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# **Original Article**

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# A comparison of high-flow nasal cannula versus non-invasive positive pressure ventilation for respiratory support in infants following cardiac surgery

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#### Abstract

Background: Following cardiac surgery, infants often remain endotracheally intubated upon arrival to the cardiac ICU. High-flow nasal cannula and non-invasive positive pressure ventilation are used to support patients following extubation. There are limited data on the superiority of either mode to prevent extubation failure. Methods: We conducted a single-centre retrospective study for infants (<1 year) and/or <10 kg who underwent cardiac surgery between 3/2019-3/2020. Data included patient and clinical characteristics and operative variables. The study aimed to compare high-flow nasal cannula versus non-invasive positive pressure ventilation following extubation and their association with extubation failure. Secondarily, we examined risk factors associated with extubation failure. Results: There were 424 patients who met inclusion criteria, 320 (75%) were extubated to high-flow nasal cannula, 104 (25%) to non-invasive positive pressure ventilation, and 64 patients (15%) failed extubation. The high-flow nasal cannula group had lower rates of extubation failure (11%, versus 29%, p = 0.001). Infants failing extubation were younger and had higher STAT score (p < 0.05). Compared to high-flow nasal cannula, non-invasive positive pressure ventilation patients were at 3.30 times higher odds of failing extubation after adjusting for patient factors (p < 0.0001). Conclusions: Extubation failure after cardiac surgery occurs in smaller, younger infants, and those with higher risk surgical procedures. Patients extubated to non-invasive positive pressure ventilation had 3.30 higher odds to fail extubation than patients extubated to high-flow nasal cannula. The optimal mode of respiratory support in this patient population is unknown.

Following congenital heart surgery, infants often remain endotracheally intubated on mechanical ventilatory support upon arrival to the cardiac ICU. These patients undergo a trial of extubation when deemed safe. The decision-making process for extubation is quite complex. 1,2 Upon extubation, additional non-invasive modes of respiratory support such as high-flow nasal cannula and non-invasive positive pressure ventilation are commonly used to support these infants.<sup>3,4</sup> Studies have shown approximately 3–27% of patients with CHD fail extubation after cardiac surgery. 1,5-11 Risk factors for extubation failure are numerous such as complex surgical repair, younger age, smaller patients, presence of airway anomalies, genetic abnormalities, pulmonary hypertension, and phrenic and diaphragmatic nerve injury to name a few. 4-7,12-14 Patients with CHD successfully extubated using non-invasive positive pressure ventilation have been shown to have shorter lengths of stay, 5,15-17 while studies in preterm infants without CHD showed non-invasive positive pressure ventilation reduced extubation failure compared to highflow nasal cannula. 18 Other studies have shown high-flow nasal cannula to decrease the need for intubation in infants with respiratory failure and may improve respiratory mechanics through unidirectional flow in the upper airway, decreasing dead space, improving minute ventilation, pulmonary compliance, and distending airway pressure. This support ultimately reduces the work of breathing and oxygen consumption, while enhancing oxygen delivery and gas exchange.19-23

Despite the use of high-flow nasal cannula and non-invasive positive pressure ventilation to support patients following extubation, there is limited data on the efficacy and superiority of either mode to prevent extubation failure in infants with CHD following cardiac surgery. We hypothesise that the use of non-invasive positive pressure ventilation will be associated with lower rates of extubation failure and a shorter length of stay when compared to high-flow nasal cannula. Our aims are to examine which mode of respiratory support (high-flow nasal cannula

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versus non-invasive positive pressure ventilation) after extubation is associated with lowest rates of extubation failure and examine risk factors that are associated with extubation failure in patients with CHD following cardiac surgery.

## **Materials and methods**

## **Cohort selection**

This single-centre retrospective cohort study included all infants (<1 year) and/or <10 kg who underwent CS for CHD from March 1<sup>st</sup> 2019, to March 31<sup>st</sup> 2020, at Children's Healthcare of Atlanta, a free-standing university-affiliated quaternary hospital. An internal surgical database was queried, and eligible surgical encounters were identified. Preterm neonates with corrected gestational age of <35 weeks were excluded. All patients were admitted to the cardiac ICU post-operatively. This project was reviewed and approved by the Children's Healthcare of Atlanta Institutional Review Board (study # 00000706). Informed consent was waived.

