Risk factors and outcomes of extubation failure in a South African tertiary paediatric intensive care unit

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Background. Extubation failure contributes to poor outcome of mechanically ventilated children, yet the prevalence and risk factors have been poorly studied in South African (SA) children.
Objective. To determine the prevalence, risk factors and outcomes of extubation failure in an SA paediatric intensive care unit (PICU).
Methods. This was a prospective, observational study of all mechanically ventilated children admitted to a tertiary PICU in Cape Town, SA. Extubation failure was defined as requiring re-intubation within 48 hours of planned extubation.
Results. There were 219 episodes of mechanical ventilation in 204 children (median (interquartile range (IQR)) age 8 (1.6 - 44.4) months). Twenty-one of 184 (11.4%) planned extubations (95% confidence interval (CI) 7.2% - 16.9%) failed. Emergency cardiac admissions (adjusted odds ratio (aOR) 7.58 (95% CI 1.90 - 30.29), dysmorphology (aOR 4.90; 95% CI 1.49 - 16.14), prematurity (aOR 4.39; 95% CI 1.24 - 15.57), and ventilation ≥48 hours (aOR 6.42 (95% CI 1.57 - 26.22) were associated with extubation failure. Children who failed extubation had longer durations of ventilation (231 hours (146.0 - 341.0) v. 53 hours (21.7 - 123.0); $p<0.0001$); longer duration of PICU (15 (9 - 20) days v. 5 (2 - 9) days; $p<0.0001$) and hospital length of stay (32 (21 - 53) days v. 15 (8 - 27) days; $p=0.009$); and higher 30-day mortality (28.6% v. 6.7%; $p=0.001$) than successfully extubated children.
Conclusions. Extubation failure was associated with significant morbidity and mortality in our setting. Risk factors for extubation failure identified in our context were similar to those reported in other settings.
Keywords. intubation, extubation failure, risk factors, paediatric intensive care unit, mechanical ventilation, outcomes.

Contributions to the field
This study provides novel data on the prevalence, risk factors and outcomes associated with extubation failure in a single-centre South African PICU. The results of this study may help identify high-risk groups for extubation failure within our local context, and forms a basis for practice improvement initiatives aimed at decreasing extubation failure rates and improving outcomes.

The proportion of children requiring mechanical ventilation in paediatric intensive care units (PICUs) ranges from 20% to over 60% in different settings.[1-3] The primary indications for assisted ventilation are respiratory failure, as a result of primary airway or lung disease or secondary to other organ failures; or for postoperative care.[4] The risks of morbidity and mortality increase with the duration of mechanical ventilation. Extubation failure is also associated with significant adverse outcomes including increased mortality, prolonged PICU and hospital stay, higher costs, and greater need for tracheostomy.[5-7] As such it is important that extubation is neither rushed nor unnecessarily prolonged.

The prediction of extubation readiness and outcome is challenging. Several factors are necessary for effective spontaneous breathing, including adequate respiratory drive, patent airways, effective airway reflexes and clearance, adequate respiratory muscle strength, effective gas exchange, ventilation-perfusion matching and haemodynamic stability.[8] There is insufficient evidence supporting a reliable method of assessing readiness for extubation and/or predicting extubation success in the paediatric population, and the routine use of any extubation readiness testing cannot currently be recommended above clinical judgement.[9,10] Objective, valid and reliable weaning and extubation readiness tests for routine use therefore remain elusive in paediatric practice and decision-making depends largely on the clinical judgment of the attending physician.[9] In our PICU, formal extubation readiness tests and spontaneous breathing trials are not routinely performed. The decision to extubate is based on clinical assessment and review of the clinical data by the attending paediatric intensivist.

There is a paucity of data on the outcomes of African children requiring mechanical ventilation, including extubation failure rates. This study therefore aimed primarily to determine the extubation failure rate (prevalence). Secondary objectives were to describe the factors associated with extubation failure and to describe and compare the outcomes of mechanically ventilated children with and without

extubation failure in the PICU of Red Cross War Memorial Children's Hospital, Cape Town, South Africa (SA).

Methods

The Human Research Ethics Committee of the University of Cape Town approved the study and the need for informed consent was waived (HREC ref. no. 166/2017).

