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Perioperative NT-proBNP Changes in Children with Congenital Heart Disease Undergoing Cardiac Catheterization

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ABSTRACT

Background: Congenital heart disease (CHD) is a structural abnormality of the heart and blood vessels present from birth and represents one of the leading causes of childhood mortality among congenital disorders. Global incidence reported 8-10 cases per 1,000 live births worldwide. Diagnostic cardiac catheterization plays an essential role in the evaluation and management of CHD, making anesthetic technique selection crucial, as it directly influences the quality of the procedure, patient safety, and comfort for patient and operator. Sevoflurane has been proposed to possess cardioprotective properties, potentially reflected by changes in N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels, a biomarker of myocardial stretch. However, data in pediatric CHD patients remain limited.

Objective: To analyze perioperative changes in NT-proBNP levels in pediatric CHD undergoing cardiac catheterization with sevoflurane inhalation anesthesia.

Research Method: This analytical observational study was conducted at Dr. Soetomo General Hospital, involving 20 patients aged 1-17 years with CHD undergoing cardiac catheterization who fulfilled inclusion and exclusion criteria. Demographic data and NT-proBNP levels were collected at three time points: pre-sevoflurane, intra-sevoflurane, and six hours post-extubation. Data were analyzed with Friedman test, Wilcoxon signed-rank analysis and Spearman's correlation.

Results: Median preoperative NT-proBNP levels were elevated compared with age-matched reference values. NT-proBNP decreased significantly during sevoflurane exposure compared with pre-sevoflurane levels ($p = 0.004$), followed by a significant increase at 6 hours post-extubation ($p = 0.014$). Significant perioperative changes were observed only in the 1-3 year group, with older groups showed no statistical differences. A moderate negative correlation was found between sevoflurane exposure duration and NT-proBNP reduction ($r = –0.446$, $p = 0.049$), with exposures >100 minutes producing greater decreases.

Conclusion: Sevoflurane anesthesia was associated with a significant intraoperative reduction in NT-proBNP, particularly in younger children, with longer exposure times enhancing this effect. These findings suggest a cardioprotective role of sevoflurane in children with CHD undergoing cardiac catheterization

KEYWORDS: Congenital Heart Disease, Nt-Probnp, Sevoflurane, Pediatric

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INTRODUCTION

Congenital heart disease (CHD) is defined as a structural abnormality of the heart or great vessels present at birth and remains one of the leading causes of mortality among congenital anomalies (Lestari, 2023). Globally, the incidence of CHD is estimated at 8–10 cases per 1,000 live births. In Indonesia, the incidence is approximately 8 per 1,000 live births, corresponding to an estimated 40,000–50,000 affected infants annually. Mortality remains high, with up to 50% of deaths occurring within the first six months of life and 80% within the first year (Lestari, 2023). Data from the World Health Organization (WHO) further highlight geographical variation, reporting incidences of 6% in Bangladesh, 15% in India, 6% in Myanmar, and 10% in Sri Lanka. The severity of CHD spans from mild to life-threatening. In severe cases, early diagnosis and intervention are essential. At Dr. Soetomo General Hospital, Surabaya, approximately 5% of pediatric intensive care admissions involve CHD with associated

cardiovascular complications (Prasanti et al., 2021; Anshori et al, 2023). Advances in medical technology have expanded the role of cardiac catheterization, both diagnostic and therapeutic, as a less invasive alternative to open surgery. Since its introduction in the 1950s, catheter-based interventions have reduced the need for thoracotomy and cardiopulmonary bypass, thereby lowering procedure-related complications and shortening hospital stay. A meta-analysis demonstrated that transcatheter closure of perimembranous ventricular septal defects (pmVSD), a type of acyanotic CHD, was associated with reduced transfusion requirements, shorter hospitalization, and lower rates of residual shunting compared with surgical closure (El-Kadeem et al., 2019).

Anesthetic management is a critical determinant of outcomes in pediatric cardiac catheterization. The primary goals include maintaining hemodynamic stability, preventing arrhythmias, and preserving the delicate balance between systemic and pulmonary circulation (Elshalakany & Salah, 2022; Syilfana et al, 2024; Garg et al, 2025). General anesthesia is frequently employed, with halogenated volatile agents such as sevoflurane widely favored. Beyond its anesthetic properties, sevoflurane has been shown to confer cardioprotective effects (Eis & Kramer, 2022). In CHD, ventricular wall stress arises from pressure or volume overload, often accompanied by impaired systolic or diastolic function. This myocardial stretch promotes the release of cardiac biomarkers, particularly brain natriuretic peptide (BNP) and its inactive fragment, N-terminal proBNP (NT-proBNP). While BNP exerts diuretic, vasodilatory, and anti-remodeling effects, NT-proBNP is biologically inactive but more stable, with a longer half-life, making it a reliable marker of sustained myocardial strain (Xie et al., 2021).

