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Risk Factors for Extubation Failure After Pediatric Cardiac Surgery and Impact on Outcomes: A Multicenter Analysis

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IMPORTANCE: Extubation failure (EF) after pediatric cardiac surgery is associated with increased morbidity and mortality.

OBJECTIVES: We sought to describe the risk factors associated with early (< 48 hr) and late (48 hr ≤ 168 hr) EF after pediatric cardiac surgery and the clinical implications of these two types of EF.

DESIGN, SETTING, AND PARTICIPANTS: Retrospective cohort study using prospectively collected clinical data for the Pediatric Cardiac Critical Care Consortium (PC4) Registry. Pediatric patients undergoing Society of Thoracic Surgeons benchmark operation or heart transplant between 2013 and 2018 available in the PC4 Registry were included.

MAIN OUTCOMES AND MEASURES: We analyzed demographics and risk factors associated with EFs (primary outcome) including by type of surgery. We identified potentially modifiable risk factors. Clinical outcomes of mortality and length of stay (LOS) were reported.

RESULTS: Overall 18,278 extubations were analyzed. Unplanned extubations were excluded from the analysis. The rate of early EF was 5.2% (948) and late EF was 2.5% (461). Cardiopulmonary bypass time, ventilator duration, airway anomaly, genetic abnormalities, pleural effusion, and diaphragm paralysis contributed to both early and late EF. Extubation during day remote from shift change and nasotracheal route of initial intubation was associated with decreased risk of early EF. Extubation in the operating room was associated with an increased risk of early EF but with decreased risk of late EF. Across all operations except arterial switch, EF portrayed an increased burden of LOS and mortality.

CONCLUSION AND RELEVANCE: Both early and late EF are associated with significant increase in LOS and mortality. Study provides potential benchmarking data by type of surgery. Modifiable risk factors such as route of intubation, time of extubation as well as treatment of potential contributors such as diaphragm paralysis or pleural effusion can serve as focus areas for reducing EFs.

KEY WORDS: congenital heart disease; congenital heart defects; early extubation failure; extubation; extubation failure; hypoplastic left heart syndrome; late extubation failure; outcomes; postoperative care; risk factor

To reduce the morbidity associated with protracted mechanical ventilation following pediatric cardiac surgery, early extubation is favored (1–3). However, attempts to minimize duration of ventilation must be balanced with extubation failure (EF), which has been associated with increased hospital length of stay (LOS) and mortality (1). Our current understanding of factors associated with EF after pediatric cardiac surgery relies mainly on single center studies with small sample sizes (4, 5). The existing multicenter studies have studied early EF occurring in the initial 48 hours after extubation, as in the previous Pediatric

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KEY POINTS

Question: What is the clinical epidemiology and impact of early and late extubation failure (EF) after cardiac surgery in children?

Findings: Analysis of the PC4 database identified an early EF rate of 5.2% and a late failure rate of 2.5%. EF at any point was associated with increased length of stay and mortality. We present risk factors by type of surgery and identify potentially modifiable risk factors such as timing of extubation.

Meaning: Better understanding of the identified modifiable factors may reduce such failures.

Cardiac Critical Care Consortium (PC4) study, which showed a EF rate of 5.8% while a study focusing on neonates showed a significant variability of EF rates (within 72 hr) between 5% and 22% across centers (1, 6–8). It remains unknown which children are at risk and what are the clinical implications in those who develop EF after this early phase of extubation. Such delayed EF may be multifactorial and may represent more contribution from overall degree of multisystem recovery and compensation.

The impact of EF appears to be significant, both on hospital stay and in-hospital mortality (1). Other registry-based studies have identified risk factors associated with EF such as center level performance, cardiac ICU staffing models as well as patient level risk factors such as airway anomaly and patient size (6, 7). We anticipate that specific information around the type of surgery performed would have an impact on the likelihood of EF but has not been previously studied. Studying this relationship is further important for bench marking and quality initiatives.

Our primary aim was to describe patient and procedural risk factors, including types of surgery, for early and late EF in pediatric patients after cardiac surgery. Secondary aims were to identify potentially modifiable risk factors for EF and to delineate the impact of EF on in-hospital mortality, and hospital LOS.

PATIENTS AND METHODS

Study Design and Participants

We performed a retrospective cohort study using the PC4 database (version 2, 2013–2018). We included all subjects 0–18 years of age who underwent a Society of Thoracic Surgeons (STS) benchmark operation or heart transplant (OHT) (9). Patients with a tracheostomy present before their index operation and those who underwent tracheostomy before an extubation attempt were excluded as they could not be included under cases or controls. Additionally, those on mechanical circulatory support before their index operation, and those who died before extubation were also excluded. Intubation events for procedures such as cardiac catheterization or imaging or after 7 days of initial extubation were excluded, as were intubations with unplanned extubations. Details regarding subject identification, methods, and data collection have been previously reported (10, 11). The data integrity of the PC4 database has been well-described highlighting a major discrepancy rate of 0.6%, which lends to the strength of the database (10, 11). For the registry, The University of Michigan institutional review board (IRB) provides oversight for the PC4 Data Coordinating Center; no IRB review was necessary for this study (and thus no number was assigned) because it did not fall under the board's guidelines as human subject research.

Predictors of EF were selected based on prior studies and mechanistic rationale and included: demographics, surgical procedure, medical/surgical factors, complications, and modifiable risk factors. Predictor variables included in the analysis are listed in the first column of **Table 1**.

