ISSUE 20

PRIME

Perfusion-Related Insights – Management and Evidence

- Specialty insights
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Editorial Letter

It is with immense pleasure that we present 20th issue of PRIME Newsletter — "Perfusion-Related Insights–Management and Evidence" — a quarterly scientific newsletter that includes review article, randomized control trial, recently published guideline, 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 is comprised of two articles. The first article summarizes recent methods for management of CPB-induced acute kidney injury. The second article under this section highlights the risk of prolonged ICU stay after cardiac surgery with CPB.

The first article of second section 'Basic Facts' outline serum biomarkers associated with severity of lung injury in pediatric patients and suggest potential therapeutic targets for future study. The second article sheds light on rewarming techniques for patient survival after hypothermic cardiac arrest.

The third section 'Practice Pearls' describes the possibility and usefulness of the autologous platelet-rich plasma collection from the CPB circuit after heparin administration. The next section 'Journal Talk' exhibits management of cardiac surgery-induced hyperlactatemia with targeted blood pressure during CPB.

The fifth section 'Expert Opinion' signifies the effectiveness of del Nido cardioplegia for myocardial protection in adults undergoing elective cardiac surgery and also to compare it with blood cardioplegia. Under the sixth and last section 'News Corner', updated guidelines on extracorporeal membrane oxygenation for COVID-19 patients is presented.

We hope this newsletter enriches your knowledge with the current practices and research updates in the field of CPB 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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PREVENTION AND MANAGEMENT OF ACUTE KIDNEY INJURY FOLLOWING CARDIOPULMONARY BYPASS

Introduction

Some associated problems with cardiopulmonary bypass (CPB) are hemolysis, capillary leak syndrome, and acute kidney injury (AKI). Around 18.2-30% of patients, who undergo CPB surgery, develops AKI, which is considered as an important predictor of morbidity and mortality in such patients. CPB-associated AKI is further responsible for poor clinical outcomes, longer hospital stays, stroke and mortality. Therefore, the mechanisms involved in CPB-associated AKI needs to be evaluated in order to prevent and manage the disease. The current study addressed the risk factors for CPB-associated AKI as well as summarized recent methods used to manage AKI after CPB.

Risk factors for CPB-associated AKI

The risk factors associated with AKI development following CPB is summarized in Table 1.

Risk factors	Significance
Age > 70 years	Relative risk 2-2.23, 95% CI, 1.33-3.76 (p<0.005)
Female sex	Odds ratio (OR) 1.21, 95% CI, 1.09-1.33 (p<0:001)
Smoking history	OR 2.01, 95% CI, 1.14-3.52 (p = 0.015)
Left ventricular ejection fraction < 35%	OR 1.25, 95% CI, 1.01-2.2 (p = 0.01)
Children with congenital heart disease	29-86% develops AKI
Estimated glomerular filtration rate < 60 mL/min/1.73m²	An independent risk factor for AKI following CPB
Serum creatinine (sCR) > 2.5 mg/dL	4.8 folds increased risk with 1mg/dL increase in sCR
Genetic polymorphisms (SNP rs1617640 in the promoter of the erythropoietin gene)	Patients with this allele causes increased erythropoietin concentrations and requires more frequent acute renal replacemernt therapy (RRT)
Hemoglobin levels < 9 g/dL	OR 1.16 per 1 g/dL decrease, 95% CI, 1.05-1.31 (p = 0.018)
Hemoglobin levels > 8 g/dL	Conservative use of red blood cell transfusion in these patients increases risk for AKI
Hematocrit < 24%	During CPB, 7% increase in relative risk of AKI per 1% decrease in the nadir haematocrit value
Lowest oxygen delivery (critical threshold of < 272 mL/min/m²) + peak postoperative serum creatinine levels	Best predictor for AKI
Delaying cardiac surgery for more than 24 hours of exposure to contrast agents	Cardiac surgery on the day of cardiac catheterization and use of higher dose of contrast agent are associated with an increased risk of AKI development
Longer CPB duration	Prolonged surgery time and time on CPB is contributing risk factor for developing AKI after CPB

Table 1: Risk factors for acute renal dysfunction following CPB

Renal Replacement Therapy

Early ultrafiltration along with RRT during postoperative period decreases the activity of the proinflammatory milieu and its effects. Moreover, in infants it prevents fluid overload and improves clinical outcomes.

Peritoneal Dialysis

- Early use of peritoneal dialysis (PD) for AKI along with low cardiac output removes fluid after cardiac surgery, that eases fluid restriction and thereby ameliorate the function of cardiopulmonary system. In addition, dialysis-associated complications does not occur during PD.
- In infants, who are susceptible to develop AKI, use of PD catheter results in an earlier negative fluid balance and extubation that improves inotrope scores and clinical outcomes.

Continuous Renal Replacement Therapy

- Continuous RRT or CRRT is a safe and effective method in infants and children undergoing cardiac surgery as it allow hyperalimentation by maintaining fluid and electrolyte homeostasis.
- Although CRRT preserves renal function in patients after operation, but its high cost limited its utilization.

Hemodialysis

- Immediate start of hemodialysis (HD) with decrease in urine output (< 30 mL/hour) increases patient survival.
- In high-risk patients, use of perioperative prophylactic HD lowers mortality and morbidity rates during the surgery.
- In comparison to PD, the modern CRRT and HD can directly remove fluid and has the facility for online monitoring of solute clearance.

Further Perspective

Some urinary biomarkers (NGAL, IL-18, L-FABP), and blood biomarkers (renin, IL-8 and macrophage migration inhibitory factor) correlates with disease severity as well as risk of CPB-associated AKI.

Conclusion

- Recent finding of two novel susceptibility loci (chr3p21.6 and BBS9) for AKI following CPB may help to identify patients at preoperative screening and to take necessary prevention for decreasing AKI development in them.
- Use of pump flow, hemoglobin, oxygen saturation, and arterial oxygen tension may deliver adequate oxygen. Other alternatives are redesign of the circuit to minimize the volume, use of retrograde autologous priming, and the management of intraoperative fluid administration. Hyperbaric oxygen therapy and oxygen preconditioning is also used to prevent AKI after CPB.
- Statin therapy is also gaining popularity as it significantly reduces sCr and reduces the incidence of postoperative AKI.
- Use of RRT is proved to be beneficial for AKI after CPB.
- Free hemoglobin and iron, excess oxidative stress, and endothelial dysfunction can be new therapeutic targets for reducing AKI after CPB surgery and for improving patient outcomes.

