ISSUE 21

PRIME

Perfusion-Related Insights – Management and Evidence

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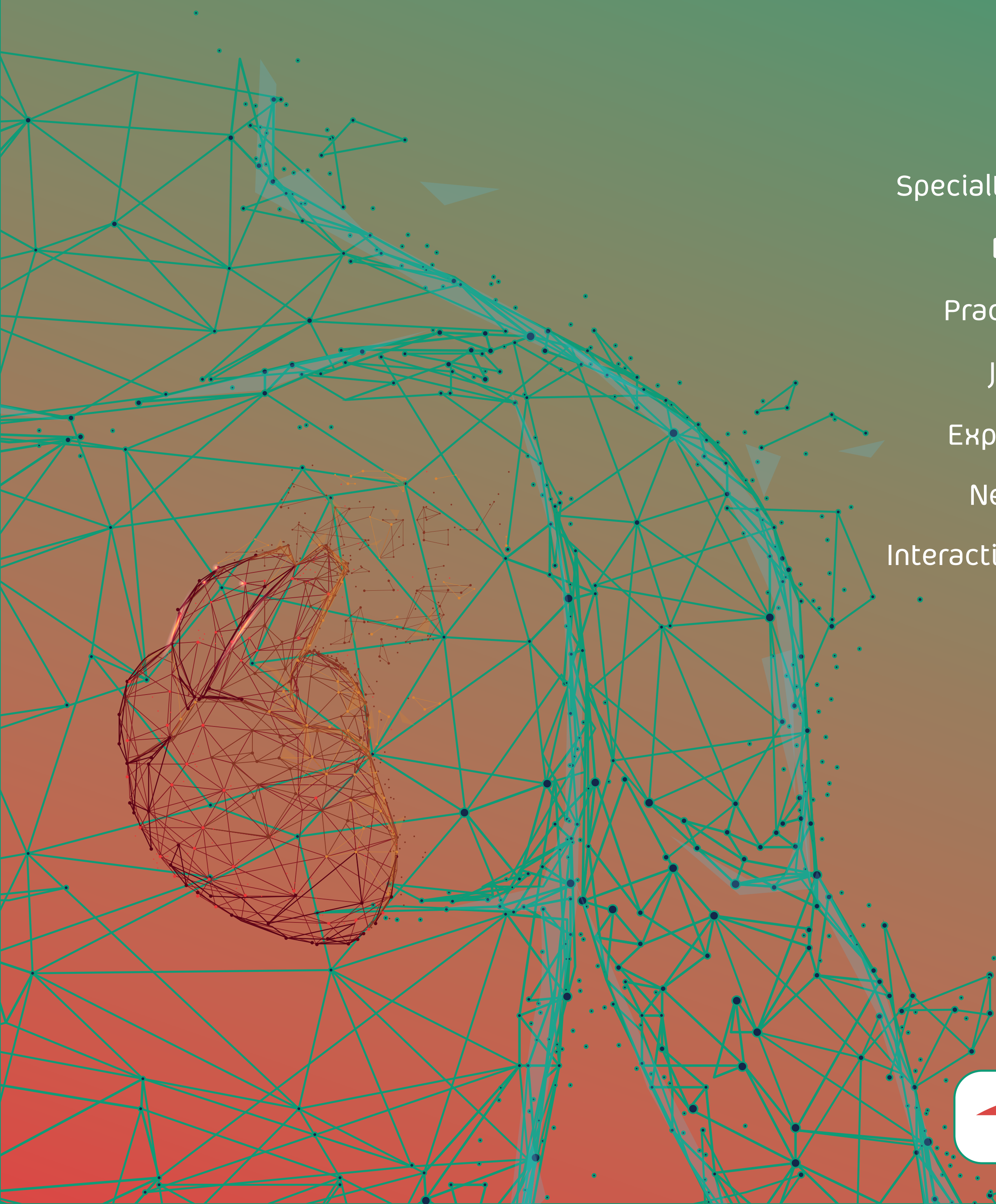

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Editorial Letter

It is with immense pleasure that we present the 21st issue of PRIME Newsletter — "Perfusion-Related Insights–Management and Evidence" — a quarterly scientific newsletter that includes review articles, case reports, randomized control trials, recently published guidelines, expert opinions, 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 is a case report which summarizes the effect of incremental administration of FFP in the intraoperative period along with hemostatic assessment in a patient with severe FXI deficiency who underwent CABG and CPB. The second article under this section highlights the use of cell saver blood transfusion over RBCs in children that reduces post-CPB pro-inflammatory cytokine response.

The second section 'Basic Facts' contains a randomized trial highlighting nitric oxide delivery during CPB to reduce AKI. The third section 'Practice Pearls' describes the effect of antiplatelet therapy on perioperative blood loss in patients undergoing Off-Pump CABG. The next section 'Journal Talk' exhibits the assessment of complications occurring during CPB in COVID-19 patients undergoing cardiac surgery.

The first article of the fifth section 'Expert Opinion' describes the perfusion techniques for extended aortic arch aneurysms & thoraco abdominal aortic aneurysms through left thoracotomy. The second article of this section highlights the effect of CPB glucose levels on inflammatory response after pediatric cardiac surgery. The sixth and last section 'News Corner' presented 2022 AHA/ACC/HFSA guidelines for the management of heart failure.

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 from the next edition.

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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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A CASE REPORT OF SEVERE FACTOR XI DEFICIENCY DURING CARDIAC SURGERY: LESS CAN BE MORE

Introduction

The severity of coagulopathy after CPB is dependent on several factors, including hemodilution, time of perfusion, and activation of the contact protein pathway. Contact protein pathway includes multiple key serine proteases, platelets, and fibrinogen, depending on the degree of heparin-mediated anticoagulation. Factor XI (FXI), a serine protease, is part of the contact protein pathway and one of the most proximate enzymes activated by thrombin. Severe congenital FXI deficiency (<20% normal activity) is rare and can be associated with severe bleeding following cardiac surgery requiring CPB. Severe FXI deficiency-related bleeding is mostly treated by FFP.

In this case report, the effect of incremental administration of FFP in the intraoperative period coupled with hemostatic assessments with ROTEM is used in a patient with severe FXI deficiency who underwent CABG and CPB.

Case study

- A 76-year-old man was admitted to the hospital due to coronary artery stenosis with left anterior descending 70–80%; obtuse marginal 70%; left circumflex, ramus 70%; and posterior descending artery 60–70%. His left ventricular ejection fraction was found at 58%.
- Twelve years prior, he was discovered with severe FXI deficiency, when having lumbar laminectomy. He was then treated with FFP prior to surgery and did not receive any blood products. He did not ever face bleeding events prior to that surgery.
- On the day of surgery, hemostatic assessment were made and ROTEM tests performed before the administration of FFP. Just before the start of surgery, 500mL of FFP (just half dose suggested by hematology service) was given to the patient and ROTEM tests were performed. The anti-fibrinolytic agent, aminocaproic acid, was administered i.v. at 5 gm loading dose followed by a 20 mg/kg/h infusion.
- No excessive bleeding was observed during the surgical dissection. The ACT of the blood sample obtained after FFP administration was above the normal range (by 18s). There was normalization of CT values in the InTem sample, indicating increased FXI activity after FFP administration.
- After completion of surgical preparation, 15,000 IU of unfractionated heparin was administered to get ACT value of 645 s which should be >480 s prior to CPB. After maintaining these conditions, CPB was then commenced.

Perioperative conditions

- CABG was performed with an aortic cross-clamp time of 63 min and a CPB perfusion time of 87 min.
- After an hour of perfusion, a blood sample was analyzed with a HepTem test along with heparinase assessment. During the CPB time period, coagulation had deteriorated compared to the InTem prior to CPB (Table 1). Additional 750 ml of FFP was added to the CBP pump over 10 min just prior to separation from CPB for prolongation of the CT. The patient was successfully separated from CPB, and the anticoagulation effect of heparin was neutralized with protamine (150 mg).

- Decannulation and chest closures were normal without observation of any meaningful bleeding.