Definitions

- EF was defined as need for intubation and reinstitution of mechanical ventilation after initial planned extubation following index surgery. Those reintubated after more than 7 days and/or those who were intubated for a cardiac catheterization or imaging study but were extubated immediately following the procedure were not classified as EF.
- Timing of extubation relative to shift change was classified as follows: "day shift" 08:00–16:00, "shift change" 06:00–07:59 and 16:01–19:59, "night shift" 20:00–05:59.
- Initial airway upon pediatric cardiac ICU (PCICU) admission was defined as the initial airway (oral or nasal) documented upon PCICU admission after cardiac procedure.
- Surgical variables used, including, definitions for benchmark operations are consistent with the Society of Thoracic Surgery Congenital Heart Surgery Database definitions and have been previously described (9). Similarly, all data fields used for the study are directly obtained from standardized

TABLE 1.
Demographics and Risk Factors For Early and Late Extubation Failure After Cardiac Surgery

Parameter	Total Cohort	No Extubation Failure (Reference Group)	Early Extubation Failure (< 48 hr)		Late Extubation Failure (48–168 hr)	
	n = 18,278 (100%)	*n* = 16,869 (92.3%)	*n* = 948 (5.2 %)	Adjusted Odds Ratio (95% CI), *p*[a]	*n* = 461 (2.5%)	Adjusted Odds Ratio (95% CI), *p*[a]
Age						
Neonate (0–30 d)	4,130 (22.6%)	3,607 (21.4%)	358 (37.8%)	2.48 (1.69–3.65), < 0.001	165 (35.8%)	2.03 (1.31–3.17), 0.002
Infant (31 d–1 yr)	9,437 (51.6%)	8,794 (52.1%)	428 (45.1%)	1.72 (1.28–2.31), < 0.001	215 (46.6%)	1.62 (1.17–2.25), 0.004
Child (> 1 yr–< 18 yr), reference	4,711 (25.8%)	4,468 (26.5%)	162 (17.1%)	–	81 (17.6%)	–
Gender						
Female, reference	7,914 (43.3%)	7,315 (43.4%)	418 (44.1%)	–	181 (39.3%)	–
Male	10,364 (56.7%)	9,554 (56.6%)	530 (55.9%)	0.96 (0.84–1.10), 0.576	280 (60.7%)	1.22 (1.05–1.41), 0.008
Hispanic/Latino ethnicity						
Yes	3,232 (17.7%)	3,002 (17.8%)	172 (18.1%)	1.11 (0.91–1.36), 0.315	58 (12.6%)	0.67 (0.52–0.87), 0.002
Unknown	874 (4.8%)	818 (4.8%)	40 (4.2%)	0.93 (0.60–1.43), 0.745	16 (3.5%)	0.67 (0.39–1.14), 0.141
No	14,172 (77.5%)	13,049 (77.4%)	736 (77.6%)	–	387 (83.9%)	–
Race						
Caucasian, reference	11,395 (62.3%)	10,495 (62.2%)	602 (63.5%)	–	298 (64.6%)	–
Asian only	640 (3.5%)	609 (3.6%)	23 (2.4%)	0.95 (0.61–1.47), 0.808	8 (1.7%)	0.63 (0.46–1.61), 0.083
Black only	2,651 (14.5%)	2,423 (14.4%)	143 (15.1%)	1.04 (0.84–1.28), 0.726	85 (18.4%)	1.15 (0.89–1.49), 0.287
Native American only	92 (0.5%)	85 (0.5%)	7 (0.7%)	1.44 (0.63–3.31)0.390,	0 (0.0%)	1.00–
Pacific Islander only	72 (0.4%)	66 (0.4%)	5 (0.5%)	1.18 (0.44–3.18), 0.749	1 (0.2%)	0.24 (0.05–1.21), 0.084
Multiracial/other	1,975 (10.8%)	1,835 (10.9%)	101 (10.7%)	0.98 (0.77–1.25), 0.892	39 (8.5%)	0.86 (0.6–1.25), 0.429
Unknown	1,453 (7.9%)	1,356 (8.0%)	67 (7.1%)	0.90 (0.61–1.32), 0.577	30 (6.5%)	1.10 (0.7–1.73), 0.675
Primary insurance type						
Public, reference	9,338 (51.1%)	8,596 (51.0%)	503 (53.1%)	–	239 (51.8%)	–
Private	7,537 (41.2%)	6,975 (41.3%)	375 (39.6%)	0.96 (0.82–1.12), 0.577	187 (40.6%)	1.02 (0.84–1.23), 0.849
Non-U.S. insurance	61 (0.33%)	56 (0.3%)	2 (0.2%)	0.74 (0.17–3.13), 0.678	3 (0.7%)	3.31 (0.43–25.30), 0.248
None/self	217 (1.2%)	202 (1.2%)	8 (0.8%)	0.61 (0.29–1.27), 0.184	7 (1.5%)	1.35 (0.59–3.11), 0.481
Unknown	1,125 (6.1%)	1,040 (6.2%)	60 (6.3%)	1.20 (0.80–1.82), 0.377	25 (5.4%)	1.04 (0.81–1.32), 0.776

(*Continued*)

TABLE 1. (*Continued*)
Demographics and Risk Factors For Early and Late Extubation Failure After Cardiac Surgery

