



## Original Contribution

# Difficult tracheal intubation and perioperative outcomes in patients with congenital heart disease: A retrospective study



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## ARTICLE INFO

## Keywords:

Difficult tracheal intubation  
Congenital heart disease  
Children

## ABSTRACT

**Background and objective:** Management of difficult tracheal intubation during induction of anesthesia in children with congenital heart disease is challenging. The aim of this study is to evaluate the incidence of difficult tracheal intubation in patients with congenital heart disease and compare the incidence of perioperative complications and outcomes in patients with and without difficult tracheal intubation.

**Design:** Retrospective cohort study.

**Setting:** Tertiary Children's Hospital.

**Participants:** 6858 patient-encounters including cardiac diagnostic, interventional or surgical procedures from 2012 to 2018 were reviewed. Exclusion criteria: age > 18 years, endotracheal tube or tracheostomy in-situ.

**Methods/interventions:** Patients' demographics, number and methods of intubation, peri-intubation hemodynamics, intensive care unit and postoperative hospital length of stay were recorded. Multivariable mixed-effects median, logistic, ordinal, and multinomial regression modeling were implemented to analyze outcomes in the matched sets.

**Results:** Of the 6014 encounters examined in the study, the incidence of DTI was 0.96% and all 58 difficult tracheal intubations (DTI) were matched using 1:2 propensity score matching to 116 non-DTI encounters. Number of intubation attempts was significantly higher among patients with difficult tracheal intubation (ordinal logistic regression odds ratio = 2; 95% CI: 1.3, 2.7;  $P < 0.001$ ). No significant differences in peri-intubation hemodynamic stability were noted. Patients with difficult tracheal intubation had longer post-operative hospital length of stay (median = 12.1 vs 7.9 days, coef. = 4; 95% CI: 1.3, 6.8;  $P = 0.004$ ) than patients without.

**Conclusion:** Despite a higher number of intubation attempts, our study shows no major differences in the peri-intubation hemodynamics in patients with and without difficult tracheal intubation. This risk can be mitigated by a good understanding of cardiac physiology, management of hemodynamics, and early use of an indirect intubation technique to maximize first attempt success.

## 1. Introduction

Management of difficult tracheal intubation (DTI), whether anticipated or unanticipated, during induction of anesthesia in children is challenging. DTI in children with congenital heart disease (CHD) is particularly challenging because it may be impossible to achieve 100%

saturation of arterial blood with oxygen prior to induction, and many of these children experience rapid deterioration in hemodynamics during periods of hypoxemia and hypercapnia [1]. In the setting of a compromised pulmonary perfusion and an altered hemodynamic response, airway complications can be associated with increased morbidity. In children undergoing anesthesia, respiratory events are the major cause

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<https://doi.org/10.1016/j.jclinane.2021.110565>

Received 29 April 2021; Received in revised form 13 October 2021; Accepted 17 October 2021

Available online 30 October 2021

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of cardiac arrest in patients with and without CHD, with the majority of these events being secondary to loss of airway patency [2,3]. Compared to children without heart disease, CHD patients are at higher risk of anesthesia related adverse events, with a higher resultant risk of hypoxic brain damage, cardiac arrest, and death [4,5].

Data from the Pediatric Difficult Intubation Registry (PeDIR) has shown that DTI occurred in 2–5 per 1000 pediatric anesthesia cases, with these cases having a 20% complication rate [6]. However, in pediatric cardiac patients, studies have shown an overall significantly higher rate of poor laryngoscopic views (3.5% versus 0.2–0.5%), with a greater incidence in patients younger than 1 year of age (5.6% versus 1.7%) and a higher likelihood of DTI [7,8].

This study aims to evaluate a single-institution's incidence of DTI in patients with CHD and to compare perioperative complications in patients with and without DTI.

## 2. Methods

Following approval from the Institutional Review Board, 6858 electronic medical records of patients with an age of 18 years or below diagnosed with CHD and who had a general anesthetic with endotracheal intubation for diagnostic or interventional cardiac catheterization, electrophysiology studies, echocardiography, magnetic resonance imaging, or cardiac surgery between December 2012 and December 2018, were reviewed. Patients older than 18 years of age, and patients who presented with an in-situ endotracheal tube or a tracheostomy were excluded.

