

Risk factors for prolonged ventilation after the modified Fontan procedure

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Original Article

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Social Media Synopsis:

Fenestration, low pulmonary artery index, and high-grade atrioventricular valve regurgitation are risk factors for prolonged ventilation after Fontan surgery.

Abstract

Objective: To investigate the risk factors associated with prolonged ventilation after Fontan surgery. **Design:** Retrospective case series. **Setting:** Tertiary childrens hospital. **Patients:** We included 123 children who underwent Fontan surgery without delayed sternal closure or extracorporeal membrane oxygenation between 2011 and 2017. **Intervention:** Fontan surgery. **Measurements and main results:** Prolonged ventilation was defined as intubation for more than 24 hours after surgery. Preoperative, intraoperative, and perioperative data were collected retrospectively from medical records. Multivariate logistic regression analysis was used to identify risk factors for prolonged ventilation. The median age and weight of patients were 2.2 years and 10.0 kg, respectively. Seventeen per cent of the patients (n = 21) received prolonged mechanical ventilation, and the median intubation period was 2.9 days. There were no 90-day or in-hospital deaths. The independent predictors of prolonged ventilation identified were fenestration (p < 0.01), low pulmonary artery index (p = 0.02), and advanced atrioventricular regurgitation (p < 0.01). The duration of ICU stay was significantly longer in the prolonged ventilation group than in the early extubation group (10 days versus 6 days, p < 0.01). **Conclusion:** Fenestration, low pulmonary artery index, and significant atrioventricular regurgitation are risk factors for prolonged ventilation after Fontan surgery. Careful preoperative and perioperative management that considers the risk factors for prolonged ventilation in each individual is important.

The treatment outcomes for CHD have improved dramatically over the past 40 years, and the number of patients surviving until Fontan surgery is increasing. The importance of early extubation and withdrawal from positive pressure ventilation has long been recognised, and these procedures are currently the standard post-operative management strategy.¹⁻³ In recent years, numerous studies have investigated fast-track care from the operating room, and the usefulness of this approach is being established.⁴⁻⁶

Prolonged ventilation often occurs due to various reasons and could lead to undesirable effects such as increased post-operative complications, prolonged ICU, and total duration of hospitalisation. This study aimed to extract a subset of Fontan patients suitable for fast-track care in cardiac ICU based on preoperative and intraoperative variables and use them in planning postoperative management strategies tailored to each case. The secondary aim was to investigate the associations of prolonged mechanical ventilation with adverse events and mortality.

Materials and methods

Patients and setting

From January, 2011 to December, 2017, 128 patients underwent Fontan surgery at the Shizuoka Children's Hospital and were admitted to the CICU after surgery. These patients were included in this study, and their medical, anaesthesia, surgery, and ICU records were retrospectively reviewed. Patients who required delayed sternal closure after Fontan surgery or extracorporeal membrane oxygenation were excluded, and details of our institute settings and operative strategy are described in the Supplementary Material. The ethical review board of Shizuoka Children's Hospital approved this study and waived the need for informed consent.

At our hospital, all cardiovascular surgery patients are admitted to the CICU receiving mechanical ventilation, and we aim to extubate as early as possible. Extubation is performed once the following criteria are met: stable circulation; systolic blood pressure above the fifth percentile for the child's age; normal lactate level (<2 mmol/l); adequate hemostasis; maintenance of respiratory function [spontaneous breathing test (fraction of inspired oxygen ≤ 0.5; positive end-expiratory pressure ≤ 5 cmH₂O, peak inspiratory pressure ≤ 10 cmH₂O)]; and awaking while maintaining a sufficient airflow through the airway.