Experimental and clinical evidence suggests that sevoflurane provides cardioprotection through mechanisms such as mitochondrial KATP channel opening, activation of p38 MAP kinase, and modulation of mitochondrial calcium and reactive oxygen species. These processes reduce cytosolic and mitochondrial calcium overload, limiting apoptosis and myocardial injury. Che et al. reported that sevoflurane anesthesia lowered NT-proBNP levels in patients with atrial fibrillation undergoing mitral valve replacement compared with propofol anesthesia. Similarly, sevoflurane demonstrated cardioprotective effects in rheumatic heart disease patients undergoing valve surgery, with benefits persisting up to 48 hours postoperatively (Lam et al., 2024). Despite these findings, no consensus has been established regarding the optimal anesthetic strategy for achieving cardioprotection in pediatric CHD, particularly in the context of cardiac catheterization. Therefore, this study was conducted to evaluate the potential cardioprotective effects of sevoflurane, as reflected by changes in NT-proBNP levels, in pediatric patients with congenital heart disease undergoing diagnostic and interventional cardiac catheterization.

MATERIALS AND METHODS

Study Design

This study was conducted as an observational analytic investigation with a single-group, pre- and post-test design. The primary objective was to evaluate changes in NT-proBNP levels, and the secondary objective was to assess the relationship between the duration of sevoflurane exposure and NT-proBNP changes in pediatric patients with congenital heart disease (CHD) undergoing cardiac catheterization.

Study Population and Setting

The study was carried out in the Operating Room of Integrated Cardiac Service Center at Dr. Soetomo General Hospital, Surabaya, Indonesia, between October 2024 and May 2025. The study population comprised pediatric patients diagnosed with CHD who were scheduled for diagnostic cardiac catheterization under general anesthesia with sevoflurane.

Inclusion and Exclusion Criteria

Inclusion criteria:

1. Pediatric patients aged 1–17 years with CHD undergoing diagnostic cardiac catheterization
2. Patients with cyanotic or acyanotic CHD
3. Cardiac catheterization procedures lasting at least 60 minutes

Exclusion criteria:

Failure to establish intravenous access prior to anesthesia procedure.

Sampling Method

Consecutive sampling was applied, and a total of 20 patients were enrolled.

Data Collection

Anesthesia and Sampling Protocol

All patients underwent intravenous line placement in the ward. Premedication with intravenous midazolam 0,05-0,1 mg/kg was given in the premedication room. General anesthesia was induced with fentanyl 1–2 µg/kg, propofol 1–2 mg/kg, and rocuronium 0.6–1.2 mg/kg to facilitate tracheal intubation. Anesthesia was maintained with inhaled sevoflurane, initiated at 2,5 Vol% to achieve 1 minimum alveolar concentration (MAC), targeting a bispectral index (BIS) of 40-60 and maintained within this range.

NT-proBNP Measurements

Venous blood was drawn at three time points:

1. Pre-Sevoflurane: immediately after intubation (pre-sevoflurane baseline),
2. Intra-Sevoflurane: after 60 minutes of stable BIS (40–60) under sevoflurane maintenance,
3. 6 Hours Post-Extubation

Demographic, clinical, and procedural data, including total sevoflurane exposure time were recorded.

Outcomes

- Primary outcome: Changes in NT-proBNP levels across the three measurement time points (pre-, intra-, and post-sevoflurane exposure).
- Secondary outcome: Correlation between duration of sevoflurane exposure and delta NT-proBNP values.

Statistical Analysis

All data were analyzed using SPSS software. Data distribution was assessed with the Shapiro–Wilk test. Continuous variables were reported as mean ± standard deviation (SD) for normally distributed data, or as range (median) for non-normally distributed data. NT-proBNP levels across the three time points were compared using the Friedman test. When significant differences were observed, pairwise comparisons were performed with the Wilcoxon signed-rank test. The association between sevoflurane exposure time and changes in NT-proBNP was evaluated using the Spearman correlation test. Statistical significance was set at $p < 0.05$.

