The use of ultrasound compared to an age-based formula to estimate endotracheal tube size in an academic hospital

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Declaration

I, Donovan Charles Heslop, declare that this research report is my own unaided work. It is being submitted for the Degree of Master of Medicine in the branch of Anaesthesiology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

Signature

01/08/2023

Date

Abstract

Background

An accurate estimation of tracheal diameter for endotracheal tube size selection is imperative in the pediatric population, with ultrasound shown to be an acceptable and superior method of endotracheal tube size estimation when compared to conventional age-based methods.

Aim

To compare the accuracy of endotracheal tube size estimation using airway ultrasound to age-based formula in the South African pediatric population.

Methods

This was a prospective observational study, with 54 patients, American Society of Anesthesiologists physical status I–III, aged two to 12 years old, scheduled for elective surgery at Chis Hani Baragwanath Academic Hospital, South Africa. Patients were allocated to two groups, the age-based method group or ultrasound method group. The accuracy of each method used for endotracheal tube estimation was assessed using a standardized leak test. Post intubation endotracheal tube cuff pressures were measured and post operative follow up was done to assess for features of airway injury.

Results

The ultrasound method was a more accurate estimate of endotracheal tube size (74.47%) compared to the age-based method (29.63%) ($p = 0.0011$). In all cases a cuffed endotracheal tube was used. No difference was seen between the mean endotracheal tube cuff pressure between the groups with a large proportion of patients having underinflated endotracheal tube cuffs.

Conclusion

Ultrasound is a more accurate predictor of appropriate ETT size in the pediatric population compared to a conventional age-based formula. The use of ultrasound for the estimation of ETT size is an accurate, non-invasive, and reproducible technique with potential for long-term cost saving and reduced complications. Ultrasound is

becoming readily accessible in the theatre setting in South Africa and with appropriate training and expertize, this bedside tool has the potential for more widespread uptake and may be a more accurate means of determining endotracheal tube size in children.

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List of Abbreviations

APL: Adjustable Pressure-Limiting

ASA: American Society of Anesthesiologists

CHBAH: Chris Hani Baragwanath Academic Hospital

cmH_20: Centimetres of water

ETT: Endotracheal tube

l/min: Litres per minute

MHz: Megahertz

mm: Millimetres

NMBA: Neuromuscular blocking agent

MRI: Magnetic Resonance Imaging

POCUS: Point of care Ultrasound

US: Ultrasound

Statement

This Research report contains a literature review, a draft article, the study proposal and appendices. The study proposal is included for background reference and not for examination. This Research Report is in the format which complies with the University of Witwatersrand's Style Guide for Theses, Dissertations and Research Reports. The draft article differs in format from the rest of the research report as to comply with the Author Guidelines of the Journal of Pediatric Anesthesia, which is the journal which it is intended to be submitted for publication.

Section 1: Literature review

1.1 Introduction

Anaesthetists require proficiency in the skill of airway management (1, 2). A knowledge of airway anatomy, physiology, and pathology is needed as they have implications on an anaesthetist's ability to secure it (1). General anaesthesia with an endotracheal tube (ETT) is the most common anaesthetic technique in paediatric patients (3, 4). The intubation of paediatric patients is a challenge due to the anatomical and physiological differences between a paediatric and adult airway, added to this selecting an appropriately sized ETT is complicated (1).

The anatomical differences between an adult and paediatric airway become less prominent with increasing age (3, 5). The paediatric patient's head is larger relative to their body size, with a prominent occiput and short neck (3, 5). They have a larger tongue, shorter mandible and the larynx is more cephalic with a longer, stiffer, U-shaped epiglottis, that sits at a 45-degree angle from the anterior laryngeal wall (3, 5). The vocal cords are angled in an anterior-inferior to a posterior-superior position (5). The mucous membranes are loosely attached by submucosa tissue and prone to airway oedema (3). These differences predispose them to airway obstruction and difficult laryngoscopy. The cricoid ring is the narrowest portion of the paediatric airway compared to the glottic opening in adults making the airway funnel shaped (3, 5). Typically, direct laryngoscopy does not enable the anaesthetist to view the narrowest point of the paediatric airway (3).

The paediatric population is prone to rapid desaturation, hypoxaemia, and hypercapnia during periods of apnoea (1, 6). This most commonly occurs during laryngoscopy. Repeated intubation attempts may also result in awareness, laryngospasm, and bronchospasm (7).

Complications also occur due to the use of incorrectly sized ETTs. If too small, there will be increased resistance to gas flow, risk of aspiration, insufficient ventilation, leakage of anaesthetic volatile agents into the theatre environment and inaccurate end tidal carbon dioxide and gas monitoring (8-10). If too large they can cause significant airway trauma, resulting in laryngeal oedema, stridor, local ischaemia, ulceration of the tracheal mucosa, granulation tissue formation, scar formation and

subglottic stenosis. These result in increased resistance to airflow and work of breathing (11-14).

