Incidence, impact and indicators of difficult intubations in the neonatal intensive care unit: a report from the National Emergency Airway Registry for Neonates

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ABSTRACT
Objective To determine the incidence, indicators and clinical impact of difficult tracheal intubations in the neonatal intensive care unit (NICU).

Design Retrospective review of prospectively collected data on intubations performed in the NICU from the National Emergency Airway Registry for Neonates.

Setting Ten academic NICUs.

Patients Neonates intubated in the NICU at each of the sites between October 2014 and March 2017.

Main outcome measures Difficult intubation was defined as one requiring three or more attempts by a non-resident provider. Patient (age, weight and bedside predictors of difficult intubation), practice (intubation method and medications used), provider (training level and profession) and outcome data (intubation attempts, adverse events and oxygen desaturations) were collected for each intubation.

Results Out of 2009 tracheal intubations, 276 (14%) met the definition of difficult intubation. Difficult intubations were more common in neonates <32 weeks, <1500 g. The difficult intubation group had a 4.9 odds ratio (OR) for experiencing an adverse event and a 4.2 OR for severe oxygen desaturation. Bedside screening tests of difficult intubation lacked sensitivity (receiver operator curve 0.47–0.53).

Conclusions Difficult intubations are common in the NICU and are associated with adverse event and severe oxygen desaturation. Difficult intubations occur more commonly in small preterm infants. The occurrence of a difficult intubation in other neonates is hard to predict due to the lack of sensitivity of bedside screening tests.

INTRODUCTION
Tracheal intubation (TI) is one of the most commonly performed procedures in the neonatal intensive care unit (NICU).1 Adverse events, oxygen desaturations and failed attempts are common during the procedure. Tracheal intubation adverse events (TIAEs) occur in 20%–40% of neonatal TIs.2 3 Severe oxygen desaturations (≥20% decrease in blood oxygen saturation [SpO2]) occur in approximately 50% of neonatal TIs.4 Overall, first attempt success rates for neonatal TI are approximately 50%, with variation depending on the provider type.4–9 First attempt success rates are higher when using videolaryngoscopy—ranging from 63% to 72%—but are still suboptimal.10 11 Failed TI has been linked to intraventricular haemorrhage and neurodevelopmental impairment in premature infants.12 13 These data suggest that additional work is needed to make neonatal TI safer.14 Accurately predicting which neonates will be difficult to intubate may improve safety. Recent studies have examined the utility of fetal biometric parameters to predict difficult TI in periviable neonates at birth.15 However, no prior studies have examined the utility of bedside screening tests of difficult intubation in the NICU.

In the adult and paediatric intensive care unit (ICU), a ‘difficult intubation’ is defined as one requiring three or more laryngoscopic attempts by an experienced provider (eg, not residents in training).16 17 The reported incidence of difficult TIs...
in the adult ICU is 8%-11%.\textsuperscript{16} The reported incidence of difficult TIs in the paediatric ICU is 9%-17.\textsuperscript{17} In the adult and paediatric ICU, patients with difficult TIs have significantly more adverse events and oxygen desaturations than those with non-difficult TIs. The incidence, impact and indicators of difficult TI in the NICU are unknown.

The primary aims of this study were to: (1) determine the incidence of difficult TIs in the NICU, (2) quantify the clinical impact of difficult TIs and (3) examine the utility of bedside screening tests of difficult neonatal TI. We hypothesised that difficult TI would be common in the NICU, that difficult TIs would be associated with TIAEs and oxygen desaturations and that bedside screening tests could predict the occurrence of difficult TI.

**METHODS**

**Study design**

This was a retrospective cohort study using prospectively collected data from the National Emergency Airway Registry for Neonates (NEAR4NEOS) database. NEAR4NEOS was established in 2014 with the goal to improve neonatal intubation safety and quality. There were 10 academic NICUs contributing data to the NEAR4NEOS at the time of the study. The current study includes data on all neonates who underwent TI in the NICUs at each of the sites between 1 October 2014 and 31 March 2017.