RESULT

Baseline Demographics

A total of 20 patients were included in the final analysis. Baseline demographic and perioperative characteristics are presented in Table 1.

Table 1. Baseline Demographics of Subjects

Characteristics	Descriptive	p value
Age	7,40 ± 5,10	0,063
Weight	6 - 46 (15,0)	0,010
Height	112,5 ± 33,49	0,105
Sevoflurane Exposure Duration	60 - 140 (90,0)	0,004
Classification of CHD		
Cyanotic	17 (70,0%)	-
Acyanotic	6 (30,0%)	
Intraoperative Fluid Administration	178,5 ± 92,55	0,051
Intraoperative Blood Loss	10 - 50 (20,0)	<0,001
Bispectral Index	43 - 58 (48,0)	0,193

*declared equal/homogeneous if the p value > 0.05

The demographic and intraoperative characteristics of the study subjects are summarized in Table 5.1. The age of the patients ranged from 1 to 16 years, with a mean ± SD of 7.40 ± 5.10 years. The body weight ranged from 6 to 46 kg, with a median of 15 kg. The height of the patients ranged from 70 to 172 cm, with a mean ± SD of 112.5 ± 33.49 cm. Duration of sevoflurane exposure ranged from 60 to 140 minutes, with a median of 90 minutes. In terms of CHD classification, 17 patients (70.0%) had cyanotic CHD, while 6 patients (30.0%) had acyanotic CHD. For intraoperative fluid administration, the range was 50 to 350 mL, with a mean ± SD of 178.5 ± 92.55 mL. Intraoperative blood loss ranged from 10 to 50 mL, with a median of 20 mL. The bispectral index (BIS) values ranged from 43 to 58, with a mean ± SD of 48.05 ± 3.91.

Normality testing using the Shapiro–Wilk test showed that age ($p = 0.063$), height ($p = 0.105$), intraoperative fluid administration ($p = 0.051$), and BIS values ($p = 0.193$) were normally distributed ($p > 0.05$). In contrast, body weight ($p = 0.010$), sevoflurane exposure duration ($p = 0.004$), and intraoperative blood loss ($p < 0.001$) were not normally distributed.

NT-proBNP levels

In this study, the dependent variable assessed was the serum level of NT-proBNP. Venous blood sampling was performed at three time points: prior to the administration of sevoflurane, 60 minutes after sevoflurane administration (intra-sevoflurane), and 6 hours post-extubation following discontinuation of sevoflurane. NT-proBNP levels were measured using the ELISA method, and results were expressed as ratios in ng/mL. The descriptive results of NT-proBNP and the corresponding normality tests are presented in the following table, including range, median, mean, and standard deviation values.

Table 3. NT-proBNP Levels Descriptive

	n	NT-proBNP	p value
Pre Sevoflurane	20	0,123 – 1,651 (0,239)	<0,01
Intra Sevoflurane	20	0,120 – 0,476 (0,191)	0,005

6 Hours Post Extubation	20	0,123 – 2,726 (0,208)	<0,01

*declared equal/homogeneous if the p value > 0.05

Based on the descriptive analysis of NT-proBNP levels from 20 samples, the pre-sevoflurane NT-proBNP values ranged from 0.123 to 1.651 ng/mL, with a median of 0.239 ng/mL. For the intra-sevoflurane NT-proBNP values, the range was 0.120 to 0.476 ng/mL, with a median of 0.191 ng/mL. At 6 hours post-extubation, NT-proBNP levels ranged from 0.123 to 2.726 ng/mL, with a median of 0.208 ng/mL. Normality testing using the Shapiro–Wilk test demonstrated that all NT-proBNP data—pre-sevoflurane, intra-sevoflurane, and 6 hours post-extubation—were not normally distributed ($p < 0.05$).

Analysis of Changes in NT-proBNP Levels with Sevoflurane Inhalation

The analysis of NT-proBNP level changes was performed across three time points: pre-sevoflurane, intra-sevoflurane, and 6 hours post-extubation. Since the NT-proBNP data were not normally distributed, the Friedman test was applied. The following table presents the results of the analysis of changes in NT-proBNP levels under sevoflurane inhalational anesthesia:

Table 4. NT-proBNP Levels Across Measurement Points

NT Pro BNP	Range (Median)	p value
Pre Sevoflurane	0,123 – 1,651 (0,239)	0,014
Intra Sevoflurane	0,120 – 0,476 (0,191)	
6 Hours Post Extubation	0,123 – 2,726 (0,208)	

