Evaluation of perioperative risk factors in pediatric patients with left ventricle outflow tract obstruction

Canan Salman Önemli¹, Kübra Evren Şahin¹, Mustafa Karaçelik², Çagatay Bilen²



¹Department of Anesthesiology and Reanimation, Saglik Bilimleri University, Dr. Behcet Uz Pediatric Diseases and Surgery Training and Research Hospital, İzmir, Turkey

²Department of Pediatric Cardiovascular Surgery, Saglik Bilimleri University, Dr. Behcet Uz Pediatric Diseases and Surgery Training and Research Hospital, İzmir, Turkey

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Abstract

Introduction: Left ventricular outflow tract obstructions (LVOTO) presents as complex cardiac diseases accompanied by other cardiac anomalies in the pediatric age group. Postoperative complications, especially cardiac, pulmonary, and renal complications, that may develop after pediatric cardiac surgery can become life-threatening. If the perioperative risk factors for these complications are known in pediatric patients with LVOTO, anesthesiologists and surgeons may take precautions to eliminate undesirable outcomes.

Aim: To evaluate the perioperative risk factors that may contribute to the development of postoperative complications in pediatric patients operated on for LVOTO in a pediatric cardiac surgery clinic.

Material and methods: The study retrospectively investigated 58 patients who were operated on for LVOTO in a pediatric cardiac surgery clinic. The patients were divided into two groups, those with and without postoperative complications. Preoperative laboratory test results, anesthesia time, operation time, aortic cross-clamp time, cardiopulmonary bypass (CPB) time, postoperative inotropes, first postoperative laboratory tests, intraoperative and postoperative complications, mechanical ventilation time, intensive care unit stay, and hospital stay were recorded.

Results: The most common postoperative complications were endocrine complications, followed by hepatic complications. The preoperative lymphocyte count was significantly higher (p < 0.05), and the neutrophil-to-lymphocyte ratio (NLR) was significantly lower (p < 0.05) in the group with postoperative complications. The postoperative pH, glucose, creatinine, and aspartate aminotransferase (AST) levels were significantly lower (p < 0.05), and the postoperative calcium level was significantly higher (p < 0.05) in the group without postoperative complications. Intraoperative platelet transfusion rate was found to be significantly lower (p < 0.05) in the group with postoperative complications.

Conclusions: It is critical to identify predictive factors to prevent postoperative complications in pediatric patients undergoing surgery for LVOTO. Preoperative NLR, intraoperative platelet transfusion, and postoperative calcium, glucose, pH and AST levels may help in the prediction of complications.

Key words: left ventricle outflow tract obstruction, pediatric, perioperative, complications, risk factors.

Introduction

The left ventricular outflow tract (LVOT) is the anatomical structure through which the left ventricular stroke volume passes as it moves towards the aorta [1]. This structure has three components – subvalvular, valvular (aortic valve) and supravalvular – and obstructions formed in this region are also referred to by these names [1, 2]. Left ventricular outflow tract obstructions (LVOTO) in the pediatric age group are generally associated with other cardiac anomalies (ASD, VSD, PDA, etc.) appearing as complex congenital heart diseases accompanying the picture [2]. LVOTO is present in 3–10% of patients with congenital heart disease [3]. The most common form of LVOTO in pediatric age is valvular stenosis, and the rarest form is supravalvular stenosis [2].

Knowing the risk factors that can predict early intraoperative and postoperative complications in pediatric patients who will undergo surgical treatment for LVOTO may reduce morbidity and mortality rates with good anesthesia management and significantly contribute to reducing the length of intensive care unit (ICU) stay, hospital stay, and hospitalization costs. It was reported that mechanical ventilation time, ICU stay, and postoperative hospital stay were prolonged in pediatric patients with postoperative complications [4]. Although developed scoring systems

Address for correspondence: Canan Salman Önemli, Department of Anesthesiology and Reanimation, Saglik Bilimleri University, Dr. Behcet Uz Pediatric Diseases and Surgery Training and Research Hospital, İzmir, Turkey, e-mail: canan_ege_35@hotmail.com Received: 24.05.2023, accepted: 29.10.2023.

such as RACHS-1, Aristotle, STS-EACTS, etc. are used to prevent mortality in pediatric cardiac surgery, the measurements in these systems were designed to prevent mortality and have prognostic value but do not have a specific feature for the prevention of post-operative complications in specific pediatric cardiac surgery patients [4]. The limited number of publications related to pediatric LVOTO indicates that the risk factors for the complications of surgical interventions in this particular group are not well known.