Demographics (age, weight, gender, and race), clinical characteristics (cardiac diagnosis, cardiac ICU length of stay, post-operative length of stay, hospital length of stay, duration of mechanical ventilation, respiratory support following extubation (high-flow nasal cannula versus non-invasive positive pressure ventilation), genetic syndrome, chromosomal abnormalities), and operative variables (cardiopulmonary bypass and cross-clamp times) were collected. Surgical procedures were categorised by complexity based on the Society of Thoracic Surgeons and the European Association for Cardio-Thoracic Surgery (STAT) Mortality Scores.<sup>24</sup> Duration of mechanical ventilation was defined as the duration of time from intubation to the first extubation attempt. Extubation failure was defined as the need for reintubation within 48 hours from the initial extubation attempt. Respiratory support following extubation was dichotomised to high-flow nasal cannula versus non-invasive positive pressure ventilation. Patients remained assigned to the initial mode of respiratory support at time of extubation even if they required escalation to the alternative modality prior to reintubation. Mortality was defined as all deaths occurring during the hospitalisation in which the operation was performed; and all deaths occurring after discharge from the hospital, but before the end of the thirtieth post-operative day.<sup>24</sup>

Airway Management: All patients were endotracheally intubated with cuffed endotracheal tubes and placed on mechanical ventilation and on a standardised analgosedation protocol on admission from the operating room. Once spontaneously breathing, and extubation readiness determined, patients were placed on a spontaneous breathing trial using continuous positive airway pressure with pressure support. Following a successful spontaneous breathing trial, patients were extubated to non-invasive respiratory support at the discretion of the cardiac ICU physician ranging from high-flow nasal cannula to non-invasive positive pressure ventilation, with RAM interface (Neotech Products LLC. Valencia, CA). The analgosedation protocol is a standard of care where sedation is adjusted in a uniform way to avoid inherent bias related to sedation and optimise sedation use and avoid over-sedating patients following extubation and minimising sedation-related extubation failure.

## Statistical analysis

Demographics were compared for patients with non-invasive positive pressure ventilation versus high-flow nasal cannula using chi-square and Fisher's exact tests for categorical variables and

using t-test and Wilcoxon rank sum tests for continuous variables. Logistic regression was conducted to determine the crude and adjusted odds ratios for extubation failure when comparing non-invasive positive pressure ventilation versus high-flow nasal cannula. Logistic modelling was also conducted stratifying the data into the following categories: weight  $\leq$  or >5 kg and neonate versus non-neonate. All demographic and clinical variables were entered into a multivariable logistic regression model and eliminated one at a time using backward selection to produce the final adjusted model. A p-value of 0.05 was considered the cut-off for statistical significance. Statistical analyses were performed in SAS Enterprise Guide version 7.15 (SAS Institute, Inc., NC).

#### **Results**

## Demographic data

There were 424 eligible patients during the study period. Patient characteristics are presented in Table 1. The median age was 97 days [interquartile range (IQR) 9–166], and median weight was 4.6 kg (IQR 3.3–6.1). Operations with STAT scores of 4 or 5 comprised 143 (34%) of all surgeries. The median duration of cardio-pulmonary bypass and cross-clamp times were 109 minutes (IQR 78–143) and 65 minutes (IQR 39–91), respectively. The median cardiac ICU length of stay was 5 days (IQR 2–10), post-operative length of stay 8 days (IQR 5–18), and the median duration of mechanical ventilation was 21 hours (IQR 12–64). Chromosomal abnormalities were present in 27% and diagnosed genetic syndromes in 36% (Table 1).

## Patients stratified by respiratory support after extubation

The 2 groups were high-flow nasal cannula versus non-invasive positive pressure ventilation. There were 320 (75%) patients in the high-flow nasal cannula group versus 104 (25%) patients in the non-invasive positive pressure group. The non-invasive positive pressure group were younger (median age 26 versus 115 days, p < 0.0007) and smaller (median weight 3.5 versus 5.1 kg, p < 0.0001) than the high-flow nasal cannula group (Table 1). The patients in the non-invasive positive pressure group had longer cardiopulmonary bypass time (median 127 versus 106 minutes, p 0.0012), longer cardiac ICU and hospital length of stay, and longer duration of mechanical ventilation (Table 1).

