

# Prevalence and risk factors analysis of early postoperative arrhythmia after congenital heart surgery in pediatric patients

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## Abstract

**Background:** Arrhythmia is one of the most common complications after cardiac surgery. The objectives of this study were to determine the prevalence and analyze the risk factors of postoperative arrhythmia in pediatric patients after cardiac surgery for congenital heart defects (CHD) at a single center in Bali, Indonesia over 2 years period. **Methods:** A cross-sectional study, among 120 pediatric patients with CHD who underwent cardiac surgery, 92 patients met inclusion criteria in this study. The data were taken from medical records included demographic data, anthropometry, electrocardiography, surgical procedures, perioperative parameters, electrolyte levels, and management of postoperative arrhythmias.

**Results:** Among 92 patients, 14 (15.2%) developed postoperative arrhythmias. Complete heart block (CHB) the most common arrhythmia, observed in five patients (35.7%), followed by supraventricular tachycardia three patients (21.4%). There were statistically significant differences between arrhythmia and nonarrhythmia groups for cardiopulmonary bypass (CPB) duration (171.23 vs. 108.01 min), aortic cross-clamp duration (115.58 vs. 73.59 min), ischemia duration (106.33 vs. 65.43 min), and potassium level (3.33 vs. 3.88 mmol/L) with  $p < .05$ . Based on multivariate linear regression analysis, CPB time and potassium level were found to be independent risk factor.

**Conclusions:** Early postoperative arrhythmia observed 15.2% in this study, dominated by CHB. CPB duration, aortic cross-clamping, ischemia time, and potassium level were statistically significantly different between arrhythmia and nonarrhythmia groups.

## KEYWORDS

arrhythmia, cardiac surgery, congenital heart defects, postoperative complication

## 1 | INTRODUCTION

Cardiac arrhythmia defined as abnormal changes in heart rhythm, is caused by impaired generation or conduction of electrical impulses in the heart.<sup>1</sup> Arrhythmia is one of the most common complications

after cardiac surgery in pediatric and adult patients. Although arrhythmias can be transient and well managed, in pediatric patients with congenital heart defects after undergoing cardiac surgery, arrhythmias are a major source of morbidity and mortality. The prevalence of postoperative arrhythmias after cardiac surgery for

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congenital heart defects is 7.3%–48%,<sup>2</sup> with a mortality rate of 9.1%.<sup>3</sup> A number recent studies shown the most type of arrhythmia observed was Junctional Ectopic Tachycardia.<sup>2–4</sup> Several factors contribute to the occurrence of cardiac arrhythmias after cardiac surgery, including patient-related risk factors and surgery-related risk factors.<sup>5</sup> Patient-related risk factors include age,<sup>4,5</sup> abnormalities of the heart anatomy<sup>2,4,5</sup> and comorbidities. Surgery-related risk factors include trauma, postsurgical inflammation,<sup>2,5</sup> hemodynamic stress,<sup>5,6</sup> postsurgical myocardial ischemia,<sup>4,5,7</sup> perioperative drugs, and electrolyte disturbances.<sup>2,4,5,7</sup>

Postoperative cardiac arrhythmias in pediatric patients with congenital heart defects are varied, include tachyarrhythmia or bradyarrhythmia. The types of rhythms found in patients with bradyarrhythmia include atrioventricular block and SA Node dysfunction (sinus bradycardia and sinus arrest). The types of rhythms found in patients with tachyarrhythmias include Atrial tachycardia (Intra-atrial reentry tachycardia, atrial flutter), Junctional Ectopic tachycardia, Ventricular tachycardia (Premature Ventricular Complex; Monomorphic VT; Torsade de Pointes; Ventricular Fibrillation).<sup>6,8</sup>

This objective of this study was to analyze the prevalence and risk factors for early postoperative arrhythmias after cardiac surgery for patients with pediatric congenital heart defects at a single center in Bali, Indonesia between January 2020 and December 2022.

## 2 | MATERIALS AND METHODS

### 2.1 | Study setting and sample

The research design is a cross-sectional study. The data of this study were taken from medical records who underwent cardiac surgery between January 2020 and December 2022 in a single center in Bali, Indonesia. The inclusion criteria in this study were patients aged less than 18 years who had congenital heart defects and underwent cardiac surgery between January 2020 and December 2022. Patients with poorly recorded data, history of arrhythmia and used antiarrhythmic drugs before cardiac surgery were excluded from this study.