An accurate estimation of tracheal diameter to select an appropriate ETT size prior to laryngoscopy would reduce airway instrumentation to a minimum, reduce the number of ETT exchanges, and reduce the risk of the complications mentioned above (7, 14-16). Different methods based on physical characteristics are available to determine the size ETT needed for the paediatric population (17). These are based on age (18, 19), height (20, 21), and the width of the fifth finger (22).

Two age-based formulae frequently utilised are the modified Coles formula and the Khine's formula (18, 19). The Modified Coles formula (age in years/4 + 4) is used for uncuffed ETTs, adapted from Cole in 1957 (6, 18). The Khine's formula (age in years/4 + 3) (19) was developed for use with cuffed ETTs. It was adapted from the Modified Coles formula, to select a smaller internal diameter ETT, which accommodates the extra space needed for the cuff (19). These methods of ETT size selection are recommended in texts (6) but little data is available on the validation of these formulae (22). Literature shows age-based formulae tend to over-estimate ETT size (7, 23). This has clinical implications as an ETT that is too big may cause complications (11-14).

The Broselow tape is a colour coded length-based tape which correlates a paediatric patient's height and weight to medical instructions such as drug dosages and equipment size, including the size of ETT needed for intubation (20). It is recommended by the Advanced Trauma Life Support (24) and Pediatric Life Support (25) groups and is used globally (20). It was validated on American and European paediatric patients (21). However, these showed an appropriate ETT size was only selected 77% of the time in American (26) and 55% in European children (20). It appeared to be more accurate than age-based formula (20, 26). Other height-based formula are available but have not been validated (21).

Another method endorsed by the Pediatric Life support (25) and Advanced Trauma Life Support (24) groups is the selection of an ETT by choosing the closest in diameter to that of the 5^{th} digit. This is done by holding an ETT over the little finger (22). There is little data available on the validation of this method (22).

These methods have been shown to lack accuracy (4, 7, 23, 27-31). Some were developed and only validated on patients from western populations (20). These methods are not able to factor in differences seen in growth, development, and organ size in different populations for various reasons such as genetic, socio-economic, and environmental factors making them likely to be inaccurate (23, 29). The application of these methods can also be subjective (22).

An alternative method of ETT size selection has been investigated involving the direct measurement of the diameter of a paediatric patient's trachea using airway ultrasound (US). The tracheal diameter can be measured prior to intubation, to select an appropriate ETT size for intubation (29, 32). There are multiple methods available to visualise tracheal diameter which include:

- Direct visualisation measurements: Direct laryngoscopy and video-assisted devices.
- Semi-direct visualisation measurements: Magnetic resonance imaging, Computer tomography, X-ray, and US (1, 29)

Ultrasound has become more readily utilised in clinical medicine as it has several advantages. It is a reliable, safe, pain free, non-invasive, more readily available, portable bedside tool, and provides real time data (31).

Ultrasound technology and quality has improved which previously hampered its use for airway procedures (33). There is growing evidence for the use of airway US in the paediatric population (33). It is used as a pre-screening intubation tool for difficult laryngoscopy, selection of ETT size, confirmation of ETT placement and depth and to detect laryngeal mask airway malrotation. It assists in procedure guidance for percutaneous cricothyroidotomy, percutaneous dilatational tracheostomy and airway nerve blocks (33-35). Airway US can be used to measure the column of air at the level of the cricoid cartilage to predict an appropriately sized ETT prior to intubation (7, 31, 32).

Lakhal et al. (32) demonstrated that US is comparable in accuracy to magnetic resonance imaging when measuring the diameter of the air column at the level of the cricoid cartilage. A non-experienced physician was able to accurately measure subglottic diameter after just 15 airway US procedures being performed before data collection (32). A study in Canada found physicians were able to accurately detect

ETT placement with 98% sensitivity and 100% specificity after one tutorial and two practice attempts (36). A study done in Turkey showed that after a one hour course and one live demonstration, anaesthesia registrars with no prior experience had an overall success rate in correct ETT size determination of 77.5% (37).

Several studies have been conducted comparing the use of the airway US method to the conventional methods of ETT size selection to determine which is more accurate in selecting the most appropriate ETT in paediatric patients. A summary of the results and methods used in some of these studies is shown in Table 1. The results from these studies show that the airway US method of ETT size selection is more accurate than conventional methods in selecting an appropriately size ETT (4, 7, 23, 27-31, 38).