Of the 320 patients in the high-flow nasal cannula group, 34 (11%) failed extubation. Those who failed extubation were younger (median age 8 versus 125 days, p < 0.0001) and smaller (median weight 3.2 versus 5.3 kg, p < 0.0001), had longer cardiopulmonary bypass times (median 150 versus 103 minutes, p < 0.0001), longer cross-clamp time (median 93 versus 58 minutes, p = 0.0017), longer cardiac ICU and hospital length of stay, and longer duration of mechanical ventilation (Table 2). They were also more likely to have a higher STAT score of 4 and 5 (47% versus 20%, and 15% versus 5%, p < 0.0001 respectively), and antenatal diagnosis (71% versus 47%, p = 0.001). Those who failed extubation in the high-flow nasal cannula group had a higher mortality rate (12% versus 1%, p = 0.0003) when compared to those who did not fail (Table 2).

Of the 104 patients in the non-invasive positive pressure group, 30 (29%) failed extubation. Those who failed extubation had longer duration of mechanical ventilation (median 137 hours versus 72, p = 0.03), longer cardiac ICU length of stay (median 24 versus 9, p = 0.0004), longer post-operative length of stay (median 36 versus 16, p = 0.0001), and higher mortality (30% versus 5%, p = 0.0006) (Table 3).

Table 1. Patient characteristics stratified by type of respiratory support following extubation.

Variables	All, n = 424	HFNC, n = 320 (75%)	NIPPV, n = 104 (25%)	<i>p</i> -value
Age (days)	97 (9–166)	115 (14–175)	26 (7–139)	0.0007
Weight (kg)	4.6 (3.3–6.1)	5.1 (3.5–6.3)	3.5 (2.8–5.1)	<0.0001
Gender				
Female	206 (49%)	145 (45%)	61 (59%)	0.02
Male	218 (51%)	175 (55%)	43 (41%)	
Race				
Black	155 (37%)	106 (33%)	49 (47%)	0.04
White	228 (54%)	182 (57%)	46 (44%)	
Other	41 (10%)	32 (10%)	9 (9%)	
Chromosomal abnormality	116 (27%)	81 (25%)	35 (34%)	0.10
Genetic syndrome	154 (36%)	112 (35%)	42 (40%)	0.32
Antenatal diagnosis	219 (52%)	159 (50%)	60 (58%)	0.16
Single ventricle	76 (18%)	57 (18%)	19 (18%)	0.91
STAT score				
1	107 (25%)	91 (28%)	16 (15%)	0.0006
2	126 (30%)	103 (32%)	23 (22%)	
3	44 (10%)	32 (10%)	12 (12%)	
4	117 (28%)	73 (23%)	44 (42%)	
5	26 (6%)	18 (6%)	8 (8%)	
% fluid overload				
<0%	181 (43%)	144 (45%)	37 (36%)	0.18
0–10%	173 (41%)	123 (38.4%)	50 (48%)	
>10%	70 (17%)	53 (16.6%)	17 (16%)	
Duration of MV (hours)	21 (12–64)	17 (11–28)	86 (43–152)	<0.0001
CPB Time (minutes)	109 (78–143)	106 (74–136)	127 (92–163)	0.0012
Cross-clamp time (minutes)	65 (39–91)	61 (39–86)	74 (43–98)	0.08
Postop LOS	8 (5–18)	7 (5–12)	20 (10–34)	<0.0001
CICU LOS	5 (2–10)	4 (2-8)	10 (6–20)	<0.0001
Hospital LOS	13 (6–29)	9 (6–19)	30 (17–46)	<0.0001
Operative mortality	21 (5%)	8 (3%)	13 (13%)	<0.0001

Results are depicted in n (per cent), median (interquartile range)

CICU LOS: Cardiac Intensive Care Unit Length of Stay; HFNC: High-Flow Nasal Cannula; LOS: Length of Stay; MV: Mechanical Ventilation; NIPPV: Non-invasive Positive Pressure Ventilation Bold p-values are significant

The most common aetiology of extubation failure was upper airway obstruction 69%, followed by deconditioning/weakness 23%, and atelectasis 11% in the entire cohort (Table 4). These findings were similar in both the high-flow nasal cannula and non-invasive positive pressure ventilation groups respectively (Table 4).

