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RESEARCH

Extubation failure after cardiac surgery in children with Down syndrome

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Abstract

Extubation failure (EF) after cardiac surgery is associated with poorer outcomes. Approximately 50% of children with Down syndrome (DS) have congenital heart disease. Our primary aim was to describe the frequency of EF and identify risk factors for its occurrence in a population of patients with DS after cardiac surgery. Secondary aims were to describe complications, length of hospital stay, and mortality rates. This report was a retrospective case–control study and was carried out in a national reference congenital heart disease repair center of Chile. This study includes all infants 0–12 months old with DS who were admitted to pediatric intensive care unit after cardiac surgery between January 2010 and November 2020. Patients with EF (cases) were matched 1:1 with children who did not fail their extubation (controls) using the following criteria: age at surgery, sex, and type of congenital heart disease. Overall, 27/226 (11.3%) failed their first extubation. In the first analysis, before matching of cases and controls was made, we found association between EF and younger age (3.8 months vs 5 months; $p=0.003$) and presence of coarctation of the aorta ($p=0.005$). In the case–control univariate analysis, we found association between an increased cardiothoracic ratio (CTR) ($p=0.03$; OR 5 (95% CI 1.6–16.7) for a CTR > 0.59) and marked hypotonia (27% vs 0%; $p=0.01$) with the risk of EF. No differences were found in ventilatory management.

Conclusions: In pediatric patients with DS, EF after cardiac surgery is associated with younger age, presence of aortic coarctation, higher CTR reflecting the degree of cardiomegaly and hypotonia. Recognition of these factors may be helpful when planning extubation for these patients.

What is Known:

- *Extubation failure after cardiac surgery is associated with higher morbidity and mortality rates. Some studies report higher rates of extubation failure in patients with Down syndrome.*

What is New:

- *In children with Down syndrome, extubation failure after cardiac surgery is associated with younger age, presence of aortic coarctation, higher CTR reflecting cardiomegaly and severe hypotonia.*

Keywords Down syndrome · Extubation failure · Congenital heart disease · Cardiac surgery · Cardiothoracic ratio

Abbreviations

CHD	Congenital heart disease
CBP	Cardiopulmonary bypass
CTR	Cardiothoracic ratio
DS	Down syndrome
EF	Extubation failure

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ETT	Endotracheal tube
MV	Mechanical ventilation
NMBA	Neuromuscular blocking agents
PICU	Pediatric intensive care unit
SE	Successful extubation

Introduction

Down syndrome (DS) is the most common chromosomal disorder. There are geographical differences in total and live birth prevalence due to increasing maternal age and the practice of prenatal diagnosis and termination of pregnancy in some countries. Reports from the United States and Europe show a rate of 11–12 per 10,000 live births [1, 2]. Latin American countries have increasing trends, with an incidence rate of up to 24 per 10,000 live births [3].

Congenital heart diseases (CHD) are commonly associated conditions for this group of patients and are a known contributor to morbidity and mortality. The reported prevalence is up to 50% of CHD, and most of them l will require cardiac surgery [4]. In addition, after cardiac surgery, patients require ventilatory management, one of the most crucial care factors in pediatric intensive care units (PICU) [5].

Extubation failure (EF) is defined as the need to reintubate within the first 24 to 72 h after endotracheal tube (ET) removal [5]. EF is associated with increased duration of mechanical ventilation (MV) and PICU stays, infections and respiratory complications, increase in health care costs, and mortality [5-7].

In the pediatric population, there is a significant variability in EF rates, ranging from 5 to 6%, reaching up to 12% in neonates. There are studies that report even higher rates of EF among patients with DS [5, 6, 8], but there is a knowledge gap on the causes or risk factors associated to this group.

This study aimed to investigate EF frequency, etiology, and risk factors for EF among children with DS after cardiac surgery.

Materials and methods

Study design and participants

This report was a retrospective case–control study. The investigation was carried out in a PICU at the UC-Christus Clinical Hospital from January 2010 and November 2020. Patients were identified through the PICU database. Eligible participants for the study were infants with DS (0–12 months old) who underwent cardiac surgery for CHD and were admitted to the PICU for postoperative care. The electronic clinical records were accessed to register preoperative data. The exclusion criteria were patients with unavailable electronic records, no extubation attempt in our center, tracheostomy or chronic MV, and those who died before the attempt of extubation.