Parameter	Pre-Op	Pre-CPB	CPB	Post-CPB
aPTT (s, 24.0–36.5)	68.6	-	-	35.1
INR (0.9–1.1)	1.0	-	-	1.0
Fibrinogen (mg/dL, 200–465)	-	-	-	290
Platelet Count (1000/μL, 130–450)	206	-	-	114
ACT (s, 100–140)	-	158	525-665	125
InTem				
CT (s, 122–208)	397	280	366*	256
α (°, 70–81)	67	75	67*	69
MCF (mm, 51–72)	57	64	56*	57
ExTem				
CT (s, 43–82)	77	65	-	85
MCF (mm, 52–70)	59	64	-	60
FibTem				
MCF (mm, 7–24)	17	17	-	15

Parameters: ACT = activated clotting time; aPTT = activated partial thromboplastin time; _ = angle, a measure of the velocity of thrombus formation; CT = clotting time, a measure of the time to onset of coagulation; INR = international normalized ratio; and MCF = maximum clot firmness, a measure of clot strength. ROTEM test types: ExTem = coagulation activated via tissue factor mediated factor VII-dependent pathway; FibTem = ExTem with platelet- inactivation; InTem = coagulation activated via the factor XII-dependent, contact protein pathway; and * InTem with heparinase to digest heparin, also known as HepTem.

Table 1. Perioperative hemostatic assessments

Post-operative period

- The ACT value was within the normal limits and InTem CT and values were similar to that observed after the first administration of FFP prior to CPB.
- Upon arrival to the cardiac ICU, the aPTT, PT, and fibrinogen concentrations were within normal limits. While the platelet count was less compared to the normal range, the normal MCF values were observed in all three ROTEM tests and a lack of clinical bleeding was observed and no platelets or other blood products were transfused.
- The following day the FXI activity was found to be 17%. Given the 50-70h half-life of FXI, it was likely that this activity was >20% the day before after FFP administration, rendering the patient no longer severely deficient.

Conclusion

This case report may serve as an evidence-based tactic for the management of hemostasis of a patient suffering from severe FXI-deficiency needed CPB.

Reference

Kazui T, Nielsen VG, Audie SD, Venkataramani RM, Bryant JT, Swenson K et al. A Case Report of Severe Factor XI Deficiency during Cardiac Surgery: Less Can Be More. J Cardiovasc Dev Dis. 2022 Apr 15; 9(4):118.

CELL SAVER BLOOD TRANSFUSIONS MAY BE ASSOCIATED WITH A DECREASE IN INFLAMMATION AND IMPROVED OUTCOME MEASURES IN PEDIATRIC CARDIAC SURGERY PATIENTS

Introduction

CPB is necessary for rectification of congenital heart disease via open-heart surgery and induces a systemic inflammatory response that causes complications such as acute lung injury and AKI. Additionally, blood transfusions are also required for this type of surgery that may further exacerbate the inflammatory response and increase morbidity and mortality. This study was aimed to replace the use of RBCs with cell saver (CS) blood transfusion that attenuate the post-CPB pro-inflammatory cytokine response.

Methods

- Patient population was divided into CS group and the control group.
- Serum cytokine concentrations of IL-10, IL-1RA, IL-6, IL-8, and TNF-α were measured preoperative period and postoperatively on days (POD) 0, 1, and 2.
- BUN and creatinine level were measured.

Results

- Anti-inflammatory IL-10 levels were significantly lower in the CS group on POD 0 than in the control group.
- BUN and creatinine levels on POD 2 were significantly lower in the CS group.
- The duration of milrinone use decreased by 80% in the CS group ($p = 0.048$)
- Time to extubation (hours) was significantly lower in the CS group.
- Hospital length of stay was decreased by 60% in the CS group ($p = 0.003$).

Parameters	Cell Saver group	Control group	*p*-value
IL-10 level (mean) at POD-0	1083.2 pg/mL	2080.2 pg/mL	0.0026
BUN level at POD-2	13.79	21.88	0.004
Creatinine level at POD-2	0.45	0.55	0.055
Median time to extubation (hour)	3.5	6.5	0.026

Table 2. Parameters assessed during preoperative and postoperative periods

Conclusion

CS transfusions in children lowered postoperative anti-inflammatory IL-10 which may be associated with improvements in renal and pulmonary functions.

Reference

Martinez MJ, Schwingshackl A, Romero T, Roach GD, Belperio JA, Federman MD. Cell saver blood transfusions may be associated with a decrease in inflammation and improved outcome measures in pediatric cardiac surgery patients. Perfusion. 2022 Apr 12: 2676591221078420.

NITRIC OXIDE DELIVERY DURING CARDIOPULMONARY BYPASS REDUCES ACUTE KIDNEY INJURY: A RANDOMIZED TRIAL

Introduction

Acute kidney injury (AKI) is a serious complication associated with CPB. Cardiac surgery patients face the development of postoperative AKI in 30-52% of cases and among them, 2-5% require renal replacement therapy. Mild AKI is also responsible for increased rates of morbidity and mortality in cardiac surgery due to the high risk of infectious complications. The current study aimed to evaluate the effects of nitric oxide supplementation on the CPB circuit in cardiac surgery.

Methods

- In this randomized controlled trial (September 2015 to April 2017), patients received either NO treatment or control (usual care) in a 1:1 ratio.
- Enrolled patients were adults and had a moderate risk of renal complications according to the Cleveland clinic foundation (CCF) acute renal failure score (CCS).
- The perfusionist alone was unblinded and was responsible for NO administration.
- NO-treatment group received standard of care with the supplementation of 40-ppm gaseous NO given via the oxygenator of the CPB machine during the entire CPB period. After CPB termination, NO supplementation was stopped (Figure 1).
- Patients in the control group were treated identically except that they were not administered with NO.
- The primary endpoint was AKI incidence. Secondary endpoints included urine output, level of uNGAL, plasma-free Hb level, and changes in the total concentration of NO metabolites (NO_2^- and NO_3^-).

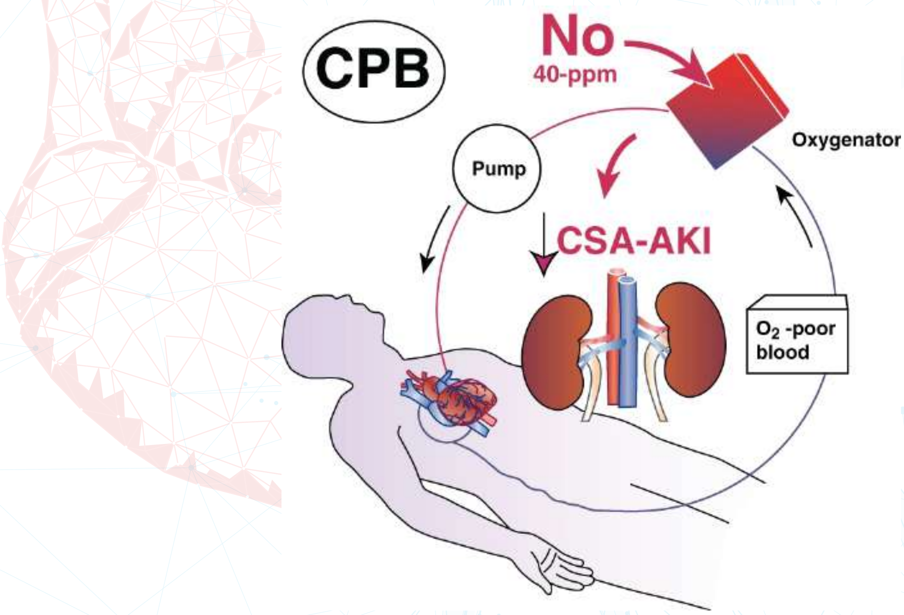


Figure 1. 40 ppm NO supplementation to CPB

Perioperative conditions

All interventions were performed through median sternotomy.