Postoperative complications, especially cardiac, pulmonary, and renal complications, that may develop after pediatric cardiac surgery can become life-threatening. If the perioperative risk factors for these complications are known in pediatric patients with LVOTO, anesthesiologists and surgeons may take precautions to eliminate undesirable outcomes. This retrospective study aimed to investigate the outcomes of pediatric patients who had cardiac surgery for LVOTO in our hospital and the perioperative risk factors that may contribute to the development of complications in these patients.

Aim

In this study, we aimed to evaluate the perioperative risk factors that may contribute to the development of postoperative complications in pediatric patients operated on for LVOTO in a pediatric cardiac surgery clinic.

Material and methods

The approval was obtained from the ethics committee of the our hospital on 21/05/2020 with protocol number 2020/08-10. The study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all patients.

The study included patients who were aged 0 to 18 years and had cardiac surgery due to LVOTO between 2012 and 2020 in our hospital. Informed consent was obtained from all patients. Patient information was obtained from patient files and the hospital information registry. The patients' data were reviewed retrospectively; their demographic data, preoperative laboratory test results, history of comorbidities, previous cardiac interventions (surgery/angiographic), concomitant cardiac anomalies, anesthesia time, operation time, aortic cross-clamp time, cardiopulmonary bypass (CPB) time, postoperative inotropes, first postoperative laboratory tests, intraoperative and postoperative complications, mechanical ventilation time, and the length of ICU and hospital stay were recorded. The patients were divided into two groups as those with postoperative complications (Group I) and those without complications (Group II), and the data for these groups were compared.

Statistical analysis

Mean, standard deviation (SD), median, minimum, maximum, frequency, and ratios were used to present the descriptive data related to the perioperative risk factors for LVOTO. The normal distributions of numerical data were tested with the Kolmogorov-Smirnov test. Analysis of variance (ANOVA) with the post-hoc Tukey test, the independent samples *t*-test, the Kruskal-Wallis test, and the Mann-Whitney *U* test were used in the analysis of independent numerical data. The χ^2 test was used in the analysis of independent qualitative data, and the Fisher test was used when the conditions for the χ^2 test were not met. The effect level was investigated with univariate and multivariate logistic regression. The program SPSS Statistics 27.0 (IBM Corp.; Armonk, NY, USA) was used in statistical analyses.

Results

The study included 58 patients, who were divided into two groups: those with or without postoperative complications. Of the patients, 77.6% were male, 22.4% were female, and 91.4% had an American Society of Anesthesiology (ASA) Physical Status Classification score of III. It was found that 5.5% of the patients (n = 3) had a syndrome (Down, Williams, tuberous sclerosis). Of the patients 36.2% previously had balloon angioplasty, and 1.7% had a PDA stent. Mechanical ventilation was not applied to any of our patients in the preoperative period. Other demographic data and the preoperative characteristics of the patients in the two groups are shown in Table I. There was no significant difference (p > 0.05) between patients with and without postoperative complications regarding the demographic and preoperative characteristics.

Concerning the intraoperative data, only 2 patients had AV block in the cardiac rhythm after CPB. It was found that cardiac arrest was not experienced in any patient during the induction and operation. It was found that the intraoperative platelet transfusion rate in the group with postoperative complications was significantly (p < 0.05) lower than in the other group. Intraoperative data for the two groups are shown in Table II. In the group with postoperative complications 39% of the patients underwent subaortic membrane resection + myectomy and 41.4% of the patients underwent additional surgical intervention.

The preoperative and postoperative laboratory results of the patients in the two groups are shown in Table III. The preoperative lymphocyte count was significantly higher (p < 0.05), and the neutrophil-to-lymphocyte ratio (NLR) was significantly lower (p < 0.05) in the group with postoperative complications. The postoperative pH, glucose, creatinine, and aspartate aminotransferase (AST) levels were significantly lower (p < 0.05), and the postoperative calcium level was significantly higher (p < 0.05) in the group without postoperative complications.