Data collection and definitions

Prolonged ventilation was defined as intubation exceeding 24 hours after admission to the CICU. Ventilation times were regarded as the total postoperative time until successful

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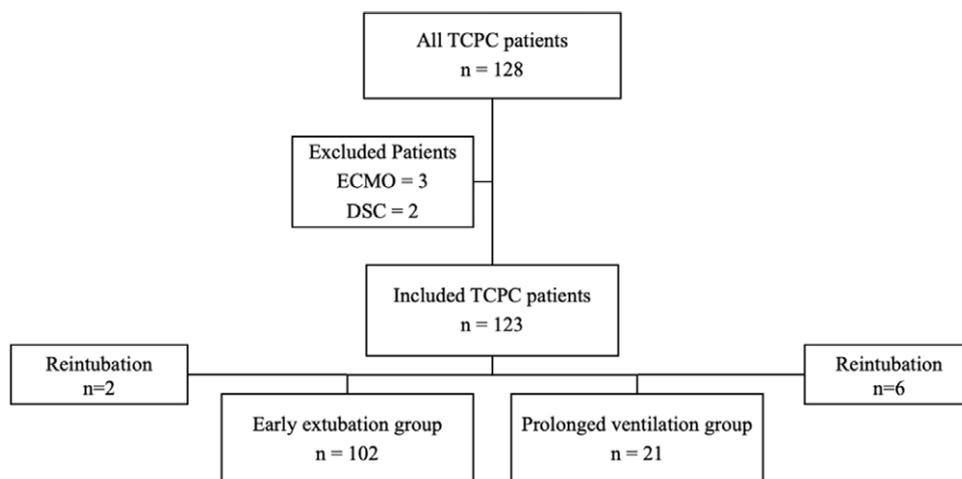


Figure 1. Patient flowchart. DSC = delayed sternal closure; ECMO = extracorporeal membrane oxygenation; TCPC = total cavopulmonary connection.

extubation. Cases requiring reintubation and those with ventilation time exceeding 24 hours were included in the prolonged ventilation group. Regarding the patients' background, we reviewed their age, sex, height, weight, body surface area, and diagnosis. The preoperative oxygen saturation (SpO₂), superior caval vein pressure (Glenn pressure), left atrial or pulmonary wedge pressure, pulmonary vascular resistance (Rp), systemic vascular resistance (Rs), pulmonary blood flow (Qp), systemic blood flow (Qs), cardiac index, volume of the main ventricle, pulmonary artery index, atrioventricular valve regurgitation, brain natriuretic peptide level, and airway and respiratory complications were recorded. Cardiac catheterization was performed in all patients 0–6 months before undergoing Fontan surgery, and the pressure in each blood vessel and oxygen saturation were measured. The ejection fraction of the main ventricle was calculated from the contrast data of cardiac catheterisation. The Qp/Qs and Rp/Rs were calculated by Fick's method. The pulmonary artery index was calculated from the diameter of the pulmonary artery just before its bifurcation; the diameter of the artery was measured during pulmonary angiography.⁷ Surgical variables, such as the main operative procedure, concurrent procedures, need for open-heart surgery, operation time, cardiopulmonary bypass time, and presence of aortic clamping, were similarly recorded. Required intra-cardiac or intra-extra-cardiac total cavopulmonary connections were recorded as concurrent operations to distinguish them from simple total cavopulmonary connections. The anaesthetic variables recorded included anaesthesia time, intraoperative drug (fentanyl) dose, muscle relaxant (vecuronium) dose, and intraoperative fluid balance. Post-operatively, we assessed the average systolic blood pressure (at admission, after 12 hours, and after 24 hours), mean arterial pressure, central venous pressure, peak lactate concentration, arterial oxygen saturation (SaO₂), vasoactive agent (inotrope) dose, inotropic score (dopamine dose (µg/kg/minute) + dobutamine dose (µg/kg/minute) + 100*epinephrine dose (µg/kg/minute))⁸, post-operative use of inhaled nitric oxide, transfusion requirements, liquid collagen usage (at 0–12 hours and 12–24 hours), final central venous pressure, incidence of arrhythmia, intubation time, reintubation, non-invasive ventilation, duration of CICU stay, duration of hospital stay, and 90-day mortality.