Data collected from the electronic medical records included age, weight, sex, intubation technique (direct laryngoscopy, video laryngoscopy, or flexible fiberoptic), total number of intubation attempts, the presence of a genetic syndrome and specific cardiac diagnoses. The International Classification of Diseases, ninth (ICD-9) and tenth Edition (ICD-10) codes were used to determine the presence of genetic syndromes and specific cardiac diagnoses (Appendix A). The incidence of airway abnormality (congenital and/or acquired), defined by ICD-9 and 10 codes, was also collected [9].

Definition of a difficult tracheal intubation was adopted from the Pediatric Difficult Intubation Registry (PeDIR), a multinational, multi-institutional collaborative [6]. PeDIR uses the following 4 criteria to define a DTI: 1. Failure to visualize vocal cords during conventional direct laryngoscopy (Cormack-Lehane  $\geq 3$ ), as attempted by an experienced provider; 2. Presence of an anatomic abnormality causing tracheal intubation using direct laryngoscopy to be physically impossible; 3. Failure of conventional direct laryngoscopy within the last 6 months; 4. Deferral of conventional direct laryngoscopy due to the assessment by an experienced anesthesiologist of a low chance of success and/or a perceived increased risk of harm.

DTI was the primary exposure variable of interest. Patients with DTI were matched to patients without DTI in a 1:2 nearest neighbor fashion based on the following matching variables: age, weight, sex, location, genetic syndromes, and cardiac diagnoses. In the matched cohort, additional data was collected from the intraoperative and postoperative records.

The primary outcomes included the need for supplemental oxygen, vasopressor use, the relative percentage change in oxygen saturation (SpO<sub>2</sub>), in heart rate (HR), in systolic, diastolic and mean blood pressures (SBP, DBP, MBP respectively) calculated by comparing preinduction values with corresponding nadir values during the anesthetic induction period (defined from the start of anesthesia medication administration until anesthesia ready time), and occurrence of cardiac arrest. Secondary outcomes included time to extubation, postoperative intensive care unit (ICU) and hospital lengths of stay (LOS), and follow up by the otolaryngology team. All tracheal intubations were performed or supervised by an anesthesiologist with advanced cardiac training and extensive experience with pediatric airway management. The staff supervise trainees who are anesthesiologists pursuing advanced training in

pediatric or pediatric cardiac anesthesia, or certified nurse anesthetists.

