Diagnostic Accuracy of Point-of-Care Ultrasound Compared to Standard-of-Care Methods for Endotracheal Tube Placement in Neonates

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Abstract

Introduction: Point of care ultrasound (POCUS) is a useful tool to determine endotracheal tube placement; however, few studies have compared it with standard methods of confirmation. We evaluated the diagnostic accuracy of POCUS and time-to-interpretation for correct identification of tracheal versus esophageal intubations compared to a composite of standard-of-care methods in neonates. Methods: A cross-sectional study was conducted in the Neonatal Intensive Care Unit (NICU) at Aga Khan University Hospital Karachi Pakistan. All required intubations were performed as per NICU guidelines. The ETT placement was determined using standard-of-care methods (auscultation, colorimetric capnography, and chest X-ray) by a clinical team, and simultaneously by POCUS. Timings were recorded for each method by independent study staff. Results: A total of 348 neonates were enrolled in the study. More than half (58%) of intubations were in an emergency scenario. Using an expert as the reference standard, POCUS user interpretation showed 100% sensitivity and 94% specificity. We found a 99.4% agreement (Kappa: 0.96; p<0.001) between the POCUS user and expert. Diagnostic accuracy of POCUS compared with at least two standard-of-care methods demonstrated 99.7% sensitivity, 91% specificity, and 98.9% agreement (Kappa:0.93; p<0.001). The median time required for POCUS interpretation was 3.0 (IQR 3.0 -4.0) seconds for tracheal intubation. The time recorded for auscultation and capnography was 6.0 (IQR 5.0 -7.0) and 3.0 (IQR 3.0-4.0) respectively. Conclusion: POCUS is a rapid and reliable method of identifying ETT placement in neonates. Early and correct identification of airway management is critical to save lives and prevent mortality and morbidity.

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Running Title: Ultrasound guided Endotracheal Intubation in Neonates

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Keywords: Point of care ultrasound, neonates, endotracheal tube, intubation.

Abstract

Introduction: Point of care ultrasound (POCUS) is a useful tool to determine endotracheal tube (ETT) placement; however, few studies have compared it with standard methods of confirmation. We evaluated the diagnostic accuracy of POCUS and time-to-interpretation for correct identification of tracheal versus esophageal intubations compared to a composite of standard-of-care methods in neonates.

Methods: A cross-sectional study was conducted in the Neonatal Intensive Care Unit (NICU) at Aga Khan University Hospital Karachi Pakistan. All required intubations were performed as per NICU guidelines. The ETT placement was determined using standard-of-care methods (auscultation, colorimetric capnography, and chest X-ray) by a clinical team, and simultaneously by POCUS. The clinical team was blinded to the POCUS images. Timings were recorded for each method by independent study staff.

Results: A total of 348 neonates were enrolled in the study. More than half (58%) of intubations were in an emergency scenario. Using an expert as the reference standard, POCUS user interpretation showed 100% sensitivity and 94% specificity. We found a 99.4% agreement (Kappa: 0.96; $p<0.001$) between the POCUS user and expert.

Diagnostic accuracy of POCUS compared with at least two standard-of-care methods demonstrated 99.7% sensitivity, 91% specificity, and 98.9% agreement (Kappa:0.93; $p<0.001$). The median time required for POCUS interpretation was 3.0 (IQR 3.0 -4.0) seconds for tracheal intubation. The time recorded for auscultation and capnography was 6.0 (IQR 5.0 -7.0) and 3.0 (IQR 3.0-4.0) respectively.

Conclusion: POCUS is a rapid and reliable method of identifying ETT placement in neonates. Early and correct identification of airway management is critical to save lives and prevent mortality and morbidity.