Definitions and matching criteria

The cases were infants with EF, which was defined as reintubation within 48 h after extubation [5, 9]; controls were infants who had successful extubation (SE), corresponding to patients who did not require reintubation or that it occurred after 48 h since extubation [5, 10]. To minimize confounding variables, we matched EF to SE patients (1:1) by age at surgery, sex, and type of CHD.

Variables and data sources

Data were retrieved from the hospital's electronic medical records. Additional information was obtained from the PICU nursing records. Preoperative data included weight at the time of surgery, nutritional diagnosis [11], airway and neuromuscular diseases (hypotonia) [12, 13], number of previous intubations and/or EF, and cardiothoracic ratio (CTR) on the preoperative chest radiography, which was calculated by a single operator according to current recommendations [14].

Intraoperative data collected were the operative risk classification of "Risk Adjustment in Congenital Heart Surgery" (RACHS-1), [9] cardiopulmonary bypass (CPB), and aortic cross-clamp time.

Regarding ventilatory management, endotracheal tube (ETT) size, duration of MV after surgery, steroid use before extubation, and use of a high-flow nasal cannula or noninvasive post-extubation ventilation were registered to observation. Other postoperative data included time of use of opioids, sedatives, or neuromuscular blocking agents (NMBAs) and the time of suspension before the extubation and post-surgical echocardiography evaluation for significant residual defects. To facilitate analysis, we used a technical performance score for assessing adequacy of repair [11]. EF etiology, such as airway obstruction, respiratory dysfunction (significant hypoxia, worsening hypercarbia, significant respiratory effort, respiratory fatigue), pulmonary congestion, atelectasis, and infectious or hemodynamic complications was registered.

Statistical methods

All analyses were performed using IBM SPSS Statistics v. 25.0. Data are presented as frequency (percentage) for categorical variables and median with interquartile range (IQR) for continuous variables. The univariate analysis included chi-square, Fisher exact test, or Mann–Whitney *U* test, used as appropriate, to determine associations between candidate predictors and EF. Odds ratio (OR) with 95% confidence interval

(95% CI) for variables that were significantly associated with EF were estimated. The optimal cut-point was obtained by using the Youden method. The ability to discriminate patients with EF versus SE was evaluated using a receiver operating characteristic curve or ROC curve, estimating their area under the curve and confidence interval. The significance level was assigned as $p < 0.05$ for all variables.

Results

Study population

During the period of study, a total of 1925 pediatric cardiac surgeries were performed; 319 (16,6%) were in patients with DS, of which 266 were infants. Seventeen patients of this group were excluded due to transfer to another hospital without an extubation attempt, six due to not available electronic records, and four users of chronic MV and tracheostomy. Of the 239 patients included in the study, 27 (11.3%) had EF (Fig. 1). Of those, 74% occurred during the first 24 h after extubation, with a median of 7.5 h (IQR 14).

Patient characteristics

The median age at surgery was lower in the EF group, 3.8 (IQR) versus 5 (IQR) months ($p = 0.008$). The CHD that led to surgery is listed in Table 1. An increase in EF rate was found in patients with coarctation of the aorta (11.1% versus 0.5%, $p = 0.006$). It is noteworthy that in the EF group, 50% of the patients with tetralogy of Fallot and two of the three patients with coarctation of the aorta also had an atrioventricular canal. In univariate analysis, a younger age (OR: 0.02; 95% CI 0.001–0.36) and coarctation of the aorta diagnosis (OR: 26; 95% CI 2.6–263) were significantly associated with EF.

Preoperative study, type of surgical repair and comorbidities according to type of extubation are shown in Table 2. In terms of clinical characteristics and comorbidities, we found an increased CTR on preoperative chest radiography in the EF group ($p = 0.03$). The optimal cut-point was established at 0.59 for the highest sensitivity and specificity. For a DS patient, a CTR of 0.59 gives five times more chance for EF (OR 5; 95% CI 1.6–16.7); with a ROC curve showing an area below the curve of 0.69 (95% CI 0.54–0.83) to discriminate patients with EF (Fig. 2). There is also a greater proportion of patients in the EF group with marked hypotonia (27% versus 0%; $p = 0.01$). Respiratory malformations were present only in the EF group (15% versus 0%, $p = 0.1$): three cases of tracheobronchomalacia and one tracheal bronchus (Table 2).

Surgical data

No significant differences were found in the operative risk classification of RACHS-1 [13], CPB, or aortic clamping time in the analysis of the surgical variables.