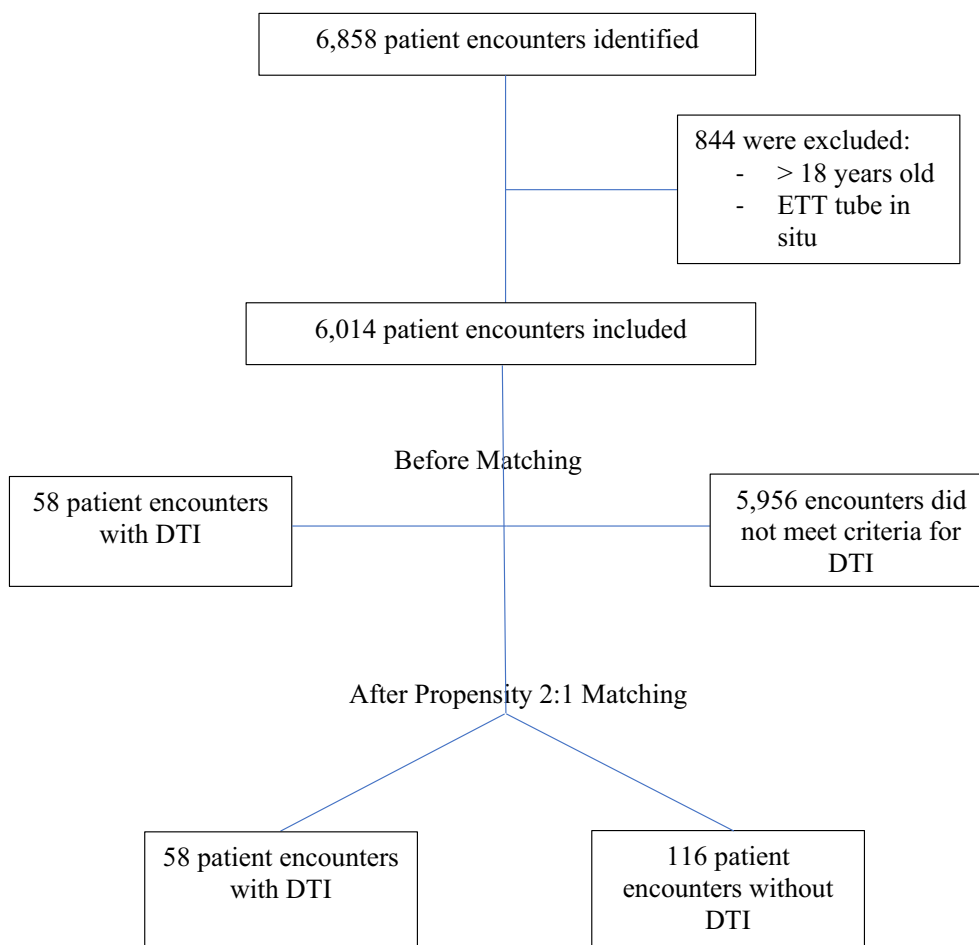
### 2.1. Statistical analysis

Continuous baseline characteristics are presented as means and standard deviations (SD) and categorical data are presented as frequencies (n) and percentages (%). Propensity score matching was implemented to match patients with DTI with patients without DTI in order to balance these two comparison groups on baseline demographic characteristics (age, weight, sex, procedure (surgical or catheterization/imaging), genetic syndromes), as well as cardiac diagnoses. The propensity scores were calculated based on the covariates above in a multivariable logistic regression model for DTI, and patients with DTI were matched to patients without DTI in a 1:2 nearest neighbor fashion based on the propensity scores. Matching was performed without replacement, as each DTI patient was matched with 2 patients without DTI with the nearest propensity scores. The absolute standardized mean difference (SMD) was calculated for each variable pre- and post-matching in order to assess the balance between the two groups. An SMD value less than 0.1 was taken to represent good post-matching balance on a given variable, and a reduction in the SMD from pre- to post-matching also represents an improvement in balance. In the matched cohort, continuous outcomes were presented as medians and interquartile ranges (IQR) due to non-normality indicated by the Shapiro-Wilk test, and binary outcomes were presented as frequencies and percentages by group. Multivariable mixed-effects median regression was used to analyze continuous outcomes while incorporating a random effect for the matched sets from propensity score matching, and conditional logistic regression was implemented to analyze binary outcomes while accounting for matched sets. Mixed-effect ordinal and multinomial logistic regression was implemented to analyze ordinal and categorical outcomes, respectively. Matching factors with SMD values  $>0.1$  were included for covariate adjustment in the multivariable regression analyses of outcomes in the matched cohort. These factors included age, weight, mitral valve anomalies, tricuspid valve anomalies, subclavian anomaly, and patent ductus arteriosus. Results from multivariable modeling in the propensity matched data are presented as adjusted coefficients or odds ratios with corresponding 95% confidence intervals and *P* values. Patients with missing data on any matching factors were excluded from the propensity score matching analysis. Denominators are reported to denote instances of missing data. A two-tailed alpha of 0.01 was used to determine statistical significance for all outcomes, in order to reduce the risk of false positive results (type I error) due to multiplicity. All statistical analyses were performed using Stata (version 16.0, StataCorp LLC., College Station, Texas) and the 'qreg2' command was implemented for median regression modeling.

The propensity-matched sample of 58 DTI cases and 116 cases without DTI (total  $N = 174$ ) provides 80% statistical power for detecting small to moderate differences (standardized effect size = 0.3) between the two groups, based on median regression analysis and assuming a two-tailed 1% alpha.

## 3. Results

In the 6-year study period, 6858 patient encounters were identified. Of these, 844 encounters were excluded for incomplete data. A total of 6014 CHD patient encounters were therefore included in the analysis. Among these encounters, 58 met the inclusion criteria for DTI (0.96%) (Fig. 1). Among the 58 DTI patients, 48 (82.8%) were anticipated to have DTI. The pre-matching comparison of baseline characteristics and cardiac diagnoses are presented in Table 1. The most commonly identified cardiac diagnoses in our cohort were pulmonary artery anomalies, aortic, mitral or tricuspid valve anomalies and septal defects. DTI encounters compared to those without DTI featured: younger patients (mean age = 2.8 years, SD = 4.5 versus mean age = 3.8 years, SD = 4.9) (SMD = 0.21); had higher rates of genetic syndromes (53.5% versus



ETT: Endotracheal tube, DTI: Difficult Tracheal Intubation.