Introduction

The newborn period, in the first 28 days of life, is the highest risk period in a child's life. Currently, there are an estimated 2.5 million global newborn deaths annually, representing nearly half of all deaths in children under the age of five.[1] Although this represents significant progress from 1990, when there were 5 million newborn deaths annually, rapid progress is still needed to achieve the Sustainable Development Goals (SDGs).[2] SDG three aims to reduce neonatal mortality rate (NMR) to 12 deaths per 1,000 live births in all countries.[3] Unfortunately, if current trends continue, it is estimated that 60 countries will miss this target by 2030.[2]

The burden of neonatal deaths is not equal across the world, and the vast majority occur in low- and middle income-countries (LMICs), particularly in sub-Saharan Africa and Central and Southern Asia. Pakistan had 251,000 neonatal deaths in 2018 and an estimated NMR of 42.[2] Half of all under-five deaths occurred in just five countries, including Pakistan.[2] To decrease the newborn deaths, the main causes of these deaths must be addressed: preterm births, intrapartum-related complications (birth asphyxia), and infections.

Intrapartum-related complications, if not fatal, are also a leading cause of long-term morbidity. Lack of oxygen to the brain in the critical few first minutes of life can result in hypoxic-ischemic encephalopathy, cerebral palsy, developmental delays, and behavioral problems.[4,5] To prevent these deaths, misclassified stillbirths, and significant morbidity, a skilled birth attendant should be present at every birth to provide immediate care to the newborn including resuscitation.[6] In facilities with neonatal intensive care units (NICU), newborn resuscitation also includes endotracheal intubation and mechanical ventilation. Unfortunately, it is common for the endotracheal tube (ETT) to be misplaced into the esophagus, depriving the lungs of oxygen at a critical period. This is less likely with providers who have more experience but has been reported to be as high as 19% in a study of varied skill level providers in 5 NICUs.[7]

To determine proper position of the ETT, several techniques can be used. Traditional clinical signs include auscultation of bilateral breath sounds, absence of breath sounds in the epigastrium, condensation in the ETT during expiration, an increase in heart rate, and chest wall movement.[8] Capnography is also commonly used which detects exhaled CO_2, and the combination of clinical signs and capnography is currently recommended for ETT confirmation in international neonatal resuscitation guidelines.[9]CO_2 detection devices may, however, result in false negative results with infants in severe respiratory failure or without cardiac output.[10,11] Chest X-ray (CXR) is the most common method of confirming ETT position; however, it requires a significant amount of time, resources, and exposes the neonate to radiation.[12]

Point of care ultrasound (POCUS) is a powerful tool that has been adapted for many uses in neonates. International evidence-based guidelines from the European Society of Pediatric and Neonatal Intensive Care determined that lung POCUS, for example, is helpful for respiratory distress syndrome (RDS), pneumonia, lung aeration, meconium aspiration syndrome (MAS), bronchiolitis, pneumothorax, chest tube insertion, pleural effusions, thoracentesis, lung edema, and atelectasis.[13] POCUS can also be helpful in determining esophageal versus tracheal ETT placement and has been shown to be faster than auscultation and capnography in adults.[14] In children, the sensitivity and specificity for POCUS ETT placement has been shown to be 98.9% and 94.1%, respectively.[15] In neonates, POCUS has mainly been used in stable intubated NICU patients to determine ETT depth,[16-20] and only few studies have compare tracheal POCUS with standard methods of intubation confirmation.[21,22]

Our group previously described a novel ultrasound simulator to train health care providers in distinguishing tracheal versus esophageal ETT placement.[23] Results of the training sessions using this simulator demonstrated decreased interpretation time and improved POCUS interpretation accuracy with repeat testing among novice users.[24] In this study, we present the findings of the application of this training program on neonates undergoing intubation, both in terms of accuracy and a time comparison to standard-of-care methods.

Methods

Study Overview

This was an observational diagnostic accuracy study that took place at the Aga Khan University Hospital (AKUH) in Karachi Pakistan, in collaboration with researchers at the Hospital for Sick Children in Toronto, Canada. AKUH is an academic teaching hospital with over 5000 deliveries per year and a level III NICU. Phase 1 of this study was completed in 2018 where a POCUS expert trained 60 health care providers on differentiating esophageal versus tracheal intubations using a novel ultrasound simulator.[25] This included an objective structured assessment of technical skills (OSATS), ten rounds of simulator-based testing, and practice on stable ventilated neonates in the NICU. In phase 2, reported here, these providers used POCUS for tracheal versus esophageal placement confirmation of ETTs in both the NICU and the labour room/operating room (LR/OR) for newborns requiring intubation. This was concurrent with standard-of-care methods including auscultation, colorimetric capnography, and CXR. Phase 2 of this study took place from July 2018 to June 2019.

