Cardiology in the Young

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Assessment of the frequency and risk factors of gastrointestinal bleeding after cardiopulmonary bypass in paediatric cases

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Abstract

Introduction and Aim: Gastrointestinal bleeding is a potential complication in paediatric patients undergoing cardiopulmonary bypass, as it develops secondary to low gastrointestinal perfusion. This study aimed to examine the incidence of gastrointestinal bleeding and identify its risk factors in these patients. *Method:* This retrospective study was undertaken to examine the demographic features, clinical findings, and operative data of paediatric patients under years old who had undergone congenital heart surgery with cardiopulmonary bypass between November 1, 2021, and November 1, 2023. The study aimed to investigate the incidence of gastrointestinal bleeding associated with cardiopulmonary bypass and to identify potential risk factors for gastrointestinal bleeding. The obtained results were statistically evaluated. *Results:* The study period included 1100 patients who underwent congenital heart surgery with cardiopulmonary bypass. Fifty-two percent of the total participants were male. The median weight of the patients was 4.4 kg, with an interquartile range of 3.5–5.8 kg. The patients were categorised by age, revealing that 62% were newborns, 24% were infants, and 14% were children. Forty-four (4.2%) of the total number of patients experienced gastrointestinal bleeding. Newborns had a significantly higher incidence of bleeding (6% or 34 patients) compared to infants (3% or 8 patients) and children (1.5% or 2 patients) ($p < 0.05$). Patients who experienced gastrointestinal bleeding had a longer median hospital stay of 24 days compared to those who did not, with a median hospital stay of 14 days. Moreover, patients who suffered from bleeding had a significantly higher mortality rate (30%) in comparison to those who did not (9.9%) ($p < 0.05$). The incidence of gastrointestinal bleeding was found to be associated with several risk factors, such as low operative age and weight, high surgical score, presence of low cardiac output syndrome, extracorporeal membrane oxygenation (ECMO) usage, high lactate levels, and low platelet count. *Conclusion:* Gastrointestinal bleeding is a potential complication for patients who undergo cardiopulmonary bypass. It is particularly relevant for newborns who have undergone prolonged surgery, have a high surgical complexity score, exhibit high lactate levels, display low cardiac output, utilise ECMO, and possess low platelet counts. In such cases, there may be a heightened incidence of gastrointestinal bleeding. It is important to consider this possibility in order to ensure the best possible patient outcomes.

Introduction

The frequency of CHD varies between 4 and 8 per thousand live births, and approximately 25% of these cases constitute critical CHDs that require treatment within the first year of life.[1] Surgical procedures for CHD patients with different anatomical and haemodynamic features can lead to various complications in intensive care after surgery.[2]

Complications of the gastrointestinal system, such as gastrointestinal bleeding due to reduced gastrointestinal perfusion after cardiac surgery following prolonged ischaemia, are among the complications that can occur. Despite advances in cardiopulmonary bypass techniques and intensive care support, these complications can still affect mortality and morbidity.[3,4]

Although there are numerous studies in the literature on gastrointestinal bleeding after cardiopulmonary bypass in adult cases, there is limited research on paediatric cases after congenital heart surgery.[5,6]

This study aimed to investigate the frequency of gastrointestinal bleeding and its risk factors in paediatric patients undergoing cardiopulmonary bypass.

Methods

Patient and study design

This study was carried out retrospectively on paediatric patients aged less than 18 years who had undergone congenital heart surgery with cardiopulmonary bypass between November 1, 2021, and November 1, 2023. Cases involving heart surgery without cardiopulmonary bypass procedures, incomplete medical records, or those experiencing gastrointestinal bleeding before the operation were excluded from the study.

The study data were obtained from the electronic medical records in our hospital's data system, and the examined variables included demographic characteristics, laboratory test data, and variables related to surgery. The study was conducted in compliance with the Declaration of Helsinki and received approval from the local committee.