# Logistic regression analysis

Using a multivariable regression analysis controlling for age, gender, race, cardiopulmonary bypass times, STAT category, and duration of mechanical ventilation to compare outcomes of extubation failure between both groups (high-flow nasal cannula versus non-invasive positive pressure ventilation), we found that patients

extubated to non-invasive positive pressure ventilation had 3.30 higher odds (95% CI 1.56–6.96, p < 0.0001) to fail extubation when compared to high-flow nasal cannula group (Table 5).

Logistic regression model demonstrated patients extubated to non-invasive positive pressure ventilation and >5 kg had 14.7 greater odds (95% CI 2.88–75.39, p = 0.0012) to fail extubation when compared to high-flow nasal cannula (adjusting for race, gender, STAT score, duration of mechanical ventilation, and cardiopulmonary bypass time). Non-neonates supported with non-invasive positive pressure ventilation had 21.7 higher odds (95% CI 5.16–91.20, p < 0.0001) to fail extubation when compared to high-flow nasal cannula (adjusting for race, gender, STAT score, duration of mechanical ventilation, and cardiopulmonary bypass time) (Table 6).

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Table 2. Patient characteristics in the high-flow nasal cannula (HFNC) group stratified by extubation failure.

Variables	HFNC Group				
	All, n = 320 (100%)	Failure, n = 34 (11%)	No failure, n = 286 (89%)	<i>p</i> -valu	
Age (days)	115 (14–175)	8 (5–22)	125 (27–181)	<0.000	
Weight (kg)	5.1 (3.5-6.3)	3.2 (2.8–4.5)	5.3 (3.7–6.5)	<0.000	
Gender					
Female	145 (45%)	10 (29%)	135 (47%)	0.049	
Male	175 (55%)	24 (71%)	151 (53%)		
Race					
Black	106 (33%)	12 (35%)	94 (33%)	0.94	
White	182 (57%)	19 (56%)	163 (57%)		
Other	32 (10%)	3 (9%)	29 (10%)		
Chromosomal abnormality	81 (25%)	9 (26%)	72 (25%)	0.87	
Genetic syndrome	112 (35%)	9 (26%)	103 (36%)	0.27	
Antenatal diagnosis	159 (50%)	24 (71%)	135 (47%)	0.01	
Single ventricle	57 (18%)	9 (26%)	48 (17%)	0.16	
STAT score					
1	91 (28%)	0 (0%)	91 (32%)	<0.000	
2	103 (32%)	8 (24%)	95 (33%)		
3	32 (10%)	4 (12%)	28 (10%)		
4	73 (23%)	16 (47%)	57 (20%)		
5	18 (6%)	5 (15%)	13 (5%)		
Duration of MV (hours)	17 (11–28)	28 (20–92)	15 (10–26)	<0.000	
CPB time (minutes)	106 (74–136)	150 (121–205)	103 (72–128)	<0.000	
Cross-clamp time (minutes)	61 (39–86)	93 (69–144)	58 (38–85)	0.001	
Missing	4 (1%)	1 (1%)	3 (0.8%)		
Postop LOS	7 (5–12)	22 (13–54)	6 (5–10)	<0.000	
CICU LOS	4 (2–8)	17 (10–28)	3 (2–6)	<0.000	
Hospital LOS	9 (6–19)	32 (17–57)	8 (6–16)	<0.000	
Operative mortality	8 (3%)	4 (12%)	4 (1%)	0.000	

Results depicted in n (per cent), median (interquartile range)

CICU LOS: Cardiac Intensive Care Unit Length of Stay; HFNC: High-Flow Nasal Cannula; LOS: Length of Stay; MV: Mechanical Ventilation Bold p-values are significant

## **Discussion**

Our study showed an association between high-flow nasal cannula and lower rates of extubation failure compared to non-invasive positive pressure ventilation when adjusting for patient factors in a multivariate analysis. There was an extubation failure rate of 15% (64/442) within 48 hours in our cohort. Risk factors associated with extubation failure were smaller, younger, and higher risk surgery patients, with longer cardiopulmonary bypass and cross-clamp time which contributed to longer length of stay and mortality.