Statistical analysis

For the patient characteristics, quantitative variables are presented as median (interquartile range), and qualitative variables are

expressed as percentages. Intergroup comparisons of continuous and nominal variables were performed using Wilcoxon rank-sum test and Fisher's exact test, respectively.

Multivariate logistic regression analysis was used to calculate the adjusted odds ratio, and 95% confidence interval with prolonged ventilation was used to identify risk factors for prolonged ventilation. We did not include factors in the multivariable model that had statistically significant differences if they were not clinically important. All analyses were performed using JMP v13 (SAS Institute Inc., Cary, NC, United States of America). Variables that showed significant differences in the bivariate analysis and those considered clinically significant were included in the multivariate model and analysed by the stepwise method. We used the backward elimination method, and the removal p-value threshold was fixed at 0.05.

Results

In total, 128 patients underwent the Fontan procedure over the 7-year study period. Figure 1 shows a flowchart of the patient enrolment process. Of the 128 patients, 3 received extracorporeal membrane oxygenation, and 2 had delayed sternal closure and were, therefore, excluded from the study. The final analysis included 123 patients; 102 (83%) of these patients were in the early extubation group, and 21 (17%) were in the prolonged ventilation group. The median ventilation time of the study patients was 8.7 hours (interquartile range: 5.0–17.5). The 24 hours set as the definition of prolonged ventilation represented the 84th percentile for all cases.

The characteristics of all patients in each group are shown in Table 1. The median age and weight of the patients were 2.2 years (interquartile range: 1.7–3.3) and 10.0 kg (interquartile range: 9.0–12.0), respectively. Sixty-nine (56%) were men and 54 (44%) were women. There were no significant differences in age, sex, weight, height, and body surface area between the two groups. The various CHD diagnosed in the early extubation group were hypoplastic left heart syndrome, heterotaxy, and other functionally univentricular heart conditions in 18 (18%), 25 (24%), and 59 (58%) patients, respectively. In the prolonged ventilation group, the diagnoses were hypoplastic left heart syndrome in 10 (48%, higher than that in the early extubation group, $p < 0.01$), heterotaxy in 7 (33%), and functionally univentricular heart in 4 (19%) patients.

Table 1. Baseline patient characteristics

	Overall cohort n = 123	Early extubation group n = 102	Prolonged ventilation group n = 21	p-value
Age (years, median, IQR)	2.2 (1.7–3.3)	2.2 (1.7–3.1)	2.2 (1.7–3.7)	0.61
Sex (n, male, %)	69 (56%)	59 (58%)	10 (48%)	0.79
Weight (kg, median, IQR)	10.0 (9.0–12.0)	10.1 (9.1–11.8)	9.9 (7.5–12.3)	0.72
Height (cm, median, IQR)	81.2 (77.1–90.5)	81.1 (77.3–92.1)	82.2 (76.0–87.0)	0.39
BSA (m ² , median, IQR)	0.48 (0.44–0.54)	0.47 (0.44–0.54)	0.48 (0.45–0.53)	0.52
Diagnosis				
HLHS (n, %)	28 (22%)	18 (18%)	10 (48%)	<0.01
Heterotaxy (n, %)	32 (26%)	25 (25%)	7 (33%)	0.42
Other FUH (n, %)	63 (51%)	59 (58%)	4 (19%)	<0.01
Main ventricle, right (n, %)	64(54%)	49(48%)	15 (71%)	0.04

BSA = body surface area; FUH = functionally univentricular heart; HLHS = hypoplastic left heart syndrome; IQR = interquartile range.

The bivariate analysis is summarised in Table 2. The pulmonary artery index was lower and severe atrioventricular regurgitation was more frequently observed in the prolonged ventilation group than in the early extubation group. Longer operation and cardiopulmonary bypass times and aortic cross-clamping were more frequently performed in the prolonged ventilation group than in the early extubation group. The intraoperative fluid balance was higher in the prolonged ventilation group than in the early extubation group. The post-operative profile and cause of the prolonged ventilation are described in the Supplementary Material.