Ventilatory and post-operative management

The size of ETT was recorded in both groups. In 77% of patients with EF, a smaller diameter was used according to international recommendations for patients with DS [15] vs. 67% used by the SE group. The relationship between the use of a more significant than recommended ETT size and the development of post-extubation stridor was 50%. The ETT (85%) used in the EF group were with cuff versus 93% in the other group. Table 3 compares the variables of ventilatory management between both groups.

We found no difference in the number of significant residual defects in postoperative echocardiogram nor in the electrocardiogram, which showed sinus rhythm in all patients at the moment of the extubation attempt. There was no significant different in terms of vasoactive and inotropic support during extubation between the groups ($p = 0.3$).

There was no significant difference in hours of infusion of opioids, benzodiazepines, or NMBAs. No differences were found between the time of suspension of these drugs before the attempt of extubation (Table 4).

Post-extubation complications in the EF group

All patients with EF had at least one respiratory complication. Fourteen developed respiratory dysfunction (significant hypoxia, worsening hypercarbia, significant respiratory effort, or respiratory fatigue); the most frequent causes in order were upper airway obstruction, atelectasis, pulmonary edema, and pleural effusion. Five patients were complicated with infectious diseases (respiratory infections and sepsis) and, less frequently, hemodynamic instability or bleeding.

Stay in the PICU and mortality

Length of stay in the PICU was 7.2 (±7.4) days in the EF group versus 11.5 (10.6) in the group with SE ($p = 0.001$). It must be taken into account that nine patients from the EF group (33%) were transferred on MV to another hospital after they failed the extubation, while from the SE group, none were transferred to another ICU.

In terms of mortality rates, one death was reported in the EF group (3.7%) and none in the SE group ($p = 0.07$).