Parameter	Total Cohort	No Extubation Failure (Reference Group)	Early Extubation Failure (< 48 hr)		Late Extubation Failure (48–168 hr)	
	n = 18,278 (100%)	n = 16,869 (92.3%)	n = 948 (5.2 %)	Adjusted Odds Ratio (95% CI), p[a]	n = 461 (2.5%)	Adjusted Odds Ratio (95% CI), p[a]
Surgical procedure						
Ventricular septal defect, reference	3,503 (19.2%)	3,368 (20.0%)	96 (10.1%)	–	39 (8.5%)	–
Coarctectomy	1,906 (10.4%)	1,803 (10.7%)	79 (8.3%)	1.77 (1.22–2.55), 0.002	24 (5.2%)	1.37 (0.70–2.68), 0.357
Tetralogy of Fallot	2,503 (13.7%)	2,360 (14.0%)	107 (11.3%)	1.3 (0.97–1.74), 0.081	36 (7.8%)	0.86 (0.46–1.61), 0.643
Fontan	2,229 (12.2%)	2,127 (12.6%)	75 (7.9%)	1.18 (0.79–1.76), 0.423	27 (5.9%)	1.24 (0.65–2.39), 0.514
Superior cavopulmonary anastomosis	2,403 (13.1%)	2,193 (13.0%)	131 (13.8%)	1.77 (1.34–2.34), < 0.001	79 (17.1%)	2.47 (1.49–4.07), < 0.001
Atrioventricular canal	1,718 (9.4%)	1,578 (9.4%)	86 (9.1%)	1.44 (1.04–1.99), 0.03	54 (11.7%)	1.46 (0.96–2.21), 0.074
Arterial switch operation	1,000 (5.5%)	925 (5.5%)	48 (5.1%)	1.13 (0.7–1.84), 0.611	27 (5.9%)	1.01 (0.48–2.11), 0.980
Arterial switch-ventricular septal defect	468 (2.6%)	412 (2.4%)	38 (4.0%)	1.94 (1.16–3.22), 0.011	18 (3.9%)	1.37 (0.78–2.38), 0.270
Truncus arteriosus	307 (1.7%)	260 (1.5%)	34 (3.6%)	2.34 (1.39–3.96), 0.001	13 (2.8%)	1.30 (0.61–2.80), 0.495
Orthotopic heart transplant	874 (4.8%)	768 (4.6%)	58 (6.1%)	2.76 (1.81–4.19), < 0.001	48 (10.4%)	3.11 (1.58–6.13), 0.001
Norwood	1,367 (7.5%)	1,075 (6.4%)	196 (20.7%)	3.4 (2.21–5.23), < 0.001	96 (20.8%)	2.36 (1.23–4.54), 0.01

[a]Odds ratios are column specific and are odds ratios for parameters compared with the specified reference for that category.

definitions in a data definitions manual that is available to all participants on the PC4 internal website (10).

Outcomes

The primary outcome was EF defined as re-institution of mechanical ventilation after initial extubation following index surgery. For analysis, EF was stratified relative to time since extubation, as early EF (< 48 hr) and late EF (48–168 hr). Only the initial EF was considered when assigning early or late EF. The secondary outcomes were hospital LOS, and mortality before hospital discharge.

Statistical Analysis

Descriptive data are presented as frequency (%) for categorical variables or median (interquartile range, IQR) for continuous variables. Variable selection was explored by evaluating the association between surgery type, candidate variables, and EF using Classification and Regression Tree (CART) and Random Forest (RF). CART is a form of binary recursive partitioning, and RF is an ensemble of trees grown using bootstrap resamples of the data (12). Candidate variables were identified using variable importance from RF analyses, stratified by surgery type: atrioventricular septal defect repair (AVC), arterial switch operation with ventricular septal defect closure (ASO-VSD), Norwood procedure, and Fontan palliation. We limited the initial candidate variable selection to these surgeries selected a priori to keep the number of variables that will allow reasonable analysis. Variable importance was assessed using mean decrease in Gini impurity (13), and the 10 most important variables for each surgery were assessed in subsequent confirmatory analyses (see below). Candidate variables that emerged repeatedly across the different surgery types' RF analyses were included as covariates in subsequent multivariable regression models for confirmatory analyses. Variables that emerged uniquely in RF analysis of specific surgical types were incorporated as interactions with surgery type and formally tested in the subsequent multivariable regression models.

Following candidate variable selection from tree-based analyses, final models for overall EF, early EF, and late EF were built using two-level multivariable logistic regression analyses with hospital-specific random intercept. Finally, the outcomes including hospital LOS and hospital mortality were reported by no EF, early EF, and late EF.

All analyses were performed using SAS, Version 9.4 (SAS Institute, Cary, NC) or STATA, Version 15 (Stata Corp, College Station, TX).

RESULTS

A total of 18,278 encounters from 32 reporting centers were available for analysis after exclusions (Consort diagram, **Fig. 1**). Of this, 22.6% (4,130) were neonates, 51.6% (9,437) were infants and 25.8 % (4,711) were children. Table 1 shows the clinical characteristics of the overall cohort. The cohort was 43.3% female, 17.7% Hispanic. Primary insurance type was public insurance in 51% of the overall cohort. Medical and surgical parameters are shown in **Table 2**. Major airway anomaly was present in 751 (4.1%) patients, whereas 4,453 (24.4%) of the total cohort had chromosomal abnormality or syndrome. A total of 27% were extubated in the operating room and the distribution of extubation in the operating room by type of surgery is shown in **Supplemental Table 1** (http://links.lww.com/CCX/B239). Overall, 88.3% required cardiopulmonary bypass (CPB) operations, and of those, the median (IQR) CPB time was 107 (75–151) minutes, and the median (IQR) duration of postoperative ventilation was 0.96 (0.42–2.92) days. Postoperatively, diagnosis of diaphragm paralysis was seen in 0.9%, whereas pleural effusion was diagnosed in 1.9% of the patients (Table 2).

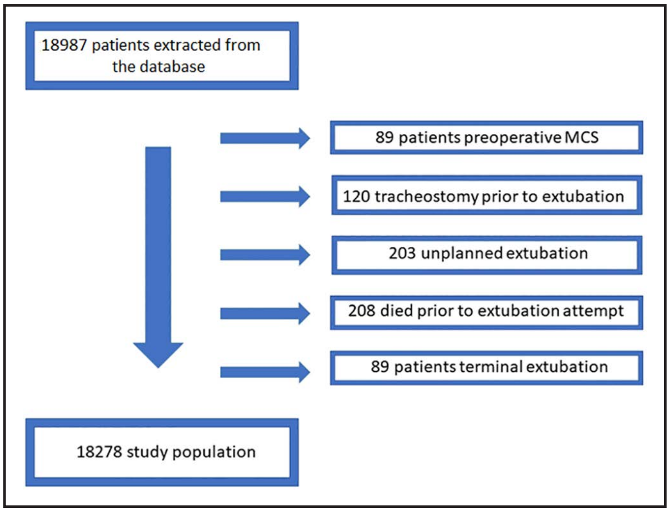

Figure 1. Consort diagram. MCS = mechanical circulatory support.