Definition and variables

During the study period, a total of 1100 patients were evaluated for cardiac surgical procedures. These procedures encompass any intrathoracic or cardiac intervention. Gastrointestinal bleeding, which is bleeding from the upper or lower gastrointestinal tract, can present in various clinical forms depending on the severity and location of the bleeding. The definition of gastrointestinal bleeding includes a positive occult blood test result in specimens such as faeces or gastric juice. For each patient who underwent a cardiac surgical procedure, the following data were recorded: demographics (age, sex, operative procedure, cardiopulmonary bypass time, temperature of cardiopulmonary bypass, perfusion mode of cardiopulmonary bypass, and postoperative factors (length of hospital stay, length of mechanical ventilation, use of renal replacement therapy, use of extracorporeal membrane oxygenation (ECMO), postoperative ejection fraction, postoperative dialysis, postoperative lactate, postoperative hepatic function [alanine aminotransferase (ALT) and aspartate aminotransferase (AST)], postoperative platelet count, and survival to hospital discharge [%]). Patient age was categorised into three groups: neonates (<28 days), infants (29 days to 1 year), and children (1–18 years). Operative procedure risk stratification was based on The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery score, and The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery mortality categories 1–5 were considered to indicate complicated surgery.[7]

In our research, we identified hepatic injury as the presence of ALT level ≥100 U/L and/or AST level ≥100 U/L 30 days post-surgery. The modified Ulate low cardiac output syndrome score was employed for the diagnosis of low cardiac output syndrome.[8] The low cardiac output syndrome score was calculated by assigning one point for each of the following criteria: (1) tachycardia (>20% above postinduction heart rate in the operating room), (2) oliguria (<1 mL/kg/hour), (3) capillary filling time >3 seconds, (4) need for volume expansion (beyond maintenance IV fluids) (>30 mL/kg/day), (5) decreased near-infrared spectroscopy (NIRS) measurements (cerebral and renal NIRS <50% and 75% of arterial saturations, respectively), (6) elevated arterial lactate levels (>2 mmol/L or >0.75 mmol/L/hour increase), and (7) need for vasoactive-inotropic infusions over 0.5 μg/kg/minute milrinone. Each parameter was allotted one point, and the low cardiac output syndrome score was calculated hourly. If the total low cardiac output syndrome score was 3 or higher at any time during the first 24 hours, the patient was considered to have low cardiac output syndrome.[9]

Blood samples for lactate level measurement were obtained from the arterial cannula inserted during surgery. Lactate levels are routinely measured on cardiac ICU admission and are frequently monitored thereafter (i.e., 6, 12, 24, and 48 h, and more often if clinically indicated) during the postoperative period.

The vasoactive inotropic score was calculated for each patient using the standard formula for the first 24 postoperative hours, and the maximum score was recorded. The vasoactive inotropic score formula is as follows: vasoactive inotropic score = Dopamine dose (μg/kg/min) + dobutamine dose (μg/kg/min) + 100 × epinephrine dose (μg/kg/min) + 10 × milrinone dose (μg/kg/min) + 10,000 × vasopressin dose (Units/kg/min) + 100 × norepinephrine dose (μg/kg/min).[10]

Statistical analysis

Data were analysed using SPSS Statistics for Windows 15.0, a software programme developed by SPSS Inc., located in Chicago, Illinois, USA. To describe continuous data, the median along with the interquartile range was utilised, while absolute count and percentages were used to present categorical data. The Pearson chi-square test and Mann–Whitney *U* test were applied to compare variables between groups. To evaluate the discrimination of factors predicting mortality and morbidity, logistic regression models were employed, and the area under the receiver operating characteristic curve was assessed using the results. The estimated area under the curve and its 95% confidence interval are presented in the results. A significance level of $p < 0.05$ was set for statistical significance.

Results

A total of 1100 patients were included in the study, with 52% being male. The patients' median age was 2 months (interquartile range: 1–3 months). The median weight was 4.4 kg (interquartile range 3.5–5.8). The patients were divided into three age groups: newborns (62%), infants (24%), and children (14%). The demographic characteristics of the patients are presented in Table 1.