### 2.2 | Data collection

The data collected were divided into preoperative, intra-operative, and postoperative data. Variables in the preoperative data were demographics (age and gender), anthropometry (weight, height, and nutritional status), type of congenital heart defects. Variables in the intra-operative data were type of surgical procedure, perioperative parameters (duration of surgery, duration of CPB, duration of aortic cross clamp time, and duration of ischemia), and electrolyte levels. Variables in the postoperative data were postoperative arrhythmia management (medication and intervention).

Early postoperative arrhythmia is defined as the changes in heart rhythm other than sinus rhythm recorded on the electrocardiogram (ECG) in the first 24h postoperatively. Arrhythmias categorized into

bradyarrhythmia including sinus node dysfunction (sinus bradycardia; sinus arrest), heart block (second-degree-third-degree block), and tachyarrhythmias including atrial tachycardia (intra-atrial reentry tachycardia, atrial flutter), junctional ectopic tachycardia, ventricular tachycardia (premature ventricular complex; monomorphic VT; Torsade de Pointes; ventricular fibrillation).

### 2.3 | Data analysis

The data were analyzed with IBM SPSS Statistic ver. 26.0. Categorical data were presented with frequencies and percentages, for numerical data were presented with mean  $\pm$  standard deviation and normality test of numerical data using Kolmogorov–Smirnov test and most of the data were not normally distributed.

The comparison between arrhythmia group and nonarrhythmia group based on risk factors such as gender and CPB using chi-square test. In addition, other risk factors like age, CPB time, ischemic time, sodium, and magnesium levels with nonnormally distributed data used the Mann–Whitney test. Surgery time, aortic cross-clamping time, potassium, and calcium level with normally distributed data used the T-independent test. Data with a *p*-value  $<.05$  in the univariate analysis will undergo multivariate testing using linear regression analysis. Results with a *p*-value less than  $.05$  were designated as significant.

## 3 | RESULTS

Out of a total of 120 pediatric patients who underwent surgical procedures for congenital heart defects from January 2020 to December 2022, 92 pediatric patients met the inclusion criteria for this study. The study characteristics can be seen in [Table 1](#). Female patients predominated, accounting for 48 samples (52.2%), and the majority of heart surgeries were performed in the early childhood age group, with 37 samples (40.2%). For anthropometric variables, the patients had an average weight of 23 ( $\pm 19.4$ )kg, with an average height of 111 ( $\pm 33.9$ )cm. Based on the nutritional status using CDC 2000 guidelines, the largest group had a normal nutritional status, with 37 (40.2%) patients. The most common diagnosis among patients who underwent heart surgery was ventricular septal defect, with 43 samples (46.7%).

In the intraoperative variable group, the most common procedure was Surgical ventricular septal defect closure, with 46 samples (50%). The duration of heart surgery was 242.83 ( $\pm 85.1$ )min, with 76 samples (82.6%) of them using cardiopulmonary bypass (CPB), and mean duration of CPB usage was 118.6 ( $\pm 54$ )min. Ultrafiltration after CPB was performed to all patients as standard procedure in our institution. The mean duration of aortic-cross clamp time (Aox time) was 80.4 ( $\pm 39.7$ )min, and the mean duration of ischemic time was 72.3 ( $\pm 37.0$ )min. The mean postoperative sodium, potassium, calcium, and magnesium levels after cardiac surgery consecutively 141.15 ( $\pm 5.6$ )mmol/L; 3.8 ( $\pm 0.71$ )mmol/L; 8.08 ( $\pm 0.91$ )mmol/L; 2.27 ( $\pm 0.95$ )mmol/L.

TABLE 1 Preoperative, intra-operative and postoperative characteristics.