At the outset of this study, our hypothesis was that non-invasive positive pressure ventilation would be associated with lower extubation failure. This was based on an assumption that higher pressures would provide adequate distending pressures and support these patients through the extubation process. However, after adjusting for age, race, gender, STAT score, duration of mechanical ventilation and cardiopulmonary bypass times, we

found patients extubated to non-invasive positive pressure ventilation had 3.30 higher odds of failing extubation when compared to high-flow nasal cannula after extubation. This surprising finding was contrary to other studies reporting less extubation failure with non-invasive positive pressure ventilation, although these studies excluded critically ill cardiac neonates and children. 25,26 Our report is the largest cohort of neonates and infants studying high-flow nasal cannula versus non-invasive positive pressure ventilation to prevent extubation failure. Jayashankar et al showed high-flow nasal cannula was comparable to non-invasive positive pressure ventilation (bi-level ventilation in particular) in preventing extubation failure in patients following cardiac surgery.<sup>4</sup> However, this report examined 100 patients (50 patients in each group). While this study was a well-designed retrospective study, the lack of similar findings could be due to the smaller sample size. Our study included a

Table 3. Patient characteristics in the non-invasive positive pressure ventilation (NIPPV) group stratified by extubation failure.

		NIPPV gro	ир		
Variables	All, n = 104 (100%)	Failure, n = 30 (29%)	No failure, n = 74 (71%)	<i>p</i> -value	
Age (days)	26 (7–139)	13 (6–129)	31 (7–144)	0.73	
Weight (kg)	3.5 (2.8–5.1)	3.7 (3.1–5.4)	3.4 (2.7–5.0)	0.62	
Gender					
Female	61 (59%)	14 (47%)	47 (64%)	0.11	
Male	43 (41%)	16 (53%)	27 (36%)		
Race					
Black	49 (47%)	13 (43%)	36 (49%)	0.54	
White	46 (44%)	4 (13%)	33 (45%)		
Other	9 (9%)	13 (43%)	5 (7%)		
Chromosomal abnormality	35 (34%)	14 (47%)	21 (28%)	0.07	
Genetic syndrome	42 (40%)	10 (33%)	32 (43%)	0.35	
Antenatal diagnosis	60 (58%)	19 (63%	41 (55%)	0.46	
Single ventricle	19 (18%)	6 (20%)	13 (18%)	0.77	
STAT score					
1	16 (15%)	5 (17%)	11 (15%)	0.79	
2	23 (22%)	6 (20%)	17 (23%)		
3	12 (12%)	5 (17%)	7 (9%)		
4	44 (42%)	11 (37%)	33 (45%)		
5	8 (8%)	3 (10%)	5 (7%)		
Duration of MV (hours)	86 (43–152)	137 (43–212)	72 (44–114)	0.03	
CPB time (minutes)	127 (92–163)	138 (95–157)	117 (90–163)	0.40	
Cross-clamp time (minutes)	74 (43–98)	82 (51–102)	73 (38–97)	0.46	
Missing	4 (1%)	1 (1%)	3 (0.8%)		
Postop LOS	20 (10–34)	36 (21–57)	16 (9–25)	0.0001	
CICU LOS	10 (6–20)	24 (8–37)	9 (5–14)	0.0004	
Hospital LOS	30 (17–46)	43 (32–123)	24 (15–37)	0.0002	
Operative mortality	13 (13%)	9 (30%)	4 (5%)	0.0006	

Results depicted in n (per cent), median (interquartile range)

CICU LOS: Cardiac Intensive Care Unit Length of Stay; HFNC: High-Flow Nasal Cannula; LOS: Length of Stay; MV: Mechanical Ventilation Bold p-values are significant

total of 424 patients (320 patients in the high-flow nasal cannula group, and 104 patients in the non-invasive positive pressure group).

Further analysis of each group, controlling for patient variables and stratifying by weight (<5 kg versus >5 kg), showed patients >5 kg extubated to non-invasive positive pressure had 15 times higher odds of extubation failure compared to high-flow nasal cannula group and 22 times higher odds in non-neonates, further suggesting that larger patients may fare better being extubated to high-flow nasal cannula rather than non-invasive positive pressure ventilation. It is possible there may be physiological benefits of high-flow nasal cannula for these patients such as the delivery of high gas flow to washout pharyngeal dead space, reducing nasopharyngeal resistance, improves lung compliance by providing positive airway pressure, all of which improve work of breathing and support respiratory dynamics.