Patient Population

During phase 2 of the study, newborns requiring intubation were eligible for enrollment. Since emergency intubation is time-sensitive, we applied a deferred consent procedure where caregivers were informed about the study protocol and procedure after the patient was stabilized. If consent was obtained, participants were included in the study. In case of refusal, images were discarded. Participants were excluded if they had abnormal anatomy of the oropharynx or airway.

Equipment

A Phillips Lumify USB ultrasound unit was used for the duration of the study. The L12-4 linear array transducer was used, set at a depth of 2.5 cm, and was connected to an Android Version 4.5 tablet computer. Two POCUS machines were available to health care providers: one in the NICU and the other in the LR/OR.

POCUS Assessment

Clinical teams, POCUS users, and research assistants were available to provide 24-hour coverage in the unit. The clinical team included an attending neonatologist, a neonatal fellow, a pediatric resident, and a staff nurse. This team assessed each newborn per standard neonatal resuscitation guidelines and determined if intubation would be required. If a neonate required intubation, it was performed by the resident or fellow as per NICU clinical guidelines and the placement of the ETT was determined using standard-of-care methods (auscultation, colorimetric capnography and CXR).

In addition to the clinical team, a POCUS user and a study research assistant were available during the intubation process. The research assistant operated independently of both the POCUS user and the clinical team. The POCUS user, following intubation, completed a POCUS examination to determine ETT placement and announced "complete" only for timing purposes. This assessment (POCUS study) was also recorded as a video. The POCUS assessment was not available to the clinical team to ensure blinding. The routine assessment of identifying placement of the endotracheal tube was carried out as per protocol without any interruption (auscultation, capnography, chest X-ray).

The POCUS user was given a maximum of 30 seconds to complete the POCUS examination, after which time the assistant notified them that their time was complete and the assessment stopped. The research assistant, who stayed in the room for the duration of the intubation, recorded the time it took for ETT confirmation from both the POCUS user and by the clinical team. If more than one intubation attempts were required for a patient, POCUS was only performed on the first attempt.

Data management and quality control

Detailed patient data including demographics, APGAR scores, reason for intubation, and patient outcome at 30 days of life were collected using the patient data collection form. This form was also used to collect data on the clinical and POCUS assessments of the ETT position (Appendix 1). After the data was collected it was transcribed into REDCap.

For quality assurance, the first 200 scans completed by POCUS users in this study were sent for review to a non-AKUH POCUS expert not involved in the study intervention. These files were deidentified and sent in Mpeg4 video format using a secure online file transfer program. The expert rated both the image quality and the interpretation of the video files.

Main Outcomes

The primary outcome of this study was diagnostic accuracy of POCUS for identifying tracheal versus esophageal intubations in newborns compared to a composite of standard-of-care methods. The secondary outcome was the time difference in determining ETT position between the POCUS user and standard-of-care methods. The tertiary outcomes were the agreement between POCUS users and standard-of-care methods, the level of agreement between POCUS users and a POCUS expert, and the level of agreement between the POCUS expert and standard-of-care methods.

Sample Size

Of the 5000 deliveries per year at AKUH, approximately 12% (600) are admitted to the NICU and approximately 70% (420) of these require intubation. Using a conservative rate of 5% for esophageal intubation, the sample size was calculated for the primary outcome using a two-sided equivalence test for correlated proportions. To achieve 80% power at a 5% significance level, a total of 222 participants were needed for the primary outcome. Details of the secondary and tertiary outcome sample size calculations are available in the protocol paper.[23]

Statistical Analysis

Data was analyzed using STATA version 16. Data was reviewed for any missing information, illegible responses, and any other inconsistencies before the analysis. Qualitative data were reported as frequencies and percentages. Quantitative data were reported as means with standard deviations and/or medians with inter quartile ranges. After checking normality of qualitative data, we carried out Wilcoxon signed-rank test to analyze the median significant difference of POCUS interpretation time with auscultation time, CO2 detection time, and chest X-ray time. Specificity statistical analysis was carried out between POCUS users and expert interpretation. Kappa statistical analysis was applied to check agreement between the POCUS expert and participant observation. P-values < 0.05 were considered as significant.