**Data collection**

A standardised NEAR4NEOS data collection tool was used to collect patient, practice, provider and outcome data on all neonatal TIs performed at each participating NICU. The institutional review board at each participating site approved the study or granted a waiver of informed parental consent for data collection and analysis. Standardised NEAR4NEOS operational definitions were used to ensure consistency of data capture across the participating sites. Each site developed a site-specific compliance plan to ensure TI capture of greater than 95%, as well as accurate and timely data entry. Patient data included gestational age and weight (both at birth and on the day of TI), comorbidities, the indication for TI and the presence or absence of bedside screening tests for difficult TI (reviewed below). Practice data included the method of intubation and all medications used. Provider data included the laryngoscopist’s training level and profession. Outcome data included the number of intubation attempts, success or failure for each attempt, TIAEs (defined below) and changes in oxygen saturations (SpO2) during TI. These data were collected by the care team at the time of TI on a NEAR4NEOS data form. These data were then entered into a password-protected secure Research Electronic Data Capture system hosted by the Data Coordinating Centre at the Children’s Hospital of Philadelphia.\textsuperscript{18}

**Inclusion and exclusion criteria**

Only TIs in the NICU were included in the analyses. Intubations performed in the delivery room were excluded due to difficulty in evaluating bedside screening tests of difficult TI at the time of birth, as well as limitations in collecting the oxygen saturation data in that group. TIs for elective endotracheal tube changes in the NICU were also excluded. For TIs requiring more than one method of approach (defined as ‘Course’ in NEAR4NEOS operational definitions), only the first course was included in the analyses.

**Difficult TI definition**

We defined a ‘difficult neonatal TI’ as one requiring three or more intubation attempts by a non-resident provider. This means that a ‘difficult TI’ would require a minimum of two failed attempts by non-resident providers (with the third attempt being successful). This definition was based on the standard definitions of difficult TI used in the adult and paediatric ICU.\textsuperscript{16} 17 There was no common algorithm for the escalation of TI approach (eg, change from direct laryngoscopy to videolaryngoscopy) among participating centres. When the first course (method of approach) failed, or non-laryngoscopy approach was used (such as fibreoptic bronchoscopy), the TI was also considered as difficult neonatal TI.

**TI adverse events**

TIAEs were classified into two categories: severe and non-severe.\textsuperscript{2} Severe TIAEs included oesophageal intubation with delayed recognition, emesis with witnessed aspiration, hypotension requiring intervention (fluid and/or vasopressors), laryngospasm, malignant hyperthermia, pneumothorax/pneumomediastinum and cardiac arrest. Cardiac arrest was defined as loss of perfusion, or severe bradycardia, requiring chest compressions for ≥ 1 min.

Non-severe TIAEs included oesophageal intubation with immediate recognition, mainstem bronchial intubation, epistaxis, lip trauma, gum or oral trauma, emesis without aspiration, hypertension requiring therapy, pain and/or agitation requiring additional medication and causing a delay in intubation and dysrhythmia. Dysrhythmia included bradycardia to less than 60 beats per minute or arrhythmia requiring treatment.

Oxygen desaturations during TI were determined using the highest SpO2, measured immediately prior to intubation (eg, after preoxygenation) and the lowest SpO2 during the intubation. The NEAR4NEOS programme defines ‘severe’ oxygen desaturation as a ≥ 20% decrease in SpO2 from the pre-TI value.\textsuperscript{2} If either the highest or lowest SpO2 were not recorded, those data were excluded from the analysis.

**Bedside screening tests of difficult intubation**

A predefined set of bedside screening tests of difficult TI were included on the NEAR4NEOS data collection form. The predictors were based on those used in the adult and paediatric ICU populations.\textsuperscript{16} 17 The presence, or absence, of each screening test in the neonate undergoing TI was determined at the time of TI by the intubating team and was recorded on the NEAR4NEOS data form. The screening tests included: a known prior history of difficult airway, upper airway obstruction, limited mouth opening, limited neck extension, micrognathia, midfacial hypoplasia, cleft palate and a short thyromental distance. Where possible, objective measures of the bedside screening tests were used, including, for example, upper airway obstruction defined as an anatomical barrier to visualise glottic opening, widest mouth opening defined as how many patient’s fingers fit between gum/incisors and thyromental space defined as how many patient’s fingers fit between chin and thyroid cartilage.