The effect of laboratory results was investigated with univariate and multivariate logistic regression analyses. In the univariate model, significant (p < 0.05) efficacy of intraoperative platelet transfusion, preoperative lymphocyte count, NLR, postoperative pH, glucose, AST, and calcium values was observed in the differentiation of patients with and without postoperative complications. In the multivariate model, significant independent (p < 0.05) efficacy of preoperative NLR, postoperative pH and calcium values

Patient characteristics	Postoperative complication (-)	Postoperative complication (+)	<i>P</i> -value
Age [years]:	8.1 ±5.8	6.9 ±5.1	0.457
Newborn	0	0	
Infant	0	1 (2.5%)	
Toddler	6 (35.3%)	9 (21.9%)	
Preschool	5 (29.4%)	11 (26.8%)	
School	4 (23.5%)	12 (29.3%)	
Adolescent	2 (11.8%)	8 (19.5%)	
Gender, <i>n</i> (%):	· · · ·	·	0.896
Male	13 (76%)	32 (78%)	
Female	4 (24%)	9 (22%)	
Weight [kg]	27.9 ±16.6	26.0 ±20.3	0.388
BSA [m ²]	0.9 ±0.4	0.9 ±0.5	0.516
ASA score, <i>n</i> (%):			1.000
	16 (94.1)	37 (90.2)	
ĪV	1 (5.9)	4 (9.8)	
Syndrome, n (%)	1 (5.9)	2 (4.9)	1.000
Drug use, n (%):			
Propranolol	12 (70.6)	26 (63.4)	0.601
ACE inhibitor	6 (35.3)	17 (41.5)	0.662
Spironolactone	5 (29.4)	15 (36.6)	0.601
Digoxin	0	2 (4.9)	1.000
 Furosemide	4 (23.5)	9 (22.0)	0.896
Prior cardiac procedure, n (%)	5 (29.4)	7 (17.1)	0.291
Interventional procedures prior to surgery, n (%)	8 (47.1)	18 (43.9)	0.826
Preoperative cardiac status:			
Arrhythmia:	0	2 (4.8%)	
Ventricular tachycardia attacks	0	1 (2.4%)	
Wolf-Parkinson-White syndrome	0	1 (2.4%)	
Hypertrophic cardiomyopathy	0	2 (4.8%)	
Heart failure	0	1 (2.4%)	
Bicuspid aortic valve, n (%)	6 (35.3)	12 (29.3)	0.652
Ventricular septal defect, n (%)	3 (17.6)	10 (24.4)	0.575
Additional valve anomalies, n (%)	6 (35.3)	16 (39.0)	0.790
Aortic regurgitation, n (%):			0.242
Trivial	10 (58.8)	32 (78.0)	
Mild	3 (17.6)	6 (14.6)	
Moderate	3 (17.6)	2 (4.9)	
Severe	1 (5.9)	1 (2.4)	
LVOT peak gradient, n (%):			0.394
< 30	4 (23.5)	16 (39.0)	
> 30–50	2 (11.8)	7 (17.1)	
> 50–90	9 (52.9)	12 (29.3)	
> 90	2 (11.8)	6 (14.6)	
LVOTO type, <i>n</i> (%):	× 117		
Subvalvular	6 (35.5)	20 (48.8)	
Valvular	3 (17.6)	10 (24.4)	
Supravalvular	0 (0.0)	1 (2.4)	
Subvalvular + Valvular	4 (23.5)	7 (17.1)	
	0	5 (12.2)	
 Subvalvular + Valvular + Supravalvular	0	2 (4.8)	

LVOT – left ventricle outflow tract, LVOTO – left ventricle outflow tract obstruction, BSA – body surface area.