Reference

Liu D, Liu B, Liang Z, Yang Z, Ma F, Yang Y, Hu W. Acute kidney Injury following cardiopulmonary bypass: a challenging picture. Oxidative Medicine and Cellular Longevity. 2021 Mar 9;2021.

RISK FACTORS ASSOCIATED TO PROLONGED ICU STAY IN PATIENTS AFTER CARDIAC SURGERY WITH CARDIOPULMONARY BYPASS

Introduction

Patient, who requires cardiopulmonary bypass (CPB) during cardiac surgery needs to stay in the intensive care unit (ICU) postoperatively, sometimes for 3-7 days. Several risk factors, viz, age, oxygen index, type and duration of surgery, hypertension, blood transfusion, etc. are responsible for such prolonged length of stay (LOS) in the ICU. Furthermore, prolonged LOS is associated with higher complication rates, hospital costs and mortality rates. Therefore, this retrospective observational study investigated the incidence of prolonged LOS in the ICU after cardiac surgery with CPB, along with the associated risk factors.

Methods

- Data of 395 ICU patients (age ≥ 18 years), who underwent cardiac surgery [including isolated coronary artery bypass grafts (CABG), isolated or multiple valve surgery, or valve surgery and CABG] with CPB and were alive for next 72 hours, was collected from hospital database and included in this study.
- Patient demographics, illness, perioperative clinical data, and ICU LOS were gathered and analysed for risk factors of prolonged ICU LOS using Univariate analysis and Binary logistic regression modelling.

Results

- Patient's mean age was 58 years, 47.1% of the patients were females, and 6.3% had previously undergone cardiac surgery.
- The median ICU LOS was 50.9 hours, and 137 (34.7%) patients had a prolonged ICU LOS (>72.0 hours). Valve surgery was the most common technique performed in majority of patients (59.5 %).
- Univariate analysis showed that 16 variables ($p<0.05$) were accountable for prolonged ICU LOS (Table 2).
- Logistic Regression analysis showed that 8 variables were significantly ($p<0.05$) associated with prolonged LOS (Table 3).

Characteristics	ICU LOS ≤72 h (n = 258)	ICU LOS ≤72 h (n = 258)
Preoperative:		
Age (years), mean ± SD	56.1 ± 11.8	61.3 ± 10.5
NT-proBNP (pg/ml), median Surgery type, median	847.0	1468.0
Surgery type, median		
◆ CABG or valve surgery	216	94
◆ CABG + valve surgery	42	43
History of cardiac surgery, median	9	16
Hypertension, median	74	56
NYHA class, median		
◆ I or II	162	71
◆ III or IV	96	66
Intraoperative:		
Surgery Time (minutes), mean ± SD	294.8 ± 67.7	338.7 ± 92.9

Characteristics	ICU LOS ≤72 h (n = 258)	ICU LOS ≤72 h (n = 258)
CPB Duration (minutes), mean ± SD	127.4 ± 41.3	156.8 ± 56.6
Red Blood Cell (U), mean ± SD	4.1 ± 2.4	5.5 ± 3.1
Aortic occlusion duration (minutes), mean ± SD	86.6 ± 36.8	95.7 ± 36.4
Postoperative:		
PaO_2/FiO_2 (within 6 hours of surgery), median		
◆ > 400 mmHg	91	14
◆ 300-400 mmHg	96	55
◆ < 300 mmHg	69	555
Postoperative atrial arrhythmia, median	26	41
Postoperative ventricular arrhythmia, median	11	32
Non-invasive assisted ventilation use, median	10	36
NT-proBNP (pg/L), median	379	848
Prolonged mechanical ventilation, median		
◆ ≤ 24 h	233	69
◆ > 24 h	25	68

Table 2: Univariate analysis of patient characteristics before, during and after cardiac surgery with CPB. NT-proBNP: N-terminal pro-brain natriuretic peptide, NYHA: New York Heart Association, PaO_2/FiO_2: Arterial blood partial pressure of oxygen/fraction of inspired oxygen

Characteristics	Odd Ratio (n = 395)	95% CI
CABG + valve surgery	2.24	1.15-4.37
CPB Duration	1.01	1.01-1.02
Red Blood Cell	1.14	1.03-1.28
PaO_2/FiO_2 (within 6 hours of surgery)		
◆ 300-400 mmHg	3.29	1.47-7.38
◆ < 300 mmHg	3.75	1.65-8.51
Postoperative atrial arrhythmia	2.52	1.18-5.40
Postoperative ventricular arrhythmia	3.15	1.30-7.62
Prolonged mechanical ventilation	4.94	2.54-9.59
Non-invasive assisted ventilation use	7.71	2.99-19.92

Table 3: Logistic Regression analysis of LOS after cardiac surgery with CPB adjusted by age and sex. PaO_2/FiO_2: Arterial blood partial pressure of oxygen/fraction of inspired oxygen

Conclusion

- Cardiac surgery patients are at risk of extended ICU stays, especially who are having CABG in combination with valve surgery, peri-operative infusion, and a longer CPB duration.
- Care should be taken during early post-operative period for correction of atrial and ventricular arrhythmia, respiratory circulation and to prevent further complications.
- A thorough assessment should be performed with early evaluation to identify patients at risk of prolonged ICU LOS.

Reference

Zhang X, Zhang W, Lou H, Luo C, Du Q, Meng Y, Wu X, Zhang M. Risk factors for prolonged intensive care unit stays in patients after cardiac surgery with cardiopulmonary bypass: A retrospective observational study. International journal of nursing sciences. 2021 Oct 10;8 (4):388-93.

PREDICTION OF CARDIOPULMONARY BYPASS-INDUCED LUNG INJURY IN PEDIATRIC PATIENTS USING PROTEIN BIOMARKERS

Introduction

Cardiopulmonary bypass (CPB) causes systemic inflammation, which causes lung injury and often necessitates the use of prolonged mechanical ventilation. To predict the risks of such consequences, biomarkers of systemic inflammation are required. The current study hypothesized that specific serum proteins may be employed as biomarkers to predict the severity of lung injury following cardiac surgery in pediatric patients. This retrospective chart review study aimed to discover serum biomarkers that can provide a prognosis of the severity of lung injury and suggest potential therapeutic targets for future study.