**Statistical analysis**

Descriptive statistics were presented as numbers and percentages. Non-parametric data were presented as a median and IQRs. The relationship between patient demographics and the occurrence of a difficult TI was analysed using a Wilcoxon rank-sum test. The relationship between
the patient, provider and practice characteristics with the occurrence of difficult TI was analysed using univariate analysis with the χ², or Fisher’s exact test for dichotomous variables, or Wilcoxon rank-sum test for numeric variables. The utility of bedside screening tests of difficult TI was evaluated by calculating the sensitivity, specificity, positive predictive value, negative predictive value and area under the receiver operator curve (ROC) for each. The clinical impact of difficult TI was assessed by univariate analysis with the occurrence of severe and non-severe TIAEs and severe oxygen desaturation. A p value <0.05 was considered significant. Statistical analysis was performed using STATA V.14.0.

### RESULTS

Data on 3023 TIs from 10 academic NICUs were collected during the study period. Of those, 1014 TIs did not meet inclusion criteria (figure 1). A total of 2009 TI encounters were analysed. Of those 2009 neonatal intubations, 276 (14%) met the definition of difficult TI, and 1733 (86%) did not meet the definition.

Patient characteristics are provided in table 1. Difficult intubations were more common in neonates <32 weeks corrected gestation and <1500 g at the time of TI. The only comorbidity associated with difficult TI was sepsis (p=0.02). Indications for intubation associated with difficult TIs included intubation for surfactant administration (p=0.02) and intubation for airway obstruction (p=0.03).

Provider and practice characteristics are provided in table 2. The most common first providers to perform TI in neonates in the difficult TI group were neonatal fellows (48.9%). The difficult TI group received less sedation/analgesia and paralytic medications prior to intubation as compared with non-difficult TI group (p=0.03 and p<0.001). Videolaryngoscopy was used less commonly in the difficult TI group (p<0.001).

Neonates in the difficult TI group experienced more TIAEs and severe oxygen desaturations during intubation (table 3). In the difficult TI group, the OR for experiencing an adverse event was 4.9 (95% CI 3.7 to 6.4; p<0.0001) and the OR for severe desaturation was 4.1 (95% CI 3.0 to 5.5; p<0.001).

The value of bedside screening tests for difficult TI are provided in table 4. Upper airway obstruction, a known history of difficult airway, micrognathia, limited mouth opening, limited neck extension, cleft palate and short thyromental distance were

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**Figure 1** Study flow diagram. NICU, neonatal intensive care unit.
all more common in the difficult TI group (p=0.03 to <0.001). The sensitivity, positive predictive value and area under the ROC for all screening tests of difficult TI were poor. 

**DISCUSSION**

We analysed the NEAR4NEOS database to determine the incidence of difficult TIs in the NICU, quantify the clinical impact of difficult TIs and examine the utility of bedside predictors of difficult neonatal TI. We found that 14% of intubations in the NICU met our definition of ‘difficult’. Difficult TIs were associated with the higher occurrence of adverse events and oxygen desaturations. Bedside screening tests of difficult TI had little value to predict the occurrence of a difficult TI. To the authors’ knowledge, this is the first report to examine difficult TI in the NICU.