TABLE 2.
Medical and Surgical Risk Factors For Early and Late Extubation Failure After Cardiac Surgery

Parameter	Total Cohort	No Extubation Failure (Reference Group)	Early Extubation Failure (< 48 hr)		Late Extubation Failure (48–168 hr)	
	n = 18,278	*n* = 16,869 (92.3%)	*n* = 948 (5.2 %)	Adjusted Odds Ratio (95% CI), *p*	*n* = 461 (2.5%)	Adjusted Odds Ratio (95% CI), *p*
Medical-surgical factors						
Cardiopulmonary bypass (per 10 min)		9.5 (6.2–14.2)	11.9 (7.7–17.3)	1.02 (1.01–1.04), < 0.001[a]	13.4 (9.0–18.5)	1.03 (1.01–1.06), 0.005[a]
Delayed sternal closure	1,841 (10.1%)	1,492 (8.8%)	228 (24.1%)	1.18 (0.93–1.51), 0.179[a]	121 (26.2%)	1.16 (0.78–1.73), 0.474[a]
Postoperative ventilator days		0.5 (0.0–1.8)	1.0 (0.0–4.8)	1.02 (1.01–1.03), 0.005[a]	2.8 (0.8–6.1)	1.04 (1.02–1.06), 0.000[a]
Patient factors						
Major airway abnormality	751 (4.1%)	636 (3.8%)	75 (7.9%)	2.14 (1.63–2.80), < 0.001[a]	40 (8.7%)	1.90 (1.38–2.62), < 0.001[a]
Chromosomal abnormality or syndrome	4,453 (24.4%)	4,050 (24.0%)	260 (27.4%)	1.38 (1.16–1.65), < 0.001[a]	143 (31.0%)	1.49 (1.20–1.86), < 0.001[a]
Potentially modifiable risk factors						
Initial airway upon CICU arrival						
Oral, reference	10,199 (55.8%)	9,337 (55.4%)	542 (57.2%)	–	320 (69.4%)	–
Nasal	3,173 (17.4%)	2,930 (17.4%)	153 (16.1%)	0.73 (0.57–0.92), 0.007[b]	90 (19.5%)	0.78 (0.57–1.08), 0.133[b]
Extubated in operating room	4,878 (26.7%)	4,578 (27.1%)	251 (26.5%)	1.93 (1.57–2.38), < 0.001[b]	49 (10.6%)	0.58 (0.34–0.98), 0.043[b]
Unknown		24 (0.1%)	2 (0.2%)	0.94 (0.19–4.53), 0.936[b]	2 (0.4%)	1.07 (0.11–10.75), 0.952[b]
Time of day, initial postoperative extubation						
Day time hours		11,668 (69.2%)	718 (75.7%)	–	328 (71.1%)	–
Evening/night time hours		5,201 (30.8%)	230 (24.3%)	0.71 (0.51–0.99), 0.041[b]	133 (28.9%)	1.23 (0.91–1.66), 0.172[b]
Time of day, reference day shift (08:00–16:00 hr)						
Day shift		10,490 (62.2%)	639 (67.4%)	–	297 (64.4%)	–
Shift changes		3,203 (19.0%)	165 (17.4%)	1.29 (1.00–1.67), 0.049[b]	91 (19.7%)	1.06 (0.69–1.62), 0.786[b]
Night shift		3,176 (18.8%)	144 (15.2%)	1.58 (1.07–2.31), 0.020[b]	73 (15.8%)	0.77 (0.50–1.18), 0.225[b]
Postoperative complications						
Diaphragm paralysis	263 (1.4%)	146 (0.9%)	71 (7.5%)	6.30 (4.56–8.71), < 0.001[b]	46 (10.0%)	7.44 (4.98–11.12), < 0.001[b]
Pleural effusion	454 (2.5%)	321 (1.9%)	91 (9.6%)	6.41 (4.89–8.42), < 0.001[b]	42 (9.1%)	6.16 (3.61–10.51), < 0.001[b]

[a]Odds ratios represent comparison between extubation failure and no extubation failure.

[b]Odds ratios are based on comparison with the reference category for that particular variable.

Primary Outcomes

EF occurred in 1,409 patients (7.6%). Early EF occurred in 5.2% (n = 948) and late EF in 2.5% (n = 461). Tables 1 and 2 show parameter distribution by no EF, early EF, and late EF as determined by multivariable logistic regression analyses.

Candidate Variable Selection/Random Forest Analyses. Candidate variable selection was done as described above and significant similarity among surgical procedures with many variables was found repeatedly. Race, gender, insurance type, presence of airway anomaly, chromosomal syndrome, age at surgery in days, CPB time, initial and final airway/intubation strategy, presence of postoperative pleural effusion, and ventilator duration in days each appeared as important variables for multiple surgical types suggesting many candidate variables are associated with EF independent of the type of surgery. Variables thus selected were included as covariates in subsequent multivariable analyses. Additionally, we performed Cox regression analysis for time to EF event and these findings are shown in **Supplemental Table 2** (http://links.lww.com/CCX/B239) and **Supplemental Figure 2** (http://links.lww.com/CCX/B239). We also performed the Cox regression analysis without pleural effusion and diaphragm paralysis included in the model and the findings were similar to those in Supplemental Table 2 (http://links.lww.com/CCX/B239).