**Fig. 1.** Flow Diagram of patients with and without Difficult Intubation before and after 2:1 Propensity Matching. ETT: Endotracheal tube, DTI: Difficult Tracheal Intubation.

18.1%; SMD = 0.79); and had higher rates of many specific cardiac diagnoses such as interrupted aortic arch, anomalies of the tricuspid and aortic valves, truncus arteriosus, septal defects and subclavian anomaly.

Following 1:2 propensity score matching, the 58 DTI encounters were matched with 116 non-DTI encounters (Table 2). In the matched cohort, balance was improved on all matching factors as measured by a decreased SMD for each variable (Supplemental Table 1). In the propensity matched data set, pulmonary artery and pulmonary valve anomalies, anomalous pulmonary venous connections, and septal defects were the most significant cardiac diagnoses found in patients with DTI.

Number of intubation attempts was significantly higher among cases with DTI (41.4% of cases with DTI had 1 intubation attempt, and 80.2% of cases without DTI had 1 intubation attempt; ordinal regression odds ratio = 2; 95% CI: 1.3, 2.7;  $P < 0.001$ ) (Table 3). Intubation technique significantly differed comparing cases with versus without DTI ( $P < 0.001$ ). Among encounters with DTI, 20.7% used DL, 72.4% used VL, 5.2% used flexible fiberoptic, and 1.7% used VL and flexible fiberoptic. Among the 58 patients with DTI, successful intubation was performed by the attending anesthesiologist in 26 patients, by a pediatric anesthesiology fellow in 28 patients and by a certified nurse anesthetist in 4 patients.

Analysis of outcomes in the matched cohort is presented in Table 4. After propensity score matching, there were no significant differences in the following outcomes when comparing encounters with versus without DTI: supplemental oxygen use (OR for DTI = 1.54; 95% CI: 0.3, 7.89;  $P = 0.606$ ), vasopressor use (OR = 2.12; 95% CI: 0.99, 4.56;  $P = 0.054$ ), having otorhinolaryngology (ORL) follow-up (OR = 3.65; 95% CI: 0.35, 37.9;  $P = 0.278$ ), relative percent change in SpO<sub>2</sub> (coefficient (coef.) = -2.4%; 95% CI: -6.3%, 1.6%;  $P = 0.247$ ), percent change in HR (coef. = -0.3%; 95% CI: -6.9%, 6.3%;  $P = 0.922$ ), percent change in systolic BP (coef. = -4.3%; 95% CI: -13.2%, 4.7%;  $P = 0.349$ ), percent change in diastolic BP (coef. = 0%; 95% CI: -8.7%, 9.7%;  $P = 0.999$ ), percent change in MAP (coef. = -1.8%; 95% CI: -11.4%, 7.8%;  $P = 0.708$ ), and time to extubation in days (coef. = 0.8 days; 95% CI: -0.1, 1.7;  $P = 0.088$ ). There were no cardiac arrests in the matched cohort. Moreover, there was no difference between the two groups in terms of time from peri-induction to anesthesia ready. The median time to anesthesia ready was 33 min (IQR: 24, 49) in the DTI group and 34 min (IQR: 21, 52) in the non-DTI group with an adjusted coefficient of 0.35 (95% CI: -8.2, 8.9;  $P = 0.936$ ), using mixed-effects median regression accounting for the propensity matched sets.

There was significantly longer postoperative hospital LOS for patients with DTI (median = 12.1 days (IQR: 6.1, 20.6)) versus patients without DTI (median = 7.9 days (IQR: 4.9, 12.9)) (coef. = 4; 95% CI: 1.3,