Study design and population

This was a prospective observational study of all children who were intubated and ventilated during their admission to the PICU from May to September 2017, including those who were intubated outside the PICU. Children admitted with a tracheostomy *in situ,* those admitted for a planned tracheostomy and children who were brain dead and admitted to the PICU for the sole purposes of organ donation, were excluded.

The 6-month study period was considered sufficient to enrol the required sample size of 139 planned extubation episodes, in order to detect a prevalence of 5 - 15% with 5% precision and a 95% confidence interval (CI) (http://sampsize.sourceforge.net/iface/#prev).

Study site

The PICU of the Red Cross War Memorial Children's Hospital is a 22-bed multidisciplinary unit situated in a tertiary paediatric hospital in Cape Town, SA. It admits ~1 400 patients aged 0 - 13 years per annum, and has a mortality rate of approximately 6%. Admissions are mainly for the management of paediatric emergencies such as pneumonia and/or sepsis, trauma and surgical emergencies, as well as post elective surgery (predominantly cardiac).

Data collection

Data were collected using a standardised, self-developed case record form. Intubation data were captured from the PICU intubation checklist, which was completed at the time of intubation by the doctor who performed the procedure. For intubations occurring outside the PICU, data were extracted from the clinical notes. The doctor who carried out the extubation filled peri-extubation data into the case record form. The level of consciousness was documented using the AVPU scale (alert, verbal, pain, unresponsiveness) and P and U were categorised as impaired. Remaining data were extracted from the patients' clinical notes, medication and observation charts. If a child needed to be re-intubated, the attending doctor provided these data. Extubation failure was defined as requiring re-intubation within 48 hours of a planned extubation.[7] The appropriateness of the endotracheal tube (ETT) internal diameter used was assessed with the (Age/4) + 4 mm formula for children 1 to 7 years for uncuffed tubes, and (Age/4) + 3.5 mm for cuffed tubes. The Advanced Pediatric Life Support (APLS) aide memoire 2015 was used for children 8 years and older. For neonates and infants, the weight-based recommendation from the *Textbook of Neonatal Resuscitation* (7th ed) was used.[11] Mallinckrodt cuffless and Parker Thin Cuff microcuff tubes were used for intubations carried out in the PICU. The bedside nurse routinely checked cuff pressure to ensure it remained between 20 and 30 cmH$_2$O. The predicted mortality risk, using the Paediatric Index of Mortality 3 (PIM3) was obtained from the PICU admissions database. The oxygenation index (OI) was calculated using the formula OI = mean airway pressure (cmH$_2$O) × fractionated oxygen (FiO$_2$) × 100/ partial oxygen pressure (PaO$_2$).