Variable		Value (N = 92)
Age (month)	Mean ( $\pm$ SD)	85.88 ( $\pm$ 65.3)
Age group		
Neonatal ( $\leq$ 1 month)	No (%)	5 (5.4)
Infant (1 month to $\leq$ 12 months)		15 (16.3)
Toddler (12 months to $\leq$ 24 months)		24 (26.1)
Early childhood (24 months to $\leq$ 60 months)		37 (40.2)
Middle childhood (60 months to $\leq$ 132 months)		10 (10.9)
Late childhood (132 months to $\leq$ 216 months)		1 (1.1)
Gender		
Male	No (%)	44 (47.8)
Female		48 (52.2)
Weight (kg)	Mean ( $\pm$ SD)	23 (19.4)
Length/Height (cm)	Mean ( $\pm$ SD)	111 ( $\pm$ 33.9)
Nutritional status (CDC, 2000)		
Severe malnutrition	No (%)	5 (5.4)
Moderate malnutrition		15 (16.3)
Mild malnutrition		24 (26.1)
Normal		37 (40.2)
Overweight		10 (10.9)
Obesity		1 (1.1)
Type of CHD		
ASD	No (%)	14 (15.2)
VSD		43 (46.7)
PDA		2 (2.2)
AVSD		1 (1.1)
VSD with PDA		5 (5.4)
TOF		19 (20.7)
Miscellaneous		8 (8.7)
Type of procedure		
Surgical ASD closure	No (%)	15 (16.3)
Surgical VSD closure		46 (50.0)
BT shunt		7 (7.6)
Total correction TOF		13 (14.1)
BCPS		3 (3.3)
Others		8 (8.7)
Duration of surgery (min)	Mean ( $\pm$ SD)	242.83 ( $\pm$ 85.1)
Cardiopulmonary bypass (CPB) time (min)		118.6 ( $\pm$ 54)
Aortic cross-clamp time (min)		80.4 ( $\pm$ 39.7)
Ischemic time (min)		72.3 ( $\pm$ 37.0)
Early postoperative arrhythmias	No (%)	14 (15.2)

TABLE 1 (Continued)

Variable		Value (N = 92)
Complete heart block		5 (6.5)
Supraventricular tachycardia		3 (3.3)
Ventricular extra systole		2 (2.2)
Atrial fibrillation		2 (2.2)
Junctional tachycardia		1 (1.1)
Atrioventricular block grade 1		1 (1.1)
Sodium levels (mmol/L)	Mean ( $\pm$ SD)	141.15 ( $\pm$ 5.6)
Potassium levels (mmol/L)	Mean ( $\pm$ SD)	3.8 ( $\pm$ 0.71)
Calcium level (mmol/L)	Mean ( $\pm$ SD)	8.08 ( $\pm$ 0.91)
Magnesium level	Mean ( $\pm$ SD)	2.27 ( $\pm$ 0.95)

Abbreviations: ASD, atrial septal defect; AVSD, atrioventricular septal defect; BCPS, bidirectional cavo pulmonary shunt; CHD, congenital heart defects; PDA, patent ductus arteriosus; SD, standard deviation; TOF, Tetralogy of Fallot; VSD, ventricular septal defect.

The prevalence rate of early postoperative arrhythmia in this study was 14 (15.2%) patients, the most common arrhythmia was complete heart block (CHB) with five (6.5%) patients, followed by supraventricular tachycardia with three (3.3%) patients. The distribution of arrhythmia based on the type of congenital heart defects in patients can be seen in Table 2.

The comparison between the arrhythmia group and the nonarrhythmia group in this study is presented in Table 3. There were statistically significant differences between the mean values of the arrhythmia and nonarrhythmia groups in terms of CPB duration ( $171.23 \pm 52.64$  min vs.  $108.01 \pm 48.44$  min), Aortic Cross-Clamp time ( $115.58 \pm 34.38$  min vs.  $73.59 \pm 37.28$  min), Ischemic time ( $106.33 \pm 30.63$  min vs.  $65.43 \pm 34.50$  min), and postoperative potassium levels ( $3.33 \pm 0.57$  mmol/L vs.  $3.88 \pm 0.70$  mmol/L) with a  $p$ -value  $<.05$ . No statistically significant differences were found between the arrhythmia and nonarrhythmia groups in terms of gender, use of CPB, nutritional status, type of CHD, operation age, and operation duration, with  $p$ -values  $>.05$ .

Based on multivariate linear regression analysis in Table 4, CPB time, Aortic Cross-Clamp time, Ischemia time, and potassium level are statistically significant as a predictor of postoperative arrhythmia ( $p = .000$ ;  $R = .540$ ), meaning all of the risk factor had 54% contribution of the arrhythmias event in this study. The results show that CPB duration ( $p = .034$ ) and potassium level ( $p = .047$ ) have  $p$ -values  $<.05$ , indicating both were found to be independent risk factors for postoperative arrhythmia.