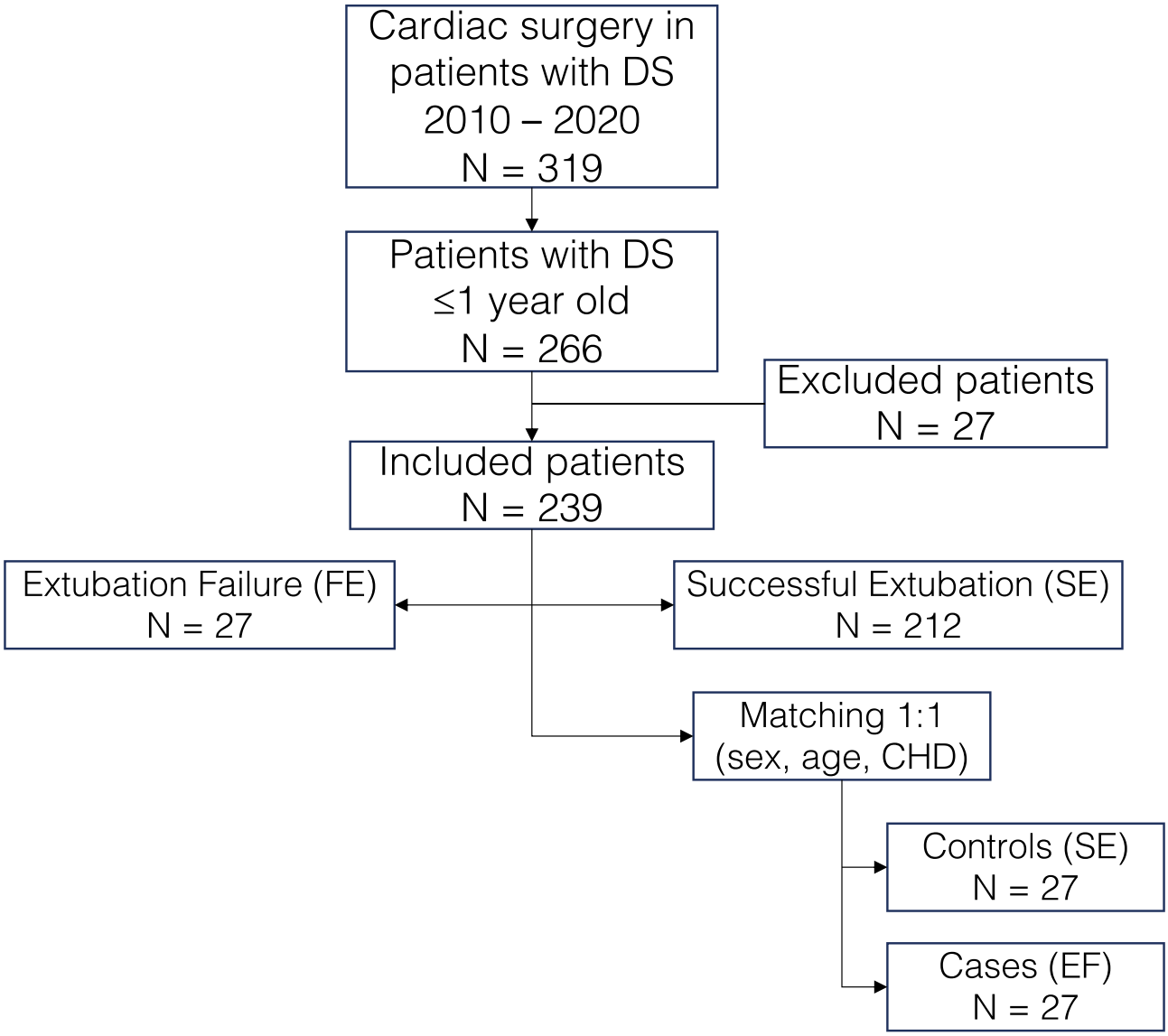

Fig. 1 Flowchart of included patients, from a total of 319 children with DS who underwent cardiac surgery registered on our database

Discussion

As expected, this study found a higher prevalence of EF in infants with DS, 11.3% vs 4–6% described in children without DS after cardiac surgery [6, 16].

The independent risk factors for EF were younger age at the time of surgery, coarctation of the aorta, marked hypotonia at admission, and cardiomegaly evaluated by an augmented CTR on chest x-ray. Finding a relation between aortic coarctation and EF was unexpected. We believe one related factor is the surgical technique. Aortic coarctation repair through left thoracotomy could compromise adequate ventilation due to intraoperative lung collapse and secondary to postoperative pain, thus affecting lung mechanics. Also in our group, 3 from 4 patients had an aortic coarctation associated with atrioventricular septal defect and they underwent coarctation repair as the first stage of surgery, without repair of the septal defect. In these cases, the increase in left ventricular afterload after withdrawing positive inthrathoracic pressure may have resulted in an increase in intracardiac shunt with pulmonary hyperflow and secondary pulmonary congestion. This effect could have been exacerbated in this group of patients who frequently have systolic hypertension, partly due to postoperative increased adrenergic discharge, resulting in more pulmonary congestion and diminishing cardiac output.

Table 1 Study population characteristics and univariate analysis

	Total ($n = 239$)	Failed extubation ($n = 27$)	Successful extubation ($n = 212$)	p value
Female	144	13 (48.1)	131 (61.8)	0.2
Age at surgery, months	4.8	3.8 (1.6)	5 (2.2)	0.003
Body weight, kg		4.57 (1.1)	4.83 (1.0)	0,38
Cardiac heart diseases:				
Ventricular septal defect	104 (43.5)	11 (40.7)	93 (43.8)	0.8
Atrioventricular canal	106 (44.3)	13 (48.1)	93 (43.8)	0.7
Tetralogy of Fallot	25 (10.5)	4 (14.8)	21 (9.9)	0.5
Associated with AVSD	5	2	3	
Isolated	20	2	18	
Aortic coarctation	4 (1.7)	3 (11.1)	1 (0.5)	0.005
Associated with AVSD	2	2	0	
Isolated	2	1	1	

Values are mean (SD) or n (%)

AVSD atrioventricular septal defect

We also found more frequently the history of previous intubation, EF in earlier hospitalizations, and the presence of respiratory malformations; however, the number of reported cases does not allow for establishing associations.