Methods

- Pediatric patients (< 8 years old), who underwent CPB surgery for similar complexity according to Society of Thoracic Surgeons-European Association for Cardiothoracic Surgery (STAT 3 or 4) were included in the study.
- Clinical variables were gathered and combined with unbiased proteomic analysis of frozen plasma samples from:
    - A study group (patients with mechanical ventilation > 48 hours post surgery)
    - A control group (patients with mechanical ventilation < 48 hours post surgery)
- Patients in both groups were well matched for age, weight, and CPB duration.

Results

- A total of 483 proteins were identified on proteomic analysis of 4 control and 4 study patients.
- There was no significant difference between the groups regarding age, weight and STAT category.
- Mean length of mechanical ventilation was 30 hours and 110 hours in the control and study group respectively ($p < 0.01$).
- 36 out of 178 proteins, 18 of 140 proteins and 25 of 166 proteins were significantly different ($p < 0.05$) before CPB, at 0 hour after CPB and at 48 hours post CPB respectively between the groups. Top increased and top decreased proteins at these time points are shown in Figure 1.
- ICU and hospital stay duration were comparabale between the groups.
- Pathway analysis revealed that the top pathway involved was cytoskeleton remodeling. Other pathways involved were immune response and blood coagulation.
- Proteoglycan 4 was validated by ELISA and no differences was found at the pre-CPB time point. However, the study group (ng/mL) had lower levels of proteoglycan 4 compared to control group (128 ± 67 vs. 195 ± 160 ng/mL, $p<0.05$) after 48 hours of CPB.

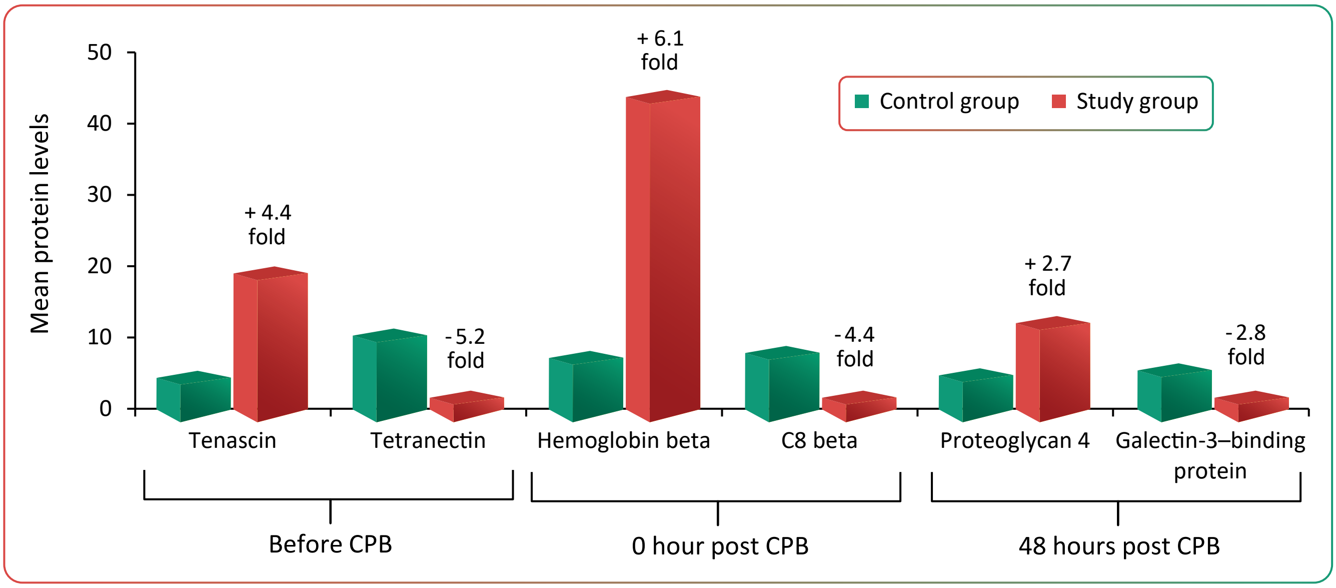


Figure 1: Comparison of top hit proteins of the proteomic analysis before CPB and 0 and 48 hours after CPB in pediatric patients of control (n=4) and study (n=4) groups

Conclusion

- Biomarkers found at pre CPB may suggest risk factors (e.g., coagulation disorders), but those found at 0 hour and 48 hours post CPB may reflect ongoing pathobiology mechanisms.
- The validation study confirmed for the first time that lower plasma levels of proteoglycan 4 were associated with longer mechanical ventilation (> 2 days) in pediatric patients after CPB.
- The proteomic analysis found multiple proteins involved in cytoskeleton remodeling, blood coagulation, complement and immune response activation, and left scope of research on the multiple pathways as well as the possible therapeutic targets in future.

Reference

Asfari A, Hock KM, Byrnes JW, Borasino S, Halloran BA, Mobley JA, Ambalavanan N. Biomarkers for Adverse Lung Injury Following Pediatric Cardiopulmonary Bypass. Critical care explorations. 2021 Sep;3(9).

REWARMING TECHNIQUES IN PATIENTS WITH HYPOTHERMIC CARDIAC ARREST

Introduction

Previous literature suggested higher survival rate with extracorporeal life support (ECLS) over cardiopulmonary bypass (CPB) after successfully rewarming and resuscitation of patients who were suffering from hypothermic cardiac arrest (HCA). The current review and meta-analyses aimed to (i) evaluate survival to hospital discharge after rewarming from HCA using ECLS, and (ii) investigate whether the probability of surviving to hospital discharge differed depending on whether the patients underwent rewarming with CPB or/and extracorporeal membrane oxygenation (ECMO).

Methodology

- Published literature including references with an abstract in English, French or German was reviewed.
- Primary outcome was survival to hospital discharge.
- Neurological outcome, differences in relative risks (RR) of survival, related to applied rewarming technique, sex, asphyxia, and witnessed or unwitnessed HCA was reviewed.
- Hypothermia outcome prediction probability score after extracorporeal life support (HOPE) was calculated in patients having individual data.