Data management and analysis

Data were transferred from the case record forms into an SPSS spreadsheet and analysed using SPSS Statistics version 27 (IBM, USA) and Statistica version 13 (Statsoft Inc, USA). Data were tested for normality using the Shapiro Wilks W test and mostly presented as medians (interquartile range (IQR)) as the majority of the data were not normally distributed. Comparisons of patient characteristics with and without extubation failure were analysed using χ^2 tests for categorical variables and Mann-Whitney U tests for continuous variables.
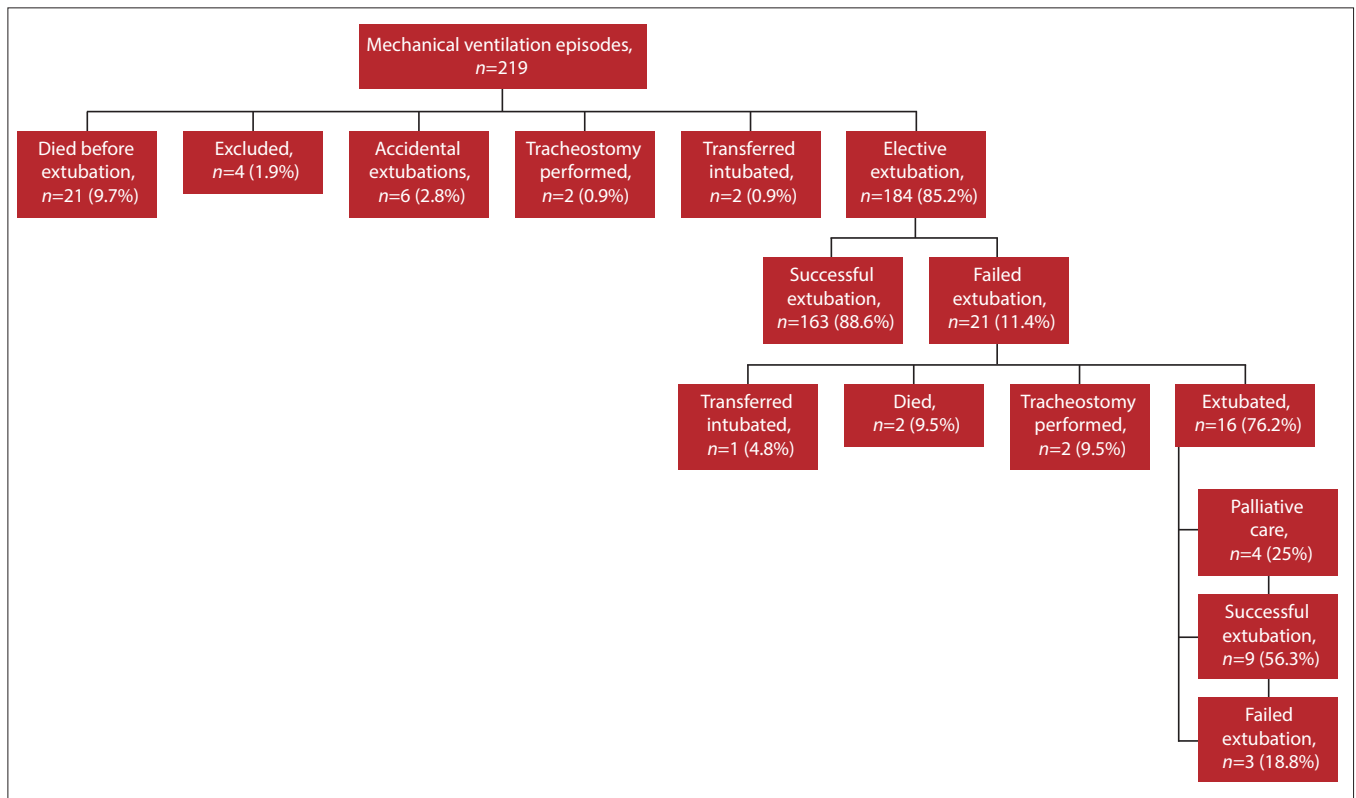

Fig. 1. Flow of participants through the study.

Variables found to be associated with the primary outcome of extubation failure on univariable analysis at $p<0.05$ were entered into a multivariable backward stepwise logistic regression model, to determine independent associations with the primary binary outcome (extubation failure). A significance level of 0.05 was chosen.

Table 1. Admission characteristics

Variables*	All planned extubations (N=184)	Failed extubation (N=21)	Successful extubation (N=163)	p-value
Age (month)	8.1 (2.0 - 43.6)	3.1(0.9 - 11.7)	8.5 (2.0 - 40.5)	0.25
Gender, male	91 (49.5)	8 (38.1)	81 (49.7)	0.34
Weight (kg)	6.7 (3.3 - 13.0)	3.9 (2.5 - 18.5)	7.0 (3.5 - 13.0)	0.23
Risk of mortality (PIM3)	0.02 (0.01 - 0.05)	0.04 (0.01 - 0.1)	0.02 (0.01 - 0.1)	0.38
Primary diagnosis				
Post cardiac surgery	60 (32.6)	4 (19.0)	56 (34.6)	0.16
Respiratory disease	38 (20.7)	4 (19.0)	34 (20.9)	0.85
Post surgery (non-cardiac)	22 (12.0)	4 (19.0)	18 (11.0)	0.3
Sepsis/septic shock	22 (12.0)	1 (4.8)	21 (12.88)	0.3
Emergency cardiac admission	16 (8.7)	5 (23.8)	11 (6.7)	0.009
Neurological disease	11 (6.0)	0	11 (6.7)	-
Trauma	10 (5.4)	2 (9.5)	8 (4.9)	0.4
Burns	6 (3.3)	0	6 (3.7)	-
Transplant	4 (2.2)	0	4 (2.5)	-
Other	8 (4.3)	1 (4.8)	7 (4.3)	0.9
Comorbid conditions				
Prematurity	20 (10.9)	6 (28.6)	14 (8.6)	0.006
Genetic syndrome or dysmorphology	30 (16.3)	7 (33.3)	23 (14.1)	0.02
Chronic lung disease	4 (2.2)	2 (9.5)	2 (1.2)	0.01
HIV infection	5 (2.7)	0	5 (3.1)	-
HIV exposure	27 (14.7)	5 (23.8)	22 (13.5)	0.2
Neuromuscular disease	2 (0.2)	1 (4.8)	1 (0.6)	0.08
Chronic kidney disease	8 (4.3)	1 (4.8)	7 (4.3)	0.9