The results of the multivariate logistic regression analysis are shown in Table 3. Fenestration, pulmonary artery index, and atrioventricular regurgitation were observed to be significant risk factors for prolonged ventilation. Cardiopulmonary bypass times, aortic cross-clamping, and intraoperative fluid balance were not found to be independent risk factors in the multivariable analysis.

Details of the post-operative complications, duration of CICU stay, and total post-operative hospital stay is shown in Table 4. In the prolonged ventilation group, the reintubation rate was high and post-operative respiratory complications were frequent compared to the early extubation group. Pleural effusion and chylothorax were the most common respiratory complications and occurred in 23 patients (19%): 15 in the early extubation group and 8 in the prolonged ventilation group. The duration of CICU stay was significantly longer in the prolonged ventilation group than in the early extubation group, and a similar trend was also observed in the total duration of hospitalisation. There were no deaths within 90 days after surgery in both groups.

Discussion

The result of this analysis found that the prevalence of prolonged mechanical ventilation after Fontan surgery was 17% (21 of 123), and the independent risk factors for prolonged ventilation after Fontan surgery were fenestration, low PA index, and advanced atrioventricular regurgitation. In the group with prolonged ventilation, not only was the length of ICU stay extended, reintubation and post-operative respiratory complications were also frequent. Detecting Fontan patients for whom fast-track care is appropriate may be beneficial for perioperative management.

The importance of early extubation after Fontan surgery has been recognised since it was first reported by Fontan et al.¹ In 1980, Schuller et al. published the first case series on the usefulness of early extubation after Fontan surgery.² Although the number of cases was small (only nine), they reported that extubation increased the SaO₂ and led to postoperative stability. Fast-track care, followed by early post-operative extubation, has become established in real-world clinical practice, and this trend is currently shifting from early extubation in the CICU to extubation in the operating room.^{4–6}

The usefulness of fast-track care after other paediatric cardiovascular operations, in addition to the Fontan procedure, was also recently demonstrated. Harris et al reported a series where all patients who underwent Fontan and Glenn operations were extubated within 24 hours, and 90% of patients who underwent any paediatric cardiovascular surgery procedure were extubated within 24 hours.⁴ Similarly, they reported that intubation before surgery, body weight ≤5 kg, cardiopulmonary bypass time ≥140 minutes, aortic cross-clamping, post-operative use of vasoactive agents, and SaO₂ <80 mmHg were risk factors for prolonged ventilation. Similar to this study, we defined prolonged ventilation as ventilator time greater than 24 hours; this benchmark (24 hours), which represented the 84th percentile for all cases in our study, was adopted because it reduces management bias, such as admission to CICU at night-time.

Fenestration is considered for installation when high central venous pressure is expected after total cavopulmonary connection. The reason fenestration was detected as an independent factor for the prolonged ventilation in this study is considered complex. This is because many cases had poor pulmonary vascular bed; hence, post-operative circulatory and respiratory disorders were thought to be more likely to occur. There have been many studies on the effects of fenestration on the Fontan procedure; however, the results remain controversial. According to the latest meta-analysis, fenestration does not contribute to failed Fontan, and in the short term, fenestration lowers pulmonary blood pressure and reduces post-surgery pleural effusion.⁹ Ventilation time has similarly been studied; however, only a few patients have been examined, and the conclusions were unclear.¹⁰ In a study by Salazar et al, similar to our study, ventilation time was extended in the fenestration group.¹¹ Our results suggest that fenestration may be a predictor