## 4 | DISCUSSION

Postoperative arrhythmias are the common complications after cardiac surgery for congenital heart defects. The prevalence rate of early arrhythmias after cardiac surgery for congenital heart defects in this study was 15.2%. Other recent studies have similar result to

TABLE 2 Distribution of arrhythmia based on the type of congenital heart defects.

Type arrhythmia	ASD (n=14)	VSD (n=43)	PDA (n=2)	AVSD (n=1)	VSD with PDA (n=5)	TOF (n=19)	Miscellaneous (n=8)
Total arrhythmias (n=14)	2 (14.2)	4 (9.3)	1 (50)	0	2 (40)	2 (10.5)	3 (37.5)
SVT (n=3)	-	1 (2.3)	-	-	-	2 (10.5)	-
CHB (n=5)	-	3 (6.9)	-	-	2 (40)	-	-
VES (n=2)	-	-	-	-	-	-	2 (25)
AF (n=2)	2 (14.2)	-	-	-	-	-	-
JET (n=1)	-	-	-	-	-	-	1 (12.5)
AVB Grade 1 (n=1)	-	-	1 (50)	-	-	-	-

TABLE 3 Analysis of risk factors early arrhythmia after pediatric cardiac surgery.

Variable	Arrhythmia (n=14)	Nonarrhythmia (n=78)	Statistical test	p-value
Gender				
Male	6	38	$\chi^2=0.163$	.776
Female	8	40		
CPB usage				
On-pump	10	66	$\chi^2=1.437$	.256
Off-pump	4	12		
Nutritional status			MW=0.512	.608
Type of CHD			MW=1.24	.212
	Arrhythmia N (Mean $\pm$ SD)	Nonarrhythmia N (Mean $\pm$ SD)	Statistical test	p-value
Age	69.71 $\pm$ 65.71	88.78 $\pm$ 65.28	MW=0.794	.427
Surgery time	271.42 $\pm$ 86.3	237.70 $\pm$ 84.44	t=1.37	.174
CPB time	171.23 $\pm$ 52.64	108.01 $\pm$ 48.44	MW=4.12	.000
Aortic cross-clamp time	115.58 $\pm$ 34.38	73.59 $\pm$ 37.28	t=3.612	.001
Ischemic time	106.33 $\pm$ 30.63	65.43 $\pm$ 34.50	MW=3.92	.000
Sodium level	143.53 $\pm$ 6.93	140.74 $\pm$ 5.28	t=1.67	.097
Potassium level	3.33 $\pm$ 0.57	3.88 $\pm$ 0.70	t=2.78	.007
Calcium level	7.75 $\pm$ 0.72	8.14 $\pm$ 0.94	t=1.39	.169
Magnesium level	2.51 $\pm$ 1.82	2.23 $\pm$ 0.74	MW=0.435	.664

TABLE 4 Multivariate linear regression analysis risk factor for early arrhythmia after pediatric cardiac surgery.

Risk factors	p-value
Cardiopulmonary bypass time (min)	.034
Aortic cross-clamp time (min)	.086
Ischemic time (min)	.085
Potassium level (mmol/L)	.047

ours, study in the United States by Delaney et al. had an arrhythmia incidence rate of 15%.<sup>9</sup> Alotaibi et al. in Saudi Arabia was 14.4%,<sup>3</sup> and also the other studies.<sup>10-14</sup> There were studies with higher prevalence rate of arrhythmias, a study from Ishaque et al. was 22.8%,<sup>2</sup> study by Abdel Gawad et al. in Egypt with an arrhythmia prevalence rate of 50%,<sup>4</sup> and a study from Grosse-Wortmann et al. showed the highest prevalence rate of previous studies with an arrhythmia prevalence of

79.1%.<sup>15</sup> The difference in results from previous studies is because of differences of the definition arrhythmia between studies and differences in measurement methods. For example, arrhythmia from Yildirim et al. defined as a change in heart rhythm that is persistent for more than 30s,<sup>12</sup> while the definition of arrhythmia by Delaney et al. is a change in heart rhythm that requires an intervention.<sup>9</sup> The difference results can also be caused by the measurement method, according to Grosse Wortman, measuring data with Holter monitoring, cause the diagnosis of arrhythmia to be more sensitive than studies using bedside monitoring, so it showed the highest prevalence compared to previous studies.<sup>15</sup>

Complete heart block (CHB) is the most common type of arrhythmia after cardiac surgery in this study, with prevalence rate of five patients (5.4%) out of all patients. The highest prevalence of CHB was found in the surgical VSD closure procedure, where out of five patients who experienced CHB, three (60%) patients had a surgical VSD procedure.

