Effect of CPB Glucose Levels on Inflammatory Response After Pediatric Cardiac Surgery

Zhi-Hua Zeng

Department of Cardiovascular Surgery, TEDA International Cardiovascular Hospital, Chinese Academy of Medical Sciences & Graduate School of Peking Union Medical College

Xin-Yi Yu

Department of Cardiovascular Surgery, TEDA International Cardiovascular Hospital, Chinese Academy of Medical Sciences & Graduate School of Peking Union Medical College

Xiao-cheng Liu

Department of Cardiovascular Surgery, TEDA International Cardiovascular Hospital, Chinese Academy of Medical Sciences & Graduate School of Peking Union Medical College

Zhi-Gang Liu (✉ liuzg@tedaich.com)

Department of Cardiovascular Surgery, TEDA International Cardiovascular Hospital, Chinese Academy of Medical Sciences & Graduate School of Peking Union Medical College

Research Article

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Abstract

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

Methods: We enrolled children with congenital heart disease who underwent surgical repair between June 2012 and December 2020. We included only patients who underwent cardiac surgery with CPB. The primary outcome was severe SIRS. A two-piece-wise regression model was applied to examine threshold effect of CPB glucose on severe SIRS.

Results: A total of 7350 patients were enrolled in the present study, of whom 3895 (52.99%) are female. After potential confounders were adjusted, non-linear relationship was detected between CPB glucose and severe SIRS, whose turning point was 8.1. By gender, the J-shaped risk curve for female patients is not significantly different from the risk curve for male patients. With CPB glucose < 8.1mmol/L, the estimated dose-response curve was consistent with a horizontal line. However, the prevalence of severe SIRS increased with increasing glucose up to the turning point (Glucose > 8.1mmol/L); the odds ratio (OR) of the Glucose was 2.13 (95% CI: 1.99-2.28).

Conclusions: The present study indicates the association of CPB glucose with inflammatory response after pediatric cardiac surgery. The patients might have the best outcomes with the optimal CPB glucose no more than 8.1mmol/L.

Background

Congenital heart disease (CHD) is the most common cause of major congenital anomalies [1]. Although surgical techniques had achieved massive breakthroughs, postoperative morbidity and mortality among infants and young children remain relatively high [2]. Systemic inflammatory response syndrome (SIRS) is a common complication after cardiac surgery. Therefore, identifying modifiable risk factors during the procedure is important for sustained improvement in outcomes.

Hyperglycemia is related to cardiopulmonary bypass (CPB) [3]. Several clinical studies have linked hyperglycemia to increased morbidity and mortality in patients undergoing cardiac surgery [4, 5]. The perioperative period for congenital heart surgery can be challenging because of the systemic inflammatory response and endocrine metabolic stress associated with these procedures [6].

Improved glycemic control at initiation of CPB in adult patients undergoing cardiac surgery was associated with reduced 30-day mortality [7]. Nevertheless, there are no definite optimal glycemic threshold or reference interval for pediatric patients receiving open-heart surgery with CPB. In this study, we aimed to investigate the association of CPB glucose with severe SIRS in pediatric patients receiving open-heart surgery with CPB.

Methods

Research population

This respective cohort study was conducted in pediatric patients who underwent cardiac surgery at TEDA International Cardiovascular Hospital. We included all patients who underwent cardiac surgery with arrested-heart CPB between June 2012 and December 2020. We excluded patients undergoing a cardiac procedure on a beating heart or required preoperative renal-replacement therapy, mechanical ventilatory support, or mechanical circulatory support. We also excluded those who had missing CPB glucose data or outcome. The present study was approved by the Ethics Committee (Internal Review Board) of TEDA International Cardiovascular Hospital. All participants were obtained a written informed consent prior to participation or if the participants had not attained age of majority, the consent was additionally provided by a parent or legal guardian in the study. All procedures in this study were in accordance with the guidelines of the 1975 Declaration of Helsinki.

Research Exposure

All blood glucose measurements during cardiopulmonary bypass were collected.

In this study, maximum CPB arterial glucose values were retrieved from a local online hospital information system for analysis and further confirmed by independent manual examination of extracorporeal circulation records.