*declared statistically significant if p<0,05

Based on Table 4, the comparison of changes in NT-proBNP levels from 20 samples using the Friedman test yielded a p-value of 0.014 (< 0.05), indicating that the differences in NT-proBNP levels across the three time points—pre-sevoflurane, intra-sevoflurane, and 6 hours post-extubation—were statistically significant. According to the median and mean values, NT-proBNP levels decreased from pre-sevoflurane to intra-sevoflurane, followed by an increase from intra-sevoflurane to 6 hours post-extubation. To further assess pairwise differences between observations (pre-sevoflurane vs. intra-sevoflurane, pre-sevoflurane vs. 6 hours post-extubation, and intra-sevoflurane vs. 6 hours post-extubation), the Wilcoxon signed-rank test was applied. The results are presented as follows:

Table 5. Changes in NT-proBNP Level

Changes in NT-proBNP level	Median (Min-Max)	Delta median NT pro BNP	p value
NT pro BNP Pre-Intra Sevoflurane	0,239 (0,123 – 1,651) --- 0,191 (0,120 – 0,476)	-0,048	0,004
NT-proBNP Pre Sevoflurane-6 Hours Post Extubation	0, 239 (0,123 – 1,651) --- 0,208 (0,123 – 2,726)	0,031	0,872
NT-proBNP Intra Sevoflurane-6 Hours Post Extubation	0,191 (0,120 – 0,476) --- 0,208 (0,123 --- 2,726)	0,017	0,014

*declared statistically significant if p<0,05

Based on Table 5, the analysis of delta NT-proBNP levels between pre- and intra-sevoflurane demonstrated a median delta of –0.171, indicating a significant decrease in intra-sevoflurane NT-proBNP levels compared with pre-sevoflurane values ($p = 0.004$). In contrast, the delta NT-proBNP between pre-sevoflurane and 6 hours post-extubation showed a median delta of 0.016, with no statistically significant difference ($p = 0.872$). Meanwhile, the comparison between intra-sevoflurane and 6 hours post-extubation revealed a median delta of 0.187, indicating a significant increase in NT-proBNP levels from intra-sevoflurane to post-extubation ($p = 0.014$). In summary, intra-sevoflurane NT-proBNP levels were significantly decreased compared with pre-sevoflurane values, while NT-proBNP levels at 6 hours post-extubation were significantly increased compared with intra-sevoflurane levels.

Age-Stratified Analysis of NT-proBNP

Recognizing that normal NT-proBNP values vary by age (Sugimoto et al., 2010), we further stratified the data into three age categories using these reference values. For greater accuracy, two patients classified as congestive heart failure grade II were excluded from this stratified analysis.

Age Group 1-3 Years

Table 6. NT-proBNP Level in Age Group 1-3 Years

NT Pro BNP	Range (Median)	p value
Pre Sevoflurane	0,198 – 0,472 (0,294)	0,021
Intra Sevoflurane	0,127 – 0,317 (0,229)	
6 Hours Post Extubation	0,187 – 0,567 (0,304)	

Table 7. Changes in NT-proBNP Level in Age Group 1-3 Years

Changes in NT-proBNP level	Median (Min-Max)	Delta median NT pro BNP	p value
NT pro BNP Pre-Intra Sevoflurane	0,294 (0,198 – 0,472) --- 0,229 (0,127 – 0,317)	-0,065	0,018
NT-proBNP Pre Sevoflurane-6 Hours Post Extubation	0,294 (0,198 – 0,472) --- 0,304 (0,187 – 0,567)	0,01	0,612
NT-proBNP Intra Sevoflurane-6 Hours Post Extubation	0,191 (0,120 – 0,476) --- 0,208 (0,123 --- 2,726)	0,017	0,028

Age Group 3-14 Years

Table 8. NT-proBNP Level in Age Group 3-14 Years

NT Pro BNP	Range (Median)	p value
Pre Sevoflurane	0,123 – 0,648 (0,180)	0,347
Intra Sevoflurane	0,120 – 0,350 (0,187)	
6 Hours Post Extubation	0,123 – 0,665 (0,141)	

Table 9. Changes in NT-proBNP Level in Age Group 3-14 Years

Changes in NT-proBNP level	Median (Min-Max)	Delta median NT pro BNP	p value
NT pro BNP Pre-Intra Sevoflurane	0,180 (0,123 – 0,648) --- 0,187 (0,120 – 0,350)	0,007	0,514
NT-proBNP Pre Sevoflurane-6 Hours Post Extubation	0,180 (0,123 – 0,648) --- 0,141 (0,123 – 0,665)	-0,039	0,208
NT-proBNP Intra Sevoflurane-6 Hours Post Extubation	0,187 (0,120 – 0,350) --- 0,141 (0,123 --- 0,665)	-0,046	0,171