**Table 1**  
Pre-matching comparison of baseline characteristics.

Variable	Difficult Intubation (n = 58)	No Difficult Intubation (n = 5956)	SMD
Age (years)	2.8 (4.5)	3.8 (4.9)	0.21
Weight (kg)	11.9 (14.2)	15.8 (17.7)	0.24
Sex:			0.13
Female	22 (37.9%)	2646/5951 (44.5%)	
Male	36 (62.1%)	3305/5951 (55.5%)	
Location:			0.09
Cath Lab	11 (19%)	924 (15.5%)	
Operating Room	47 (81%)	5032 (84.5%)	
Any genetic syndrome	31 (53.5%)	1075 (18.1%)	0.79
Interrupted aortic arch	1 (1.9%)	112 (1.9%)	0.01
Double aortic arch	0 (0%)	61 (1%)	0.14
Coarctation of the aorta	0 (0%)	19 (0.3%)	0.08
Anomalies of aortic arch	18 (31%)	2285 (38.4%)	0.15
Pulmonary artery anomalies	34 (58.6%)	2708 (45.5%)	0.27
Single ventricle	8 (13.8%)	1468 (24.7%)	0.28
Aortic valve anomalies	35 (60.3%)	3710 (62.3%)	0.04
Mitral valve anomalies	31 (53.5%)	3469 (58.2%)	0.09
Pulmonary valve anomalies	30 (51.7%)	2359 (39.6%)	0.24
Tricuspid valve anomalies	9 (15.5%)	919 (15.4%)	0.002
Anomalous pulmonary venous connections	5 (8.6%)	643 (10.8%)	0.07
Aortopulmonary window	1 (1.7%)	48 (0.8%)	0.08
Truncus arteriosus	1 (1.7%)	92 (1.5%)	0.01
Septal defects	50 (86.2%)	5086 (85.4%)	0.02
Cor triatriatum	0 (0%)	57 (1%)	0.14
Coronaries	9 (15.5%)	940 (15.8%)	0.06
Subclavian anomaly	1 (1.7%)	124 (2.1%)	0.03
Transposition of the great arteries	5 (8.6%)	782 (13.1%)	0.15
Double inlet left ventricle	1 (1.7%)	422 (7.1%)	0.21
Double outlet ventricle (Right or Left)	9 (15.5%)	798 (13.4%)	0.06
Ebstein's anomaly	0 (0%)	146 (2.5%)	0.22
Patent ductus arteriosus	10 (17.2%)	1298 (21.8%)	0.11
Persistent left superior vena cava	0 (0%)	122 (2.1%)	0.22
Tetralogy of Fallot	14 (24.1%)	1034 (17.4%)	0.17

Data are presented as mean (standard deviation) or n (%). Absolute standardized mean differences (SMD) were calculated to compare the two groups pre-matching.

6.8;  $P = 0.004$ ). However, postoperative ICU LOS was not significantly longer in DTI patients (median = 6 days (IQR: 1.9, 13.2)) versus patients without DTI (median = 3.9 days (IQR: 1.9, 8.9)) (coef. = 2.1; 95% CI: -1.3, 5.5;  $P = 0.227$ ). The time to extubation calculated from time of intubation to time of extubation was not significantly longer in the DTI group (median = 1.8 days (IQR: 0.7–5.1)) than in the in the non-DTI group (median = 1.1 days (IQR: 0.4–2.9) coef = 0.8; 95% CI: -0.1, 1.7;  $P = 0.088$ ). In the DTI group, 22/58 (37.9%) patients had airway abnormality, and in the non-DTI group 34/116 (29.3%) patients had airway abnormality ( $P = 0.144$ ).

#### 4. Discussion

In this study population, among the 6014 included patients, 58 (0.96%) had a DTI. There were no cardiac arrests in the matched cohort and no significant difference between patients with DTI and those without DTI in terms of peri-induction physiologic changes with no change in SpO<sub>2</sub>, HR, SBP, DBP and MBP, and no significant differences in supplemental oxygen and vasopressor use.

The incidence of DTI in this study is slightly lower than previously reported. In a computerized survey of 10,000 anesthetics the incidence of serious airway difficulties was 1.3% [10] Similarly, the incidence of DTIs was reported as 1.25% in 1278 pediatric patients with CHD undergoing cardiac surgery [7]. This difference in incidence is likely related to differences in the definition of DTI. In our study, PeDIR was

