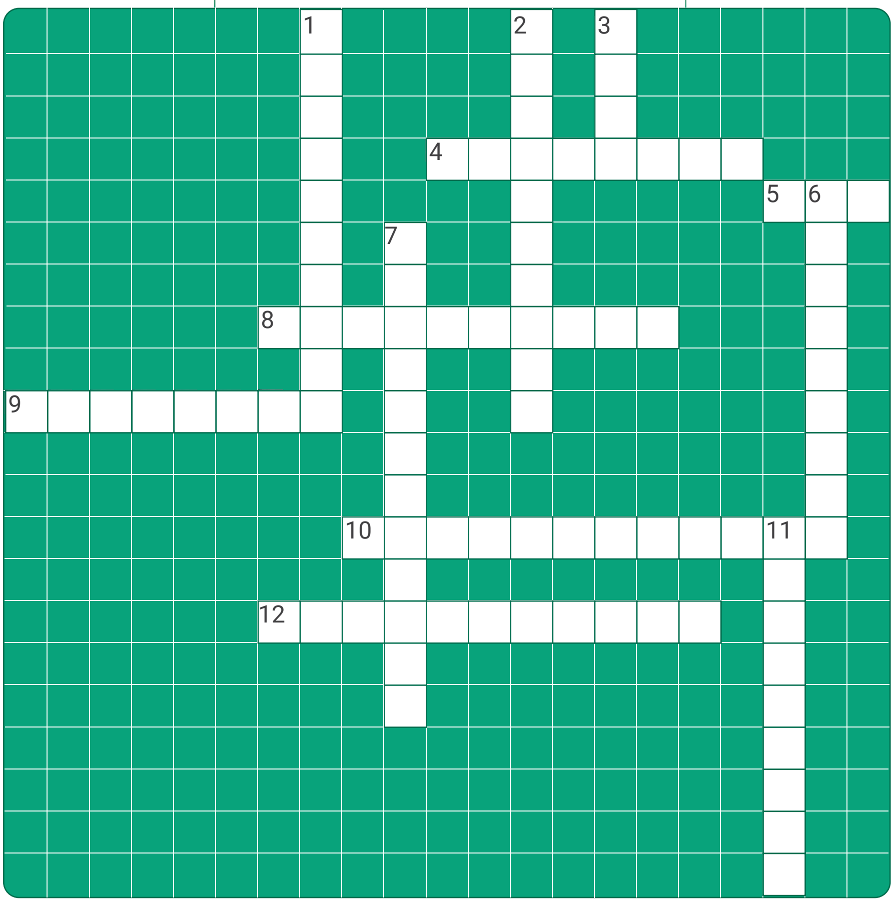
5. ______________ transfusion is safe during CPB surgery in FXII deficient patients.

8. ________________ is a protein, plays an essential role in clot formation.

9. _____________ generation during CPB is associated with increased bleeding.

10. CPB induced ________________ lead to excessive bleeding and worse patient outcomes.

12. ___________ is used as vasopressor to treat vasoplegic syndrome in patients undergoing CPB.



DOWN

1. A high-fidelity ________ environment can measure cognitive, technical and motion analysis of a basic CPB task.

2. A surgical opening in the middle of the chest to access the chest cavity for heart surgeries.

3. ________ allows a bloodless field during cardiac surgery similar to CPB, but unlike CPB it provides longer support for days to weeks.

6. The HRV components can be categorized into time domain, _________ domain and nonlinear measures.

7. A healthcare professional who operates an artificial heart-lung blood pump during surgery.

11. A device designed to measure activated clotting time during CPB surgery.

Coagulopathy	Angiotensin	Frequency	Simulation	FFP	Thrombin	Normoxic	ECMO	Perfusionist	Sternotomy	Fibrinogen	Hemochron

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