Age Group >14 Years

Table 10. NT-proBNP Level in Age Group >14 Years

NT Pro BNP	Range (Median)	p value
Pre Sevoflurane	0,138-0,304 (0,221)	0,223
Intra Sevoflurane	0,131 – 0,173 (0,152)	
6 Hours Post Extubation	0,198 – 0,201 (0,199)	

Table 11. Changes in NT-proBNP Level in Age Group >14 Years

Changes in NT-proBNP level	Median (Min-Max)	Delta median NT pro BNP	p value
NT pro BNP Pre-Intra Sevoflurane	0,221 (0,138 – 0,304) --- 0,152 (0,131 – 0,173)	-0,069	0,180
NT-proBNP Pre Sevoflurane-6 Hours Post Extubation	0,221 (0,138 – 0,304) --- 0,199 (0,198 – 0,201)	-0,022	0,665
NT-proBNP Intra Sevoflurane-6 Hours Post Extubation	0,152 (0,131 – 0,173) --- 0,199 (0,198 – 0,201)	0,047	0,180

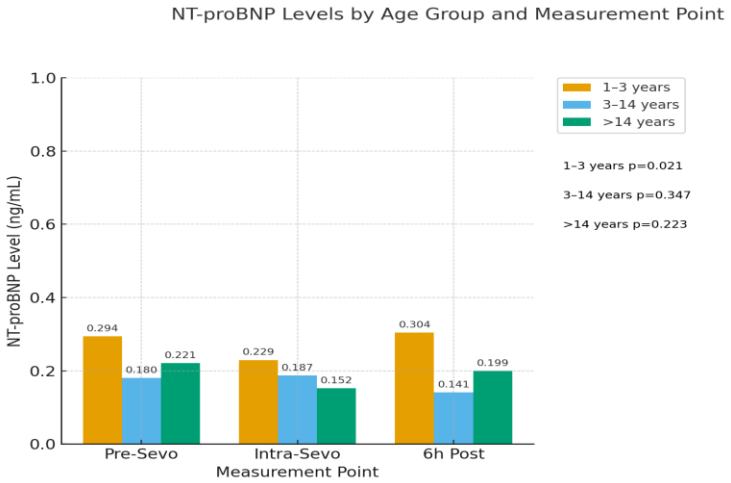

Figure 1. NT-proBNP Levels by Age Group and Measurement Point

Following stratification by age group, significant NT-proBNP changes were observed predominantly in age group 1-3 years, whereas older children exhibited more stable biomarker profiles. In age group 1-3 years, pairwise comparisons revealed decreased in median value of intra-sevoflurane NT-proBNP level from pre-sevoflurane, with delta median of -0,065 ng/mL. Comparison of pre-sevoflurane and 6 hours post-extubation demonstrated a slight increase of NT-proBNP level, with median from 0,294 ng/mL to 0,304 ng/mL. In contrast, comparison between intra-sevoflurane and 6 hours post-extubation showed an incrrase in NT-proBNP from 0,191 ng/mL to 0,208 ng/mL, with delta median of 0,017 (p=0,028). Overall, in age group 1-3 years demonstrate that NT-proBNP levels decreased significantly during sevoflurane anesthesia but increased significantly after discontinuation of sevoflurane exposure.

Sevoflurane Exposure Duration and NT-proBNP Changes

To further evaluate factors beyond age, an additional analysis was performed to examine the association between sevoflurane exposure duration and changes in NT-proBNP levels. This analysis was conducted using Spearman's correlation test, given the non-normal distribution of the data, to assess whether longer exposure times were correlated with greater reductions in NT-proBNP (delta values).

Table 12. Sevoflurane Exposure Duration and Delta NT-proBNP

	Description	p value
Sevoflurane Exposure Duration	60 - 140 (90,0)	0,004
Delta NT-proBNP (Intra Sevoflurane-Pre Sevoflurane)	-1,53 – 0,09 (-0,028)	<0,01

The duration of the procedure ranged from 60 to 140 minutes, with a median of 90 minutes. Normality testing demonstrated that operative duration was not normally distributed ($p = 0.004$, $p < 0.05$). Descriptive analysis of delta NT-proBNP, defined as the difference between pre-sevoflurane and intra-sevoflurane levels, showed values ranging from –1.53 to 0.09, with a median of –0.028. This indicates that most patients experienced a decrease in NT-proBNP levels during sevoflurane administration. Normality testing confirmed that delta NT-proBNP values were also not normally distributed ($p < 0.01$). Given the non-normal distribution of both variables, the relationship between sevoflurane exposure duration and delta NT-proBNP was assessed using the Spearman correlation test. The results of this correlation analysis are summarized in the following table.