Table II. Patients' intraoperative and ICU data

RACHS score 9.7 ±5.2 10.0 ±4.2 0).537
After CPB heart rhythm, n (%):	.684
Normal sinus rhythm 14 (82.4) 30 (73.2)	
Sinus rhythm after defibrillation3 (17.6)9 (22.0)	
Atrioventricular block 0 2 (4.9)	
Pace, n (%) 1 (5.9) 2 (4.9) 1	.000
Transfusion, n (%):	
Blood transfusion 10 (58.8) 15 (36.6) 0).120
Fresh frozen plasma transfusion14 (82.4)38 (92.7)0).345
Platelet transfusion 5 (29.4) 2 (4.9) 0	0.009
Intraoperative drug, n (%):	
Tranexamic acidw 5 (29.4) 7 (17.1) O).291
Milrinone 2 (11.8) 6 (14.6) 0).773
Dopamine 14 (82.4) 29 (70.7) C).358
Dobutamine 12 (70.6) 34 (82.9) 0).291
Noradrenaline 3 (17.6) 8 (19.5) C	.869
Aortic cross-clamping time [min] 91.5 ±40.9 78.6 ±35.5 0).233
CPB time [min] 138.0 ±47.7 116.7 ±40.5 C	0.089
Surgery, n (%):	
Brom aortoplasty 0 8 (19.5)	
Subaortic membrane resection (SMR)4 (23.5)8 (19.5)	
SMR + myectomy 6 (35.3) 16 (39)	
Aortic commissurotomy 5 (29.4) 2 (4.8)	
Aortic valve replacement2 (11.7)8 (19.5)	
Mitral valve replacement 0 2 (4.8)	
VSD closure 3 (17.6) 10 (24.4)	
ASD closure 0 2 (4.8)	
Aortic aneurysm excision1 (5.8)0	
Hypoplastic arcus aorta repair 0 1 (2.4)	
Tumor resection 0 1 (2.4)	
AICD implantation 0 1 (2.4)	
Surgical time [min] 329.2 ±86.4 289.0 ±79.8 C	0.094
Anesthesia time [min] 365.9 ±89.1 324.2 ±80.2 C	.086
ICU stay [days] 6.1 ± 6.8 4.3 ± 2.3 C	.420
Hospital stay [days] 16.8 ±13.6 13.5 ±5.9 O).258

CPB – cardiopulmonary bypass, ICU – intensive care unit, RACHS – risk adjustment for congenital heart surgery, AICD – automated implantable cardioverter defibrillator.

was observed in the differentiation of patients with and without postoperative complications (Table IV).

Discussion

It was found that endocrine complications were the most common postoperative complications, followed by hepatic complications (Table V). The rate of exploration due to bleeding was 1.7%; the postoperative mortality was 5.1%. Regarding the causes of mortality, 3 patients died as a result of low cardiac output syndrome (LCOS). No significant difference was found between the two groups (p > 0.05) regarding the causes and rates of mortality. There was no intraoperative mortality. In order to prevent postoperative complications in pediatric congenital heart surgery, first of all, it is necessary to know what these may be, to determine the risk factors and to follow them clinically. In this study, we examined patients who were operated on for LVOTO and tried to determine both the complications that may occur and the risk factors related to them. When we examined the complications of all systems, we found that the highest rate was in the endocrine system (29.3%), while the second highest rate was in the hematological (10.3%) and pulmonary

Patient characteristics	Postoperative complication (–)	Postoperative complication (+)	<i>P</i> -value
Preoperative:			
Hemoglobin [g/dl]	12.8 ±1.3	12.4 ±1.5	0.356
Hematocrit [%]	38.3 ±4.2	37.2 ±4.1	0.468
White blood cells [× 10 ³ /UI]	7.8 ±2.0	8.7 ±2.4	0.180
Neutrophils [N] [× 10 ³ Ul]	4.1 ±1.4	3.9 ±1.7	0.581
Lymphocytes [L] [× 10 ³ /Ul]	2.7 ±1.5	3.8 ±1.6	0.010
NLR	1.7 ±0.7	1.2 ±0.6	0.011
Platelets [× 10 ³ /Ul]	302.4 ±91.0	311.7 ±94.2	0.452
рН	7.5 ±0.0	7.4 ±0.0	0.274
Lactate [mmol/l]	1.6 ±0.5	1.5 ±0.5	0.644
Postoperative:			
pН	7.40 ±0.05	7.43 ±0.04	0.005
Lactate [mmol/l]	2.8 ±1.0	2.7 ±0.8	0.731
Glucose [mg/dl]	160.3 ±23.4	198.2 ±50.0	0.005
BUN [mg/dl]	11.6 ±2.5	12.4 ±3.2	0.314
Creatinine [mg/dl]	0.5 ±0.2	0.6 ±0.1	0.017
ALT [U/l]	14.4 ±3.2	20.4 ±28.7	0.345
AST [U/I]	50.3 ±11.8	89.0 ±69.1	0.029
Total bilirubin [mg/dl]	1.0 ±0.5	1.2 ±0.6	0.573
Direct bilirubin [mg/dl]	0.4 ±0.2	0.4 ±0.2	0.739
CRP [mg/dl]	0.3 ±0.9	0.2 ±0.4	0.513
Sodium [mmol/l]	141.6 ±1.8	141.6 ±2.9	0.922
Potassium [mmol/l]	3.8 ±0.3	3.9 ±0.7	0.521
Calcium [mg/dl]	8.4 ±0.5	8.1 ±0.5	0.028
Hemoglobin [g/dl]	10.4 ±1.5	9.9 ±1.7	0.289
Hematocrit [%]	31.1 ±4.8	29.1 ±4.9	0.159
White blood cells [× 10 ³ /UI]	14.8 ±6.1	15.9 ±6.2	0.361
Neutrophils [N] [× 10 ³ /Ul]	12.2 ±5.6	12.8 ±5.6	0.708
Lymphocytes [L] [× 10 ³ /Ul]	1.9 ±1.0	2.3 ±1.7	0.388
NLR	7.5 ±3.9	6.5 ±3.4	0.334
Platelets [× 10 ³ /Ul]	167.4 ±44.9	179.8 ±63.9	0.468