Research Covariates

For each patient, those baseline and clinical characteristics, including Gender, Age of surgery (month), Age category of surgery, Body surface area (m^2), BMI (kg/m^2), Hemoglobin, Residence, Residence location, Residence altitude, Inpatient season, Hemodynamic pathology, Extracardiac malformations, Genetic anomalies, Clinical pathway implementation, pulmonary arterial hypertension (PAH), Aristotle complexity score and level were collected.

Research Outcome

The primary outcome variable was severe systemic inflammatory response syndrome (SIRS), which we defined as the time of onset of SIRS from admission to the intensive care unit (ICU), postoperative day 5, or discharge [8]. According to the International Consensus on Pediatric Sepsis: Definition of Pediatric Sepsis and Organ Dysfunction, SIRS is defined as the presence of at least 2 of 4 age-specific criteria: temperature, heart rate, respiratory rate, and leukocyte count, one of which must be abnormal temperature or leukocyte count [9]. In the present study, severe SIRS was defined as according with all 4 above criteria

[10]. Secondary outcomes included SIRS and total hospital costs, postoperative hospital days, and all-cause mortality at 30 days postoperatively.

Statistical analysis

All analyses were performed using EmpowerStats (<http://www.empowerstats.com>). Baseline and clinical materials were grouped by gender. Categorical variables are presented as percentages. Continuous variables are reported as medians with interquartile range (IQR). Comparisons between groups were performed using χ^2 testing for categorical variables and Kruskal–Wallis testing for continuous variables.

Adjusted smoothing spline plots were used to compare the nonlinear risk of severe SIRS between gender-specific groups along the continuum of CPB glucose levels. And we applied a two-piece-wise regression model to examine threshold effect of CPB glucose on severe SIRS. To examine the cumulative incidence of severe SIRS by age at surgery, we used Kaplan-Meier estimates, using age as the time scale [11]. *P-value* < 0.05 was defined as statistically significant.

Results

Patient characteristics and primary outcome

A total of 7350 patients were enrolled in the present study (Figure 1), of whom 3895 (52.99%) are female. 37.5 months (IQR 18.91-69.83) was the median age at the time of surgery, 5950 (80.95%) were from rural areas, and the median glucose during CPB was 6.40 (IQR 5.3-7.8) mmol/L. Baseline characteristics of patients with female and male are shown in Table 1. Female patients were older but congenital heart disease clinical pathways were less frequently implemented (Table 1).

Table 1
Characteristics and results between female and male patients.

	All patients(N=7350)	Female(N=3895)	Male(N=3455)	<i>P-value</i>
Sociodemography				
Age of surgery,month	37.53(18.91-69.83)	39.10 (20.13-70.87)	35.93 (17.67-68.15)	<0.001
Age category of surgery				0.018
Infants	2127 (28.94%)	1067 (27.39%)	1060 (30.68%)	
Toddlers and preschoolers	3526 (47.97%)	1899 (48.75%)	1627 (47.09%)	
School age	1415 (19.25%)	772 (19.82%)	643 (18.61%)	
Teenagers	282 (3.84%)	157 (4.03%)	125 (3.62%)	
Body surface area, m ²	0.59 (0.47-0.75)	0.59 (0.47-0.75)	0.59 (0.47-0.75)	0.880
BMI, kg/m ²	15.19 (14.07-16.53)	15.01 (13.89-16.33)	15.41 (14.27-16.77)	<0.001
Hemoglobin	128.00 (119.00-136.00)	128.00 (119.00-136.00)	128.00 (119.00-137.00)	0.140
Residence				0.309
Countryside	5950 (80.95%)	3136 (80.51%)	2814 (81.45%)	
Urban	1400 (19.05%)	759 (19.49%)	641 (18.55%)	
Residence location				0.673
Eastern China	1724 (23.46%)	930 (23.88%)	794 (22.98%)	
Northern China	1010 (13.74%)	543 (13.94%)	467 (13.52%)	
Central China	1499 (20.39%)	780 (20.03%)	719 (20.81%)	
Western China	3117 (42.41%)	1642 (42.16%)	1475 (42.69%)	
Residence altitude				0.456
Low altitude	5038 (68.54%)	2655 (68.16%)	2383 (68.97%)	
High altitude	2312 (31.46%)	1240 (31.84%)	1072 (31.03%)	
Inpatient Information				