Table 13. Correlation between Sevoflurane Exposure Duration and Delta NT-proBNP

	Spearman coefficient correlation (r)	p value
Sevoflurane Exposure Duration ---- Delta NT Pro BNP	-0,446	0,049

Based on Table 13, the correlation analysis between sevoflurane exposure duration and delta NT-proBNP demonstrated a statistically significant association, with a p-value of 0.049 (< 0.05). The Spearman correlation coefficient (r) was –0.446, indicating a negative correlation. This result suggests that longer sevoflurane exposure duration was associated with a greater decrease in NT-proBNP levels. The strength of this correlation falls within the moderate range (r = 0.400–0.600).To further explore the relationship between sevoflurane exposure and NT-proBNP dynamics, the analysis was stratified by procedure duration. Patients were categorized into two groups based on the median value of operative time: those with exposure durations of less than 100 minutes and those exceeding 100 minutes. This stratification allowed for a clearer comparison of NT-proBNP changes relative to shorter versus longer sevoflurane administration.

Table 14. NT-proBNP levels in Patients with Sevoflurane Exposure <100 minutes

NT Pro BNP	Range (Median)	p value
Pre Sevoflurane	0,123-0,472 (0,205)	0,212
Intra Sevoflurane	0,120 – 0,350 (0,190)	
6 Hours Post Extubation	0,123 – 0,567 (0,199)	

Table 15. Changes in NT-proBNP levels in Patients with Sevoflurane Exposure <100 minutes

Changes in NT-proBNP level	Median (Min-Max)	Delta median NT pro BNP	p value
NT pro BNP Pre-Intra Sevoflurane	0,205 (0,123 – 0,472) --- 0,190 (0,120 – 0,350)	-0,015	0,254
NT-proBNP Pre Sevoflurane-6 Hours Post Extubation	0,205 (0,123 – 0,472) --- 0,199 (0,123 – 0,567)	-0,006	0,328
NT-proBNP Intra Sevoflurane-6 Hours Post Extubation	0,190 (0,120 – 0,350) --- 0,199 (0,123 – 0,567)	0,009	0,060

Table 16. NT-proBNP levels in Patients with Sevoflurane Exposure >100 minutes

NT Pro BNP	Range (Median)	p value
Pre Sevoflurane	0,141-0,648 (0,315)	0,011
Intra Sevoflurane	0,123 – 0,317 (0,202)	
6 Hours Post Extubation	0,131 – 0,665 (0,286)	

Table 17. Changes in NT-proBNP levels in Patients with Sevoflurane Exposure >100 minutes

Changes in NT-proBNP level	Median (Min-Max)	Delta median NT pro BNP	p value
NT pro BNP Pre-Intra Sevoflurane	0,315 (0,141 – 0,648) --- 0,202 (0,123 – 0,317)	-0,113	0,028
NT-proBNP Pre Sevoflurane-6 Hours Post Extubation	0,315 (0,141 – 0,648) --- 0,286 (0,131 – 0,665)	-0,029	0,753
NT-proBNP Intra Sevoflurane-6 Hours Post Extubation	0,202 (0,123 – 0,317) --- 0,286 (0,131 – 0,665)	0,084	0,028