Prior reports described extubation failure rates of 15-20% in critically ill children and 3-27% following cardiac surgery. 1,5,7-11,27 Neonates and infants with higher mortality after extubation failure were likely due to these patients with more vulnerable physiology. 1,4,13,28 In our cohort, the overall mortality rate was 5% (21/424) with a mortality rate of 8% (8/320) in the high-flow nasal cannula group and 13% (13/104) in the non-invasive positive pressure group. Those who failed extubation had a much higher mortality rate 12% (4/34) and 30% (9/30), respectively. It is unclear if extubation failure is a sign of mortality risk versus an antecedent cause as it relates to severity of illness and complexity of patient hospital course. Also, consistent with our findings, previous studies have also shown smaller and younger patients with longer duration of mechanical ventilation and length of stay were at higher risk of extubation failure. Surgical risk factors associated with

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Table 4. Etiology of extubation failure.

Etiology	All, n = 64	HFNC, n = 34 (53%)	NIPPV, n = 30 (47%)	<i>p</i> -value
Upper airway obstruction	44 (69%)	19 (56%)	25 (83%)	0.03
Deconditioning/weakness	15 (23%)	10 (29%)	5 (17%)	0.25
Atelectasis	7 (11%)	6 (18%)	1 (3%)	0.11
Pneumothorax	2 (3%)	0 (0%)	2 (7%)	0.22
Low cardiac output	2 (3%)	1 (3%)	1 (3%)	>0.99
Sepsis	2 (3%)	1 (3%)	1 (3%)	>0.99
Pleural effusion	1 (2%)	1 (3%)	0 (0%)	>0.99
Neurological issues	1 (2%)	0 (0%)	1 (3%)	0.47
Diaphragm paresis	0 (0%)	0 (0%)	0 (0%)	-
Vocal cord paralysis	0 (0%)	0 (0%)	0 (0%)	_
Pneumonia	0 (0%)	0 (0%)	0 (0%)	-
Pulmonary oedema	0 (0%)	0 (0%)	0 (0%)	-

Results depicted in n (per cent)

HFNC: High-Flow Nasal Cannula; NIPPV: Non-invasive Positive Pressure

Bold p-values are significant

Table 5. Crud and adjusted odds ratio for extubation failure by support type.

	Odds ratio (OR) (95% CI)	<i>p</i> -value
NIPPV versus HFNC (crude OR)	3.41 (1.96-5.93)	<0.0001
NIPPV versus HFNC (adjusted OR)	3.30 (1.56–6.96)	<0.0001

Adjusted for age, race, gender, STAT score, duration of mechanical ventilation, and CPB time Bold *p*-values are significant

extubation failure in our cohort likely reflected the fragile state and tenuous physiology of this age group and were consistent with previous studies.<sup>1,13,17,27–29</sup>

This study is subject to the typical limitations inherent to single-centre retrospective cohort studies. As a single-centre study, the demographics, clinical characteristics, as well as surgical and medical management of these patients are specific to our institution and might not be generalisable to other healthcare systems. Ventilation weaning protocols and extubation readiness testing may be institution-specific. Also, we compare in our study high-flow nasal cannula versus non-invasive positive pressure ventilation using nasal RAM interface, which is a common practice in some cardiac ICU,

but not a widely adapted respiratory interface. Also, the choice of respiratory support mode was at the discretion of the cardiac ICU team taking care of the patients and this might have added bias in the selection of one mode over the other. This is a difficult property to control for when conducting retrospective studies as personal training, and clinical experiences, and patient clinical condition and complexity of hospital course all factor in when deciding which mode to use after extubation adding the potential for selection bias. Despite these limitations, this large cohort of patients with CHD can shed light on post-cardiac surgery respiratory support.