A systematic review by Saravia et al. (39) and Gupta et al. (40) confirmed that the US method of ETT size selection is a reproducible and more accurate method when compared to age-based formulae used for the estimation of ETT size in the paediatric population. The US method was shown to have a mean accuracy of 86% across the studies analysed but the accuracy did range widely from 48% to 100%. The accuracy of age-based formulae was reported to be lower (mean accuracy of 54%), also with a wide range of accuracy of 24% to 95% (39).

To determine if an ETT is appropriately sized, the standard leak test can be done (6, 41, 42). This test is performed once a paediatric patient is intubated with an ETT. The fresh gas flow rate is set to 5 litres/min, the patient is positioned supine with the head in neutral position (43). A pressure of 25 cmH_20 is applied to the breathing circuit. An audible air leak around the ETT is listened for by placing a stethoscope over the skin of the larynx (42). If a leak is present, the ETT is appropriately sized and if no audible leak is detected, the ETT is too large and should be exchanged. Studies have found that 50% of patients who developed post intubation croup (described as any feature of airway obstruction i.e., hoarseness, stridor or sternal retraction) did not have a leak around their ETT at a pressure of 25 cmH_2O (41).

This method does have limitations (44). Factors which may influence the pressure at which a leak occurs include head position, the degree of neuromuscular blockade, the depth of the ETT and the inspiratory flow rate. There has also been significant inter-observer difference noted when conducting the leak test (45). There is currently

Table 1: Studies comparing US method to conventional methods used to determine appropriate ETT size in paediatric patients

Study Author, Year:	Country and Population:	ETT type: CETT, UCETT, or both	Condition of US measurement:	US Measurement CC level:	Appropriate leak pressure (cmH_2O):	Results: Accuracy of comparator method (%)	Results: Accuracy of US method (%)
Shibasaki et al., 2010 (7).	Japan n: 192 Age: 1 mo - 6yrs	Both	Apnoea with NMBA	Lower border	10 - 20	Aged-based formula: Agreement ratio: 35 (CETT) 60 (UCETT).	Agreement ratio: 98 (CETT) 96 (UCETT) (p<0.001)
Bae et al., 2011 (27).	Korea n: 141 Age: < 8 yrs	Not specified	Apnoea with NMBA, CPAP of 10 cmH20	Mid	15 - 30	Age-based formula: 31	60 (p<0.001)
Sutagatti et al., 2017 (31).	India n: 75 Age: 1 - 14 yrs	Both	Patients awake	At CC	10 - 20	Age-based formula: 75 Height-based formula: 36	89 (p<0.001 when compared with height-based formula).
Altun et al., 2017 (23).	Turkey n: 152 Age: 1 - 10 yrs	CETT	Apnoea with NMBA	At CC	10 - 25	Age-based formula: 47 Height-based formula: 59	88
Laksono et al., 2020 (29).	Indonesia n: 40 Age: 1 - 5 yrs	CETT	Apnoea with NMBA	Lower border	10 - 30	Height-based formula: 64 Fifth finger method: 69	92 (p<0.05)
Elshazly et al., 2020 (28).	Egypt n: 54 Age: 1 - 6 yrs	CETT	Apnoea with NMBA	Lower border	10 - 30	Age-based formula: 68	92 (p<0.05)
Agrawal et al., 2020 (30).	India n: 60 Age: up to 12 yrs	Both	Apnoea with NMBA	At CC	10 - 25	Age-based formulae: 60	88 (p<0.001)
Gnanaprakasam et al., 2021 (4).	India n: 150 Age: 2 - 6 yrs	UCETT	Apnoea with NMBA	At CC	10 - 20	Age-based formula: 45	75 (p<0.001)
Ekor et al., 2022 (38)	North-west Africa n: 106 Age: 1-10 yrs	CETT	Apnoea with NMBA	Lower border	10-20	Age-based formula: 66	98 (p<0.001)

n: number, mo: months, yrs: years, CETT: cuffed ETT, UCETT: uncuffed ETT, CPAP: continuous positive airway pressure, CC: cricoid cartilage NMBA: neuromuscular blocking agent, p: p-value

no suitable alternative method available to determine an appropriately sized ETT (27, 43).

There are two types of ETT type available for clinical use, which are cuffed and uncuffed, with literature showing no preference for use of either type (39, 46). There are known advantages and disadvantages to the use of either cuff type.

Advantages with the use of uncuffed ETTs are that a larger internal diameter ETT is often used which decreases resistance to airflow. This lowers work of breathing and allows for easier suctioning. Uncuffed ETTs cause less trauma to the airway mucosa and cost less than cuffed ETTs (19). Disadvantages include a higher incidence of re-intubation which leads to a higher incidence of complications (46, 47). Oversized tubes can cause airway injury and as there is no cuff air leaks occur, which cause ventilation difficulties, inaccurate end tidal gas concentration measurements and atelectasis. There is also environmental contamination of anaesthesia gases and risk of aspiration (47).