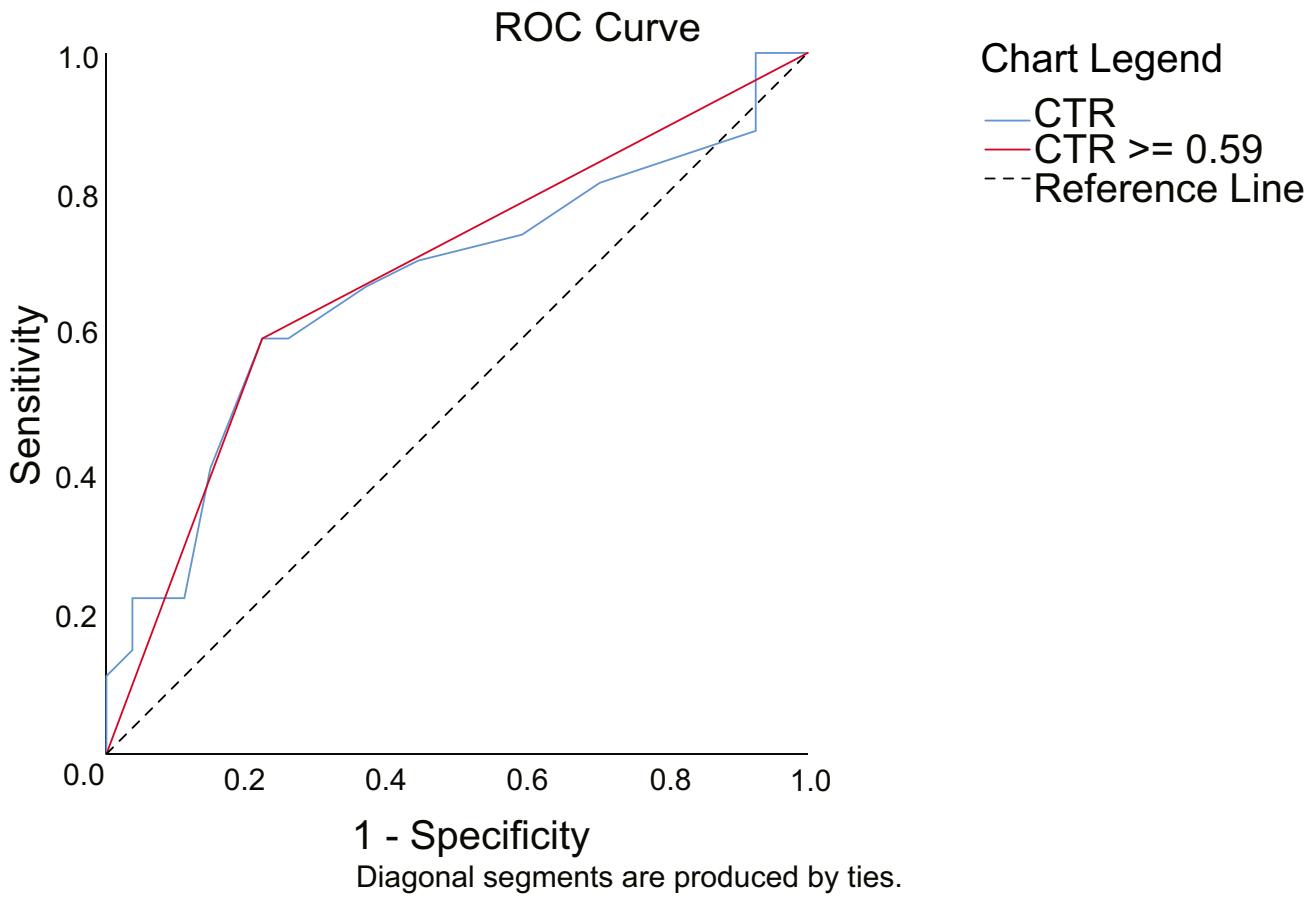

Fig. 2 ROC curve for prediction of extubation failure based on the cardiothoracic ratio (CTR). The optimal cut point was stablished at 0.59 for the highest sensitivity and specificity. AUC (area under the curve) of 0.69 to discriminate patients with EF

Table 2 Preoperative study, type of surgical repair, and comorbidities according to type of extubation

	Extubation failure ($n=27$)	Successful extubation ($n=27$)	p value
Cardiac heart diseases:			
Ventricular septal defect	11 (40.7%)	11 (40.7%)	1
VSD closure	11 (100%)	11 (100%)	1
AP banding	0	0	
Atrioventricular septal defect (isolated)	9 (33.3%)	13 (48.1%)	0.4
AVSD repair	9 (100%)	13 (100%)	1
AP banding	0	0	
Tetralogy of Fallot (isolated)	2 (7.4%)	2 (7.4%)	0.67
ToF repair	2 (100%)	1 (50%)	1
BTT shunt	0	1 (50%)	
ToF associated with AVSD	2 (7.4%)	0	0.5
BTT shunt	2 (100%)		
Aortic coarctation (Isolated) repair	1 (3.7%)	0	1
Aortic coarctation Associated with AVSD	2 (7.4%)	1 (3.7%)	1
AVSD + CoA repair	0	0	
Only CoA repair	2 (100%)	0	
CoA repair + PA banding	0	1 (100%)	
Presurgical chest x-ray			
CTR	0.58 (0.04)	0.55 (0.04)	0.03
CTR ≥ 0.59	16 (59)	6 (22)	0.006
Previous cardiac surgery	2 (7.4)	0	0.49
Previous use of IMV	9 (33.3)	5 (18.5)	0.4
Previous EF	2 (7.4)	1 (3.7)	1.0
Airway malformations	4 (15.4)	0	0.19
Marked hypotonia	7 (26.9)	0	0.01