The first aim of this study was to determine the incidence of difficult TIs in the NICU. We found that 14% (276 of 2009) of intubations in the NICUs we studied were difficult TIs. This incidence is higher than in prior multicentre studies reports from the adult and paediatric ICU.16 17 We believe this difference fundamentally comes from our study population. Inherently, the airway features in neonatal population are different from adult and paediatric population. However, we also found that difficult TIs were more frequently performed by fellows and less frequently performed with video laryngoscopy and premedication. The association between fellows as first laryngoscopist and difficult TI may be explained by experience. Fellows, particularly early on, may have little experience in performing TIs in neonates, certainly less than that of a consultant/attending physician. Video laryngoscopy was only used in 13% of difficult TIs and in 30% of non-difficult TIs. Video laryngoscopy has been associated with higher first attempt intubation success in trainees when compared with direct laryngoscopy.19 It is possible that higher use of video laryngoscopy in adult and paediatric TI studies may be associated with higher TI success and thus with lower incidence if difficult TI in their population. Future studies are needed whether video laryngoscopy will decrease number of TI attempts and difficult TIs. Analgesia/sedation was given in 65% of non-difficult intubations and 58% of difficult intubations; and paralytics were given in 50% and 23% of cases. This means that more than a third of the time, premedication was not used. Premedication has been associated with increase TI success rates.2 These therefore, is the possibility that the prevalence of difficult intubation could be—at least partly—explained by insufficient use of premedication. Given the higher incidence of difficult TI in the NICU, we believe that specific attention should be paid to improving neonatal TI safety. This includes careful consideration of the first laryngoscopist, the device and premedication.24

The second aim of this study was to examine the clinical impact of difficult neonatal TI. We found that TIs that met the definition of ‘difficult’ had more TIAEs and severe desaturations. In the difficult TI group, the OR for experiencing an adverse event was 4.9, and the OR for severe desaturation was 4.1. This suggests that the definition we used was clinically meaningful. We believe establishing this definition of difficult neonatal TI sets the stage for future studies in this area and may help NICUs develop quality improvement approaches to address difficult neonatal TIs. The Paediatric Difficult Intubation registry recommends that the number of laryngoscopy attempts is limited to two or less and advocates for quickly transitioning to direct intubation techniques when direct laryngoscopy fails after two attempts.19 One of the NEAR4NEOS study sites has established a difficult airway pathway in which two failed TI attempts by an experienced practitioner triggers the activation of an airway response team that includes an anaesthesiologist, an otolaryngologist and a respiratory therapist.20

The third aim of this study was to examine the utility of bedside screening tests of difficult neonatal TI. We found that difficult TIs occurred more commonly in younger and smaller patients. Prior reports from the paediatric ICU have found similar results.17 The reason why younger and smaller patients are more difficult to intubate cannot be determined from the results of this study. However, the smaller size of the airway, proportionately larger head, more cephalad position of the larynx, proportionately larger tongue and the large and floppy epiglottis are all potential factors.21 22

We found that the sensitivity, positive predictive value and area under the ROC for all the bedside screening tests

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Provider and practice characteristics stratified by intubation difficulty</th>
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<tr>
<td>Provider and practice characteristic</td>
<td>Non-difficult intubation (n=1733)</td>
</tr>
<tr>
<td>First intubator</td>
<td></td>
</tr>
<tr>
<td>Neonatology fellow, n (%)</td>
<td>474 (27)</td>
</tr>
<tr>
<td>Nurse practitioner/physician assistant/hospitalist</td>
<td>698 (40)</td>
</tr>
<tr>
<td>Paediatric resident</td>
<td>266 (15)</td>
</tr>
<tr>
<td>Neonatology attending</td>
<td>122 (7)</td>
</tr>
<tr>
<td>Respiratory therapist</td>
<td>44 (3)</td>
</tr>
<tr>
<td>Other</td>
<td>129 (7)</td>
</tr>
<tr>
<td>Device used</td>
<td></td>
</tr>
<tr>
<td>Direct laryngoscope</td>
<td>1353 (78)</td>
</tr>
<tr>
<td>Videolaryngoscope</td>
<td>380 (30)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Medications given</td>
<td></td>
</tr>
<tr>
<td>Analgesic/sedative</td>
<td>1125 (65)</td>
</tr>
<tr>
<td>Paralytic*</td>
<td>865 (50)</td>
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</tbody>
</table>

*Ten neonates were reported to receive paralysis only. From the data, it is unclear whether these neonates were already sedated before TI procedure was initiated.