The results of the univariate analysis for gastrointestinal bleeding after cardiopulmonary bypass are presented in Table 2. Among the 1100 children, 44 (4.2%) developed gastrointestinal bleeding as a postoperative complication. Of these patients, 30% died, while 70% survived to hospital discharge. The incidence of gastrointestinal bleeding was 4.9% in neonates (34/682), 3.0% in infants (8/264), and 1.2% in children (2/154).

In this cardiopulmonary bypass cohort (1100 children), 44 (4.2%) had postoperative gastrointestinal bleeding. Patients with gastrointestinal bleeding were younger (30 vs. 120 days, $p < 0.001$) and had lower weight compared to those without gastrointestinal bleeding. The The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery category, which is influenced by the CHD diagnosis, differed significantly between the two groups. Patients with gastrointestinal bleeding had longer cardiopulmonary bypass (120 vs. 90, $p < 0.001$) and aortic cross-clamp times (80 vs. 50, $p < 0.001$). Additionally, patients with gastrointestinal bleeding had lower postoperative platelet counts (80 vs. 150, $p < 0.001$) and higher postoperative arterial lactate levels (6.5 vs. 2.4, $p < 0.001$).

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Table 1. Demographics and patient characteristics

Variables	Median (IQR) or *n*%
n	1100
Age (months)	2 (1–3)
Weight (kg)	4.4 (3.5–5.8)
Body surface area (m^2)	0.28 (0.24–0.32)
Male	572 (52)
STAT category	
1–2	420 (38)
3–5	680 (62)
Syndrome	54 (4.9)
Emergent procedure	172 (15.6)
Physiology	
Single ventricle	311 (28)
Biventricular	789 (72)
Main procedure	
ASD closure	65 (5.9%)
Arch reconstruction	108 (9.8%)
Arterial switch operation	97 (8.8%)
AVSD repair	58 (5.2%)
Bidirectional cava pulmonary anastomosis	34 (3.1%)
DORV repair	10 (0.9%)
Fontan operation	5 (0.4%)
Norwood	25 (2.3%)
Pulmonary artery banding	62 (5.7%)
Shunt	26 (2.4%)
TAPVC repair	42 (3.9%)
Tetralogy of fallot total repair	93 (8.4%)
Truncus repair	12 (1%)
Valve repair	34 (3.1%)
VSD closure	212 (19.3%)
Other	217 (19.8%)

ASD = Atrial Septal defect; AVSD = Atrioventricular Septal Defect; DORV = Double outlet right ventricle; STAT = The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery; TAPVC = Total abnormal pulmonary venous connection; VSD = ventricular septal defect.

Table 2. Univariate analysis for gastrointestinal bleeding after cardiopulmonary bypass in children

Variables	GIS bleeding ($n = 44$)	No GIS bleeding ($n = 1056$)	*p*
Age/days	30 (15–60)	120 (90–150)	<**0.001**
Age Group			
Newborn	34 (77.5)	648 (61)	<**0.001**
İnfant	8 (18)	256 (24)	
Children	2 (4.5)	152 (15)	
Weight/kg	3.6 (3–4.2)	6 (4.5–7.5)	<**0.001**
Male	22 (50)	550 (52.1)	0.890
Saturation	89 (85–93)	91 (88–96)	0.840
Paliative surgery	9 (21)	158 (15)	0.320
STAT category			
1–2	10 (22)	410 (38)	**0.001**
3–5	34 (78)	646 (62)	
CPB time/min	120 (100–145)	90 (70–110)	<**0.001**
Cross clamp time/min	80 (60–100)	50 (30–70)	<**0.001**
Ventilation time/hour	20 (15–25)	12 (8–16)	**0.002**
ECMO	14 (31.8)	24 (2.3)	<**0.001**
Vazoactive Inotrope score <10	31 (70)	845 (80)	0.080
Arrhythmias	4 (9)	74 (7)	0.280
Hepatic İnjury	11 (25)	21 (2)	<**0.001**
Acute Kidney Injury	6 (13.6)	35 (8.9)	**0.020**
LCOS	28 (63.6)	170 (16)	<**0.001**
Peak Artery lactate level (mmol/L)	6 .5 (5–7.5)	2.4 (1.8–3.2)	<**0.001**
Postoperative platelet (109/L)	80 (60–100)	150 (110–190)	<**0.001**
ICU stay (days)	9 (7–13)	3 (2–4)	**0.001**
Post-op hospital stay (days)	25 (20–30)	14 (10–18)	<**0.001**
Mortality	13 (30%)	105 (9.9%)	<**0.001**