Values are mean (SD) or *n* (%)

VSD ventricular septal defect, *AVSD* atrioventricular septal defect, *ToF* tetrallogy of Fallot, *CoA* aortic coarctation, *PA* pulmonary artery, *BTT* Blalock−Taussig, *CTR* cardiothoracic ratio, *IMV* invasive mechanical ventilation, *CTR* cardiothoracic ratio

Analyzing the relationship between MV time and EF, although there is a trend towards a longer duration, it was not significantly different, which we attribute to the small number of patients. In terms of sedoanalgesia and NMBAs, although there was a tendency for an increasing number of hours of infusion, but with no significant difference. We must clarify we did not quantitate the cumulative doses of opioids, benzodiazepines nor neuromuscular blocking agents administered. We speculate that cumulative exposure was likely greater in the extubation failure group.

As seen in other series, the most frequent post-extubation complications were progressive respiratory dysfunction with hypoventilation and poor gas exchange, pulmonary congestion, and obstruction of the upper airway. The presence of marked hypotonia, having a younger age and the factors related to aortic coarctation that we mentioned, could contribute to the development of these complications.

Regarding the stay in the PICU, it is striking that the group with SE had a longer length of stay than the group that failed. An explanation for this finding, it considers that

Table 3 Ventilatory management characteristics

	Extubation failure ($n=27$)	Successful extubation ($n=27$)	p value
MV prior to surgery, mean (SD), days	5.15 (14.7)	0.93 (2.9)	0.4
MV post-surgery, median (IQR), hours	53 (59)	45 (32)	0.24
Dexamethasone use pre extubation, *n* (%)	9 (34.6)	13 (48.1)	0.4
Post-extubation use of HFNC, *n* (%)	6 (22.2)	4 (14.8)	0.72
Post-extubation NIV, *n* (%)	5 (18.5)	4 (14.8)	1.0

MV mechanical ventilation, *HFNC* high flow nasal cannula, *NIV* non-invasive mechanical ventilation

Table 4 Use of sedoanalgesia and neuromuscular blocking agents

	Failed extubation ($n=27$)	Successful extubation ($n=27$)	p value
Morphine, h Min–max range	21.5 (79) 4–165	22.5 (22) 12–65	0.93
Fentanyl, h Min–max range	48 (39) 17–94	23.5 (26) 13–105	0.64
Midazolam, h Min–max range	42.5 (45) 8–165	41 (28) 0–104	0.4
NMBA blockers, h Min–max range	20 (33) 12–96	18.5 (7) 0–28	0.54
Suspended SA, h	7 (17)	4 (8)	0.23

Values are median (IQR) or *n* (%)

NMBA neuromuscular muscular blocking agents, *SA* sedoanalgesia

nine of the twenty-seven patients with EF were transferred to another PICU on MV. The actual length of their stay in these critical units is unknown.

This study has the limitations inherent in a single-center, retrospective cohort study. In addition, given the selected group of patients included with a rare event, we obtained a limited cohort for the analysis. We also found limitations at the time of registering the variables. The absence of weaning and extubation protocols can affect the analysis because they are not homogeneous, as well as the lack of registration and objectivity of other variables, such as hypotonia.

Conclusions

In conclusion, in pediatric patients with Down syndrome, extubation failure after congenital cardiac surgery is associated with younger age, presence of aortic coarctation, a higher CTR before surgery reflecting the degree of cardiomegaly, and severe hypotonia. Recognition of these risk factors may allow clinicians to anticipate high-risk patients and consider a more conservative approach to their extubation strategy or help them for more rapid reintervention to limit adverse outcomes".

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Authors contribution Fernanda Salgado, Guillermo Larios, and Paulo Valderrama conceived and designed the study, coordinated and supervised data collection, carried out the analyses, and drafted the initial manuscript. Rodolfo Amstein and Patricio Valle contributed to clinical data acquisition for the study, coordinated and supervised data collection, and revised the manuscript. Gonzalo Valenzuela reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

Declarations

Consent to participate In this study, clinical data were collected from databases and clinical records which contained anonymized records. Given our study design, the ethics committee waived the need to obtain informed consent from individual patients. The protocol ID: 200311006 was approved by the Health Sciences Scientific Ethics Committee at Pontificia Universidad Católica de Chile.

Competing interests The authors declare no competing interests.

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