Perioperative details
Anesthesia was induced by fentanyl (3.0-5.0 μg/kg) + propofol (1.5 μg/kg) and supported by the Inhalation of sevoflurane 2–3 vol % before and after CPB. Sevoflurane was blended into CPB circuit gas source during perfusion.
Central venous catheter was installed in right internal jugular vein. Radial artery was catheterized using 20G arterial cannula to monitor the arterial pressure and to obtain blood samples for gas analyzer.
Metabolic parameters, acid-base blood balance, and plasma ionograms were monitored.
Processed EEG (BIS) was monitored and maintained in the range of 40 to 60.
During surgery
Hypotension was prevented by inhibiting hyperchloremic acidosis and renal vasoconstriction. Saline solution (0.9%) was not infused. Balanced crystalloids solution was used.
CPB was performed in a non-pulsatile mode using Stockert system with disposable membrane oxygenators. Perfusion index was 2.6 L/min/m². Initially, 500 mL of 4% succinylated (modified fluid) gelatin and 500 mL of balanced crystalloid solution were used for circuit prime.
Prior to CPB, patients were administered heparin (3 mg/kg), and activated clotting time was maintained at >500 s.
Mean arterial blood pressure during CPB (≥65 mmHg), the temperature of the nasopharynx (36.4–36.6 °C), Hb level (≥80 g/L) and hematocrit (≥24) were maintained. Norepinephrine was given if perfusion pressure >65 mmHg was not maintained with a perfusion index of 2.6 L/min/m².
$PaCO_2$ and PaO_2 were maintained within 35–40 and 100–120 mmHg, respectively.
Myocardial protection in case of aortic insufficiency was achieved by perfusion of the ascending aorta or coronary artery with cold crystalloid solution (5–8 °C) for 6–8 min.
Local hypothermia with ice gruel was used.
After surgery, all patients were transported to the ICU and ICU-management was performed according to the KDIGO guidelines.
NO supplementation
In the NO group, an additional NO supplementation line was connected to the gas-air mixture supply circuit under aseptic conditions.
NO supplementation line connector with a bacterial filter was as close to CPB oxygenator as possible.

Results

- A total of 96 patients (61 male and 37 female) were included of which 48 (mean=64 years) received NO supplementation and 26 (mean=63 years) received usual care.
- Primary outcome: Nitric oxide administration was linked with a significant ($p=0.023$) decrease in total AKI rate in the NO-treatment group compared to the control group (Table 3).

Characteristics	NO-treatment group (n=48)	Control group (n=48)	*p*-value
AKI, total n (%)	10 (20.8%)	20 (41.6%)	0.023
AKI, stage 1 n (%)	8 (16.6%)	13 (27.3%)	0.016
AKI, stage 2 n (%)	2 (4.1%)	5 (10.4%)	0.22
AKI, stage 3 n (%)	0	1 (2%)	0.5
ICU stay (h)	22	30	0.22
Hospital stays (days)	10	12	0.17
Mechanical ventilation time (h)	9	10	0.2
Mortality	0	1	0.5
Infusion volume in ICU mL/kg	76	74.8	0.26
Perioperative conditions			
Perioperative transfusion, n (%)	18 (37.5)	18 (37.5)	0.42
CPB duration, min	118	119	0.8

Table 3. Post-operative characteristics of patients

Secondary outcomes: (Table 4)

- Urine output was found significantly more in the NO-treatment group during CPB.
- The uNGAL level was significantly lower in the NO-treatment group after 4 h of surgery.
- There were no differences in plasma-free Hb changes between NO and the control group but remained increased compared with the initial values even after 24 h.
- Changes in the total concentrations of NOx (combination of the NO_2^- and NO_3^-) metabolites (μM/mL) in blood plasma had significantly higher values in the NO-treatment group starting from 5 min post clamping to the end of surgery.

Secondary endpoints	NO-treatment group (n=48)	Control group (n=48)	*p*-value
Urine output during CPB (mL/kg/h)	2.6	1.7	0.0002
uNGAL level (ng/mL)	1.12	4.62	0.005
NO_{total} 5 min post clamping (μM/mL)	13.5±1.4	10.8±2.5	0.0073
NO_{total} 5 min after declamping (μM/mL)	15.3±1.6	9.4±2.1	0.0004
NO_{total} end of surgery (μM/mL)	10.8±1.1	9.2±2.3	0.028

Table 4. Secondary endpoints characteristics of perioperative period in patients

Conclusion

Administration of nitric oxide during CPB in adult patients at moderate risk for renal complications was linked with a significant decrease in AKI.

Reference

Kamenshchikov NO, Anfinogenova YJ, Kozlov BN, Svirko YS, Pekarskiy SE, Evtushenko VV et al. Nitric oxide delivery during cardiopulmonary bypass reduces acute kidney injury: A randomized trial. J Thorac Cardiovasc Surg. 2022 Apr; 163(4):1393-1403.

Practice Pearls

EFFECT OF ANTI-PLATELET THERAPY ON PERIOPERATIVE BLOOD LOSS IN PATIENTS UNDERGOING OFF-PUMP CORONARY ARTERY BYPASS GRAFTING

Introduction

The formation of platelet-rich intracoronary thrombi during CABG is the main cause of morbidity and mortality. Clopidogrel with aspirin is used as the gold standard for the prevention of intra-coronary stent thrombosis. The combination of aspirin and clopidogrel in the pre-operative conditions is a cause for concern because complete inhibition of platelet functions causes severe bleeding. This study aimed to review the effect of the preoperative use of clopidogrel and aspirin on perioperative bleeding, blood product transfusion, and resource utilization after CABG.

Methods

- In this study, data of 1200 patients (age: 31-70 years) who underwent off-pump CABG were reviewed. The patients were divided into three groups as shown below:
- Group 1: discontinued aspirin and clopidogrel 6 days prior to surgery (n = 468)
  Group 2: discontinued both drugs 3 to 5 days prior to surgery (n = 621)
  Group 3: discontinued both drugs 2 days prior to surgery (n = 111)
- Anesthetic techniques, heparin (1 mg/kg i.v), and protamine management were standardized for all patients during surgery.
- Aspirin 150 mg and clopidogrel 75 mg were administered on the first post-operative day.
- Primary endpoint: to determine the effects of antiplatelet drug usage on perioperative bleeding patterns.
- Secondary endpoints: to evaluate the morbidity and mortality rates associated with the use of antiplatelet drugs prior to surgery.

Results

- Group 2 patients had a higher rate of bleeding, low level of Hb, PCV and platelet count (Table 5) as compared with other groups on day 1 of the post-operative period.
- Group 2 patients (60.39%) required more blood and blood product transfusion units as compared to other groups (Table 6).
- Transfusion of platelets and FFP in groups 2 and 3 compared to group 1 were found higher, which suggests that stopping anti-platelet medication 6 days prior to surgery is associated with decreased bleeding and less transfusion of blood and blood products.
- Patients of groups 2 and 3 were associated with higher blood loss in terms of drainage at 12 and 24 hours. Post-operatively, this was statistically significant (Table 6).
- Re-exploration was statistically significant in patients of group 3 (9.01%) than in groups 2 (2.58%) and 1 (1.07%) (Table 6).

Parameters	Group 1	Group 2	Group 3	*p*-value
Hb level				
Pre-operative	12.404±1.8	12.427±1.953	12.61±1.604	0.573
Post OP Day 1	11.97±1.563	9.26±2.38	1.71±1.20	<0.001
Post OP Day 3	10.285±1.515	10.505±5.049	10.218±1.788	0.561
Post OP Day 5	10.468±1.33	10.335±1.366	10.262±1.177	0.164
On discharge	10.857±1.299	10.785±1.734	10.661±1.078	0.444
Packed Cell Volume (PCV)				
Pre-operative	36.757±5.584	36.159±6.153	37.458±5.173	0.050
Post OP Day 1	35.05±5.70	28.84±6.61	34.78±3.89	<0.001
Post OP Day 3	30.853±4.953	31.419±15.27	30.762±5.321	0.679
Post OP Day 5	31.419±4.006	31.009±4.206	30.786±3.532	0.159
On discharge	32.57±3.897	32.362±5.199	31.984±3.233	0.449
Platelet count				
Pre-operative	223.13±71.914	226.035±81.621	221.261±83.694	0.751
Post OP Day 1	202.05±98.85	189.04±72.455	185.207±69.732	0.021
Post OP Day 3	171.699±72.694	176.823±71.89	171.748±70.294	0.470
Post OP Day 5	180.481±69.931	191.448±81.559	195.234±83.179	0.038
On discharge	212.244±83.441	221.953±93.66	239.018±103.941	0.014

A platelet count of < 80,000 was an indication for platelet transfusion.
The values of PT, aPTT, and INR of more than 1.5 times the control were treated with FFP.
A hematocrit of less than 24% was corrected by transfusion of red blood cells.
The indications for re-exploration were blood losses greater than 500 ml over the first hour, more than 300 ml for 2 consecutive hours, more than 200 ml for 3 consecutive hours, and more than 1 liter over the first 8 hours.