PIM3 = paediatric index of mortality 3; IQR = interquartile range.
*Continuous variables: median (IQR); categorical variables *n* (%).

Table 2. Peri-intubation factors

Variables	All planned extubations (N=184), n (%)	Failed extubations (N=21), n (%)	Successful extubations (N=163), n (%)	p-value
Location				
Theatre	98 (53.3)	8 (38.10)	89 (54.60)	0.31
PICU	31 (16.8)	5 (23.81)	26 (15.95)	
Another hospital	36 (19.6)	6 (28.57)	30 (18.40)	
Medical ER	8 (4.3)	0	8 (4.91)	
Ward	6 (3.3)	2 (9.52)	4 (2.45)	
Trauma ER	1 (0.5)	0	1 (0.61)	
Out of hospital	4 (2.2)	0	4 (2.45)	
Primary indication				
Airway protection	5 (2.7)	0	5 (3.1)	0.32
Respiratory distress/failure	58 (31.5)	7 (33.3)	51 (31.3)	
Cardiovascular instability	20 (10.9)	5 (23.8)	18 (11.0)	
Neurology	23 (12.5)	3 (14.3)	20 (12.3)	
Postoperative	93 (50.5)	7 (33.3)	86 (52.8)	
Other factors				
NIV support prior to intubation	71 (38.6)	13 (61.9)	58 (35.6)	0.04
Emergency intubation	88 (47.8)	14 (66.7)	74 (45.4)	0.07
Previous endotracheal intubation	64 (34.8)	8 (38.1)	56 (34.4)	0.74
>Two attempts at intubation	21 (11.4)	3 (14.3)	18 (11.0)	0.54
Nasal intubation route	151 (82.1)	14 (66.7)	137 (84.0)	0.05
Cuffed ETT	116 (63.0)	11 (52.4)	105 (64.4)	0.26

PICU= paediatric intensive care; ER = emergency room; NIV = non-invasive ventilation; ETT = endotracheal tube.

Results

There were 446 admissions during the study period, with 219 (49.1%) episodes of invasive mechanical ventilation in 204 children (n=104 (51.0%) male; median (IQR) age 8.0 (1.6 - 44.4) months). Twenty-one (10.3%) of the mechanically ventilated children died before extubation was planned and four were excluded. There were six accidental extubations, all of which required re-intubation shortly afterwards. The final dataset for inferential analysis included 184 elective extubation cases, in 179 children. Twenty-one (11.4% (95% CI 7.2% - 16.9%)) of these 184 elective extubations failed within 48 hours, with a median (IQR) time to re-intubation of 7 (2 - 26) hours (Fig. 1).

The most common reason for admission to PICU was for postoperative management of children after cardiac surgery, followed by respiratory disease (Table 1), and the primary indications for intubation were for postoperative support followed by respiratory distress or respiratory failure (Table 2). A greater proportion of children who failed extubation were admitted as emergencies for treatment of cardiac conditions (Table 1).

Comorbid conditions were common, with dysmorphology or genetic syndromes occurring most frequently. Of the 34 children with documented dysmorphology, 14 had Trisomy 21, 5 had fetal alcohol syndrome, 2 each had 22q deletion and VACTERL, 1 case each had CHARGE (coloboma, heart defects, atresia choanae, growth retardation, genital abnormalities, and ear abnormalities), VATER (vertebral abnormalities, anal atresia (absence or closure of anus) and cardiac (heart) defects), Noonan syndrome, Alagille syndrome and Rett syndrome, while 6 were unclassified. Although overall the proportion

of comorbidities was not significantly different between groups, on *post hoc* analysis a significantly greater proportion of failed extubation cases presented with dysmorphology, prematurity and chronic lung disease compared with the successfully extubated group (Table 1).