In conclusion, extubation failure is common in infants following cardiac surgery with smaller, younger infants, and those with higher risk surgical procedures at highest risk. There were no racial, ethnic, or socio-economic risk factors associated with extubation failure. Overall, patients extubated to non-invasive positive pressure ventilation had 3.30 higher odds of failing extubation versus patients extubated to high-flow nasal cannula. Furthermore, patients weighing >5 kg and non-neonates who were extubated to non-invasive positive pressure ventilation had even higher odds of failing extubation when compared to similar patients extubated to high-flow nasal cannula. Based on these findings, clinicians may

**Table 6.** Crude and adjusted odds ratio for non-invasive positive pressure ventilation (NIPPV) versus high-flow nasal cannula (HFNC) respiratory support type, stratified by weight, and neonates.

	Weight ≤5 kg		Weight >5	Weight >5 kg	
	Odds ratio (OR)	<i>p</i> -value	Odds ratio (OR)	<i>p</i> -value	
NIPPV versus HFNC (crude OR)	1.81 (0.96–3.45)	0.07	11.2 (3.50-35.61)	<0.0001	
NIPPV versus HFNC (adjusted OR)	1.65 (0.68-4.0)	0.27	14.7 (2.88–75.39)	0.0012	
	Neonate		Non-neona	Non-neonate	
	Odds ratio	<i>p</i> -value	Odds ratio	<i>p</i> -value	
NIPPV versus HFNC (crude OR)	1.31 (0.63–2.72)	0.47	9.15 (3.55–23.57)	<0.0001	
NIPPV versus HFNC (adjusted OR)	0.80 (0.28–2.28)	0.67	21.7 (5.16–91.20)	<0.0001	

Adjusted for race, gender, STAT score, duration of mechanical ventilation, and CPB time Bold  $\emph{p}\text{-}\text{values}$  are significant

need to re-evaluate their extubation practices. It is difficult to draw a definitive conclusion regarding the optimal type of respiratory support in these patients; however, these findings contribute to the literature and make a compelling case for a prospective trial in this fragile population. Currently, our institution is undergoing such a study to further clarify this important aspect of critical care support following cardiac surgery.

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#### Conflicts of interest. None.

**Ethical standards.** The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and have been approved by the institutional committees (Institutional Review Board at the Children's Healthcare of Atlanta).

### **References**

- Miura S, Hamamoto N, Osaki M, Nakano S, Miyakoshi C. Extubation failure in neonates after cardiac surgery: prevalence, etiology, and risk factors. Ann Thorac Surg 2017; 103: 1293–1298.
- Chang AC, Hanley FL, Lock JE, Castaneda AR, Wessel DL. Management and outcome of low birth weight neonates with congenital heart disease. J Pediatr 1994; 124: 461–466.
- Richards-Belle A, Davis P, Drikite L, et al. FIRST-line support for assistance in breathing in children (FIRST-ABC): a master protocol of two randomised trials to evaluate the non-inferiority of high-flow nasal cannula (HFNC) versus continuous positive airway pressure (CPAP) for non-invasive respiratory support in paediatric critical care. BMJ Open 2020; 10: e038002.
- Jayashankar JP, Rajan P, Kottayil BP, Jayant A, Balachandran R. Comparison of nasal bi-level positive airway pressure versus high-flow nasal cannula as a means of noninvasive respiratory support in pediatric cardiac surgery. Anesth Essays Res 2020; 14: 283–287.
- Gupta P, Kuperstock JE, Hashmi S, et al. Efficacy and predictors of success of noninvasive ventilation for prevention of extubation failure in critically ill children with heart disease. Pediatr Cardiol 2013; 34: 964–977.
- Harrison AM, Cox AC, Davis S, Piedmonte M, Drummond-Webb JJ, Mee RB. Failed extubation after cardiac surgery in young children: prevalence, pathogenesis, and risk factors. Pediatr Crit Care Med 2002; 3: 148–152.
- Mastropietro CW, Cashen K, Grimaldi LM, et al. Extubation failure after neonatal cardiac surgery: a multicenter analysis. J Pediatr 2017; 182: 190– 196. e194.
- Manrique AM, Feingold B, Di Filippo S, Orr R, Kuch BA, Munoz R. Extubation after cardiothoracic surgery in neonates, children, and young adults: one year of institutional experience. Pediatr Crit Care Med 2007; 8: 552–555.
- Yamasaki Y, Shime N, Miyazaki T, Yamagishi M, Hashimoto S, Tanaka Y. Fast-track postoperative care for neonatal cardiac surgery: a single-institute experience. J Anesth 2011; 25: 321–329.
- Gupta P, McDonald R, Gossett JM, et al. A single-center experience of extubation failure in infants undergoing the Norwood operation. Ann Thorac Surg 2012; 94: 1262–1268.