Results

- Outcomes of 464 patients with HCA from 23 case observation studies who underwent rewarming with CPB (n=245) or/and ECMO (n=219) were included.
- 172 patients (37%) survived to hospital discharge, with 76 (31%) surviving after CPB and 96 (44%) surviving after ECMO.
- 87% and 75% of CPB and ECMO group respectively had good neurological outcomes. The chance of survival in ECMO group, compared to CPB group in terms of good vs. poor neurological outcome was RR 0.86, CI 95% 0.75–0.99 (p = 0.047), i.e., 14 % less probability of good neurological outcome with ECMO.
- In comparison to CPB, the possibility of surviving with a poor neurological outcome (instead of dying) was ~200% higher after using ECMO. Overall, ECMO had a 41% (p = 0.005) higher chance of survival than CPB.
- A man and a woman had 46% (p = 0.043) and 31% (p = 0.115) higher chances of survival with ECMO than CPB, respectively.
- Avalanche victims had the lowest chance of survival, followed by drowning and people losing consciousness in cold environments (Figure 2).
- Asphyxia, unwitnessed HCA, male sex, high initial body temperature, low pH, and high serum potassium (s-K+) levels were all linked to a lower chance of survival when analysed using logistic regression.
- Overall mean predictive surviving probability (HOPE score; n=134) in patients with individual data was 33.9 ± 33.6% with no significant difference between ECMO and CPB-treated patients.

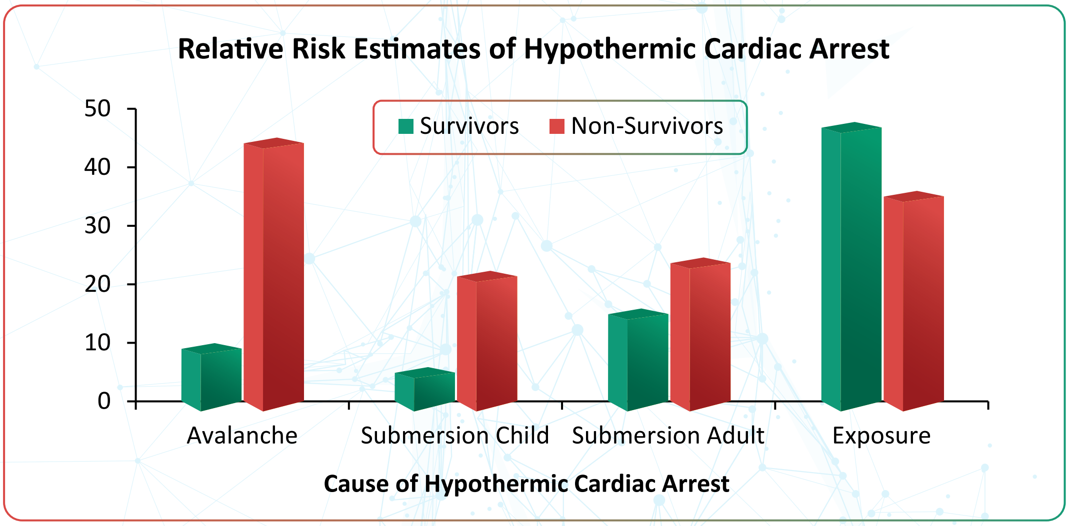


Figure 2: Relative risk estimates of hypothermic cardiac arrest

Conclusion

- The chance of surviving was significantly higher after rewarming with ECMO, as compared to CPB, and in patients with witnessed compared to unwitnessed HCA.
- Avalanche victims had the lowest probability of survival.
- Male sex, high initial body temperature, low pH, and high s-K+ were all factors linked to a low chance of survival.

Reference

Bjertnæs LJ, Hindberg K, Næsheim TO, Suborov EV, Reierth E, Kirov MY, Lebedinskii KM, Tveita T. Rewarming from hypothermic cardiac arrest applying extracorporeal life support: a systematic review and meta-analysis. Frontiers in medicine. 2021;8.

AUTOLOGOUS PLATELET-RICH PLASMA COLLECTION FROM CARDIOPULMONARY BYPASS CIRCUIT AFTER EXTRACORPOREAL CIRCULATION INDUCTION DURING SURGERY

Introduction

During cardiac surgery, when blood is exposed to the cardiopulmonary bypass (CPB) circuit, this results in intraoperative thrombocyte impairment that affects both thrombocyte count and function. Notably, homologous platelet transfusion is used to treat platelet impairment. Autologous platelet-rich plasma (PRP) collection is suitable before the injection of heparin and establishment of cardiopulmonary bypass (CPB); however, preoperative PRP collection takes ~90 minutes and thus delays the surgery. The current study aimed to evaluate the possibility and usefulness of the autologous PRP collection from the CPB circuit after heparin administration and to assess its effect on the aggregative function.

Methods

- Using the Haemonetics Component Collection System®, autologous PRP was prepared from 72 CPB patients by drawing blood from the CPB circuit immediately after CPB was started.
- Blood samples were obtained at three time points for analysis:
  - A: beginning of surgery before heparin administration
  - B: immediately after heparin reversal with protamine and the cessation of CPB
  - C: after the collected autologous PRP was returned to the patient
- Platelet count and platelet aggregation ability were analyzed.
- Adenosine diphosphate (ADP, 1.0 μM and 3.0 μM), and collagen (0.25 μg/ml and 2.0 μg/ml) were used to induce platelet aggregation.

Results

- The mean patient age was 72.4 ± 12.9 years, with male to female ratio of 49:23.
- 42 cases had valvular disease surgery, 26 had aortic aneurysm surgery, and 4 cases had coronary artery bypass surgery or other surgeries. The average operation time was 378.6 ± 141.8 minutes.
- In autologous PRP, the mean platelet count was 5.5 (range: 3–14) units.
- Platelet count decreased by 118.3 (±31.4) × 1000/μl from A to B and increased by 27.3 (± 17.2) × 1000/μl from B to C.
- Maximum agglutination ability was decreased significantly ($p<0.01$) from point A to point B using both ADP (1.0 μM and 3.0 μM) and collagen (0.25 μg/ml and 2.0 μg/ml). On the other hand, agglutination ability was increased ($p<0.01$) from point B to point C using ADP (1.0 μM and 3.0 μM, $p<0.01$) and collagen (0.25 μg/ml, $p=0.10$ and 2.0 μg/ml, $p<0.01$) as shown in Figure 3.