Median (IQR) *n* (%).
CPB = Cardiopulmonary bypass; ECMO = Extracorporeal membrane oxygenation; ICU = Intensive care unit; LCOS = Low cardiac output syndrome; STAT = The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery.

Overall, patients with gastrointestinal bleeding had longer hospital (25 vs. 14, $p < 0.001$) and ICU stays (9 vs. 3, $p<0.001$). The mortality rate was significantly higher among patients with gastrointestinal bleeding than among those who did not develop gastrointestinal bleeding (30% vs. 9.9%, $p < 0.001$).

The results of the multivariate analysis of the risk factors for gastrointestinal bleeding after cardiopulmonary bypass in children are presented in Table 3. The multivariate analysis revealed that cardiopulmonary bypass time (odds ratio [OR] 1.2, 95% confidence interval [CI]: 1–1.5; $p < 0.001$), age (OR 1, 95% CI: 0.9–1.1; $p = 0.01$), complicated surgery (OR 2.3, 95% CI: 1.6–3.2; $p < 0.001$), weight (OR 0.9, 95% CI: 0.8–1; $p = 0.02$), low cardiac output syndrome (OR 2, 95% CI: 1.5–2.7; $p < 0.001$), use of ECMO (OR 4.1, 95% CI: 2.2–6.1; $p < 0.001$), hepatic injury (OR 1.3, 95% CI: 1–1.8; $p = 0.01$), arterial lactate level (OR 1.2, 95% CI: 1.1–1.3; $p = 0.01$), and postoperative platelet counts (OR 0.8, 95% CI: 0.65–0.95; $p < 0.001$) were associated with gastrointestinal bleeding in CHD surgery patients with cardiopulmonary bypass.

Discussion

In this study, we examined the prevalence of gastrointestinal bleeding and its potential risk factors in children with CHD who underwent cardiopulmonary bypass. Our findings indicate that gastrointestinal bleeding occurred in 4% of the cases and was associated with increased mortality. We also identified several

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Table 3. Multivariate logistic regression analysis of risk factors for gastrointestinal bleeding after cardiopulmonary bypass in children

Variables	*p*	Odds Ratio	95% Confidence Interval
Age/days	0.01	1	0.9–1.1
Weight	0.020	0.9	0.8–1
STAT category	<0.001	2.3	1.6–3.2
CPB Time	<0.001	1.2	1–1.5
ECMO	<0.001	4.1	2.2–6.1
Hepatic injury	0.010	1.3	1–1.8
LCOS	<0.001	2	1.5–2.7
Peak Artery lactate level	0.010	1.2	1.1–1.3
Postoperative platelet	<0.001	0.8	0.65–0.95

CPB = Cardiopulmonary bypass; ECMO = Extracorporeal membrane oxygenation; LCOS = Low cardiac output syndrome; STAT = The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery.

independent risk factors for gastrointestinal bleeding, including newborn cases, prolonged operation duration, high surgical complexity score, elevated lactate levels, low cardiac output, ECMO usage, and low platelet count. Our study contributes to the limited research on this topic in children with these characteristics.