The location of intubation and primary indications for intubation were not significantly different between failed and successfully extubated groups (Table 2). Cuffed ETTs were used in most cases (63%; Table 2), with uncuffed ETTs used in 48.8% of children <12 months old. There was no difference in the proportion of cuffed v. uncuffed tubes between successful and failed extubation groups (Table 2). The ETT size used was within the recommended range in 55.4% (n=102), larger than recommended in 30.4% (n=56) and smaller than recommended in 14.1% (n=26). There was no association between the disparity in ETT size and post-extubation stridor (p=0.18), extubation failure (p=0.08) or extubation failure secondary to upper airway obstruction (p=0.24).

Sixty-three (34.2%) children received steroids prior to extubation (Table 3), 19 for indications other than the risk of upper airway oedema (including post-solid-organ transplant immunomodulation (n=6), hypotension (n=4) and tuberculous meningitis (n=3)). Dexamethasone was used for upper airway oedema, methylprednisolone or prednisolone for transplant immunomodulation and hydrocortisone for hypotension. The median duration from time of the first steroid dose to time of extubation was 5.5 hours in the extubation failure group and 23.5 hours in the successful extubation group (p=0.06).

At the time of extubation, 41 (22.3%) cases were receiving one or more inotrope/s and/or vasopressors: milrinone (n=29), adrenaline (n=25)

Table 3. Pre- and peri-extubation factors				
	All planned extubations	**Failed extubations**	**Successful extubations**	
Variables*	**(N=184)**	**(N=21)**	**(N=163)**	**p-value**
Steroid administered prior to extubation	63 (34.2)	11 (52.4)	52 (31.9)	0.06
Inotrope/vasopressor support at time of extubation	41 (22.3)	5 (23.8)	36 (22.1)	0.86
Neuromuscular blocking agent in preceding 24 hours	21 (11.4)	0 (0)	21 (12.9)	0.07
Analgesic/sedative infusion in preceding 24 hours	166 (90.2)	19 (90.5)	147 (90.2)	0.73
Analgesic/sedative infusion at time of extubation	93 (50.5)	6 (28.6)	87 (52.1)	0.06
Mode of ventilation prior to extubation				
Pressure control ventilation	136 (73.9)	16 (76.2)	120 (73.6)	0.8
Pressure support ventilation	48 (26.1)	5 (23.8)	43 (26.4)	
Ventilator settings prior to extubation				
FiO_2	0.30 (0.25 - 0.32)	0.30 (0.21 - 0.33)	0.30 (0.25 - 0.30)	0.63
Peak inspiratory pressure (cmH_2O)	15.0 (14.0 - 16.0)	15.0 (14.0 - 15.0)	15.0 (14.0 - 16.0)	0.80
Positive end-expiratory pressure (cmH_2O)	5.0 (5.0 - 5.0)	5.0 (5.0 - 5.0)	5.0 (5.0 -5.0)	0.22
Mean airway pressure (cmH_2O)	9.0 (8.0 - 10.0)	8.0 (7.0 - 10.0)	9.0 (8.0 - 10.0)	0.60
Tidal volume (ml/kg)	6.4 (5.1 - 7.9)	5.7 (5.0 - 7.0)	6.5 (5.2 - 8.0)	0.075
Duration of ventilation prior to extubation (hours)	57.6 (22 - 123)	112.0 (50 - 174)	49.0 (21 - 116)	0.012
Duration of ventilation >48 hours	102 (55.4)	18 (85.7)	84 (51.5)	0.003
Blood gas analysis done	174 (94.6)	21 (100)	153 (93.9)	
pH	7.39 (7.34 - 7.43)	7.39 (7.37 - 7.43)	7.44 (7.38 - 7.45)	0.51
pCO_2 (kPa)	5.53 (4.88 - 6.28)	6.23 (5.22 - 6.9)	5.5 (5.3 - 5.6)	0.09
pO_2 (kPa)	13.10 (8.91 - 17.60)	9.23 (6.05 - 11.2)	18.7 (11.0 - 20.6)	0.21
Base excess	−0.01 (-3.7 - 4.3)	1.9 (-3.5 - 6.7)	−0.2 (-3.7 - 4.1)	0.22
Bicarbonate (mmol/L)	24.2 (21.2 - 27.7)	27.8 (25.7 - 29.2)	27.9 (27.7 - 29.2)	0.23
Oxygenation index	19.4 (13.8 - 28.2)	17.9 (13.8 - 36.8)	19.7 (13.8 - 27.6)	0.70
Cumulative fluid balance (% body weight)	1.87 (0.12 - 7.01)	6.33 (1.12 - 9.12)	1.68 (0.11- 6.32)	0.10
Hb (g/dL)	11.0 (9.4 - 12.7)	11.1 (10.0 - 12.6)	11.0 (9.4 - 12.7)	0.75
Transfused prior to extubation	56 (30.4)	5 (23.8)	51 (31.3)	0.45
Impaired level of consciousness	5 (2.7)	2 (9.5)	3 (1.8)	0.04