**Table 2**  
Post-matching comparison of baseline characteristics.

Variable	Difficult Intubation (n = 58)	No Difficult Intubation (n = 116)	SMD
Age (years)	2.8 (4.5)	2.1 (3.5)	0.18
Weight (kg)	11.9 (14.2)	10 (10.6)	0.15
Sex:			0.05
Female	22 (37.9%)	47 (40.5%)	
Male	36 (62.1%)	69 (59.5%)	
Location:			0
Catheterization	11 (19%)	22 (19%)	
Laboratory/Imaging			
Operating Room	47 (81%)	94 (81%)	
Any genetic syndrome	31 (53.5%)	63 (54.3%)	0.02
Interrupted aortic arch	1 (1.9%)	1 (0.9%)	0.08
Double aortic arch	0 (0%)	0 (0%)	0
Coarctation of the aorta	0 (0%)	0 (0%)	0
Anomalies of aortic arch	18 (31%)	32 (27.6%)	0.08
Pulmonary artery anomalies	34 (58.6%)	66 (56.9%)	0.04
Single ventricle	8 (13.8%)	20 (17.2%)	0.10
Aortic valve anomalies	35 (60.3%)	66 (56.9%)	0.07
Mitral valve anomalies	31 (53.5%)	70 (60.3%)	0.14
Pulmonary valve anomalies	30 (51.7%)	57 (49.1%)	0.05
Tricuspid valve anomalies	9 (15.5%)	31 (26.7%)	0.28
Anomalous pulmonary venous connections	5 (8.6%)	9 (7.8%)	0.03
Aortopulmonary window	1 (1.7%)	1 (0.9%)	0.08
Truncus arteriosus	1 (1.7%)	2 (1.7%)	0
Septal defects	50 (86.2%)	102 (87.9%)	0.05
Cor triatriatum	0 (0%)	0 (0%)	0
Coronaries	9 (15.5%)	21 (18.1%)	0.07
Subclavian anomaly	1 (1.7%)	4 (3.5%)	0.11
Transposition of the great arteries	5 (8.6%)	12 (10.3%)	0.06
Double inlet left ventricle	1 (1.7%)	1 (0.9%)	0.09
Double outlet ventricle (Right or Left)	9 (15.5%)	18 (15.5%)	0
Ebstein's anomaly	0 (0%)	0 (0%)	0
Patent ductus arteriosus	10 (17.2%)	30 (25.9%)	0.21
Persistent left superior vena cava	0 (0%)	0 (0%)	0
Tetralogy of Fallot	14 (24.1%)	23 (19.8%)	0.1

Data are presented as mean (standard deviation) or n (%). Propensity score matching was performed 2:1 using the nearest-neighbor method. Absolute standardized mean differences (SMD) were calculated to compare the two groups post-matching.

**Table 3**  
Intubation technique and number of attempts in the matched cohort.

Variable	Difficult Intubation (n = 58)	No Difficult Intubation (n = 116)	P value
Number of Intubation Attempts			
1	24 (41.4%)	93 (80.2%)	<0.001*
2	15 (25.9%)	19 (16.4%)	
3	12 (20.7%)	4 (3.5%)	
4	4 (6.9%)	0 (0%)	
5 or more	3 (5.2%)	0 (0%)	
Intubation Technique			
Direct Laryngoscopy	12 (20.7%)	104 (89.7%)	<0.001*
Video Laryngoscopy	42 (72.4%)	12 (10.3%)	
Flexible Fiberoptic, Video Laryngoscopy	1 (1.7%)	0 (0%)	
Flexible Fiberoptic	3 (5.2%)	0 (0%)	

Data are presented as n (%). Mixed-effects ordinal and multinomial logistic regression were implemented to analyze ordinal and categorical variables, respectively, while accounting for matched sets from propensity score matching.

Models are adjusted for variables with SMD  $\geq 0.1$  in the matched cohort.

\* Statistically significant.