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

	All patients(N=7350)	Female(N=3895)	Male(N=3455)	<i>P-value</i>
Inpatient season				0.440
Spring	1198 (16.30%)	651 (16.71%)	547 (15.83%)	
Summer	2086 (28.38%)	1078 (27.68%)	1008 (29.18%)	
Autumn	2140 (29.12%)	1132 (29.06%)	1008 (29.18%)	
Winter	1926 (26.20%)	1034 (26.55%)	892 (25.82%)	
Hemodynamic pathology				0.814
Non cyanotic	6262 (85.20%)	3322 (85.29%)	2940 (85.09%)	
Cyanotic	1088 (14.80%)	573 (14.71%)	515 (14.91%)	
Extracardiac malformations				<0.001
Absence	7053 (95.96%)	3690 (94.74%)	3363 (97.34%)	
Presence	297 (4.04%)	205 (5.26%)	92 (2.66%)	
Genetic anomalies				0.003
Non	6964 (94.74%)	3662 (94.02%)	3302 (95.57%)	
Presence	386 (5.13%)	233 (5.98%)	153 (4.43%)	
Clinical pathway implementation				0.556
Non	1299 (17.67%)	698 (17.92%)	601 (17.40%)	
Presence	6051 (82.33%)	3197 (82.08%)	2854 (82.60%)	
PAH				0.035
Non	4585 (62.38%)	2386 (61.26%)	2199 (63.65%)	
Presence	2765 (37.62%)	1509 (38.74%)	1256 (36.35%)	
Surgical factors				
Aristotle complexity score	6.00 (6.00-7.00)	6.00 (6.00-7.00)	6.00 (6.00-7.00)	0.165
Aristotle complexity level				0.190

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

	All patients(N=7350)	Female(N=3895)	Male(N=3455)	<i>P-value</i>
Level 1	1197 (16.29%)	666 (17.10%)	531 (15.37%)	
Level 2	5020 (68.30%)	2630 (67.52%)	2390 (69.18%)	
Level 3	1005 (13.67%)	527 (13.53%)	478 (13.84%)	
Level 4	128 (1.74%)	72 (1.85%)	56 (1.62%)	
Exposure				
Glucose, mmol/L	6.40 (5.30-7.80)	6.30 (5.30-7.80)	6.40 (5.30-7.80)	0.079
Outcomes				
Primary outcome				
Severe SIRS	1600 (21.77%)	844 (21.67%)	756 (21.88%)	0.826
Secondary outcome				
SIRS	5637 (76.69%)	2937 (75.40%)	2700 (78.15%)	0.005
Length of hospitalization, d	6.00 (4.00-8.00)	6.00 (4.00-8.00)	6.00 (4.00-8.00)	0.010
Hospitalization fee,	28831.28 (24462.60-34586.62)	28867.32 (24518.17-34592.53)	28795.06 (24422.48-34586.62)	0.652
Inpatient mortality rate	27 (0.37%)	11 (0.28%)	16 (0.46%)	0.201
BMI, Body mass index; PAH, Pulmonary arterial hypertension; SIRS, systemic inflammatory response syndrome. *Data are n (%) or median (IQR) other indicated mean (SD)				

Female patients had a higher frequency of extracardiac malformations, genetic anomalies and pulmonary hypertension in comparison to male patients (Table 1). There were no significant differences between the two groups in terms of residence, inpatient season, hemodynamic pathology, and clinical pathway implementation (Table 1). The overall incidence of severe SIRS was 21.77%, and the incidence of severe SIRS in female patients and male patients was 21.67% and 21.88% (Table 1).

Secondary Outcome

Male patients had a significantly longer postoperative hospital stay in comparison to female patients ($P=0.010$) and a higher incidence of SIRS ($P<0.01$). There was no significant differences in hospitalization fee and inpatient mortality rate.