Results

Altogether, 20 health care providers including Neonatal Fellow/Neonatal attending physicians (40%), postgraduate medical trainees (25%) and senior nursing staff (35%) performed POCUS on neonates requiring intubation. All neonatal health care providers were trained and certified for airway POCUS (Table 1).

A total of 348 neonates were enrolled in the study from July 2018 to June 2019. The mean gestational age of newborns was 32.6 (SD$\pm$ 4.8) weeks. More than half (58%) of intubations were in an emergency scenario while others were elective for procedures under anesthesia. The major reasons of emergent intubations included hemodynamic compromise (31.2%), respiratory failure (29.7%) and administration of surfactant (20.8%). The most common medical diagnosis of enrolled participants was respiratory distress syndrome, which accounted for 199 (57.2%) neonates. The mortality among the entire cohort was 23.6% (Table 2).

In total, 318 (91.3%) were tracheal intubations while 30 (8.7%) were esophageal intubation as proven by at least two standard methods (auscultation, capnography, and chest radiography). Moreover, 266 (76.4%) intubations were confirmed by all three methods. X-ray was not available for 82 (23.6%) intubations.

We evaluated the diagnostic accuracy of POCUS user interpretation compared with at least two standard-of-care methods. Altogether, 344 POCUS user interpretations were consistent with standard of care; however, three were reported as false positive and one as false negative. Therefore, the sensitivity and specificity were 99.7% and 91%, respectively, with 98.85% agreement (Kappa: 0.93; $p < 0.0001$).

The median time required for POCUS interpretation was 3.0 seconds (IQR: 3.0-4.0) with tracheal intubation as 3.0 seconds (IQR: 3.0-4.0) and esophageal intubations as 4.5 seconds (IQR: 3.0-8.0). Similarly, the recorded time measured for auscultation and capnography was 6.0 seconds (IQR: 5.0-7.0) and 3.0 seconds (IQR: 3.0-4.0), respectively. When applying the Wilcoxon signed-rank test to the time required for gold standard methods, auscultation and X-ray times were significantly higher than to POCUS interpretation time. However, CO_2 detector time (p-value: 0.594) was similar to POCUS interpretation time (Table 4).

We also compared the interpretation of POCUS images by user in the NICU and the POCUS expert and found the same interpretation as the expert assessment (97.7% images). Only two images were inconsistent between user and expert interpretations. This analysis yielded 94% specificity and 100% sensitivity. Furthermore, there was 99.4% agreement (Kappa: 0.96; $p < 0.0001$) between the POCUS user and expert.

Discussion

This study found that simulator-based training for identification of endotracheal tube placement was efficacious in training novice users with high sensitivity and specificity. Our study showed POCUS to be an accurate and rapid method to detect correct position of the endotracheal tube (3.0 (IQR 3.0-4.0) seconds).

The majority of intubations were for emergent causes including respiratory failure, surfactant administration, and hemodynamic compromise; similar to those reported by Foglia et al. in 2019.[26] Another study also listed reasons for ETT intubations such as prematurity (57.8%), respiratory failure (24.3%), life-threatening apneas (13.4%), and re-intubation after accidental displacement of ETT (4.5%).[27]