Table III. Preoperative and postoperative laboratory data

ALT – alanine aminotransferase, AST – aspartate aminotransferase, BUN – blood urea nitrogen, CRP – C-reactive protein, NLR – neutrophil/lymphocyte ratio.

Table IV. Multivariate logistic regression analysis of laboratory results

Laboratory results	Univariate logistic regression		Multivariate logistic regression			
	OR	95% CI	<i>P</i> -value	OR	95% CI	<i>P</i> -value
Intraop platelet transfusion	0.12	0.02-0.72	0.020			
Preop lymphocyte	1.69	1.06–2.70	0.027			
Preop NLR	0.33	0.13-0.82	0.017	0.26	0.08–0.80	0.018
Postop pH	> 1000	74.98 ≥ 1000	0.014	> 1000	220.66–1000	0.012
Postop glucose	1.03	1.01–1.04	0.010			
Postop AST	1.03	1.00–1.07	0.039			
Postop calcium	0.28	0.09–0.90	0.032	0.23	0.06-0.86	0.029

AST – aspartate aminotransferase, CI – confidence interval, NLR - neutrophil/lymphocyte ratio, OR – odds ratio.

systems (10.3%). We found that the risk factors that we can use to predict the development of complications are related to preoperative NLR, intraoperative platelet transfusion, postoperative calcium, glucose and AST levels.

Among all possible complications after pediatric cardiac surgery, it was found that those related to the endocrine system were most common. The most common endocrine complication was hypocalcemia, followed by hyperglycemia [5]. Metabolic disorders are the most common complications of transfusion, dependent on age, and the most dominant one is hypocalcemia resulting from citrate toxicity [6]. Blood products with the highest citrate concentration as an anticoagulant are whole blood, fresh frozen plasma and irrated packed red blood cells [7]. Reducing bleeding during the operation and therefore the use of blood products may help protect the patient from hypocalcemia. Hyperglycemia, another endocrine complication, prolongs the intubation time and the length of stay in the intensive care unit in children who have undergone cardiac surgery [8]. Blood glucose levels above 175 mg/dl were found to be associated with postoperative bacteremia following pediatric cardiac surgery [9]. In addition, postoperative hyperglycemia was found to be associated with an increased risk of morbidity and mortality in infants undergoing postoperative cardiac surgery [10]. Since endocrine complications were considered physiological consequences of CPB, they were not covered frequently in previous studies. In our study, endocrine complications were also considered among postoperative complications and were found to be the most common complications after cardiac surgery.

It was found that the mortality rate increased in patients who had postoperative complications following pediatric cardiac surgery [4]. Therefore, preventing postoperative complications can be life-saving. To develop a preventive strategy, it is important to determine the predictive factors for these complications. When the patients who developed postoperative complications were compared with the patients who did not develop complications, it was found that preoperative risk factors may be effective in the group that developed complications [4]. Potential predictors for major complications after pediatric cardiac surgery were found to be complex cardiac pathologies, cyanotic congenital heart disease, prolonged CPB (> 90 min), high-dose inotropic drug use during the operation, and increased blood lactate level [5, 11]. In our study, it was found that increased preoperative lymphocyte level, lower preoperative NLR, increased postoperative glucose and AST, and low postoperative calcium level were significantly associated with the development of complications.