Table 5. Values of Hb level, PCV and platelet counts for evaluation of rate of bleeding

Parameters	Group 1	Group 2	Group 3	*p*-value
Drainage (n)				
After 12 hour	232.107±223.063	314.994±240.081	289.919±142.343	<0.001
After 24 hour	216.475±188.928	333.939±258.845	283.682±191.915	<0.001
Total transfused blood unit n (%)				
1-2	141 (30.13)	273 (43.96)	48 (43.24)	<0.001
3-6	56 (11.97)	96 (15.46)	15 (13.51)	<0.001
>6	0 (0.00)	6 (0.97)	1 (0.90)	<0.001
Random Donor Platelet transfusion unit n (%)				
1-2	64 (13.68)	162 (26.09)	19 (17.12)	<0.001
>2	3 (0.64)	9 (1.45)	2(1.80)	<0.001
Fresh Frozen Plasma transfusion unit n (%)				
1-2	26 (5.56)	91 (14.65)	14 (12.61)	<0.001
>2	0 (0.00)	32 (5.15)	1 (0.90)	<0.001
Re-exploration n (%)	5 (1.07)	16 (2.58)	10 (9.01)	<0.001

Table 6. Distribution of drainage, total transfused blood, RDP and FFP transfusions, and Re-exploration among the study groups

Conclusion

- The preoperative use of clopidogrel and aspirin (discontinued 2-5 days prior) together in patients undergoing off-pump CABG surgery showed a significantly increased risk of bleeding and blood product transfusion.
- Hence, the use of clopidogrel and aspirin should be stopped 5 to 6 days prior to surgery to reduce the morbidity, days of hospital stay and resource utilization.

Reference

Kapoor S, Singh G, Arya RC, Singh V, Garg A, Ralhan S et al. Effect of anti-platelet therapy on peri-operative blood loss in patients undergoing off-pump coronary artery bypass grafting. Ann Card Anaesth. 2022 Apr-Jun; 25(2):182-187.

THE ASSESSMENT OF PATIENTS UNDERGOING CARDIAC SURGERY FOR COVID-19: COMPLICATIONS OCCURRING DURING CARDIOPULMONARY BYPASS

Introduction

Outcomes of cardiac surgical patients who have COVID-19 in the perioperative period are extremely poor with extended hospital stay and high mortality. It seems that the pathophysiologic conditions in COVID-19 patients may cause a challenge in the conduct of CPB. The present study has shown the results of a national registry on COVID-19 testing and complications associated with extracorporeal flow in patients undergoing cardiac surgery with CPB.

Methods

- This is a retrospective observational study that included 5,612 patients from Specialty Care Operative Procedure registry (SCOPE) from 176 hospitals throughout the U.S and Puerto Rico (November 2020 and January 2021).
- During the study period, all adult surgical patients (3283) who underwent a cardiac procedure (CABG-only) requiring CPB were included (Figure 2).
- The four groups were established based on the assessment and result of COVID-19 testing. They were negative test (Neg Test), positive test (Pos Test), unknown test (Unk Test) and no test (No Test).
- The primary endpoint was any complication during CPB. Secondary endpoints were coagulation and gas exchange complications during CPB.

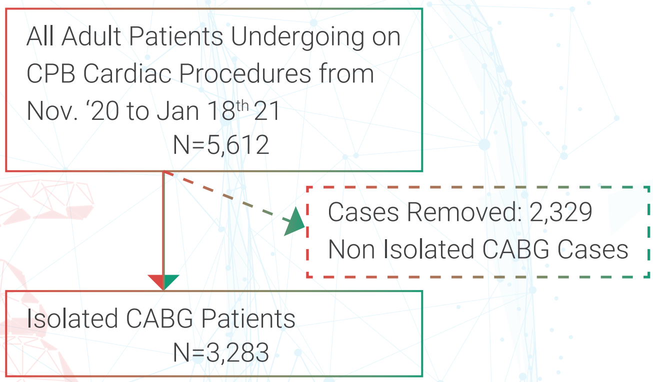


Figure 2. Distribution of patients among the groups

Results

- A total of 5,612 patients record were distributed basis of the COVID-19 test (Figure 3).
- The primary surgical procedure performed was a CABG which ranged from 58.3% (404 of 693 patients) in the Unk to 71.4% (35 of 49 patients) in the Pos Test group.
- Demographic and intraoperative parameters were shown in Table 6. There were similar findings for weight and women which were significantly more in the Pos Test group when compared to the others.

- The Pos Test group had shown the lowest on-CPB hematocrit and the highest red blood cell transfusion rate (Table 7).
- Bivariate analysis showed the higher oxygenator gas exchange complications in the Pos Test group while this finding was not statistically significant (p = 0.088) (Figure 4).
- There was a higher incidence of coagulation complications in the Pos Test group compared to all other groups (p < 0.001) (Figure 5).
- Any complications during CPB were more than ten times in the Pos test group than in the Neg test group (Figure 6).
- The total heparin given during CPB was significantly lower in the Pos Test Group as compared to the negative test group (p = 0.001). However, there were no differences in the number of patients with on-CPB ACT values under 400 seconds.