- Gupta P, McDonald R, Goyal S, et al. Extubation failure in infants with shunt-dependent pulmonary blood flow and univentricular physiology. Cardiol Young 2014; 24: 64–72.
- Sağıroğlu G, Baysal A, Copuroğlu E, Gül Y, Karamustafaoğlu Y, Dogukan M. Does early use of bilevel positive airway pressure (bipap) in cardiothoracic intensive care unit prevent reintubation? Int J Clin Exp Med 2014; 7: 3439–3446.
- Laudato N, Gupta P, Walters HL III, Delius RE, Mastropietro CW. Risk factors for extubation failure following neonatal cardiac surgery. Pediatr Crit Care Med 2015; 16: 859–867.
- Thiagarajan RR, Bratton SL, Martin LD, Brogan TV, Taylor D. Predictors of successful extubation in children. Am J Resp Crit Care Med 1999; 160: 1562–1566.
- Kloth RL, Baum VC. Very early extubation in children after cardiac surgery. Crit Care Med 2002; 30: 787–791.
- Mittnacht AJ, Thanjan M, Srivastava S, et al. Extubation in the operating room after congenital heart surgery in children. J Thorac Cardiovasc Surg 2008; 136: 88–93.
- Davis S, Worley S, Mee RB, Harrison AM. Factors associated with early extubation after cardiac surgery in young children. Pediatr Crit Care Med 2004; 5: 63–68.
- Ferguson KN, Roberts CT, Manley BJ, Davis PG. Interventions to improve rates of successful extubation in preterm infants: a systematic review and meta-analysis. JAMA Pediatr 2017; 171: 165–174.
- Mikalsen IB, Davis P, Øymar K. High flow nasal cannula in children: a literature review. Scand J Trauma Resusc Emerg Med 2016; 24: 93.
- Ejiofor BD, Carroll RW, Bortcosh W, Kacmarek RM. PEEP generated by high-flow nasal cannula in a pediatric model. Respir Care 2019; 64: 1240–1249.
- Nishimura M. High-flow nasal cannula oxygen therapy in adults: physiological benefits, indication, clinical benefits, and adverse effects. Respir Care 2016; 61: 529–541.
- Sztrymf B, Messika J, Bertrand F, et al. Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study. Intens Care Med 2011; 37: 1780–1786.
- Mikalsen IB, Davis P, Øymar K. High flow nasal cannula in children: a literature review. Scand J Trauma Resusc Emerg Med 2016; 24: 93.
- O'Brien SM, Clarke DR, Jacobs JP, et al. An empirically based tool for analyzing mortality associated with congenital heart surgery. J Thorac Cardiovasc Surg 2009; 138: 1139–1153.
- Aghai ZH, Saslow JG, Nakhla T, et al. Synchronized nasal intermittent positive pressure ventilation (SNIPPV) decreases work of breathing (WOB) in premature infants with respiratory distress syndrome (RDS) compared to nasal continuous positive airway pressure (NCPAP). Pediatr Pulmonol 2006; 41: 875–881.
- Lemyre B, Davis PG, De Paoli AG, Kirpalani H. Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation. Cochrane Database Syst Rev 2017; 2: Cd003212.
- Harrison AM, Cox AC, Davis S, Piedmonte M, Drummond-Webb JJ, Mee RB. Failed extubation after cardiac surgery in young children: prevalence, pathogenesis, and risk factors. Pediatr Crit Care Med 2002; 3: 148–152.
- Fontela PS, Piva JP, Garcia PC, Bered PL, Zilles K. Risk factors for extubation failure in mechanically ventilated pediatric patients. Pediatr Crit Care Med 2005; 6: 166–170.
- Baisch SD, Wheeler WB, Kurachek SC, Cornfield DN. Extubation failure in pediatric intensive care incidence and outcomes. Pediatr Crit Care Med 2005; 6: 312–318.