This is consistent with previous studies, CHB is the most common complication after congenital heart defect surgery,<sup>2-4,7,9</sup> and it occurred 1%–6% after congenital heart defects surgery.<sup>16</sup> Atrioventricular node is found in a specific area called the triangle of Koch within the bottom part of the right atrium. From there, it continues as the His bundle, which goes through the right fibrous trigone and emerges at the base of the noncoronary aortic cusp in the upper part of the ventricular septum. The His bundle, along with its branches, is located in the wall that separates the ventricles, making it prone to injury during surgical procedures involving that area.<sup>17</sup> This study contradicts other research that found Junctional ectopic tachycardia to be the most common type of arrhythmia.<sup>2,11-13</sup>

Based on age, the average age of patients undergoing heart surgery in this study was 85.88 ( $\pm 65.3$ ) months, and there was no significant difference in age between the arrhythmia group and the nonarrhythmia group. This study is consistent with research by Ishaque et al. ( $p = .492$ ). However, this study contradicts the findings of research by Delaney et al. and Abdel Gawad et al., which showed a statistically significant difference, with the arrhythmia group having a younger average age than the nonarrhythmia group. Therefore, the younger age of a child undergoing surgical procedures, the higher the risk of early postoperative arrhythmia.<sup>4,9</sup> Based on gender, the frequency of females with congenital heart defects in this study dominated at 48 patients (52.2%), which is consistent with previous research findings,<sup>7,18</sup> and it is not consistent with other studies that show males dominate congenital heart defects.<sup>2,3,9</sup> Despite the difference results from previous research, based on statistical tests, there was no significant difference between gender and the rate of early postoperative arrhythmia in congenital heart surgery, which is consistent with the findings of this study.<sup>2,3,7,9,18</sup>

The pathophysiology of early postoperative arrhythmias caused by various conditions such as direct injury at the time of myocardial incision, injury during cannulation, sutures in the cardiac conduction system, and excessive pressure and volume changes that occur acutely after surgery,<sup>19</sup> and our study showed similar result, early postoperative arrhythmia in this study is related to intra-operative factors. There were significant statistical differences between the arrhythmia and nonarrhythmia groups for the duration of cardio pulmonary bypass (CPB time), duration of aortic cross-clamping (AoX time), duration of ischemia (ischemic time), and potassium levels with  $p$ -values of .000, .001, .000, and .007, respectively. However, there was no significant difference in the duration of surgery between the arrhythmia and nonarrhythmia groups, with a  $p$ -value of .174. Based duration of surgery, our result is not in line with study from Ishaque et al., which found a  $p$ -value of  $<.001$  (OR: 4.33 [2.81–7.14] 95% CI), indicating that patients with longer surgical durations have a higher risk of early arrhythmia.<sup>2</sup> Based on the duration of CPB, our study showed that the arrhythmia group had a longer CPB duration, with a mean of  $171.23 \pm 52.64$  min compared to the nonarrhythmia group with mean of  $108.01 \pm 48.44$  min, and it showed a significant difference with a  $p$ -value of .000. This result is in line with previous studies.<sup>3,10,20</sup> Regarding the duration of Aortic Cross Clamp (AoX Time), this study found that the mean duration of AoX time was longer in the arrhythmia group, with  $115.58 \pm 34.38$  min compared

to the nonarrhythmia group with a mean of  $73.59 \pm 37.28$  min, and it showed a significant difference with a  $p$ -value of .001. This result is in line with previous studies by Shalby et al.,<sup>7</sup> Delaney et al.,<sup>9</sup> and Alotaibi et al.,<sup>3</sup> but it is not in line with the previous study by Sidra et al.<sup>2</sup> Based on the duration of ischemia (ischemic Time), this study found that the mean duration of ischemic time in the arrhythmia group was longer, with  $106.33 \pm 30.63$  min compared to the nonarrhythmia group with a mean of  $65.43 \pm 34.50$  min, and it showed a significant difference with a  $p$ -value of .000. This result is in line with the previous study by Abdel Gawad et al.<sup>4</sup>