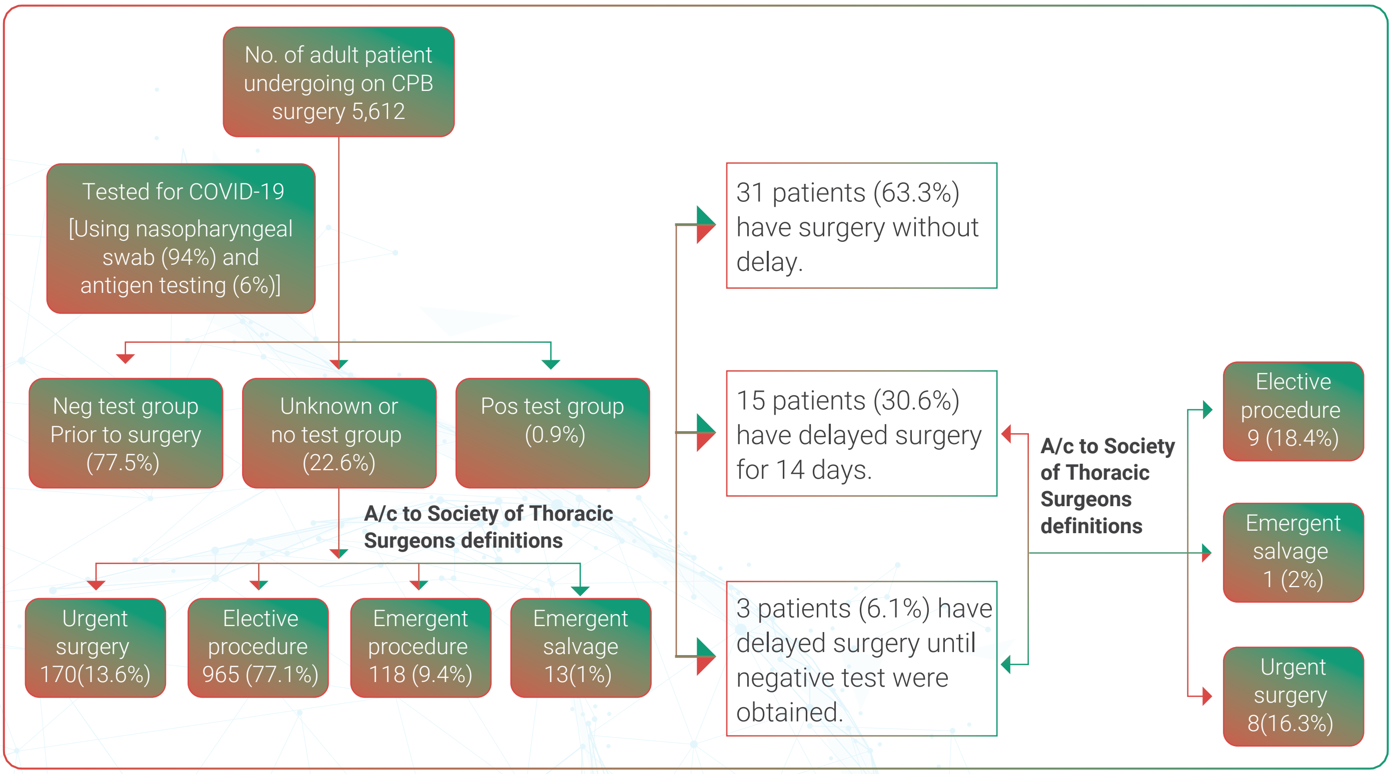
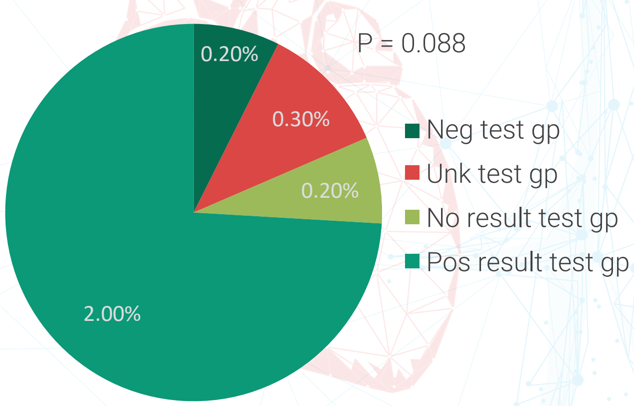


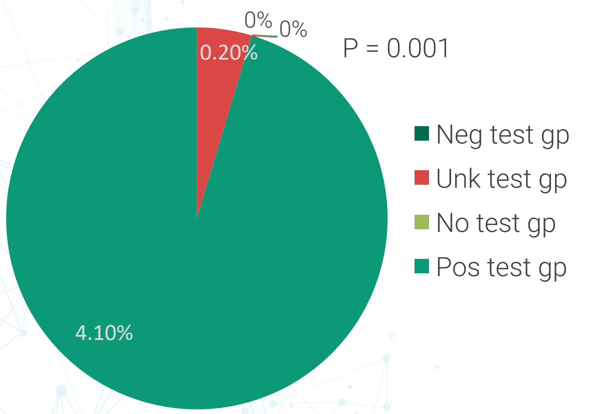
Figure 3. Distribution of patients underwent CPB

Oxygenator gas exchange complications (% cases) during CPB by test group (Figure 4)



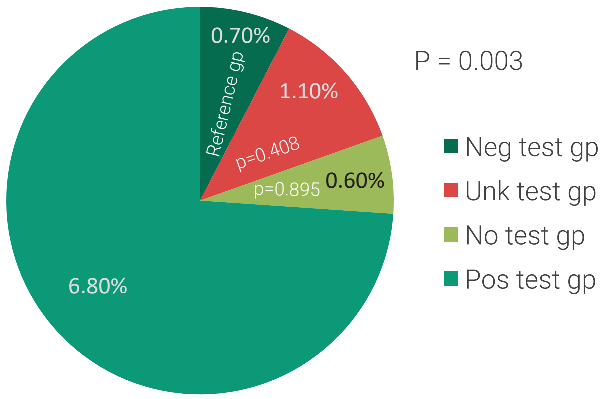
Results are shown as average and confidence interval

Coagulation complications (% cases) during CPB by test group (Figure 5)



Results are shown as average and confidence interval

Model-adjusted % cases with any complication during CPB (Figure 6)



Results are shown as average and confidence interval.

	All N=5612	Neg test N=4297	Unk test N=693	No test N=573	Pos test N=49	*p*-Value
Gender, n (%)						0.006
Men	4058 (72.3)	3149 (73.3)	483 (69.7)	398 (69.5)	28 (57.1)	
Women	1554 (27.7)	1148 (26.7)	210 (30.3)	175 (30.5)	21 (42.9)	
Patient age (years), mean (SD)	64.3 (12.5)	64.2 (12.6)	64.3 (12.2)	65.2 (12.2)	65.3 (10.6)	0.34
Patient weight (kg), mean (SD)	88.3 (20.8)	88.7 (20.9)	88.2 (20.5)	86.3 (20.5)	84.7 (15.0)	0.041
BMI (kg/m²), mean (SD)	29.9 (6.9)	30.0 (6.7)	30.0 (8.9)	29.2 (5.9)	29.5 (5.6)	0.084
Lowest CPB Hct, mean (SD)	25.9 (4.8)	26.0 (4.8)	25.7 (4.6)	25.3 (4.8)	24.1 (4.6)	<0.001
Intraop RBC transfusion, n (%)						0.019
No	3986 (71.2)	3060 (71.4)	481 (69.7)	419 (73.3)	26 (53.1)	
Yes	1609 (28.8)	1224 (28.6)	209 (30.3)	153 (26.7)	23 (46.9)	
Total heparin during CPB (KIU), mean (SD)	17.6 (13.6)	18.3 (14.1)	16.1 (13.2)	14.3 (9.8)	14.0 (9.9)	<0.001
Total heparin during CPB (KIU), median [25th, 75th percentile]	13.0 [10.0;20.0]	15.0 [10.0;25.0]	10.0 [10.0;20.0]	10.0 [10.0;20.0]	10.0 [10.0;20.0]	<0.001
ACT during CPB (seconds), n (%)						<0.419
<400 seconds	66 (1.18)	49 (1.14)	11 (1.59)	5 (0.87)	1 (2.04)	
>400 seconds	5546 (98.8)	4248 (98.9)	682 (98.4)	568 (99.1)	48 (98.0)	

ACT: activated clotting time; BMI: body mass index; CPB: cardiopulmonary bypass; Hct: hematocrit; KIU: thousands per international unit; Neg: negative; Pos: positive; RBC: red blood cell; SD: standard deviation; Unk: unknown.

Table 7. Demographic and perioperative evaluation among the groups

Conclusion

- Intraoperative complications were higher in COVID-19 positive cases during CPB.
- Coagulation disturbances such as visual observation of clots in the field or circuit during systemic heparinization and heparin resistance with the requirement of high heparin utilization have been observed.

Reference

Stammers AH, Mongero LB, Tesdahl EA, Patel KP, Jacobs JP, Firstenberg MS et al. The assessment of patients undergoing cardiac surgery for Covid-19: Complications occurring during cardiopulmonary bypass. Perfusion. 2022 May; 37(4): 350-358.

PERFUSION TECHNIQUES FOR EXTENDED AORTIC ARCH ANEURYSMS & THORACO ABDOMINAL AORTIC ANEURYSMS THROUGH LEFT THORACOTOMY

Introduction

Aortic arch and thoraco-abdominal aortic aneurysms (TAAA) surgeries are extremely challenging and require staged corrections. A one-stage operation is highly effective and improves long-term survival along with the quality of life in patients. Perfusion strategies for this kind of surgery play an important role to yield favorable outcomes.