Early Extubation Failure. The highest odds of early EF were associated with OHT and Norwood procedures. In comparison to the repair of VSD, surgical procedures not associated with increased or decreased odds of early EF were TOF, Fontan, and ASO; otherwise, all operations were associated with an increased risk of early EF. Overall, the following risk factors were associated with increased risk of early EF: extubation in the operating room, extubation at the time of shift change, nighttime extubation, presence of postoperative diaphragm paralysis, and pleural effusion.

We specifically examined the interaction of the initial airway on arrival at pediatric cardiac ICU (PCICU) and the type of surgery. Early EF was decreased by returning to the PCICU with a nasotracheal tube (OR 0.73; CI, 0.57–0.92; p = 0.007) relative to an orotracheal tube for most surgeries (**Fig. 2*A***). Extubation in the operating room was associated with early EF after the Norwood, ASO, OHT, ASO-VSD, and truncus arteriosus (TA) operations (**Fig. 2*C***). The risk of early EF, when diaphragm paralysis was present was significantly increased after the following operations: coarctation of the aorta repair via thoracotomy (CoA), VSD, superior cavopulmonary anastomosis (SCPA), AVC, AO/VSD, OHT, and Fontan (**Fig. 3*A***). The risk of early EF when drainage of pleural effusion was required was significantly increased after the following operations: ASO, Norwood, VSD, CoA, ASO-VSD, TOF, and SCPA (**Fig. 3*C***).

Late Extubation Failure. In comparison to the repair of VSD, the following operations were associated with late EF: SCPA, OHT, and Norwood procedure. Other procedures such as coarctation, Fontan, TOF, AVC, and ASO were not associated with increased odds of late EF compared with VSD. Presence of pleural effusion and diaphragm paralysis was associated with late EF.

When examining the interaction of surgical procedure and route of intubation, late EF was less likely after SCPA with nasotracheal intubation (**Fig. 2*B***). Extubation in the operating room was associated with late EF only after ASO (**Fig. 2*D***). Late EF was statistically more likely if diaphragm paralysis was present after the following operations: CoA, ASO-VSD, SCPA, and ASO (**Fig. 3*B***). Late EF was statistically more likely if pleural effusion requiring drainage was present after the following operations: ASO, ASO-VSD, AVC, OHT, and SCPA (**Fig. 3*D***).

Shift-Change and Extubation Failure. Initial extubations occurred predominantly during the day shift (69.2%), whereas 30.8% of extubations were done during the night shift (Table 2).

Relative to the day shift (08:00–16:00 hr) we assessed the risk of EF at shift change as well as night shift. The risk for early EF at shift change was significantly higher (OR 1.29 [1.00–1.67], p = 0.049). Similarly, the risk for early EF at the night shift relative to the reference day shift was significantly higher at 1.58 (1.07–2.3), p = 0.020. Such association was not seen for late EF (Table 2). Impact of shift changes/night shift on EFs for various types of surgeries is shown in **supplemental Figure 1*A–D*** (http://links.lww.com/CCX/B239).

Impact of Extubation Failure

We assessed the impact of early and late EF on outcomes such as hospital mortality and hospital LOS.