pCO_2 = partial pressure of carbon dioxide; pO_2 = partial pressure of oxygen; Hb = haemoglobin.
*Continuous variables: median (IQR); categorical variables n (%).

Table 4. Outcomes of planned extubations

Variable*	All planned extubations (N=184)	Failed extubation (N=21)	Successful extubation (N=163)	p-value
Total duration of mechanical ventilation (hours)	69.5 (22 - 149)	231.0 (146.0 - 341.0)	53.0 (21.7 - 123.0)	<0.0001
Post-extubation stridor	47 (25.5)	8 (38.1)	39 (23.9)	0.358
Total NIV post extubation	98 (52.3)	16 (76.2)	82 (50.3)	0.03
Elective NIV	57 (58.2)	11 (68.8)	46 (56.1)	0.35
Type of NIV (n=98)				
HFNC	30 (30.6)	7 (43.8)	23 (28.0)	0.21
CPAP	63 (64.3)	7 (43.8)	56 (72.0)	0.06
BiPAP	5 (5.1)	2 (12.5)	3 (3.7)	0.14
PICU LOS (days)	6.0 (3.0 - 12.0)	15.0 (9.0 - 20.0)	5 (2.0 - 9.0)	<0.0001
PICU mortality	4.0 (2.2)	2.0 (9.5)	2.0 (1.2)	0.014
Mortality 30 days post PICU discharge	17.0 (9.2)	6.0 (28.6)	11.0 (6.7)	0.001
Hospital LOS of survivors (days)	16.0 (8.0 - 28.0)	32.0 (21.0 - 53.0)	15.0 (8.0 - 27.0)	0.009

NIV = non-invasive ventilation; HFNC = high-flow nasal cannula; CPAP = continuous positive airway pressure; BiPAP = bi-level positive airway pressure, PICU = paediatric intensive care unit; LOS = length of stay;.
*Continuous variables: median (IQR); categorical variables n (%).

and noradrenaline (n=3). None was on dopamine or dobutamine. There was no evidence of a significant association between inotrope/vasopressor use and failed extubation.

Standard practice in this unit is to ensure minimal yet effective sedation; however, sedation scoring is not routinely used. Unit protocol is generally to stop sedative infusion prior to extubation, but analgesic infusions may continue for optimal pain management. The vast majority (n=166; 90.2%) of patients received analgesic or sedative infusions in the 24 hours preceding extubation and at the time of extubation, 93 (50.5%) were on one or more ongoing infusions, mainly for analgesic purposes: morphine (n=84); fentanyl (n=10); dexmedetomidine (n=5); ketamine (n=1) and midazolam (n=1). Notably, over half the cohort were extubated after surgery and/or traumatic injury, and all of these patients received opioid infusions for pain control. There was no evidence of a difference in the proportion of patients receiving sedative infusions between successful v. failed extubation groups (Table 3).

A cumulative fluid balance ≥10% body weight occurred in 14.7% (n=27) at the time of extubation. Fluid balance was not associated with extubation failure (p=0.1; Table 3) even when those with upper airway obstruction were excluded (p=0.47). On univariate analysis, impaired level of consciousness was more prevalent in those who failed extubation, but other assessed variables were similar between groups (Table 3).

On multivariable analysis, emergency cardiac admissions (adjusted odds ratio (aOR) 7.58 (95% CI 1.90 - 30.29); p=0.004), dysmorphology/genetic syndrome (aOR 4.90 (95% CI 1.49 - 16.14); p=0.009), prematurity (aOR 4.39 (95% CI 1.24 - 15.57); p=0.02), decreased level of consciousness (aOR 12.05 (95% CI 1.57 - 92.52); p=0.02), and ventilation duration ≥48 hours (aOR 6.42 (95% CI 1.57 - 26.22); p=0.01), were found to be associated with extubation failure.