**Table 4**  
Analysis of Outcomes in the Matched Cohort.

Outcome Variable	Difficult Intubation (n = 58)	No Difficult Intubation (n = 116)	Adjusted Odds Ratio or Coefficient	95% CI	P value
Supplemental Oxygen	56 (96.6%)	111 (96.5%)	1.54	(0.30, 7.89)	0.606
Vasopressor Use	16 (27.6%)	19 (16.4%)	2.12	(0.99, 4.56)	0.054
Percent change in SpO <sub>2</sub>	-2.6 (-17.8, 0)	-2.1 (-8.2, 0)	-2.4	(-6.3, 1.6)	0.247
Percent change in HR	-11 (-22.7, -2.2)	-9.4 (-18.3, -0.9)	-0.3	(-6.9, 6.3)	0.922
Percent change in Systolic BP	-23 (-33.3, -13)	-20.4 (-34.5, -5.4)	-4.3	(-13.2, 4.7)	0.349
Percent change in Diastolic BP	-33.3 (-48.1, -14.9)	-32.8 (-46.2, -17.2)	0	(-8.7, 9.7)	0.999
Percent change in MAP	-28.8 (-40, -17)	-27.5 (-39.3, -14.6)	-1.8	(-11.4, 7.8)	0.708
Cardiac Arrest Time to Extubation (days)	0 (0%) 1.8 (0.7, 5.1)	0 (0%) 1.1 (0.4, 2.9)	0.8	(-0.1, 1.7)	0.088
Postop ICU LOS (days)	6 (1.9, 13.2)	3.9 (1.9, 8.9)	2.1	(-1.3, 5.5)	0.227
Postop Hospital LOS (days)	12.1 (6.1, 20.6)	7.9 (4.9, 12.9)	4	(1.3, 6.8)	0.004*
Had ORL follow-up**	2 (3.5%)	3 (2.6%)	3.65	(0.35, 37.9)	0.278
Airway anomalies	22 (37.9%)	34 (29.3%)	1.67	(0.84, 3.34)	0.144

Data are presented as n (%) or median (IQR).

Conditional logistic regression was implemented to analyze dichotomous outcomes while accounting for matched sets from propensity score matching.

Mixed-effects median regression was used to analyze continuous outcomes while accounting for matched sets from propensity score matching.

Models are adjusted for variables with SMD  $\geq 0.1$  in the matched cohort.

HR: Heart Rate, BP: Blood Pressure, MAP: Mean Arterial Pressure, ICU: Intensive Care Unit, LOS: Length of stay, ORL: Otolaryngology.

\* Statistically significant.

\*\* ORL follow up included: a flexible exam in 3 patients, a bronchoscopy in 1 patient and a consult with no additional procedure in 1 patient.

used to define DTI. DTI data prospectively entered into the institution specific PeDIR was used in our study. Apkek et al. defined DTI based on number of attempts, aids during intubation, and laryngoscopic view of 3 or 4. In that study 43.7% of difficult tracheal intubations were attributed to an anteriorly displaced larynx (grade 3 or 4 direct views in the Cormack and Lehane classification) and 50% of the DTIs occurred in children with other congenital anomalies [7]. In another study, a higher incidence of DTI in pediatric cardiac patients (4.6%) was attributed to nasopharyngeal intubation being the preferred intubation method and to the higher difficulty encountered in Down syndrome patients [11,12]. In our study, the incidence of airway anomalies was not different between patients with and without DTI.

In our study, an indirect intubation technique such as VL, flexible fiberoptic or a combination of both was more commonly used in patients with DTI. Early recognition of a DTI with rapid transition from direct to indirect laryngoscopy may be more effective in a pediatric DTI situation [6]. Studies comparing VL to the classic conventional laryngoscopy demonstrated a better glottic view, shorter time to intubate, less difficulty with intubation and decreased complication rate when using the VL [13–15]. Moreover, VL has been associated with higher first attempt intubation success in trainees when compared with DL [13,16,17].

DTI, whether anticipated or unanticipated is a challenging

management problem in children, and has been shown to increase the risk of perioperative respiratory complications and cardiac arrest in the pediatric population [4,6,18]. It has also been associated with high rates of failed intubation and a 30% incidence of severe complications, such as cardiac arrest and severe airway trauma, followed by pneumothorax, aspiration and death [6]. The Pediatric Difficult Intubation Registry (PeDIR) reports that 20% of children with difficult tracheal intubations suffered at least one complication, with cardiac arrest occurring in nearly 2% of the patients [6]. In addition, DTIs were associated with a higher occurrence of adverse events and oxygen desaturations according to a retrospective review of prospectively collected data on intubations performed in the Neonatal Intensive Care Unit (NICU) from the National Emergency Airway Registry for Neonates [19]. Data from the Pediatric Perioperative Cardiac Arrest (POCA) registry has shown that cardiac events leading to cardiac arrest occurred most commonly in children with CHD, while respiratory events mostly related to loss of airway patency were the most common cause of cardiac arrest in patients without heart disease [3]. It has been estimated that 75% of all critical pediatric perioperative adverse events are respiratory in nature with the major cause of hypoxia being inadequate ventilation or tube misplacement [2,20]. In our study, there were no cardiac arrests and no significant difference between patients with DTI and those without in terms of hemodynamic changes during induction. Our results may be explained by the fact that patients with CHD undergoing cardiac procedures are cared for by experienced pediatric cardiac anesthesiologists who are knowledgeable in cardio/respiratory physiology and management of hemodynamic lability while also facile in airway management. In fact, the experience of the provider was an important independent risk factor associated with a lower incidence of severe critical events according to the Anesthesia Practice In Children Observational Trial (APRICOT) study. That study demonstrated a significantly lower incidence of adverse cardiovascular events when comparing care by dedicated providers versus occasional providers [18]. Despite a higher number of tracheal intubation attempts in the DTI group, the absence of significant differences in hypoxemic events between the two groups suggests a good understanding of hemodynamic goals as well as expertise in handling and managing DTI with a rapid shift to mask ventilation between intubation attempts.