- Duration of surgery, CPB and cross clamp was significantly higher in hypothermic aortic surgery group, whereas, the lowest body temperature was significantly low in hypothermic aortic surgery group.
- Hypothermic aortic surgery group required greater number of platelet blood transfusions.

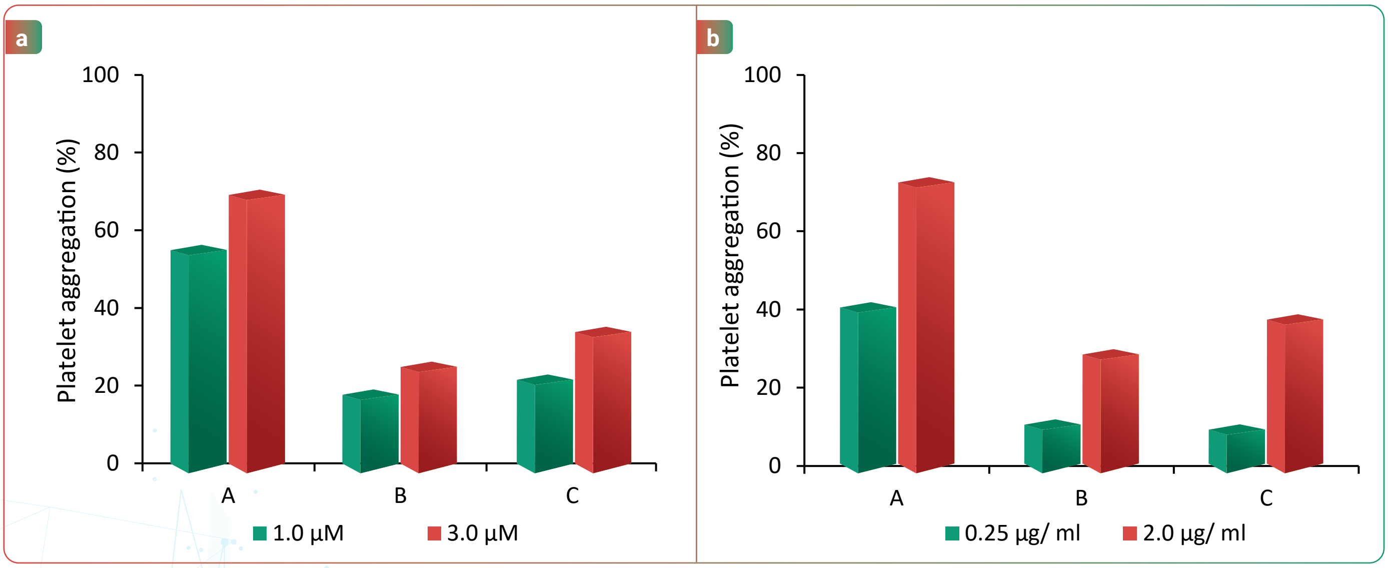


Figure 3: Percentage change in maximum platelet aggregation ability between different time points using (a) ADP and (b) collagen

Conclusion

- Autologous PRP with effective agglutination ability can be safely collected by drawing blood from the CPB circuit.
- Platelet count and aggregation ability both dropped considerably after CPB, including autologous PRP collection.
- Returning autologous PRP to patients after they stopped receiving CPB, enhanced their blood platelet count and aggregation ability.
- This strategy could be an effective countermeasure to the blood product shortages that our society perhaps going to face in the near future.

Reference

Honda T, Kanaoka Y, Furukawa H, Tamura T, Kuwada N, Yamasawa T, Watanabe Y, Yunoki Y, Tabuchi A, Tanemoto K. Intraoperative collection of autologous platelet-rich plasma from the cardiopulmonary bypass circuit upon initiation of extracorporeal circulation. Journal of Cardiothoracic Surgery. 2021 Dec;16(1):1-9.

MANAGEMENT OF CARDIAC SURGERY-INDUCED HYPERLACTATEMIA WITH TARGETED BLOOD PRESSURE DURING CARDIOPULMONARY BYPASS

Introduction

Hyperlactatemia is a common complication of cardiac surgery that has been linked to a poor prognosis as well as mortality. Postoperative hyperlactatemia reduction is necessary for improving the prognosis of cardiac patients. High mean arterial pressure (MAP) during cardiopulmonary bypass (CPB) decreases blood flow to capillaries and microcirculation perfusion, resulting in lowered blood lactate levels. According to European Adult Cardiac Surgery CPB Guidelines, 2019 peri-CPB MAP can be safely maintained between 50 and 80 mmHg. Therefore, this study aimed to test the primary hypothesis that MAP (70–80 mmHg), maintained by norepinephrine titration during CPB may reduce the post-surgical lactate level and helps in recovery of the patient.

Methods

- This single-center, randomized controlled trial included adult patients (age >18 years, blood lactate level <1.6 mM•L −1), undergoing cardiac valve surgery and devided them into two groups (n=): low MAP (L-MAP) (50-60 mmHg) and high MAP (H-MAP) (70 and 80 mmHg).
- Blood lactate levels were detected before the operation (T_0), at the end of CPB (T_1), at the end of the operation (T_2), 1 hour after the operation (T_3), 6 hours after the operation (T_4) and 24 hours after the operation (T_5).
- The primary endpoint was measurement of blood lactate level at T_2.
- The secondary endpoints were measurement of the blood lactate level at T_1, T_3, T_4, and T_5; the dose of epinephrine and dopamine at T_5; time to extubation; length of ICU stay; need of readmission within 30 days; and mortality within 1 year.

Results

- A total of 40 patients were enrolled in this study, in whom, the median MAP was successfully maintained within their target blood pressure range (57 mmHg in L-MAP vs. 76 mmHg in H-MAP). Maintenance of MAP (within their target blood pressure range) before, during and after the surgery is shown in Figure 4.