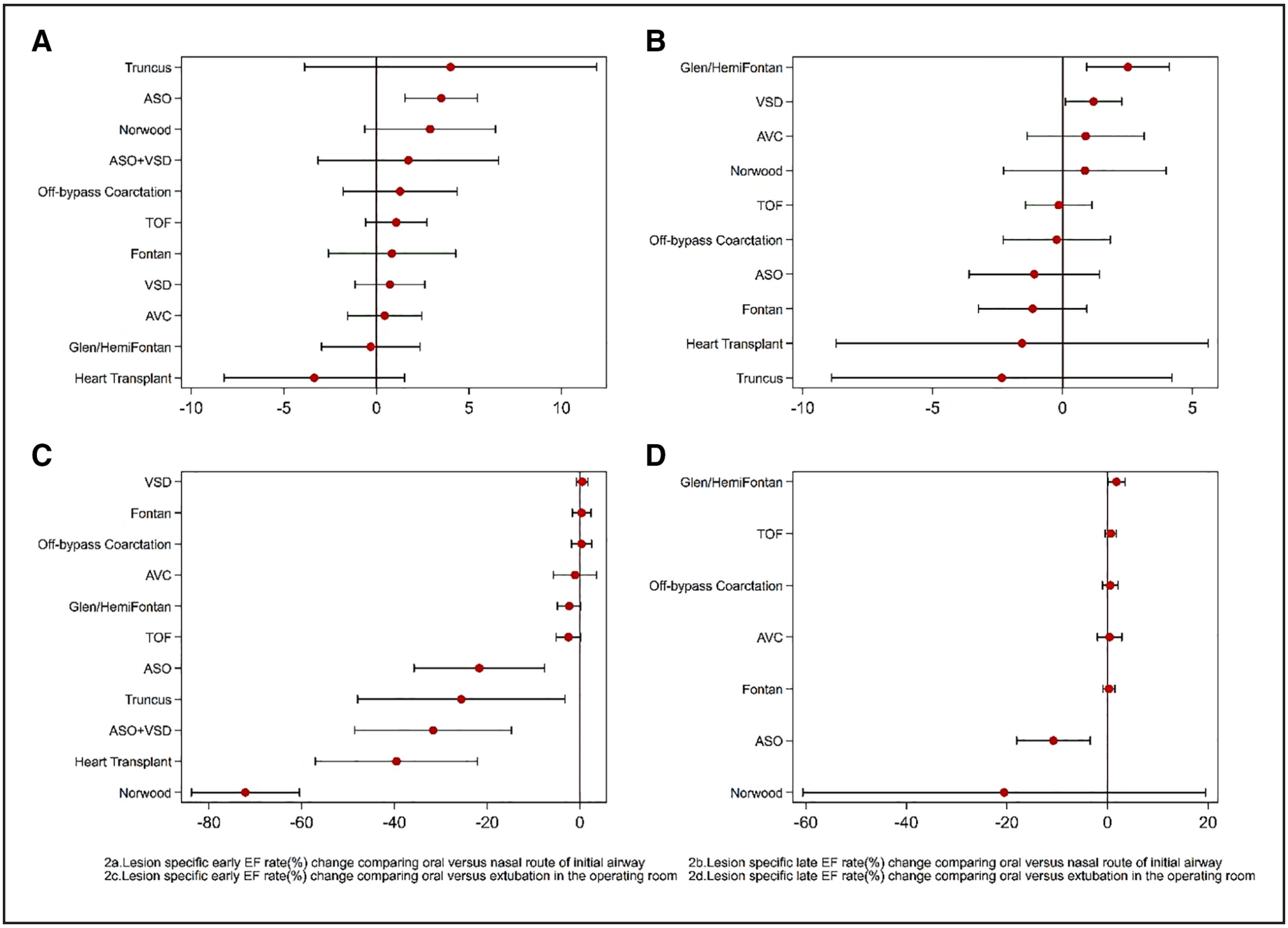

Figure 2. Interaction effect of route of initial airway with lesion and relative risk of early and late extubation failure (EF). **A**, Lesion-specific relative risk of early EF oral vs nasal route of initial airway. **B**, Lesion-specific relative risk of late EF oral vs nasal route of initial airway. **C**, Lesion-specific relative risk of early EF oral vs extubation in the operating room. **D**, Lesion-specific relative risk of late EF oral vs extubation in the operating room. ASO = arterial switch operation, AVC = atrioventricular canal repair, TOF = Tetralogy of Fallot, VSD = ventricular septal defect.

These are shown in **Table 3**. We also assessed the impact of EF by type of surgery (Table 3). The in-hospital mortality was 66 of 948 (6.96%) for those with early EF and 34 of 461 (7.38%) for those with late EF compared with 104 of 16,869 (0.62%) for those with no EF ($p < 0.0001$). Hospital LOS was significantly longer for those with early EF (24 d, IQR 12–48 d) and for late EF (33 d, IQR 19–70 d) compared with no EF (8 d, IQR 5–14 d) ($p < 0.0001$).

There was variation in the impact of EF depending on the type of surgery. With early EF, increased hospital mortality ranged from no increased risk (ASO) to an increased risk of 79-fold (ASO + VSD). Similarly, LOS was increased by a factor of 1.5-fold (ASO and Fontan) to a factor of 2.8-fold (VSD repair). Late EF conferred no increased risk of hospital mortality in ASO (0%), but hospital mortality was increased 37-fold after the Fontan procedure and LOS was increased by a factor of 1.8-fold (Fontan) to a factor of 4.8-fold (CoA) (Table 3).

DISCUSSION

In this multisite study of 18,278 hospitalizations, we show that EF; regardless of whether early or late, is associated with a 10-fold increase in mortality and an overall 3- to 4-fold increase in hospital LOS. We identified 10 independent risk factors of EF, four of which have not been previously described to our knowledge—initial airway after surgery, timing of extubation relative to shift change, male gender, and Hispanic ethnicity. Additionally, the study identified potentially