Association Of Continuous Glucose With Outcome

Adjusted smoothed plots suggest a nonlinear relationship between CPB glucose and severe SIRS. Overall, there was a gradual J-shaped risk curve among total patients (Figure 2A). By gender, the J-shaped risk curve for female patients is not significantly different from the risk curve for male patients (Figure 2B, 2C).

By two-piece-wise linear regression model, we calculated the turning point was 8.1. With a Glucose<8.1mmol/L, the estimated dose–response curve was consistent with a horizontal line. However, the prevalence of severe SIRS increased with increasing glucose up to the turning point (Glucose>8.1mmol/L); the *odds ratio* (OR) of the Glucose was 2.13 (95% CI: 1.99-2.28) (Table 2). The threshold of glucose would result in a risk probability of roughly 1.12 or greater for severe SIRS (Table 2).

Table 2 Threshold effect analysis of CPB glucose on severe SIRS using two-piece-wise regression model.

Severe SIRS	
Adjusted β/OR (95% CI) p-value	
Model I	
One line slop	1.46 (1.41, 1.50) <0.0001
Model II	
Turning point (K)	8.1
Glucose<8.1mmol/L	1.01 (0.95, 1.07) 0.7372
Glucose>8.1mmol/L	2.13 (1.99, 2.28) <0.0001
LRT test	<0.001#

LRT test: Logarithmic likelihood ratio test. # indicates that Model II is significant different from Model I.

Adjusted: Gender, Age of surgery (month), Age category of surgery, Body surface area (m²), BMI (kg/m²), Hemoglobin, Residence, Residence location, Residence altitude, Inpatient season, Hemodynamic pathology, Extracardiac malformations, Genetic anomalies, Clinical pathway implementation, pulmonary arterial hypertension (PAH), Aristotle complexity score, Aristotle complexity level.

Severe SIRS-free Probability By Age

Figure 3 shows the severe SIRS-free probability by age separately for female and male patients and overall patients. For both groups and all patients, this age gradient was steeper for those with glucose>8.1mmol/L, and the patients with glucose<8.1mmol/L have the lower risk probability (*P* < 0.001) whatever subgroups and overall (Figure 3A,B,C).

Discussion

This study demonstrated for the first time the dose-dependent effect of CPB glucose on the inflammatory response after pediatric cardiac surgery. Our findings demonstrate the optimal levels of CPB glucose for children undergoing CHD surgery. Non-linear relationship was detected between CPB glucose and severe SIRS, whose turning point was 8.1. The probability of postoperative severe SIRS increased with elevated CPB glucose up to the turning point (Glucose = 8.1mmol/L). Using the overall rate of severe SIRS as reference, CPB glucose threshold of SIRS might lower 8.1mmol/L, which conduce to management of extracorporeal circulation.

In the present study (Fig. 2), we found that the relationship between CPB glucose and severe SIRS was non-linear (after adjusting Gender, Age of surgery (month), Age category of surgery, Body surface area (m^2), BMI (kg/m^2), Hemoglobin, Residence, Residence location, Residence altitude, Inpatient season, Hemodynamic pathology, Extracardiac malformations, Genetic anomalies, Clinical pathway implementation, pulmonary arterial hypertension (PAH), Aristotle complexity score, Aristotle complexity level). This indicated that CPB glucose was related to severe SIRS after pediatric cardiac surgery. Overall, there was a gradual J-shaped risk curve among total patients (Figure 2A). By gender, the J-shaped risk curve for female patients is not significantly different from the risk curve for male patients (Figure 2B, 2C).

Intraoperative hyperglycemia was related to worse hospital outcomes after cardiac surgery, including death [4, 12, 13]. A study showed that strict glycemic control significantly decreased morbidity and mortality in critically ill children[14]. Strict intraoperative and postoperative glycemic control protects the myocardium and reduces the inflammatory response in neonatal cardiac surgery [6].

The optimal postoperative glycemic range in children undergoing complex congenital heart surgery was likely to be 6.1 to 7 mmol/L [7]. Peri-operative mean glucose ≤ 8.3 mmol/L may decreased adverse events in infants receiving open cardiac surgery [15]. In the present study, there was a non-linear relationship between CPB blood glucose and severe SIRS and the incidence of severe inflammatory response syndrome increased with increased glucose in the extracorporeal circulation. Based on the nonlinear effect of CPB blood glucose on severe SIRS in our study, CPB blood glucose levels below 8.1 mmol/L may be the optimal threshold.