Table 2. Bivariate analysis

	Early extubation group, n = 102	Prolonged ventilation group, n = 21	p-value
Preoperative profile			
SpO ₂ (% , median, IQR)	86 (83–88)	85 (84–87)	0.66
SVCP (mmHg, median, IQR)	11 (10–12)	12 (11–12)	0.65
Qp/Qs (median, IQR)	0.70 (0.61–0.83)	0.70 (0.64–0.82)	0.55
Pp/Ps (median, IQR)	0.20 (0.18–0.22)	0.21 (0.18–0.23)	0.34
Rp (wood units/m ² , median, IQR)	1.5 (1.1–1.9)	1.4 (1.1–2.5)	0.70
Rp/Rs (median, IQR)	0.10 (0.08–0.15)	0.13 (0.09–0.15)	0.97
Cardiac index (L/minute/m ² , median, IQR)	3.6 (3.1–4.3)	3.6 (3.2–4.1)	0.78
EDVI (ml/m ² , median, IQR)	79 (65–94)	82 (70–90)	0.88
ESVI (ml/m ² , median, IQR)	32 (24–40)	38 (33–42)	0.13
EF (% , median, IQR)	58 (54–63)	52 (48–58)	<0.01
PA Index (mm ³ /m ² , median, IQR)	199 (143–262)	168 (114–207)	0.02
BNP (pg/mL, median, IQR)	30 (16–60)	53 (33–98)	0.06
AVR >moderate (preoperative, n, %)	14 (14%)	11 (52%)	<0.01
Respiratory complication* (n, %)	13 (13%)	4 (19%)	0.46
Operative and anaesthesia profile			
Operation time (hours, median, IQR)	6.6 (5.8–7.5)	7.6 (6.6–8.7)	<0.01
CPB time (hours, median, IQR)	2.3 (1.8–2.9)	3.0 (2.6–3.5)	<0.01
Aortic cross-clamping (n, %)	34 (33%)	16 (76%)	<0.01
TCPC only (n, %)	61 (60%)	6 (29%)	
+ Fenestration (n, %)	11 (11%)	10 (48%)	<0.01
+ Other operation (n, %)	48 (47%)	14 (67%)	0.05
Anaesthesia time (hours, median, IQR)	8.1 (7.3–9.0)	9.6 (8.3–10.6)	<0.01
Fentanyl (µg/kg, IQR)	30 (25–38)	36 (30–38)	0.39
Vecuronium (mg/kg, IQR)	9 (7–12)	10 (7–10)	0.84
Fluid balance in OR (ml, IQR)	578 (479–808)	825 (561–1000)	0.02

*Respiratory complications include preoperative upper airway obstruction, phrenic nerve palsy, and chronic lung disease. AVR = aortic valve regurgitation; BNP = brain natriuretic peptide; CPB = cardiopulmonary bypass; CVP = central venous pressure; EDVI = end-diastolic volume index; EF = ejection fraction; ESVI = end-systolic volume index; IQR = interquartile range; MAP = mean arterial pressure; NIV = non-invasive ventilation; NO = nitric oxide; OR = operating room; PA index = pulmonary artery index; Pp/Ps = pulmonary artery–systemic blood pressure ratio; Qp/Qs = pulmonary–systemic shunt ratio; Rp = pulmonary vascular resistance; Rp/Rs = pulmonary–systemic resistance ratio; SaO₂ = oxygen saturation; SAP = systolic arterial pressure; SpO₂ = oxygen saturation; SVCP = superior caval vein pressure; TCPC = total cavopulmonary connection.

Table 3. Multivariable analysis

	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)	p-value
Fenestration	7.52 (2.60–21.7)	5.36 (1.60–17.9)	<0.01
PA index (per increase in mm ² /m ²)	0.99 (0.98–0.99)	0.99 (0.98–0.99)	0.02
Valve regurgitation >moderate (preoperative)	6.91 (2.48–19.3)	6.73 (2.13–21.3)	<0.01
CPB time (per additional hour)	2.00 (1.20–3.34)	1.38 (0.72–2.66)	0.32
Aortic cross-clamping	4.21 (1.43–12.40)	1.55 (0.38–6.30)	0.54
Intraoperative fluid balance (per additional ml)	1.00 (1.00–1.00)	1.00 (0.99–1.00)	0.12

CI = confidence interval; CPB = cardiopulmonary bypass; PA index = pulmonary artery index.