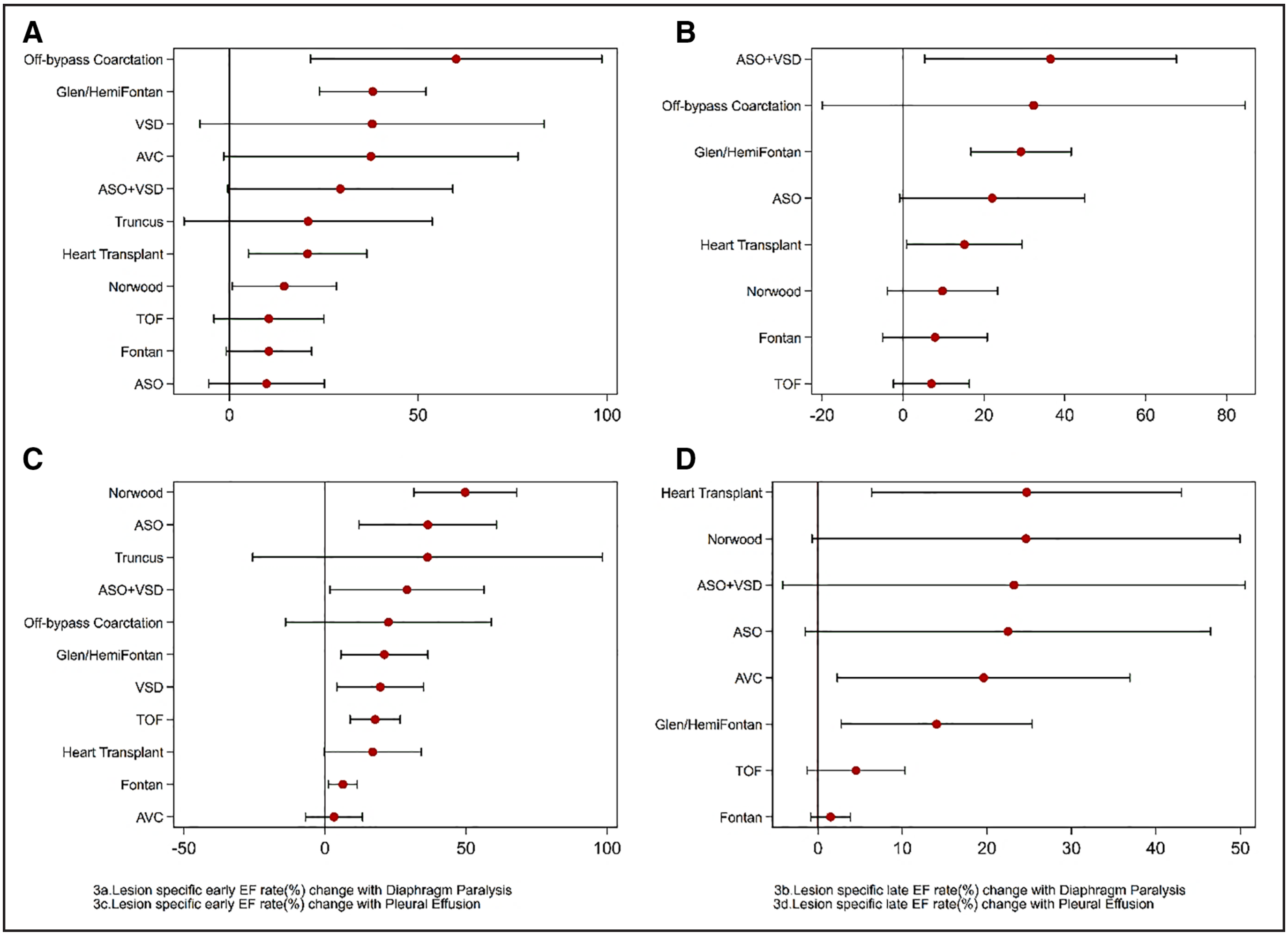

Figure 3. Lesion-specific interaction effect of diaphragm paralysis and pleural effusion with relative risk of early and late extubation failure (EF). **A**, Lesion-specific relative risk of early EF with diaphragm paralysis. **B**, Lesion-specific relative risk of late EF with diaphragm paralysis. **C**, Lesion-specific relative risk of early EF with pleural effusion. **D**, Lesion-specific relative risk of late EF with pleural effusion. ASO = arterial switch operation, AVC = atrioventricular canal repair, TOF = Tetralogy of Fallot, VSD = ventricular septal defect.

modifiable factors such as: timing of extubation during the day relative to shift change, initial airway upon return to the PCICU after surgery, presence of pleural effusion, and diaphragm paralysis. Lastly, the study provides information on EF by type of surgery and its impact on outcomes.

Overall, our early EF rate of 5.2% was similar to prior studies including the previous PC4 study which had a rate of 5.8% (1). However, the late extubation rate of 2.5% is a novel finding, to the best of our knowledge. The sample size of overall 1,409 EFs across these index operations allowed us to address the aims of the study.

Risk Factors for Extubation Failure

The principal risk factors are similar for early and late EF as well across surgical procedures. The impact of gender and race on EF is difficult to explain. Male gender was found to be a risk factor for late EF but not for early EF. Male gender as an overall risk factor for postoperative morbidity and mortality has been previously identified (14, 15) and therefore there may be a relationship that is not clearly understood from mechanistic standpoint. Hispanic ethnicity was protective for late EF but had no impact on early EF. Similar to gender, this relationship cannot be well explained. One potential explanation may be survival bias. Hispanic children have been shown to have significantly higher mortality after congenital heart surgery compared with White children (16). It may be possible that these events occur early in the postoperative periods potentially before first extubation. However, this needs to be studied further.

TABLE 3.
Unadjusted Association Between Extubation Failure and Outcomes

Parameter	No Extubation Failure	Early Extubation Failure	Late Extubation Failure
Overall cohort (*n*)	16,869	948	461
In-hospital mortality, *n* (%)	104 (0.62%)	66 (6.96%)	34 (7.38%)
Hospital LOS days (interquartile range)	8 (5–14)	24 (12–48)	33 (19–70)
Operation-specific outcomes			
Ventricular septal defect	*n* = 3,368	*n* = 96	*n* = 39
Mortality (%)	0.2	3.1	2.6
LOS (d)	5 (4–7)	14 (8–26)	18 (13–49)
Coarctectomy	*n* = 1,803	*n* = 79	*n* = 24
Mortality (%)	0.4	1.3	4.2
LOS (d)	6 (4–9)	16 (9–30)	28.5 (18–47.5)
Tetralogy of Fallot	*n* = 2,360	*n* = 107	*n* = 36
Mortality (%)	0.2	4.7	5.6
LOS (d)	7 (5–10)	14 (9–29)	27 (14–51)
Fontan	*n* = 2127	*n* = 75	*n* = 27
Mortality (%)	0.2	6.7	7.4
LOS (d)	10 (7–14)	15 (11–35)	22 (15–32)
Superior cavopulmonary anastomosis	*n* = 2193	*n* = 131	*n* = 79
Mortality (%)	0.5	6.9	6.3
LOS (d)	7 (5–12)	17 (10–35)	29 (17–35)
Atrioventricular canal	*n* = 1578	*n* = 86	*n* = 54
Mortality (%)	0.6	5.8	7.4
LOS (d)	8 (6–14)	20 (11–42)	26 (15–58)
ASO	*n* = 925	*n* = 48	*n* = 27
Mortality (%)	0.4	0	0
LOS (d)	12 (9–16)	18 (14–26.5)	22 (15–37)
ASO-ventricular septal defect closure	*n* = 412	*n* = 38	*n* = 18
Mortality (%)	0.2	15.8	5.6
LOS (d)	13 (9–20)	25.5 (15–44)	28 (19–33)
Truncus arteriosus	*n* = 307	*n* = 34	*n* = 13
Mortality (%)	1.2	8.8	7.7
LOS (d)	17.5 (11–30.5)	27 (15–73)	36 (28–71)
Orthotropic heart transplantation	*n* = 768	*n* = 58	*n* = 48
Mortality (%)	1.3	8.6	16.7
LOS (d)	17 (12–28)	33 (21–52)	42.5 (24.5–72.5)
Norwood operation	*n* = 1075	*n* = 196	*n* = 96
Mortality (%)	3.9	12.9	9.4
LOS (d)	31 (21–52)	54.5 (34–101)	73 (38.5–124)

ASO = arterial switch operation, LOS = length of stay.