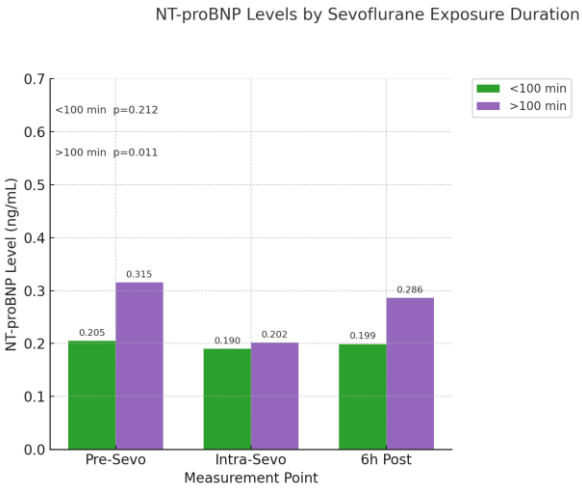

Figure 2. NT-proBNP Levels by Sevoflurane Exposure Duration

In the subgroup with sevoflurane exposure <100 minutes, pre-sevoflurane NT-proBNP levels ranged from 0.123–0.472 ng/mL with a median of 0.205 ng/mL. Intra-sevoflurane values were comparable, with a median of 0.190 ng/mL, and levels at six hours post-extubation showed only a slight increase to 0.199 ng/mL. Pairwise comparisons revealed no statistically significant changes across the three time points. Specifically, the median delta between pre- and intra-sevoflurane was –0.015 (p = 0.254), between pre-sevoflurane and 6 hours post-extubation was –0.006 (p = 0.328), and between intra-sevoflurane and 6 hours post-extubation was 0.009 (p = 0.060). These findings suggest that shorter exposure to sevoflurane did not produce meaningful alterations in NT-proBNP levels. In contrast, the subgroup with sevoflurane exposure >100 minutes demonstrated more pronounced changes. Pre-sevoflurane NT-proBNP levels ranged from 0.141–0.648 ng/mL with a median of 0.315 ng/mL, which significantly declined to 0.202 ng/mL during sevoflurane administration (delta median –0.113, p = 0.028). However, by six hours post-extubation, NT-proBNP levels rebounded to a median of 0.286 ng/mL, significantly higher than intra-sevoflurane values (delta median 0.084, p = 0.028), while remaining slightly lower than pre-sevoflurane values (delta median –0.029, p = 0.753). Taken together, these results indicate that longer sevoflurane exposure (>100 minutes) was associated with a significant intraoperative reduction in NT-proBNP, followed by a rebound after anesthetic withdrawal, whereas shorter exposures did not produce significant changes. This pattern reinforces the hypothesis that the cardioprotective effect of sevoflurane is both dose- and time-dependent, consistent with the mechanisms of volatile anesthetic preconditioning.

DISCUSSION

In this study of 20 pediatric patients with congenital heart disease (CHD) undergoing cardiac catheterization, the median preoperative NT-proBNP levels were elevated compared with normal reference values. This finding aligns with Sugimoto et al. (2015), who described a pathological cycle in which structural abnormalities in CHD lead to heart failure, myocardial stretch, and subsequent NT-proBNP release. Elevated NT-proBNP thus reflects ventricular wall stress caused by persistent pressure and volume overload. In CHD, right-sided volume overload and pulmonary hypertension further increase myocardial workload, contributing to sustained biomarker elevation and heightened vulnerability to heart failure. Sugimoto et al. also reported a direct relationship between NT-proBNP levels and heart failure severity, ranging from 0.219 ng/mL in class I to 19.784 ng/mL in class IV pediatric patients.

The primary aim of this study was to evaluate changes in NT-proBNP level during sevoflurane anesthesia in pediatric patients with CHD. NT-proBNP was selected as a surrogate marker of left ventricular stretch caused by CHD-related hemodynamic load. Statistical analysis showed a significant decrease in NT-proBNP during sevoflurane exposure compared with pre-sevoflurane

values (p=0,004). Conversely, NT-proBNP increased significantly at 6 hours post-extubation compared with intra-sevoflurane levels (p=0,014). These findings suggests that sevoflurane exerts a cardioprotective effect during exposure, which diminishes once the anesthetic agent is discontinued. The cardioprotective effect of sevoflurane aligns with experimental evidence showing that volatile anesthetics reduce cytosolic and mitochondrial calcium loading, thereby inhibiting myocardial apoptosis and necrosis, decreasing inflammation, and attenuating biomarker release (Li, 2015). Furthermore, the pharmacological profile of sevoflurane—maintaining systemic vascular resistance, cardiac output, and right atrial pressure while reducing heart rate—contributes to a favorable balance of oxygen supply and demand in CHD patients during anesthesia (Stoelting, 2015).