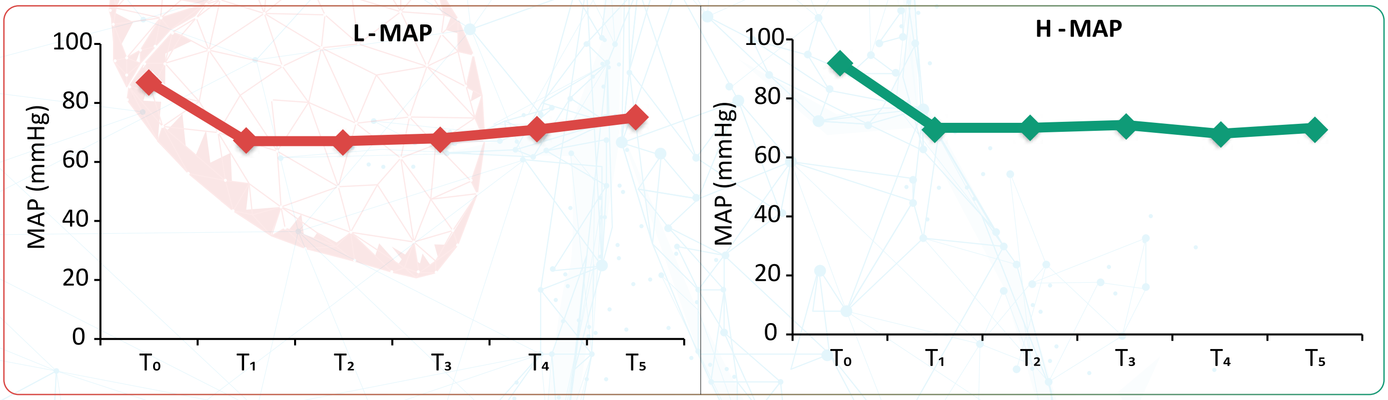


Figure 4: Median MAP during CPB in the two groups

- The lactate level in the H-MAP group was significantly lower than that in the L-MAP group at the end of the operation (3.1 vs. 2.1, $p=0.008$) and at the end of CPB and 1 hour after surgery.
- Blood lactate levels in both the groups significantly increased from T_0 to T_4 and decreased from T_4 to T_5.
- No significant difference was found in anesthetic and vasopressor usage between the two groups.
- The dose of epinephrine within 24 hours after the operation, time to extubation and length of stay in the ICU in the L-MAP group were significantly higher than those in the H-MAP group (Table 4).

	L-MAP Group (n=20)	H-MAP Group (n=20)
Baseline Characteristics:		
Operation Time (minutes), median	270	260
Aortic Occular Time (minutes), median	90	110
CPB Time (minutes), median	140	150
Post CPB Time (minutes), median	84	70
Perioperative Variables:		
Blood Glucose during CPB ($mM \cdot L^{-1}$), median	8.4	8.6
Urine volume during CPB, median	300	600
Extubation Time (hours) , median	17	11*
Length of ICU Stay (hours) , median	43	36*
Readmission within 30 days, frequency	0	0
Mortality in 1 year, %	0	0

Table 4: Clinical data of the patients. *p<0.05

Conclusion

- Maintaining a relatively higher MAP during CPB resulted in a lower blood lactate level at the end of surgery, lower epinephrine consumption, and a shorter extubation time and length of stay in the ICU after surgery.
- A relatively high blood pressure may be more conducive for enhancing tissue perfusion and oxygen flow in cardiac surgery patients.

Reference

Miao Q, Wu DJ, Chen X, Xu M, Sun L, Guo Z, He B, Wu J. Target blood pressure management during cardiopulmonary bypass improves lactate levels after cardiac surgery: a randomized controlled trial. BMC anesthesiology. 2021 Dec;21(1):1-8.

Expert Opinion

THE EFFECTIVENESS OF DEL NIDO CARDIOPLEGIA FOR MYOCARDIAL PROTECTION IN ADULTS

Introduction

Myocardial protection during cardiac surgery provides hypothermia-induced metabolic activity reduction and cardioplegia-induced diastolic arrest of the heart's electrical activity, which in turn creates a still, bloodless field for surgical accuracy. del Nido cardioplegia (DNC) with prolonged arrest time is traditionally employed for pediatric congenital heart surgery for protection of their immature heart. However, it is now widely used in adult cardiac surgery. The current historical cohort study aimed to collect secondary data to compare the safety and efficacy of DNC with blood cardioplegia (BC).

Methods

- Patients (18 to 80 years, n=286) who underwent elective cardiac surgery [coronary artery bypass grafting (CABG), aortic (AVR) and mitral (MVR) valve replacement, double valve replacement (DVR), MVR with tricuspid annuloplasty (MVR+TAP), and DVR with tricuspid annuloplasty (DVR+TAP)] with cardiopulmonary bypass (CPB), requiring cross-clamping of the aorta as well as the cardioplegia, were included in the study.
- 143 patients were selected in each BC and DNC groups, who had either of CABG (n=45), AVR (n=34), MVR (n=27), DVR (n=28), MVR+TAP (n=5), or DVR+TAP (n=4) surgery.
- Patient demographics, intraoperative variables, and postoperative variables were studied and analyzed.

Results

- Both the groups were well matched for age, gender, ejection fraction and cardiac risk factors.
- CPB and clamp time was comparable between the groups (Table 5).
- Patients in DNC group (1.13) required significantly less ($p<0.001$) redosing of cardioplegia, compared to BC group (2.35).
- Intraoperative and postoperative blood transfusions were comparable between the groups.
- The rate of clamp release ventricular fibrillation was comparable between the groups.
- The DNC group had a lower postoperative left ventricular ejection fraction than the BC group (53.4 vs. 56.0, $p=0.001$).
- In both groups, there was no 30-day mortality or postoperative myocardial infarction.