<table>
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<tr>
<th>Table 3</th>
<th>Adverse events in neonates with difficult intubation*</th>
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<tbody>
<tr>
<td>Adverse events</td>
<td>Non-difficult intubation (n=1733)</td>
</tr>
<tr>
<td>Any tracheal intubation adverse event, n (%)</td>
<td>241 (14)</td>
</tr>
<tr>
<td>Severe tracheal intubation adverse events, n (%)</td>
<td>51 (3)</td>
</tr>
<tr>
<td>Non-severe tracheal intubation adverse events, n (%)</td>
<td>210 (12)</td>
</tr>
<tr>
<td>Severe desaturation, n (%)†</td>
<td>732 (42)</td>
</tr>
</tbody>
</table>

*Severe desaturation was defined as a drop in SpO2 by >20% from highest SpO2 before intubation to lowest SpO2 during intubation attempt.
†Difficult intubation was defined as three or more failed intubation attempts by a non-resident provider.
of difficult TI we studied were poor. Therefore, their clinical utility is questionable. The screening tests we chose were based on those used in paediatric and adult patients. This is the first report of using these screening tests in neonates. As they were not developed specifically for neonates, there is some inherent difficulty in applying the screening tests in the neonatal population, particularly in very preterm babies. However, the lack of consistent strong predictors for difficult TI is also an issue with paediatric and adult TI.\textsuperscript{22–24} A recent Cochrane review of adult TI cautioned that ‘standard bedside airway examination tests should be interpreted with caution, as they do not appear to be good screening tests’.\textsuperscript{24} Based on our results, we suggest that gestational age, weight, indication for intubation and bedside screening tests of difficult TI all be considered when deciding who will perform an intubation in the NICU. This is especially important in extremely premature neonates where failed intubations have been associated with intraventricular haemorrhage and impaired neurodevelopmental outcomes.\textsuperscript{12 13} Based on the risk of difficult TI in small premature neonates, and the potential for adverse events, it seems prudent to have more experienced providers intubate those patients. Consideration should also be given to using videolaryngoscopy and premedication with paralysis as these have both been linked to greater first attempt success and fewer adverse events.\textsuperscript{10 11 25 26}

This study has several limitations. First, some readers may not support our definition of difficult TI as one requiring three or more intubation attempts by a non-resident provider. Some would argue that a neonatal fellow early in training, or a new nurse practitioner, is still a novice intubator and no different than a resident. We believe that creating any arbitrary cut point of experience (eg, fellows with 6 months of training) has inherent limitations. The definition we used is the same as that used in the adult and paediatric ICU.\textsuperscript{16 17} We chose to use that definition to ensure a consistent definition across studies and the ability to allow analysis across the different ICU populations. Second, the intubation data used in this analysis was self-reported by the medical teams at the time of intubation. This places our results at risk for reporting bias. Third, the bedside screening tests for difficult TI were determined by the medical teams at the time of the intubation. Therefore, the accuracy of the assessments of each screening test was dependent on the team’s review of the patient’s history and accurate assessment of the physical exam features. Inaccurate determination of the screening tests could bias our results. Third, this study was conducted on a cohort of neonates from 10 academic (non-community) NICUs, and neonates intubated in the delivery room were not included. This may limit the generalisability of our findings. Fourth, the data here represents the number of TIs that met our definition, not the number of neonates. It is possible that some neonates were repeatedly intubated and were counted more than once in this study dataset. Finally, we were not able to obtain long-term data on the outcomes of neonates with and without difficult TIs. Additional studies are needed to determine the impact of difficult TI on long-term neonatal outcomes.

CONCLUSION
The occurrence of difficult TI in the NICU was 14%, which is higher than in the paediatric and adult ICUs. The occurrence of difficult TIs was strongly associated with adverse events and severe oxygen desaturations. Difficult TIs occurred more common in small premature neonates. The ability of bedside screening tests to predict difficult TI was poor. These results suggest that when intubating neonates, healthcare teams should carefully consider who will perform TI, as well as what medications and devices should be used in order to improve neonatal TI safety.

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