Methods

- This is a retrospective study that included 12 arch/hemi-arch and thoraco-abdominal aneurysm patients (January 2019 and August 2021).
- The primary endpoints were perfusion techniques, neurological outcome, renal function and the postoperative outcome.
- Operative techniques included – (Figure 3)
  - CPB was established with cannulation on pulmonary artery and radial artery/femoral vein and left femoral artery/descending aorta.
  - The surgery was performed under moderate hypothermic conditions (26 °C) and systemic potassium (30-40 mmol) was administered through a cardiotomy/venous reservoir to arrest the heart.
  - Retrograde cerebral perfusion was performed through the long femoral venous cannula or RA cannula.
  - In cases of arch involvement, SACP (selective antegrade cerebral perfusion) was carried out through the AP grip flow catheters (10 -14 Fr).
  - NIRS was well maintained above the baseline for all the cases.
  - Once the hemi arch/ proximal aorta anastomosis is done, the upper body flow is established by the side arm of the aortic arch plexus graft (Terumo Gel-weave).

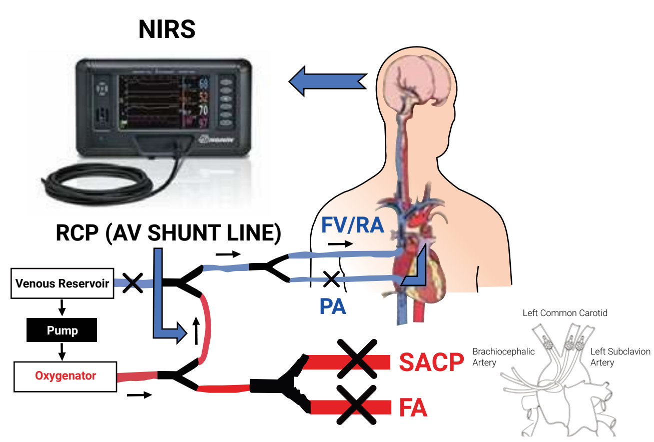


Figure 3. Circuit and design of CPB

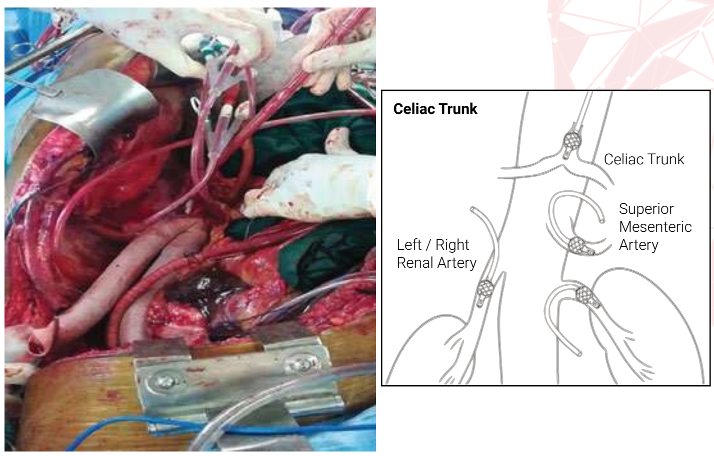
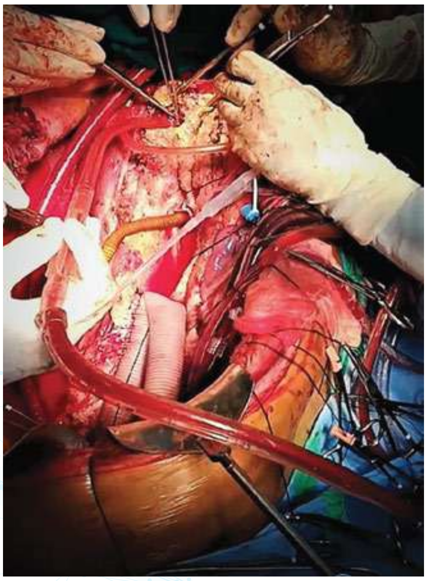


Figure 4. Visceral perfusion through superior mesenteric artery, coeliac and renal arteries

- The rise in serum K was tackled by performing zero balanced ultrafiltration.
- The abdominal vessels coelic plexus, superior mesenteric artery, and both the renal arteries are perfused with the help of AP grip flow 10 Fr – 14 Fr catheters (Figure 4). The intercostal arteries are visualized and are anastomosed to the Gel-weave graft.
- Renoplegia was administered in a few patients by the cardioplegia pump since it was available to use as the heart started beating soon after the proximal aorta anastomosis. The perfusion pressure was monitored continuously for all the visceral and renal perfusion (Figure 5).



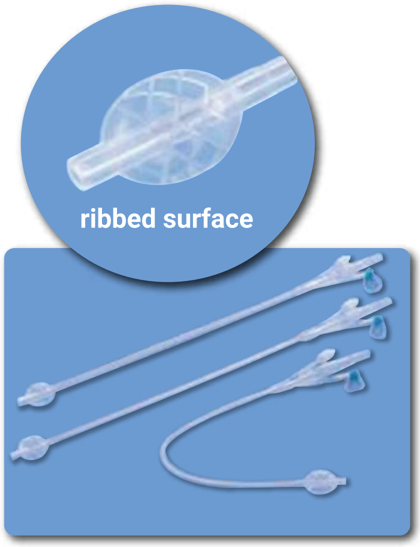
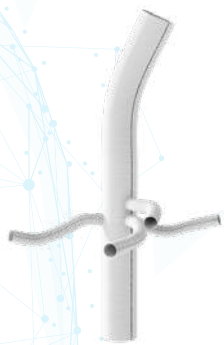


Figure 5. Renoplegia through renal arteries using AP grip flow catheters

- The descending thoracic aortic graft is anastomosed with the coselli graft for the lower abdominal aorta and the clamp was removed and rewarmed to 36°C. The visceral vessels and the renal arteries are anastomosed one after another to the coselli neo-aorta (Terumo Gel-weave Graft) (Figure 6).

(a) Arch Plexus Graft



(b) Coselli Graft

Figure 6. (a) Arch Plexus Graft; (b) Coselli Graft

Results

- None of the patients had any gut ischemia or abdominal-related complications.
- Neurologically, all the patients have no neurological deficits.
- One patient died due to post-operative renal artery hemorrhage.
- The patients with renoplegia had better post-operative serum creatinine values.
- 11 patients, out of 12, have an uneventful post-operative stay and got discharged.

Conclusion

The Techniques of whole-body perfusion with myocardial and cerebral protection are the key steps involved in the management of Aortic Arch and TAAA surgeries. This study recommended that with a holistic approach among the surgical team and safe perfusion practice, these complex surgeries can be carried out successfully as a single-stage operation.

Reference

Prakash PVS, Selvakumar R, Kalaimani D, Stevenson R, Rakesh Kumar, Ann Maria et al.
Narayana Institute of Cardiac Sciences, Bangalore. An Institutional Experience.

EFFECT OF CPB GLUCOSE LEVELS ON INFLAMMATORY RESPONSE AFTER PEDIATRIC CARDIAC SURGERY INTRODUCTION

Introduction

Systemic inflammatory response syndrome (SIRS) is a common complication after cardiac surgery. There is no definite optimal glycemic threshold for pediatric patients receiving open-heart surgery with CPB. The study aimed to investigate the optimal CPB glucose in patients undergoing cardiac surgery.

Methods

- This is a cohort study conducted on pediatric patients undergoing cardiac surgery with arrested heart CPB at TEDA International Cardiovascular Hospital (June 2012 and December 2020).
- The primary outcome variable was SIRS.
- Secondary outcomes included SIRS length of mechanical ventilation, ICU stay and all-cause mortality at 30 days postoperatively.