Variables	DNC (n=143)	BC (n=143)
Intraoperative:		
CPB Time (min), median	90.0	87.0
Cross Clamp Time (min), median	59.0	57.0
Cardioplegia Doses, mean	1.13	2.35

Variables	DNC (n=143)	BC (n=143)
Hb a (g/dL), mean	13.2	12.9
Hb b (g/dL), mean	8.0	7.9
Blood Products, mean	75	67
RBC 1, frequency	35	36
RBC 2, frequency	23	20
RBC 3, frequency	13	10
RBC 4, frequency	1	0
Fresh Frozen Plasma 1, frequency	1	1
Fresh Frozen Plasma 2, frequency	1	1
Fresh Frozen Plasma 3, frequency	4	0
Platelets, frequency	8	7
Postoperative:		
Hb ICU 6 h (g/dL), mean	10.2	9.9
Hb ICU 24 h (g/dL), mean	9.6	9.3
Blood Products, mean	30	36
RBC 1, frequency	18	26
RBC 2, frequency	4	5
RBC 3, frequency	3	0
RBC 4, frequency	2	2
Fresh Frozen Plasma 1, frequency	0	1
Fresh Frozen Plasma 2, frequency	1	0
Fresh Frozen Plasma 3, frequency	0	1
Platelets, frequency	7	4
ICU (days), mean	3.1	3.1
Postoperative Complications, median	8	12
Postoperative Hospital days, frequency	7	7
Stroke, frequency	1	1

Table 4: Characteristics of the patients in DNC versus BC groups during and after the surgery. Hb: Hemoglobin, a: baseline and before anesthesia, b: during CPB 10–15 min after giving cardioplegia, RBC: Red Blood Cell, ICU: Intensive Care Unit

Conclusion

- This study showed diversity in type of cardiac surgery and use of DNC in such patients.
- DNC requires substantially less redosing and the subsequent less hemodilution and lower need of transfusion, allowing surgeons to do an uninterrupted surgery with improved productivity.
- DNC provides similar surgical workflow as BC as well as showed to have similar clinical outcomes and myocardial protection.
- Therefore, DNC is a safe alternate to BC in adult patients undergoing CABG and valve surgeries.

Reference

George G, Varsha AV, Philip MA, Vithayathil R, Srinivasan D, Princy FS, Sahajanandan R. Myocardial protection in cardiac surgery: del Nido versus blood cardioplegia. Annals of Cardiac Anaesthesia. 2020 Oct;23(4):477.

UPDATED 2021 GUIDELINES ON EXTRACORPOREAL MEMBRANE OXYGENATION FOR COVID-19 PATIENTS

Introduction

Extracorporeal membrane oxygenation (ECMO) becomes more apparent with the unfolding of the pandemic and evident to be a therapeutic option for patients suffering from acute respiratory distress syndrome (ARDS) due to coronavirus disease 2019 (COVID-19). The current article is an updated guideline from the extracorporeal life support organization (ELSO) describing the role of ECMO for those patients. This guideline summarizes currently available literature for updating the previous guidelines, as well as to highlight the required care for COVID-19 patients receiving ECMO, and to recommend an alteration of ECMO utilization during a pandemic.

Indication of ECMO

Recommended ARDS management and indication for ECMO use is shown in Figure 5.

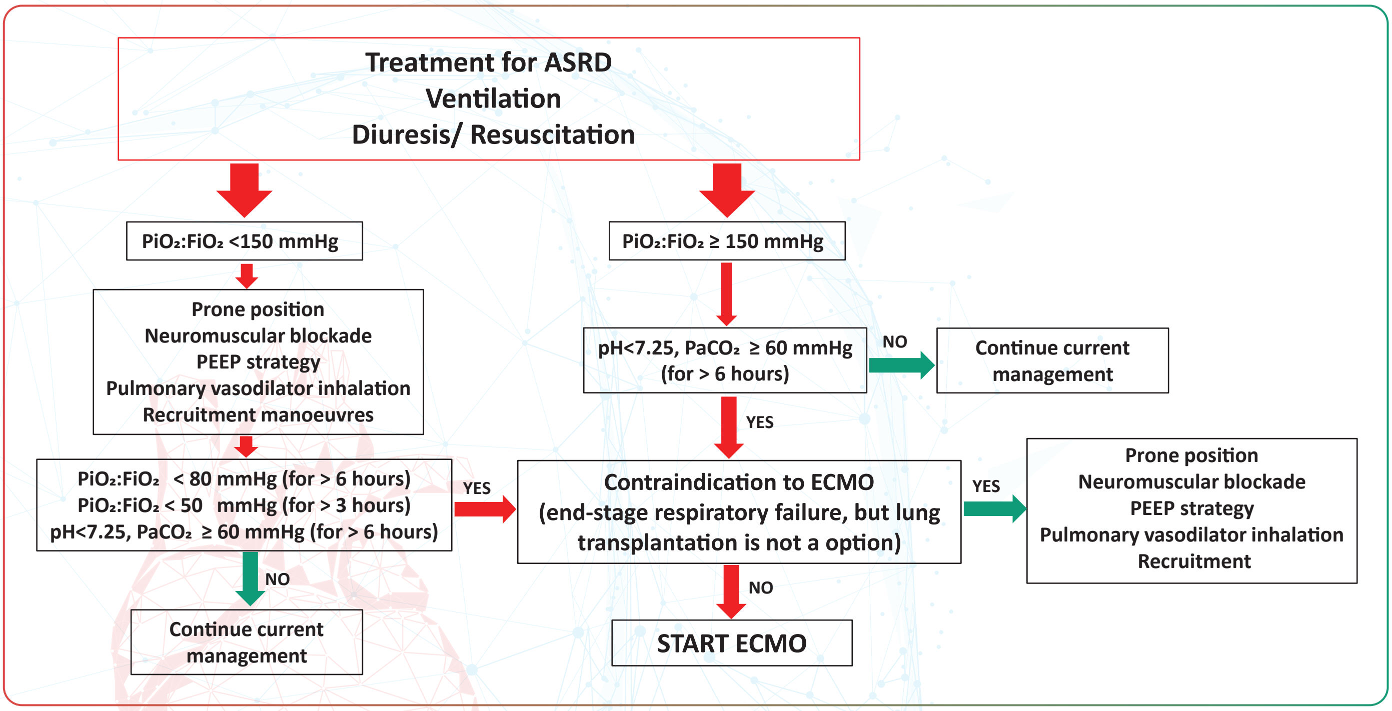


Figure 5: Conventional therapies for ARDS management. PaO_2:FiO_2 is partial pressure of oxygen in arterial blood to the fractional concentration of oxygen in inspired air, $PaCO_2$ is partial pressure of carbon di-oxide in arterial blood, PEEP is positive end-expiratory pressure

Cannulation strategy

Conventional venovenous (V-V), venoarterial (V-A), veno-arteriovenous (V-AV), and V-V dual-lumen cannulas are recommended depending on the patient's need.