NLR is a new biomarker used to predict the level of preoperative systemic inflammation in children with congenital heart disease [12, 13]. It has been found that systemic inflammatory response syndrome seen in children who have undergone pediatric cardiac surgery under CPB prolongs the duration of postoperative mechanical ventilation, ICU stay, and hospital stay [14]. Inflammatory reactions induced by CPB will also affect postoperative cardiac and pulmonary Table V. Postoperative complications

Postoperative complications	N (%)
Cardiac:	
Hypertension (nitroglycerin infusion requirement)	5 (8.6)
Arrhythmias	3 (5.1)
LCOS	4 (6.8)
Re-exploration	1 (1.7)
Pulmonary:	
Atelectasis	6 (10.3)
Pleural effusion	1 (1.7)
Pulmonary infiltration	1 (1.7)
Re-intubation (> 3)	1 (1.7)
Hematologic:	
Hemoglobin < 8 g/dl	6 (10.3)
Anemia + thrombocytopenia	2 (3.4)
Bleeding	1 (1.7)
Renal:	
Oliguria	1 (1.7)
Anuria	2 (3.4)
Hepatic:	
AST elevation	5 (8.6)
Endocrine:	
Hyperglycemia	17 (29.3)
Hypocalcemia	13 (22.4)
Infectious:	
Postoperative fever	3 (5.1)
Wound site infection	2 (3.4)
Pneumonia	1 (1.7)
Gastrointestinal:	
Decreased motility	2 (3.4)
Neurologic:	
Convulsions	1 (1.7)
Mortality	3 (5.1)

AST – aspartate aminotransferase, LCOS – low cardiac output syndrome.

In our study, it was found that the elevation of postoperative AST levels had a significant effect on the development of complications. Causes of the elevation of AST in a postoperative cardiac patient include damage to heart and skeletal muscles, hemolysis due to a CPB device, and liver damage. Since cardiac surgery poses a traumatic risk for both heart and skeletal muscle, AST levels can rise earlier than alanine aminotransferase (ALT) levels [16]. Postoperative complications such as pleural effusion, heart rhythm disorders, postoperative infections, and the need for total parenteral nutrition also increase the risk of cardiac hepatopathy [17]. It was suggested that pediatric patients with elevated transaminases undergoing cardiac surgery are also in the high-risk group in terms of postoperative mortality [16].

Although the relationship between increased serum lactate level and complications and mortality in pediatric cardiac surgery remains uncertain, high lactate levels were considered as a risk factor for increased postoperative adverse events and prolonged ICU stay [18–20]. It was found that high lactate levels were correlated with the RACHS-1 subgroup, CPB time, aortic cross-clamp time, high inotropic score, anesthesia time, and operation time [18, 21]. Especially, lactate levels \geq 4.5 mmol/l are an important risk factor for complications [21]. In our study, we did not find a significant difference between the group with and without complications in terms of postoperative lactate levels, which can be attributed to the limited number of patients in our study.

Patient blood management in pediatric cardiac surgery should involve an appropriate multidisciplinary (surgeon, anesthesiologist, and intensive care specialist) approach to prevent complications [22]. This is because blood product transfusion is associated with prolonged postoperative mechanical ventilation, pulmonary complications, and prolonged hospital stay [23, 24]. Platelet dysfunction and thrombocytopenia occur as a result of CPB use in pediatric cardiac surgery and increase the risk of bleeding complications, which is also related to the duration of CPB and the degree of hemodilution [25]. Platelet transfusion is recommended in the presence of excessive bleeding despite adequate protamine administration after CPB. In our study, we found that intraoperative thrombocyte transfusions were performed less frequently, and fresh frozen plasma was used more frequently in the group with postoperative complications.

The first important limitation of this study is that it was conducted in a single center with a limited number of patients. Conducting multi-center studies with a larger number of patients may provide clearer results. The second important limitation is the loss of data due to the retrospective design of the study. Prospective and randomized studies could yield more significant results.

It is important to identify predictive factors to prevent postoperative complications in pediatric patients undergoing surgery for LVOTO. Preoperative NLR, intraoperative platelet transfusion, and postoperative calcium, glucose, and AST levels can help identify risks. We may predict the development of complications by looking at simple laboratory tests performed in the preoperative and postoperative periods. The ability to predict complications will not only reduce morbidity and mortality but will also help reduce the length of hospital stay and hospitalization costs.

Disclosure

The authors report no conflict of interest.

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