Results

- A total of 7350 patients (median age-37.5 months) were enrolled in the present study (Fig. 7), of whom 5821 (78.20%) patients had CPB glucose less than 8.1 mmol/L. 3895 (52.99%) are female and the median glucose during CPB was 6.40 mmol/L.
- Baseline characteristics of patients with low (<8.1 mmol/L) and high (>8.1 mmol/L) glucose are shown in Table 8. Low glucose patients were older and CHD clinical pathways were more frequently implemented.
- Low glucose patients had a higher frequency of genetic anomalies and pulmonary hypertension, but had a lower frequency of hemodynamic pathology in comparison to high glucose patients.
- The incidence of severe SIRS in low glucose patients and high glucose patients was 17.23% and 39.05% (Table 8).
- The prevalence of severe SIRS increased with increasing CPB glucose level greater than 8.1 mmol/L (Table 9)

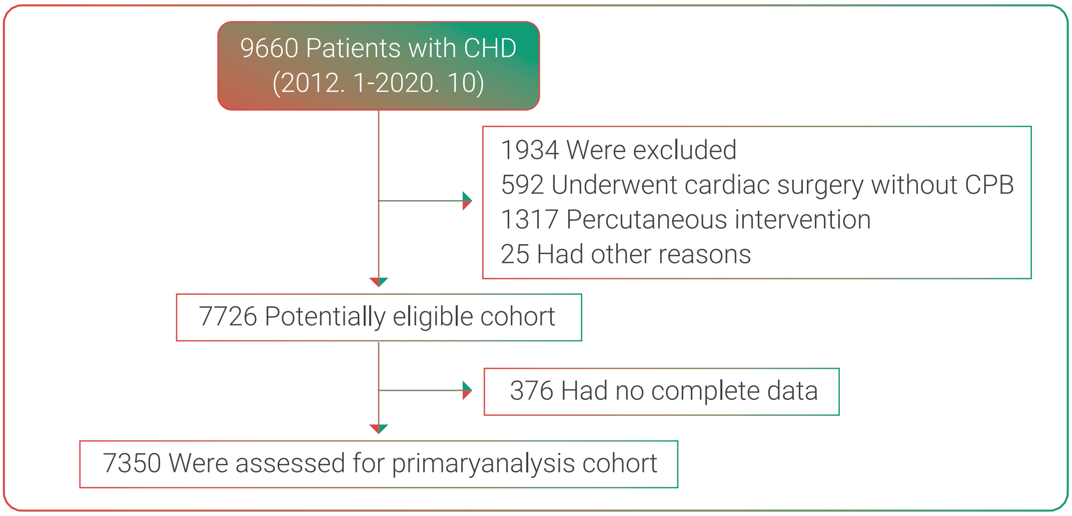


Figure 7. Selected patients for the study

Secondary outcomes:

- High glucose patients had a significantly longer postoperative length of mechanical ventilation and ICU stay in comparison to low glucose patients.
- Higher incidence of SIRS and inpatient mortality were also observed in high glucose patients group (Table 8).

	All patients (N = 7350)	Low glucose patients (N = 5821)	High glucose patients (N = 1529)	*p*-value
Surgical factors				
Aorta crossclamp time, min	34.00 (23.00–52.00)	32.00 (22.00–45.00)	51.00 (32.00–89.00)	<0.001
Red cell need, U	1.00 (0.00–2.00)	1.00 (0.00–1.00)	1.00 (1.00–2.00)	<0.001
Steroids need				<0.001
No	7052 (95.95%)	5674 (97.47%)	1378 (90.12%)	
Yes	298 (4.05%)	147 (2.53%)	151 (9.88%)	
Glucose infusion				0.072
No	7179 (97.67%)	5695 (97.84%)	1484 (97.06%)	
Yes	171 (2.33%)	126 (2.16%)	45 (2.94%)	
Insulin need				<0.001
No	6712 (91.32%)	5821 (100.00%)	891 (58.27%)	
Yes	638 (8.68%)	0 (0.00%)	638 (41.73%)	
Aristotle complexity score	6.00 (6.00–7.00)	6.00 (6.00–7.00)	6.00 (6.00–7.00)	0.127
Aristotle complexity level				0.003
Level 1	1197 (16.29%	943 (16.20%)	254 (16.61%)	
Level 2	5020 (68.30%)	4024 (69.13%)	996 (65.14%)	
Level 3	1005 (13.67%)	762 (13.09%)	243 (15.89%)	
Level 4	128 (1.74%)	92 (1.58%)	36 (2.35%)	
Exposure				
Glucose, mmol/L	6.40 (5.30–7.80)	5.90 (5.10–6.80)	9.60 (8.70–11.10)	<0.001

	All patients (N = 7350)	Low glucose patients (N = 5821)	High glucose patients (N = 1529)	*p*-value
Outcomes				
Primary outcome				
Severe SIRS	1600 (21.77%)	1003 (17.23%)	597 (39.05%)	<0.001
Secondary outcome				
SIRS	5637 (76.69%)	2937 (75.40%)	2700 (78.15%)	0.005
Length of mechanical ventilation, hours	3.15 (2.10–5.20)	3.00 (2.00–4.44)	4.40 (2.55–20.27)	<0.001
ICU stay, hours	22.08 (19.00–39.58)	21.92 (18.83–23.83)	22.75 (20.00–46.75)	<0.001

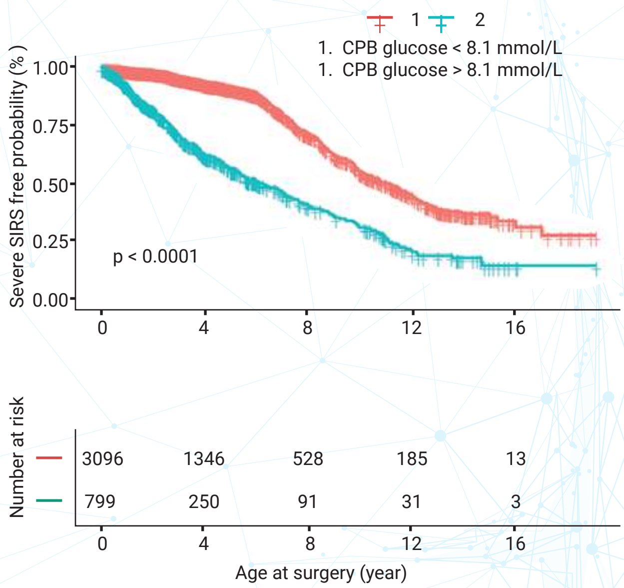
BMI, Body mass index; PAH, Pulmonary arterial hypertension; SIRS, systemic inflammatory response syndrome; ICU, intentive care unit
*Data are n (%) or median (IQR) other indicated mean (SD)

Table 8. Characteristics and results between low and high glucose patients

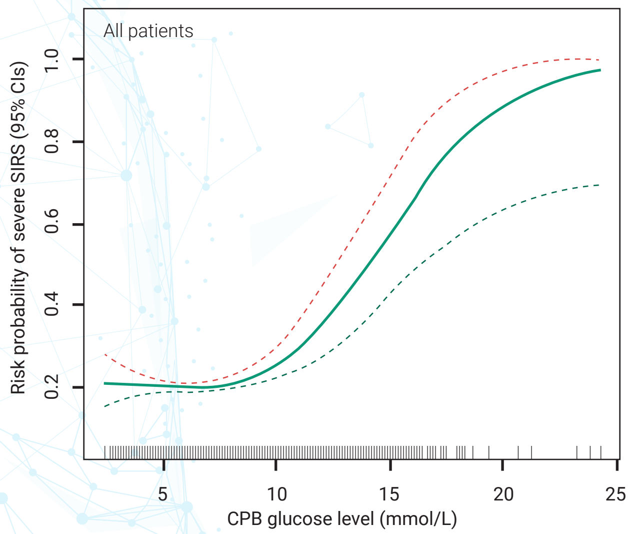
	Severe SIRS
	Adjusted β/OR (95% CI) *p*-value
Model I	
One line slop	1.08 (1.03, 1.13) 0.0008
Model II	
Turning point (K)	8.1
Glucose < 8.1mmol/L	0.98 (0.92, 1.04) 0.4151
Glucose > 8.1mmol/L	1.35 (1.21, 1.50) < 0.0001
LRT test	< 0.001#

LRT test, Logarithmic likelihood ratio test
#Model II is significant different from Model I

Table 9. Threshold effect analysis of CPB glucose on severe SIRS using two-piece-wise regression model



Severe SIRS-free probability with increasing age by glucose category for overall patients. The figure represents the severe SIRS-free probability by age separately for all patients depending on glucose category