When the data were stratified by age, significant changes in NT-proBNP were observed only in the 1-3 year age group, whereas the 3-14 year and >14 year groups showed no stastistically significant differences across the measurement points. Several explanations may account for this finding. First, younger children with CHD typically have higher baseline myocardial stress and limited compensatory reserve, making NT-proBNP more sensitive to both hemodynamic fluctuations and anesthetic modulation (Sugimoto et al., 2010). In contrast, older children generally demonstrate more stable ventricular function, with smaller biomarker variations that do not reach statistical significance. Second, physiological age-related differences in NT-proBNP should be considered. Infants and toddlers naturally exhibit higher NT-proBNP levels due to ongoing myocardial maturation and relatively reduced renal clearance, with levels declining progressively with age (Cantinotti et al., 2015). This makes perioperative shifts more readily detectable in younger children than in older patients, who tend to have lower and more stable baseline values. In older children, the relative stability of NT-proBNP may indicate a reduced sensitivity of the biomarker rather than absence of sevoflurane's protective effect. This may explain why the decline in NT-proBNP during sevoflurane anesthesia was statistically significant only in the youngest age group.

Beyond age-related differences, this study also highlighted the role of exposure time. The duration of sevoflurane exposure significantly correlated with NT-proBNP reduction, with Spearman's correlation showing r = -0,446 (p=0,049), indicating a moderate negative correlation. Subgroup analysis further revealed that longer exposure time (>100 minutes) were associated with greater reductions in NT-proBNP, making this finding consistent with Guerrero-Orriach et al, (2013), who demonstrated that the cardioprotective effects of volatile anesthetic preconditioning are both dose- and time-dependent.

Findings from adult cardiac surgery further support the present results. Julier et al. (2003), in a randomized trial of 72 CABG patients, reported significantly lower postoperative NT-proBNP concentrations in the sevoflurane group compared with placebo. Similarly, Likhvantsev et al. (2016), in a large randomized trial of 900 patients undergoing CABG with cardiopulmonary bypass, reported that NT-proBNP levels at both 24 and 48 hours postoperatively were significantly lower in the sevoflurane group compared with propofol-based total intravenous anesthesia. In contrast, Kuppuswamy et al. (2018) found no significant differences in perioperative NT-proBNP levels between isoflurane and propofol, highlighting that the cardioprotective effects of volatile anesthetics varies across volatile agents. Combined together, these studies reinforce that sevoflurane possesses a stronger cardioprotective profile than isoflurane or desflurane, attributable to its superior pharmacological stability in maintaining cardiac output, systemic vascular resistance, and pulmonary vascular resistance (Stoelting, 2015). Taken together, the findings of this study support the cardioprotective role of sevoflurane in pediatric CHD patients undergoing cardiac catheterization. Sevoflurane anesthesia was associated with a significant reduction in NT-proBNP during exposure, particularly in 1-3 year age group, and longer exposure times were linked to greater decreases. These results suggest that sevoflurane may be recommended as an optimal anesthetic choice in pediatric CHD, not only for its anesthetic efficacy but also for its potential to attenuate myocardial stress and improve perioperative outcomes. Clinically, these findings indicate that sevoflurane may be advantageous in pediatric CHD catheterization by reducing perioperative myocardial stress, with its protective effect most evident during the period of anesthetic exposure. Although the effect appears to diminish after anesthetic withdrawal, the intraoperative reduction remains clinically meaningful, as it coincides with the highest-risk period for myocardial stress.

This study has several limitations that should be considered when interpreting the findings. The wide age range of the study population may have introduced variability, as NT-proBNP levels and myocardial responses differ across pediatric developmental stages. In addition, this study did not stratify patients by type of congenital heart disease, such as cyanotic versus acyanotic forms, which may influence both baseline NT-proBNP values and the degree of perioperative changes. The severity of disease also varied among participants, likely contributing to heterogeneity in biomarker responses. These factors may have affected the consistency of the results, and future studies with more detailed stratification by CHD type and severity should be considered.

CONCLUSION

This study demonstrated that pediatric patients with CHD undergoing cardiac catheterization had elevated baseline NT-proBNP levels, reflecting underlying myocardial stress. Sevoflurane anesthesia was associated with significant reduction in NT-proBNP level during exposure, suggesting cardioprotective effect that diminishes after discontinuation, as levels rebounded 6 hours post-extubation. The protective effect was most pronounced in the youngest age group (1-3 years), likely due to higher baseline myocardial vulnerability and greater biomarker sensitivity, while older children exhibited more stable NT-proBNP profiles. In addition, longer exposure times (>100 minutes) correlated with greater NT-proBNP reduction, supporting the concept that sevoflurane cardioprotection is dose- and time-dependent. Overall, these findings highlight sevoflurane not only as a safe and effective anesthetic agent in pediatric CHD, but also as one with meaningful cardioprotective properties, making it a preferred choice for facilitating cardiac catheterization in this population.

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