Table 4. Post-operative complications and ICU and hospital stays

	Early extubation group, n = 102	Prolonged ventilation group, n = 21	p-value
Post-operative complications			
Reintubation (n, %)	2 (2%)	6 (29%)	<0.01
Respiratory complications (n, %)	22 (22%)	14 (67%)	<0.01
Arrhythmia (n, %)	9 (9%)	3 (14%)	0.43
ICU stay (days, IQR)	6 (5–8)	10 (9–17)	<0.01
Hospital stay (days, IQR)	19 (16–26)	24 (22–39)	0.31

IQR = interquartile range.

of prolonged ventilation in the short term, but further data collection is needed.

Poor pulmonary arterial development may contribute to Fontan circulation failure in the acute post-operative phase. We hypothesised that the pulmonary artery index affected prolonged ventilation. Although it has been reported that the pulmonary artery index is not related to the long-term prognosis in the Fontan circulation,¹² narrowing of the pulmonary artery can theoretically impede perfusion from the systemic veins, resulting in decreased pulmonary blood flow and cardiac output. Similarly, studies show that pulmonary artery hypoplasia does not affect ventilator time; however, only a few studies have been reported, and there seems to be room for further consideration.¹³ It is not uncommon to experience difficulties in early extubation when the pulmonary blood flow is significantly restricted or when the pulmonary parenchyma is damaged. Pulmonary artery narrowing and poor growth reflect poor respiratory and circulatory functions before surgery and should be considered when determining perioperative management strategies.

Ovrouiski et al examined the incidence of major complications after Fontan surgery. They suggested that the presence of a right ventricle as the main ventricle and heterotaxia were risk factors for prolonged ventilation and inotropic support.¹⁴ Many cases of heterotaxia and those wherein the right ventricle was the main ventricle resulted in impaired ventricular systolic function because of the configuration of the myocardium and the morphology of the ventricles. In addition, these cases are often associated with abnormal morphology of the atrioventricular valve. The presence of severe atrioventricular valve regurgitation strongly suggests poor preoperative conditions, such as chronic heart failure. There are many cases wherein additional procedures, such as fenestration preparation and valvuloplasty under cardiac arrest, were performed simultaneously in patients with concomitant atrioventricular regurgitation and anatomical abnormalities. For these combined reasons, recovery and ventilation time was prolonged, explaining that atrioventricular valve regurgitation was detected as an independent factor for prolonged ventilation.

By analysing numerous variables from the perioperative period to CICU admission, we identified predictors of prolonged ventilation. To allow for early extubation, the depth of anaesthesia during surgery, post-operative pain management, avoidance of fluid overload, and haemorrhage control are important operative and perioperative factors.⁶ In patients at high risk of prolonged ventilation, the management strategy should be established, focusing on these points.

This study's limitations include its single-centre setting and retrospective design. In addition, the number of patients was small,

and the patient selection may have been biased. Furthermore, extubation and weaning of mechanical ventilation were performed at the discretion of the CICU physician or cardiovascular surgeon rather than according to a standard protocol. In addition, our multivariate analysis did not include postoperative variables; management after CICU admission may affect the extension of ventilator time. Although our results agree with the findings of previous studies, a large multicentre study is needed for further confirmation.

In conclusion, fenestration, low pulmonary artery index, and high-grade atrioventricular valve regurgitation are risk factors for prolonged ventilation after Fontan surgery. Early extubation is useful in stabilising the post-operative circulation and shortening the duration of CICU stay. Careful preoperative and perioperative management that considers the risk factors for prolonged ventilation in each individual is important.

Supplementary material. To view supplementary material for this article, please visit <https://doi.org/10.1017/S1047951121003498>.

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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 Declaration of Helsinki and have been approved by the ethical review board of Shizuoka Children's Hospital.

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