In the current study, The probability of severe SIRS significantly increased with elevated CPB glucose up to the turning point (Glucose = 8.1mmol/L). Furthermore, We examined the cumulative incidence of severe SIRS by age at surgery and found that the patients with glucose<8.1mmol/L had the lower risk probability ($P<0.001$) whatever subgroups and overall patients (Figure 3A, 3B, 3C). These results highlighted that a significant take away maybe to maintain on CPB glucose<8.1mmol/L for all patients. Our study indicates that male patients were associated with significantly greater longer postoperative

stay despite similar percentage of in-hospital mortality and hospitalization cost in comparison with those female patients, highlighting differential CPB glucose control for CHD children in the management of extracorporeal circulation.

Limitations Of The Study

Our study has several potential limitations. The small set of variables available for covariate-adjusted analyses leaves the possibility of residual confounding. Other unavailable potential confounders, such as CPB time, might change the recorded association between CPB glucose and the risk of severe SIRS. It is the highest arterial glucose that we selected for association analysis in our study that may not be comprehensive enough to reveal the clinical significance of glucose in postoperative inflammatory responses, so further study using the average arterial glucose may more reasonable. This study only studied blood glucose during extracorporeal circulation, and further studies should be conducted in conjunction with postoperative blood glucose.

Conclusion

To the best of our knowledge, this is the first study to investigate the optimal CPB glucose in pediatric cardiac surgery. Our study provides evidence supporting that patients might have the best outcomes with the optimal CPB glucose no more than 8.1mmol/L. These findings can promote to management of CPB glucose.

Abbreviations

CHD

Congenital heart disease

CPB

Cardiopulmonary bypass

SIRS

Systemic inflammatory response syndrome

BMI

Body mass index

PAH

Pulmonary arterial hypertension

IQR

Interquartile range

ICU

Intensive care unit

OR

Odds ratio

SD

Indicated mean
CI
Confidence Interval.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee (Internal Review Board) of TEDA International Cardiovascular Hospital. All participants were obtained a written informed consent prior to participation or if the participants had not attained age of majority, the consent was additionally provided by a parent or legal guardian in the study. All procedures in this study were in accordance with the guidelines of the 1975 Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Competing interests

No conflicts of interest, financial or otherwise, are declared by the authors.

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of the data; preparation or review of the manuscript and, decision to submit for publication.

Authors' contributions

ZZH, LZG and LXC conceived the study. ZHZ, YXY, LZG and LXC planned the study and contributed to data collection. LZG, ZHZ, LXC contributed to data analysis. ZHZ, YXY, and LZG contributed to writing and preparation of the manuscript. All authors have reviewed and approved the final manuscript.

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Not applicable.