After cardiopulmonary bypass, a series of physiological changes can occur due to the redistribution of blood flow in the tissues. Cardiopulmonary bypass prioritises ensuring effective blood flow to the brain and other vital organs.This may result in decreased blood flow to the gastrointestinal mucosa, which could potentially lead to gastrointestinal bleeding. The literature reports a frequency of gastrointestinal bleeding after cardiopulmonary bypass in 0.2–2% of cases, with mortality reaching up to 19%.[11–13] In a recent study, the incidence of gastrointestinal bleeding was reported to be 1.9%, and the mortality rate was 15.9%.[4] In our study, we observed a gastrointestinal bleeding incidence of 4.2% and a mortality rate of 30%, which may be attributed to the smaller size of our study population compared to other studies.

Previous studies have identified several clinical, laboratory, and perioperative factors associated with gastrointestinal bleeding. Prolonged cardiopulmonary bypass and aortic cross-clamp times during surgery have been linked to gastrointestinal perfusion impairment and worsening of metabolic insufficiency.[4,11–14] Andersson et al.[15]suggested that during cardiac surgery, if the duration of cardiopulmonary bypass exceeds 150 minutes, it can be considered an independent risk factor predicting gastrointestinal complications. In another study, the duration of cardiopulmonary bypass was found to be associated with the release of biomarkers indicating ischaemic-reperfusion injury and endotoxemia in the gastrointestinal mucosa.[16]

In our study, the cardiopulmonary bypass duration was significantly longer in patients with gastrointestinal bleeding compared to those without (120 vs. 90 minutes, $p < 0.001$), and the prolonged cardiopulmonary bypass duration was an independent risk factor.

Intestinal ischaemia is highly sensitive in all organs, especially during postoperative low cardiac output syndrome. Various factors such as catecholamines, immobilisation, high doses of inotropic agents and opioid drugs, and delayed or absent enteral feeding can exacerbate intraoperative mucosal damage after cardiopulmonary bypass.[11–14] Prolonged and severe hypoperfusion might result in insufficient splanchnic blood flow. Pathophysiological events include uneven blood flow distribution, oxygen supply abnormalities, oxygen demand imbalance, and systemic inflammation. This may cause by neonates likelier to have low cardiac output syndrome and the sensitivity of neonatal gastrointestinal.[4,17] In our study, we found patients with gastrointestinal bleeding were younger than non-gastrointestinal bleeding cases.

It is crucial to be aware of the potential complications associated with ECMO, which can further complicate the clinical picture. Bleeding and thrombotic events are the most common complications, and anticoagulation management significantly affects the occurrence of such events. It is important to note that postoperative ECMO use may be a risk factor for gastrointestinal bleeding after cardiopulmonary bypass in children.[18] The results of our study suggest that postoperative use of ECMO ($p < 0.001$) may be a risk factor gastrointestinal bleeding after cardiopulmonary bypass in children.

A large cohort which involved 21,893 pediatric cases, used multivariate logistic regression to evaluate potential risk factors for gastrointestinal bleeding. In addition to age, weight, complicated surgery, operation time, and ECMO usage, factors such as low cardiac output syndrome, hepatic injury, arterial lactate level, and postoperative platelet count were identified as risk factors that increased the incidence of gastrointestinal bleeding.[4] Similarly, our study observed an increase in the incidence of gastrointestinal bleeding in newborns, in patients with prolonged operation duration, high surgical complexity score, elevated lactate levels, low cardiac output, ECMO usage, and low platelet count.

Limitations

The main limitation of this study is that it is a retrospective, single-centre investigation. Another constraint was that it was an observational study, showing correlation rather than causation. Conducting the study prospectively and evaluating the severity of gastrointestinal bleeding may have yielded more significant results.

In conclusion, gastrointestinal bleeding should be taken into account as a potential complication among patients who undergo cardiopulmonary bypass. An increase in the incidence of gastrointestinal bleeding has been noted in situations involving newborns, extended operation durations, high surgical complexity scores, elevated lactate levels, low cardiac output, ECMO usage, and low platelet counts. Prediction models developed based on these findings will assist future studies in quickly and safely predicting gastrointestinal bleeding.

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Competing interests. All authors declare that they have no conflict of interest.

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