Stridor occurred in 47 (25.5%) children after planned extubation, of whom 18 (38.3%) had received at least one dose of a steroid prior to extubation (Table 4). Ninety-eight (52.3%) children were placed on non-invasive ventilation (NIV) after extubation; in 57 cases this was electively initiated immediately after extubation.

Upper airway obstruction (n=7; 33.3%) was the most common indication for re-intubation within 48 hours of planned extubation, followed by respiratory distress or failure (n=6; 28.6%), heart failure (n=3; 14.3%), reduced level of consciousness (n=3; 14.3%), and cardiac

arrest (n=2; 9.5%). One child had respiratory failure as a result of critical illness neuromyopathy and 2 had poor diaphragm function. For the children with upper airway obstruction, laryngeal oedema was noted during reintubation in 3 patients and 1 had oedema and vocal cord paralysis. Microlaryngoscopy was carried out for 3 children, with laryngeal web (congenital), vocal cord paralysis (following severe traumatic brain injury) and laryngeal injury (from intubation), respectively.

Post-extubation non-invasive respiratory support was initiated in 98 (52.3%) cases, with a significantly higher proportion of NIV or high-flow nasal cannula (HFNC) use in the failed extubation group (Table 3). NIV or HFNC was started electively, immediately after extubation, in 57 (58.2%) cases considered by clinicians to be at high risk of extubation failure, while rescue NIV was initiated in 41 (41.8%) cases who developed respiratory failure within 48 hours of extubation. Eleven (19.3%) cases who received NIV electively immediately after extubation were re-intubated within 48 hours, compared with 5 out of 41 children (12.2%) who received non-elective, rescue NIV (p=0.35). Complications of NIV occurred in 3 children (3.1%). One developed a pneumothorax and 2 had mild pressure ulceration of the nasal septum.

The median (IQR) durations of mechanical ventilation and PICU stay were 69.5 (22 - 149) hours and 6 (3 - 12) days respectively, with 2% mortality in the study cohort (Table 4). By comparison, the overall mortality rate for all invasively ventilated admissions over the study period was 14.6%. Of the 21 children who failed extubation, 2 died, 1 was transferred intubated, 2 had tracheostomies and 16 were eventually extubated (Fig. 1). Eleven of the 16 (68.8%) who were extubated received steroids prior to their second extubation; 3 (18.8%) failed their second extubation and 1 failed a third extubation. The median (IQR) duration of re-intubation was 126 (60.5 - 190.0) hours.

Extubation failure was associated with significantly increased total duration of invasive mechanical ventilation; prolonged PICU and hospital stay (p=0.009), as well as higher PICU and 30-day mortality (Table 4).

Discussion

We report an invasive ventilation rate of 48.4%, median duration of ventilation of 69.5 hours and median PICU stay of 6 days for mechanically ventilated children, which is comparable with data from other PICUs.[1,2,12] Our extubation failure rate at 48 hours was 11.4%,

in support of previous suggestions that, in the absence of valid and reliable markers of paediatric extubation readiness, in the majority of cases clinician judgement alone may be sufficient.[13] Most reports on extubation failure rates in children range between 4% and 20%,[14-16] with no clear recommendation for an acceptable extubation failure rate. Very low extubation failure rates may indicate overly conservative weaning and extubation practices. Kapnadak *et al.*[17] related ventilator-free days, ICU-free days and mortality to the extubation failure rates in ICU over a 9-year period and found that periods of extubation failure rate between 7% and 15% had higher ventilator and ICU-free days compared with failure rates of <7% or >15%, with no significant difference in mortality.[17] This was, however, a single-site study in adults and may not be applicable to children.