References

1. Murray CJ, Richards MA, Newton JN, Fenton KA, Anderson HR, Atkinson C, Bennett D, Bernabé E, Blencowe H, Bourne R et al. UK health performance: findings of the Global Burden of Disease Study 2010. *Lancet*. 2013; 381(9871):997–1020.
2. O'Brien SM, Clarke DR, Jacobs JP, Jacobs ML, Lacour-Gayet FG, Pizarro C, Welke KF, Maruszewski B, Tobota Z, Miller WJ et al. An empirically based tool for analyzing mortality associated with congenital heart surgery. *J Thorac Cardiovasc Surg*. 2009; 138(5):1139–1153.
3. Doenst T, Wijeyesundera D, Karkouti K, Zechner C, Maganti M, Rao V, Borger MA. Hyperglycemia during cardiopulmonary bypass is an independent risk factor for mortality in patients undergoing cardiac surgery. *J Thorac Cardiovasc Surg*. 2005; 130(4):1144.
4. Gandhi GY, Nuttall GA, Abel MD, Mullany CJ, Schaff HV, Williams BA, Schrader LM, Rizza RA, McMahon MM. Intraoperative hyperglycemia and perioperative outcomes in cardiac surgery patients. *Mayo Clin Proc*. 2005; 80(7):862-866.
5. Yates AR, Dyke PC, 2nd, Taeed R, Hoffman TM, Hayes J, Feltes TF, Cua CL. Hyperglycemia is a marker for poor outcome in the postoperative pediatric cardiac patient. *Pediatr Crit Care Med*. 2006; 7(4):351–355.
6. Vlasselaers D, Mesotten D, Langouche L, Vanhorebeek I, van den Heuvel I, Milants I, Wouters P, Wouters P, Meyns B, Bjerre M et al. Tight glycemic control protects the myocardium and reduces inflammation in neonatal heart surgery. *Ann Thorac Surg*. 2010; 90(1):22–29.
7. Polito A, Thiagarajan RR, Laussen PC, Gauvreau K, Agus MS, Scheurer MA, Pigula FA, Costello JM. Association between intraoperative and early postoperative glucose levels and adverse outcomes after complex congenital heart surgery. *Circulation*. 2008; 118(22):2235–2242.
8. Liu H, Hu YJ, Zheng SQ, Chen T, Zeng ZH, Wu DD, Zhao S, Zeng B, Liu ZG, Shao YF. Effect of perfusate oxygenation on inflammatory response in congenital heart disease children from low versus high altitude. *J Thorac Cardiovasc Surg*. 2021; 161(6):2180–2190.
9. Goldstein B, Giroir B, Randolph A. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med*. 2005; 6(1):2-8.
10. Lindman BR, Goldstein JS, Nassif ME, Zajarias A, Novak E, Tibrewala A, Vatterott AM, Lawler C, Damiano RJ, Moon MR et al. Systemic inflammatory response syndrome after transcatheter or surgical aortic valve replacement. *Heart*. 2015; 101(7):537–545.
11. Qizilbash N, Gregson J, Johnson ME, Pearce N, Douglas I, Wing K, Evans SJW, Pocock SJ. BMI and risk of dementia in two million people over two decades: a retrospective cohort study. *The lancet Diabetes & endocrinology*. 2015; 3(6):431–436.
12. Ouattara A, Lecomte P, Le Manach Y, Landi M, Jacqueminet S, Platonov I, Bonnet N, Riou B, Coriat P. Poor intraoperative blood glucose control is associated with a worsened hospital outcome after cardiac surgery in diabetic patients. *Anesthesiology*. 2005; 103(4):687–694.
13. Puskas F, Grocott HP, White WD, Mathew JP, Newman MF, Bar-Yosef S. Intraoperative hyperglycemia and cognitive decline after CABG. *Ann Thorac Surg*. 2007; 84(5):1467–1473.

14. Vlasselaers D, Milants I, Desmet L, Wouters PJ, Vanhorebeek I, van den Heuvel I, Mesotten D, Casaer MP, Meyfroidt G, Ingels C et al. Intensive insulin therapy for patients in paediatric intensive care: a prospective, randomised controlled study. *Lancet*. 2009; 373(9663):547–556.
15. Song L, Fan D, Cun L, Jinping L, Ju Z, Zhengyi F. Effects of peri-operative glucose levels on adverse outcomes in infants receiving open-heart surgery for congenital heart disease with cardiopulmonary bypass. *Perfusion*. 2011; 26(2):133–139.

Figures

Figure 1

The selected study patients. CHD, Congenital heart diseases; CPB, cardiopulmonary bypass.

Figure 2

The relationship between CPB glucose and risk probability of severe SIRS. **A.** A gradual J-shaped risk curve among total patients. **B.** A gradual J-shaped risk curve among female patients. **C.** A gradual J-shaped risk curve among male 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 (m^2), BMI (kg/m^2), Hemoglobin, Residence, Residence location, Residence altitude, Inpatient season, Hemodynamic pathology, Extracardiac malformations, Genetic anomalies, Clinical pathway implementation, pulmonary arterial hypertension (PAH), Aristotle complexity score, Aristotle complexity level.

A **B** **C** **Figure 3**

Severe SIRS-free probability with increasing age by glucose category for female (A) and male (B) patients and overall patients (C). The figure represents the severe SIRS-free probability by age separately for female and male patients and all patients depending on glucose category.

Supplementary Files

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- [rawdata.xlsx](#)