Some of the factors identified in this study do lend themselves as potentially modifiable risk factors. The influence of the timing of ICU shift (day, night, shift change) on EF in pediatric cardiac population is not well known. Previous studies focusing on noncardiac patients did not find a significant association with daytime or nighttime extubation and reintubation needs or other complications (17, 18). Although the literature in adult ICUs has shown divergent findings (19, 20). In cardiac ICU, shift changes are associated with changing of care providers at multiple levels. During these times, it is plausible that subtle clinical signs of deterioration may not be recognized, contributing to increased rate of early EF across cardiac operations. It was noteworthy that even in the noncardiac ICU, most EFs occurred in the shift opposite to that when extubation occurred (22). Given the current changes in healthcare workforce, especially as it relates to expert nursing, it is important to keep these findings in consideration when planning an extubation. There may be differences in the overall level of experience (experience mix) between day shift and night shift nursing. Similarly, there may be significant variation in the physician and advance practice provider level coverage and expertise. All of these could impact the ability to monitor patients closely. Based on this study, consideration may be given to choosing times of the day to maximize the likelihood of successful extubation.

In addition, initial airway upon arriving to the PCICU was found to be important in influencing EF. First, extubating patients in the operating room was demonstrated to be a predictor of early EF in neonates and infants, but not of late EF (except after an ASO). These may reflect a complex interplay between young age, long duration of anesthesia and therefore readiness from pulmonary or wakefulness standpoint. Thus, it may be reasonable to defer such extubations to the ICU rather than performing them in the OR. Another finding was that patients returning to the PCICU with nasotracheal tubes were less likely to suffer from early EF. This finding could possibly be related to a larger endotracheal tube applied by orotracheal route versus nasotracheal route for the same sized child or more movement of the tube with head movement in the case of orotracheal tubes leading to more edema and/or obstruction at the level of the glottis; however, our study was not able to control for the size of the endotracheal tube.

Post-operative factors of diaphragm paralysis and pleural effusion had a significant relationship with EF (greater than 10-fold increase in odds ratio [OR]) for many surgeries, in particular, with neonatal surgeries. Based on these findings, consideration may be given to judicious removal of the postoperative chest tubes rather than expeditiously. Similarly, consideration may be given for early plication of diaphragm to potentially mitigate its impact on the overall outcome.

Procedures Portraying Greater Risk for Extubation Failure

Variability in rates of early and late EF manifested across the surgical procedures. We intentionally based this analysis using the benchmark operations defined by STS as those are commonly used to compare outcomes across institutions as well as for quality improvement purposes (9, 21). Procedures performed in younger infants had an increased risk of EF; in particular, CoA, TA, ASO-VSD, and Norwood procedures. The peculiar exception is the ASO, which was not associated with an increased risk of early EF. This is likely related to a lack of residual lesions and relative rarity of association of this lesion with genetic disease. In contrast, infants undergoing SCPA and TOF operations are known to carry a higher risk of other congenital defects and genetic disease, and these infants were noted to have a higher risk of early EF. Lastly, OHT was associated with early EF. One previous single center study of OHT patients reported an EF rate of 12.5% of patients with an overall in-hospital mortality rate of 2% as opposed to our rate of early EF of 6.6% and late EF of 5% with mortality rates of 8.6% and 16.7%, respectively (22). Neither our study nor the previous study allows assessment of other transplant-related patient morbidities that may have influenced our findings.

Although not commonly reported, late EF (48–168 hr) may be related to residual lesions that may not be recognized initially, persistence of significant heart failure beyond surgery, poor nutritional status, and chronic lung disease. These factors may lead to a more gradual decline in the respiratory status as compared with conditions such as upper airway edema or sedation related issues which cause acute respiratory decompensation and may result in early EF. Increasing application of noninvasive positive pressure ventilation in PCICUs may modify the risk; however, the current study was not designed or able to assess the impact on mode of noninvasive support based on data availability (23–25). This is the first time to our knowledge that late EF has been studied in the cardiac ICU setting. Delayed EF has been widely studied in the neonatal ICU setting in relationship to premature infants (26–28). For example, in the study by Kidman et al (27), the median time to EF was 60 hours. Additionally, they found that EF up to 7 days was associated with increased morbidity and longer hospitalizations (27). In our study, with a very different population, we found that adding later extubation times beyond the usual 48–72 hours allowed us to identify additional 2.5% of the EFs. Additionally, late EF portrayed higher mortality and longer hospital LOS than the traditionally reported early EF after congenital heart surgery. We anticipate further studies, including our future work, will continue to evaluate the risk factors for delayed EF especially related to residual lesions, preoperative status, and postoperative optimization in this cohort of congenital heart disease patients.

Limitations

Our study was limited by the inherent nature of observational study design, which can only imply association. The analysis was limited to the selected candidate variables collected within the PC4 Registry. The burden of residual lesions influences EF but could not be analyzed in this study because if a subject required postoperative intervention (surgical or catheter-based), the subject would be intubated which would skew results. Although the model controlled for surgical procedures, we were limited by a small number of EFs for any given lesion (potentially leading to the wider CIs) and were only able to make post hoc analyses and analyze interaction effects. Preoperative acuity, invasive mechanical ventilation, nutrition status, cardiopulmonary health could all directly impact success and timing of postprocedural extubation but have limited capture in the database. Again, given the potential for uneven distribution of EF patients by center, there is potential for centers with large contribution to sway the results. We did not control for center effect as practices have continued to evolve within centers over time and may vary based on the type of surgery, attending physician preference, level of experience; and therefore, these center-based practices are not static and not analyzed.

CONCLUSIONS

This analysis of the PC4 database representing the largest analysis of EF in children undergoing cardiac surgery to date, showed that EF at any point was associated with an overall increased LOS and mortality with variable impact by type of surgery. The study identified potentially modifiable factors and non-modifiable factors by type of surgery that may be important in bench marking as well as planning interventions to reduce EF and associated morbidity and mortality.

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