The factors we found to be associated with extubation failure are similar to those reported in other studies: prematurity or a history of prematurity in infants, dysmorphology, duration of ventilation ≥48 hours, and a decreased level of consciousness.[14,15,18,19] Even though the median age for those who failed extubation was 3.1 months, younger age in itself was not found to be a risk factor for extubation failure, unlike in other studies.[5,14,15] This may be because 60% of children extubated were <12 months old and 17.9% were neonates. Prematurity is associated with even greater age-related vulnerabilities, such as increased risk of apnoea, small airways, and higher chest wall compliance coupled with immature lungs with poorer compliance, a higher risk of infection, and sequelae of prematurity in infants.[19,20]

Emergency cardiac admissions had the highest extubation failure rate (31.3%). Haemodynamic instability and accompanying poor perfusion are known risk factors for respiratory failure.[9] Unlike the findings of Fontela *et al.*,[15] that children receiving dopamine and dobutamine were at higher risk of extubation failure on univariate analysis, the use of inotropes at the time of extubation in itself was not associated with extubation failure in our study.

Like other studies, a longer duration of ventilation was associated with increased extubation failure rates.[7,15,19] Prolonged ventilation is usually associated with prolonged use of sedatives, which may cause respiratory depression, and immobilisation, which may result in dysfunction of the diaphragm and myopathy with increased risk of respiratory failure.

Early fluid overload has been associated with increased PICU morbidity.[21-23] The fluid balance reported here was at the time of extubation and not necessarily during the acute phase of the first 24 - 48 hours of admission. Close attention is paid to fluid balance in the unit as standard practice, which may explain why it was not a predictive factor. Randolph *et al.*,[24] in a multicentre study of 301 mechanically ventilated children, also found that fluid balance at the time of extubation was not a predictor of extubation outcome. However, although our study was adequately powered to determine prevalence, it was likely underpowered for the multiple subanalyses conducted, and findings must therefore be interpreted with caution.

Upper airway obstruction was the primary reason for re-intubation in a third of failed extubations, as found in other studies.[5,19] The prophylactic use of corticosteroids for the prevention of post-extubation stridor and extubation failure remains controversial, though targeted use for at-risk populations maybe beneficial.[25-28] During our study, dexamethasone was administered prior to extubation to those assessed to be at high risk of upper airway obstruction. These generally were children who had multiple attempts at intubation, prolonged intubation or pre-existing concerns about upper airway compromise, or the absence of a leak around the ETT. However, this study was not designed to determine the efficacy of steroid use.

NIV and HFNC are being increasingly employed to facilitate earlier extubation and to prevent re-intubation across different disciplines;[7,29-32] their use is therefore not considered to be extubation failure. Unsurprisingly, a greater proportion of patients who failed extubation in our study received NIV after extubation, in an effort to avoid re-intubation. It has previously been reported that patients receiving elective NIV immediately after extubation have a lower rate of extubation failure compared with later 'rescue' NIV initiation;[33] however, we were unable to show a similar association.

Extubation failure was associated with increased duration of ventilation, increased adverse events during ventilation, longer PICU stay, and higher mortality, which is consistent with many other studies.[5-7,19,34] Unlike in other reports[35,36] where re-intubation rates following accidental extubation were 16 - 65%, all accidental extubations were re-intubated. The adverse event rates are high and present an opportunity for quality improvement programmes to optimise patient outcome. Although there are no clear standards for assessment of extubation readiness, implementing a minimum local standard process, which includes a pre-extubation spontaneous breathing trial and establishing clearer criteria for initiating post-extubation non-invasive support,[9,13] may improve extubation success rates, particularly in the groups designated at being of higher risk of extubation failure. This requires further investigation.

While this study was strengthened by its prospective design and use of standardised data capture forms, it was limited by being from a single centre, with resulting poor external validity and lack of standardised or protocolised determination of both extubation readiness and response to impending extubation failure (e.g. using NIV or other measures). Furthermore, the relatively small sample size, and particularly the small number of failed extubations, limits the power to draw firm conclusions regarding predictive factors for extubation failure. Further, multisite research is required to determine the risk factors for extubation failure and to identify optimal tests for extubation readiness in the SA and global PICU population.

Conclusions and recommendations

The planned extubation failure rate was 11.4% (95% CI 7.2% - 16.9%). Emergency cardiac admissions, genetic syndromes or dysmorphology, prematurity, and ventilation for 48 hours or more were independently associated with extubation failure in our setting. Extubation failure was associated with longer duration of ventilation, longer PICU and hospital stay and a fourfold increase in mortality. Ensuring patient readiness for extubation, improving sedation and weaning practices and optimising post-extubation respiratory support are critical areas for further research and clinical quality improvement initiatives, in order to avoid the need for reintubation.

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