Pulmonary strategy

- There is no data suggesting that COVID-19 patients getting V-V ECMO should be treated differently than patients with low-volume, low-pressure ventilators.
- Percutaneous tracheostomy appears to be a safe for COVID-19 patients.
- Investigation is still going on for prone position.
- It is feasible to use awake ECMO during early extubation in COVID-19.

Hematologic & hemodynamics monitoring

- COVID-19-induced coagulopathy appears to increase the risk of both thrombotic and hemorrhagic events that when normalized in COVID-19 patients, it matches the previous published data.
- Low threshold to pursue imaging for suspected deep venous thrombosis is suggested.
- Elevated cytokine profiles have been observed in COVID-19, but seem to be lower than in other causes of ARDS, sepsis and chimeric antigen receptor T-cell-mediated cytokine release syndrome. Extracorporeal hemadsorption or elimination therapies can only be recommended within the context of clinical trials.
- Currently, there is no evidence to support deviation from usual institutional practice for blood transfusion thresholds during ECMO.
- Remaining vigilant to detect acute hemodynamic deterioration during V-V ECMO (a result of COVID-19 mediated cardiac complications like acute coronary syndrome, myocarditis, acute right ventricular failure, stress cardiomyopathy, or pulmonay embolism) is recommended.

General recommendation

- The local institutional policies and previous ELSO COVID-19 guidelines should be referred for recommendations on methods for PPE use and conservation, when facing inadequate supply.
- Although SARS-CoV-2 does not spread from the blood to the gas side of polymethylpentene membrane lungs, but routine scavenging of membrane lungs gas outlet or use of viral filter is still not recommended.
- Remaining vigilant is suggested for high rates of ventilator associated pneumonia and bacteremia.
- ECMO mobilization may improve outcomes for extended runs and may act as a bridge to transplant, but the latest data do not refute or support rehabilitation on ECMO.

ECMO for pediatric patients with COVID-19

- According to ELSO guidelines, similar strategy is suggested for selection of pediatric patients with COVID-19 induced respiratory failure, requiring ECMO.
- Dual-lumen or two-site cannulation with necessary size is recommended. V-A support is suggested instead of V-V, in case of children with COVID-19–related myocarditis or severe respiratory disease.
- Institutional and national guidelines for ECMO management should be followed.

Conclusion

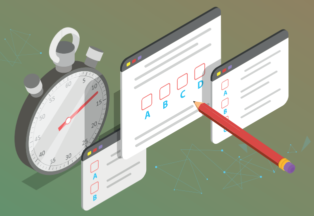
- Patients with COVID-19 and severe respiratory failure can be treated with V-V ECMO.

- Conventional guidelines should be followed for the selection and management of ECMO patient across a geographic region.
- Networks within geographic regions should be formed by ECMO centers to pool resources and coordinate patient referrals for ECMO. Mobile ECMO is also feasible and may be conducted safely for patients with COVID-19.
- Potential discontinuation of ECMO in case of perceived futility should be clearly discussed with patients and their surrogate decision-makers.
- Children may rarely require ECMO support for severe ARDS, myocarditis, or multisystem inflammatory disease. In case they require, the recommended guidelines should be followed.

Reference

Badulak J, Antonini MV, Stead CM, Shekerdemian L, Raman L, Paden ML, Agerstrand C, Bartlett RH, Barrett N, Combes A, Lorusso R. Extracorporeal membrane oxygenation for COVID-19: updated 2021 guidelines from the Extracorporeal Life Support Organization. Asaio Journal. 2021 May;67(5):485.

Interactive Capsule



Perfusion Quiz (Multiple Choice Questions)

1. One of the reason for prolonged length of ICU stay after cardiac surgery is:

a) Short mechanical ventilation
b) Younger age
c) Coronary artery bypass grafts in combination with valve surgery
d) Shorter CPB duration

2. Which of the following is a risk factor for CPB-associated acute kidney injury?

a) Serum creatinine < 2.5 mg/dL
b) Optimum oxygen delivery
c) Young patient
d) Hemoglobin levels < 9 g/dL

3. Maintaining a relatively higher mean arterial pressure during CPB resulted in the following conditions, except:

a) Post-surgery hyperlactatemia
b) Low epinephrine consumption
c) Shorter extubation time
d) Shorter ICU stay

4. Myocardial protection by means of del Nido Cardioplegia during cardiac surgery provides all of the following except:

a) Lower need of transfusion
b) Frequent cardioplegia redosing
c) Less hemodilution
d) Still and bloodless field for surgeons

5. Top pathway involved with severity of lung injury in children is:

a) FoxO signaling pathway
b) Blood coagulation pathway
c) Cytoskeleton remodeling pathway
d) MAPK signaling pathway

6. Treatment for acute kidney injury includes:

a) Reduce antioxidant level
b) Start renal replacement therapy
c) Lower hemoglobin concentration
d) Start hemodialysis after increased urine output

7. Extracorporeal membrane oxygenation is recommended when:

a) End stage respiratory failure
b) $PiO_2:FiO_2$ > 190 mmHg, pH <7.25, $PaCO_2$ ≥ 80 mmHg (for > 6 hours)
c) $PiO_2:FiO_2$ > 90 mmHg, pH >7.25, $PaCO_2$ ≤ 80 mmHg (for > 6 hours)
d) $PiO_2:FiO_2$ >/< 150 mmHg, pH <7.25, $PaCO_2$ ≥ 80 mmHg (for > 6 hours)

8. According to European Adult Cardiac Surgery CPB Guidelines, mean arterial pressure during CPB must be:

a) 40-50 mmHg
b) 80-110 mmHg
c) 50-80 mmHg
d) 70-100 mmHg

Coronary artery bypass grafts in combination with valve surgery	Hemoglobin levels < 9 g/dL	Post-surgery hyperlactatemia	Frequent cardioplegia redosing	Cytoskeleton remodeling pathway	Start renal replacement therapy	$PIO_2:FIO_2$ >/< 150 mmHg, pH <7.25, $PaCO_2$ ≥ 80 mmHg (for > 6 hours)	50-80 mmHg

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The author **WorkSure India** & **NeoCrest Life Sciences** and the reviewer have, as far as it is possible taken care to ensure that the information given in this PRIME Newsletter Issue 20 is accurate and up to date.

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