The relationship between CPB glucose and risk probability of severe SIRS. A gradual J-shaped risk curve among total patients. Red dotted lines represent the spline plots of CPB glucose and blue dotted lines represent the 95% CIs of the spline plots. Adjusted for Gender, Age of surgery (month), Age category of surgery, Body surface area (m²), BMI (kg/m²), Surgery year, Preoperative hemoglobin, Residence altitude, Hemodynamic pathology, Extracardiac malformations, Genetic anomalies, Clinical pathway implementation, pulmonary arterial hypertension (PAH), Aorta crossclamp time (min), Red Cell need (U), Steroids need, Glucose infusion, Insulin need, Aristotle complexity score, Aristotle complexity level

Figure 8. (a) Severe SIRS free probability with increased age by glucose category; (b) Risk probability of severe SIRS with glucose level

Conclusion

- The patients with glucose <8.1 mmol/L had a lower risk of probability ($P<0.001$) for severe SIRS in overall patients by age in cardiac surgery (Figure 8a).
- The probability of severe SIRS significantly increased with elevated CPB glucose (Glucose = 8.1 mmol/L) (Figure 8 b).
- High glucose patients were associated with significantly longer postoperative ventilation and ICU stays, and a higher incidence of mortality which indicates the importance of the control of glucose in CHD children in the management of extracorporeal circulation.

Reference

Zeng ZH, Yu XY, Liu XC, Liu ZG. Effect of CPB glucose levels on inflammatory response after pediatric cardiac surgery. BMC Cardiovasc Disord. 2022 May 14; 22(1):222.

2022 AHA/ACC/HFSA GUIDELINE FOR THE MANAGEMENT OF HEART FAILURE: A REPORT OF THE AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION JOINT COMMITTEE ON CLINICAL PRACTICE GUIDELINES

Introduction

The 2022 AHA/ACC/HFSA Guideline replaces the 2013 ACCF/AHA Guideline and the 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA Guideline for the Management of HF. The 2022 guideline is proposed to provide patient-centric recommendations for clinicians to prevent, diagnose and manage HF patients.

Methods

Recommendations are based on a comprehensive literature search that was conducted (May 2020 and December 2020) including clinical studies, reviews, and other evidence conducted on human subjects which were published in the English language from MEDLINE (PubMed), EMBASE, the Cochrane Collaboration, the Agency for Healthcare Research and Quality and other relevant databases. Additional relevant clinical trials and studies are also included which are published through September 2021. This guideline was harmonized with other American Heart Association or American College of Cardiology guidelines published through December 2021.

Key messages of 2022 AHA/ACC/HFSA guideline

- Guideline-directed medical therapy (GDMT) for HF with HFrEF now includes 4 medication classes, including SGLT2i.
- SGLT2i have a Class of Recommendation 2a in HF with HFmrEF. Weaker recommendations (Class of Recommendation 2b) are made for ARNi, ACEi, ARB, MRA and beta-blockers in this type of patient.
- New recommendations for HFpEF are made for SGLT2i, MRAs and ARNi. Several prior recommendations have been renewed including treatment of hypertension (Class of Recommendation 1), treatment of atrial fibrillation (Class of Recommendation 2a), use of ARBs (Class of Recommendation 2b), and avoidance of routine use of nitrates or phosphodiesterase-5 inhibitors (Class of Recommendation 3: No Benefit).
- Improved LVEF is used to refer to those patients with previous HFrEF (LVEF >40%). These patients should continue their HFrEF treatment.
- Value statements were created for selected recommendations where high-quality, economical studies of the intervention have been published.
- Amyloid heart disease has new recommendations for treatment including screening for serum and urine monoclonal light chains, bone scintigraphy, genetic sequencing, tetramer stabilizer therapy and anticoagulation.
- Data have been shown that increased filling pressures are important for the diagnosis of HF (LVEF >40%). It can be evaluated with non-invasive (natriuretic peptide, diastolic function on imaging) or invasive testing (hemodynamic measurement).
- For the prolonged survival of patients with advanced HF should be referred to a team specializing in HF. An HF specialty team reviews HF management by evaluating the suitability for advanced HF therapies and uses palliative care including suitable inotropes which consistent with the patient's goals of care.

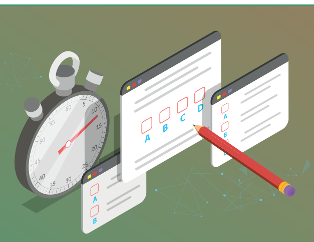
- Primary prevention is important for those at risk for HF (stage A) or pre-HF (stage B). Stages of HF was revised to emphasize the new terminologies such as the use of "at risk" for stage A-HF and pre-HF for stage B.
- Recommendations are also provided for selected patients of HF with iron deficiency, anemia, hypertension, sleep disorders, type 2 diabetes, atrial fibrillation, coronary artery disease and malignancy.

Reference

Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022 May 3; 145(18):e895-e1032.

Abbreviations

ACEi	Angiotensin-converting enzyme inhibitor
ACT	Activated clotting time
AKI	Acute kidney injury
ARB	Angiotensin receptor blockers
ARBs	Angiontensin receptor neprilysin inhibitor
BUN	Blood urea nitrogen
CABG	Coronary artery bypass grafting
CHD	Congestive heart disease
COVID	Coronavirus disease
CPB	Cardiac pulmonary bypass
CS	Cell saver
CT	Clotting time
FFP	Fresh frozen plasma
FXI	Factor XI
Hb	Hemoglobin
HF	Heart failure
HFrEF	Heart failure with reduced ejection fraction
HPpEF	Heart failure with preserved ejection fraction
ICU	Intensive care unit
IL	Interleukin
LVEF	Left ventricular ejection fraction
MCF	Macrophage chemotactic factor
MRA	Magnetic resonance angiography
NO	Nitric oxide
POD	Postoperative day
PT	Prothrombin time
pTT	Partial thromboplastin time
RDP	Random donor platelets
ROTEM	Rotational thromboelastometry
SCOPE	Specialty care operative procedure registry
SGLT2i	Sodium/glucose cotransporter-2 inhibitors
SIRS	Systemic inflammatory response syndrome
uNGAL	Urinary neutrophil gelatinase-associated lipocalin.



Perfusion Quiz (Multiple Choice Questions)

1. According to 2022 AHA/ACC/HFSA guideline, new recommendations for heart failure with preserved ejection fraction (HFpEF) are:

a) SGLT2i, MRAs and ARNi
b) SGLT2i, MRAs and beta-blockers
c) ACEi, SGLT2i, ARNi
d) None

2. Severe congenital FXI deficiency is defined when:

a) <20% normal activity
b) >20% normal activity
c) <2% normal activity
d) >2% normal activity

3. Nitric oxide supplementation during CPB in adult patients at moderate risk for renal complications is associated with:

a) Higher incidence of AKI
b) Lower incidence of AKI
c) Higher incidence of mortality
d) None

4. The preoperative use of clopidogrel and aspirin may be discontinued for reducing the bleeding and blood product transfusion in patients undergoing off-pump CABG surgery:

a) 2-5 days prior to surgery
b) 5 to 6 days prior to surgery
c) 3 to 5 days prior to surgery
d) 1 day prior to surgery

5. Complications during CPB may increase in cardiac surgical patients who have COVID-19 is:

a) Lowest CPB hematocrit level
b) Coagulation disturbances
c) Higher oxygenator gas exchange complications
d) All of the above

6. One-stage operation in the aortic arch and thoracoabdominal aortic aneurysms (TAAA) surgeries improve by:

a) Safe perfusion practice
b) Holistic approach of the surgical team
c) Both
d) None

7. The probability of severe SIRS significantly increased with:

a) Elevated CPB glucose level
b) Reduced CPB glucose level
c) Does not depend on CPB glucose level
d) None

SGLT2i, MRAs and ARNi	<20% normal activity	Higher incidence of AKI	5 to 6 days prior to surgery	All of the above	Both	Elevated CPB glucose level

The author **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 21 is accurate and up to date.

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