Based on the postoperative electrolyte levels, there were no statistically significant difference found between the arrhythmia and nonarrhythmia groups for sodium levels, while the potassium levels showed the opposite with a  $p$ -value of less than .05. The presence of hypokalemia can lead to postoperative arrhythmias by affecting the electrophysiological properties of cardiac myocytes. This includes changes such as increased phase 3 depolarization, enhanced automaticity, and decreased conduction velocity.<sup>5</sup>

This study showed that longer durations of CPB, AoX time, ischemia time, and lower potassium levels increase the risk of early postoperative arrhythmia, and based on multivariate linear regression analysis, CPB time and potassium levels, indicating both were found to be independent risk factor for patients with congenital heart defects who underwent cardiac surgery. This is related to the complexity of heart surgery,<sup>4,21</sup> inflammation caused by the use of CPB,<sup>2,11,22</sup> and the use of cardioplegia, which leads to electromechanical arrest and potentially causes arrhythmia.<sup>23</sup> Additionally, ultrafiltration after CPB was performed on all patients as a standard procedure in our institution.

The management of postoperative arrhythmias is differentiated based on the specific type of arrhythmia. In patients with bradycardia, the management typically involves the routine use of temporary pacemaker, especially in cases of hemodynamic instability resulting from cardiopulmonary bypass, the effects of cardioplegia, and hypothermia during surgical procedures.<sup>5,17</sup> The management of patients with complete heart block in this study use temporary pacemakers in four patients, resulting in a return to sinus rhythm. However, one patient experienced persistent symptom and required the placement of a permanent pacemaker. Patients with first-degree heart block did not receive any intervention and spontaneously returned to sinus rhythm. The management of supraventricular tachyarrhythmias, patients are at an increased risk of thromboembolism. Thus, the management strategy involves the administration of antithrombotic therapy and antiarrhythmic agents, encompassing both rate control and rhythm control strategies. In this study, the management of patients with supraventricular tachycardia (SVT) varied depending on the specific condition. One patient with SVT underwent synchronized cardioversion followed by the administration of amiodarone. Unfortunately, despite these interventions, the patient had unstable hemodynamics and, regrettably, did not survive. The management for two other patients with SVT, a different approach was taken. They received a bolus dose of amiodarone (60 mg) and were subsequently placed on a maintenance dose of 5–15 mcg/kg/min. This regimen aimed to control and stabilize their heart rhythm. Additionally, two patients diagnosed with

atrial fibrillation were managed differently. They use beta blockers, which help control heart rate and warfarin, an anticoagulant medication to prevent the formation of blood clots. On the other hand, patients diagnosed with junctional ectopic tachycardia (JET) had stable hemodynamics and did not require any specific interventions. Their condition did not necessitate immediate medical management. In the case of ventricular tachyarrhythmias, where patients are asymptomatic and stable hemodynamics, acute intervention is typically unnecessary. However, therapeutic options such as lidocaine, procainamide, and amiodarone are considered for the management of this condition. Cardioversion or defibrillation techniques are reserved for cases involving ventricular fibrillation or unstable ventricular tachycardia.<sup>5</sup> In this study, patients with ventricular extra systole exhibited stable hemodynamics and did not require any specific interventions regarding the arrhythmia.

#### 4.1 | Study limitation

The limitations of this study include the use of a cross-sectional method, our hospital regularly monitors patients with a bedside system, which may result in a lack of documentation of arrhythmia events in postoperative patients.

## 5 | CONCLUSIONS

The prevalence rate of arrhythmia in this study was 15.2%. The most common arrhythmia was CHB with five (6.5%) patients, followed by supraventricular tachycardia with three (3.3%). The longer duration of CPB, aortic cross-clamp time, and ischemic time during cardiac surgery and lower potassium levels after cardiac surgery, the higher the risk of arrhythmia. CPB time and potassium level were independent factor as early postoperative arrhythmia after pediatric cardiac surgery for congenital heart defects. Further research is needed to analyze the risk factors associated with postoperative arrhythmia after heart surgery in the future.

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#### CONFLICT OF INTEREST STATEMENT

Authors declare no conflict of interests for this article.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in <https://doi.org/10.6084/m9.figshare.25018286.v1>.

#### ETHICS STATEMENT

This research has acquired approval by the Universitas Udayana Faculty of Medicine Research Ethics Committee (No. 2146/UN14.2.2.VII.14/LT/2023).

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#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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