Several methods are considered as standard-of-care methods for ETT position confirmation including bilateral chest auscultation, capnography, and chest radiography. Studies in adults have demonstrated disposable CO_2 detectors to be highly sensitive and specific for confirmation of ETT placement and reported a sensitivity and specificity of 91% and 100% when compared to clinical examination.[27] Likewise, POCUS sensitivity and specificity for identification of an ETT was reported to be 0.98 (95% CI 0.97 to 0.99) and 0.98 (95% CI 0.95 to 0.99), respectively in a meta-analysis of f 323 adult intubations . They recorded a sensitivity of 91% and specificity of 97% of POCUS compared to standard methods.[28] Similarly another meta-analysis reported sensitivities of 93-98% and specificities of 97-98% for POCUS.[29]

In contrast to adult POCUS, the use of this modality for ETT placement is somewhat scarce in pediatrics. Chou et al. in 2013 reported a sensitivity and specificity of 100% in children that underwent resuscitation and intubation.[30] In our study, the sensitivity and specificity compared to standard care was 99.7% and 91.7%, respectively.

The time it takes to confirm ETT placement is critical regardless of the method chosen. Chest auscultation can be unreliable in a noisy environment during resuscitation and takes approximately 77 seconds to appreciate audible breath sounds.[31] However, in our study, we recorded a short time of only 6.0 seconds with the auscultation method. The possible reasons could be the rigorous mandatory NRP training and certification that the health care providers in NICU undergo with repeated refresher trainings, leading to excellence in competency.

Capnography, although a reliable method with high sensitivity[10] can depict false negative results in conditions with low cardiac output, inadequate pressure to inflate the lungs,[10,32] and presence of secretions in ETT.[33] However, it is a rapid method and studies have reported the time for capnography confirmation as 1.6 seconds (SD +/- 2.4).[31] In a study by Aziz et al., the time required to confirm ETT position via capnography was 6 to 12 seconds.[27] We reported a similar time of 3 seconds (IQR 3.0-4.0).

Use of POCUS is gradually gaining popularity with its rapid assessment and ease of interpretation in infants and newborns. It does not interfere during chest compression and is not affected by environmental noise and cardiac output.[30] The average time required for POCUS used in emergency situations by physicians and anesthesiologists reported in literature is 9 seconds.[29] Several studies have also measured the time to perform transtracheal ultrasound in emergent situations with a wide range from 5-45 seconds,[15,28,34,35] while few studies have shown time to ultrasound to be shorter than capnography.[28,36,37] However, our study showed no difference in interpretation time with both modalities.

This is the first study of its kind to assess diagnostic accuracy of POCUS for endotracheal tube placement in a neonatal population in the country. It was a prospective design with the largest sample size of newborns to date. We did not only measure the accuracy of POCUS with standard-of-care methods, but also measured the time to interpretation for each method in a real-time scenario. Moreover, POCUS and standard-of-care methods were interpreted independent of each other, thus minimizing the risk of bias.

The study has some potential limitations. In our setting we did not have each of the three standard-of-care methods for all intubations and hence the analysis was done by composite of at least two current methods. In addition, this was a single-centre study and hence the results may not be generalized.

Point of care ultrasound has various advantages and its clinical prevalence is increasing in adults and older children. Many of these applications and benefits can be translated to a neonatal population. This may improve resuscitation by timely recognition of ETT placement and minimize traditional unmeasured radiation exposure.

Conclusion

POCUS is an easy and rapid approach for identification of endotracheal tube placement. Compared to standard-of-care methods, it is faster than auscultation and chest X-ray. All health care providers, regardless of their qualification and experience, were able to learn POCUS skills via a low-cost simulator-based training to build proficiency.

Ethical Considerations

The study was approved by the Research Ethics Boards at The Hospital for Sick Children (REB #1000057021), the AKUH Ethical Review Committee (ERC#: 4927-Ped-ERC-17), and the National Bioethics Committee of Pakistan (4–87/NBC-319/18/552).

Authors' contributions

SA is the PI of the study and has reviewed the final draft. SA drafted the 1st draft of the manuscript. UA performed the analysis. KA, MT, SM, SBS & HM provided critical feedback on the manuscript. All authors have read and approved the final manuscript.

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Conflict of interest

All authors declared no conflict of interest

Availability of data and materials

The data available is available on request.

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