Children with CHD are at higher risk of perioperative adverse events than those without [3]. For instance, a diagnosis of CHD was associated with an incremental risk of mortality in children undergoing non cardiac surgery with a greatest incremental risk in neonates and infants [21]. These critical events related to perioperative cardiopulmonary instability and complications can lead to increased hospital LOS, and worsened outcomes [22]. Moreover, the presence of major airway anomalies and young age (<1 year) were found to be independently associated with an increased ICU LOS [23]. In our cohort, there was a significantly longer hospital but not ICU LOS for patients with DTI compared to patients without DTI. Despite being not statistically significant, we have observed higher odds of 1.54 and 2.52 in oxygen and vasopressor use respectively in the DTI than in the non-DTI group. Clinically, that is a significant difference with patients with DTI being twice as likely to receive vasopressor support as patients in the non-DTI group. In our study, the presence of airway abnormalities was not significantly different between the DTI and non-DTI groups, the median time to anesthesia ready and median time to extubation were not significantly higher in the DTI group. However, we acknowledge that anesthesia ready times are influenced by additional factors such as placement of arterial line and transesophageal echocardiography.

The primary limitations of this study are the use of retrospective data and the inherent bias related to missing data, variations in charting practice by individual providers, unrecorded or erroneously recorded diagnoses, and the preemptive and elective use of VL in anticipation of a DTI. Data related to residual cardiac disease and management in the ICU as well as procedures required within the same hospitalization, was not collected. Therefore, it is not possible to differentiate whether the

prolonged LOS is related to the difficult intubation or other post-operative non-airway events. The sample size of encounters following propensity score matching provides potentially limited statistical power for detecting small to moderate yet clinically meaningful differences between those with versus without DTI.

In conclusion, despite the increased risk of perioperative events, the higher number of intubation attempts, and the increase in overall hospital LOS in patients with CHD and DTI, our study did not show any major differences in the immediate peri-intubation period in terms of hemodynamic stability, or occurrence of cardiac adverse events in patients with and without DTI. This risk can be mitigated by a good understanding of cardiac physiology and management of the hemodynamics, and the early use of an indirect intubation technique to maximize first attempt success.

## Funding

This study was solely supported by the Department of Anesthesiology, Critical Care and Pain Medicine at Boston Children's Hospital, Harvard Medical School.

## Author statement

Carine Foz, MD- This investigator participated in the conception and design of the study; was responsible for data acquisition, and interpretation; and drafting of the manuscript. She has approved the manuscript for submission and publication.

Steven J. Staffa, MSc- This investigator/biostatistician performed all statistical analyses and made a substantial contribution to the conception and design of the study, analysis and interpretation of the data, and drafting of the manuscript. He has approved the manuscript for submission and publication.

Raymond Park, MD- This author made a significant contribution to data collection and drafting of the manuscript. He has approved the manuscript for submission and publication.

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Meena Nathan, MD MPH- This author made a significant contribution to data collection and drafting of the manuscript. She has approved the manuscript for submission and publication.

James A. DiNardo, MD- This author made a significant contribution to data collection and drafting of the manuscript. He has approved the manuscript for submission and publication.

Viviane G. Nasr, MD MPH- This investigator was responsible for the conception and design of the study; data acquisition, analysis, and interpretation; and drafting of the manuscript. She has approved the manuscript for submission and publication.

## Declaration of Competing Interest

No conflict of interest.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jclinane.2021.110565>.

[org/10.1016/j.jclinane.2021.110565](https://doi.org/10.1016/j.jclinane.2021.110565).

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