Advantages with the use of cuffed ETTs are that they allow for lower fresh gas flow rates, with less use of inhalational agents, allowing for economical anaesthesia delivery. The seal created by the cuff reduces air pollution, lowers the incidence of reintubations and improves ventilation and end tidal gas monitoring (19, 48-50). Disadvantages are that cuffed ETTs are costly. A smaller internal diameter ETT needs to be used causing increased work of breathing due to higher resistance to airflow, with a higher chance of ETT obstruction and difficulty in suctioning. They are more complicated to use, require additional cuff pressure monitoring and are prone to inappropriate placement due to variations in design and lack of appropriate depth markers. Tracheal mucosa damage may still occur from the cuff (47).

ETT cuff pressure monitoring in theatre is not routine practice (51). Tracheal injury caused by an overinflated ETT cuff is related to the absolute pressure of the ETT cuff and duration of exposure to this pressure. The former contributing more, but tracheal mucosal injury can also occur within 15 minutes of exposure to a high ETT cuff pressure (52). Endotracheal tube cuff pressures are a dynamic process and are affected by body temperature, head position, movement, depth of anaesthesia, neuromuscular blockade, and the use of nitrous oxide. This makes cuff pressure monitoring complex (44, 47).

Guidelines for optimal ETT cuff pressure ranges are not available in paediatric patients (52). It is suggested that ETT cuff pressures in adults be kept less than 20 - 30 cmH_20 (44). In normotensive adults, tracheal mucosal blood flow becomes compromised at pressures of 30 cmH_20 and completely occluded at pressures of 50 cmH_20 (53). No studies have been conducted on paediatric patients and the actual value is unknown, but mucosal capillary pressures may be lower (47, 52). The 2015 American Heart Association Pediatric Life Support guidelines have suggested a pressure range of 20 - 25 cmH_20 in children under 9 years old (54).

Anaesthetists use free inflation techniques to inflate the cuffs of ETTs which have been shown to be unreliable (47, 52, 55, 56). Measuring cuff pressure is a definitive method for keeping pressures in an acceptable range. ETT cuff pressure measurement is done by attaching a manometer to the pilot balloon of the ETT via a 3 way stop-cock (57). This allows for the cuff pressure to be recorded and adjusted appropriately, yet these are not routinely available in theatres (44, 47, 57).

Determining the size of the narrowest portion of a paediatric patient's airway to select the most clinically appropriately sized ETT remains a challenge for anaesthetists. An inappropriately sized ETT can result in complications which may cause significant morbidity to paediatric patients presenting to theatre (8-14). Conventional methods of ETT size selection lack accuracy and visualisation of the trachea with US has been shown to be a better alternative (4, 7, 23, 27-31, 39, 40).

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Section 3: Draft Article

The use of ultrasound compared to an age-based formula to estimate endotracheal tube size in an academic hospital.

By Donovan Charles Heslop, BHSc–Biomed(Wits), BSc hons-Pharm(Wits), MBBCh(Wits), DA(SA)[1,2]

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Key words (Mesh): Ultrasound, Endotracheal tube size, age-based formula, cricoid cartilage

Abstract

Background

An accurate estimation of tracheal diameter for endotracheal tube size selection is imperative in the pediatric population, with ultrasound shown to be an acceptable and superior method of endotracheal tube size estimation when compared to conventional age-based methods.

Aim

To compare the accuracy of endotracheal tube size estimation using airway ultrasound to age-based formula in the South African pediatric population.

Methods

This was a prospective observational study, with 54 patients, American Society of Anesthesiologists physical status I–III, aged two to 12 years old, scheduled for elective surgery at Chis Hani Baragwanath Academic Hospital, South Africa. Patients were allocated to two groups, the age-based method group or ultrasound method group. The accuracy of each method used for endotracheal tube estimation was assessed using a standardized leak test. Post intubation endotracheal tube cuff pressures were measured and post operative follow up was done to assess for features of airway injury.

Results

The ultrasound method was a more accurate estimate of endotracheal tube size (74.47%) compared to the age-based method (29.63%) ($p = 0.0011$). In all cases a cuffed endotracheal tube was used. No difference was seen between the mean endotracheal tube cuff pressure between the groups with a large proportion of patients having underinflated endotracheal tube cuffs.

Conclusion

Ultrasound is a more accurate predictor of appropriate ETT size in the pediatric population compared to a conventional age-based formula. The use of ultrasound for the estimation of ETT size is an accurate, non-invasive, and reproducible technique with potential for long-term cost saving and reduced complications. Ultrasound is becoming readily accessible in the theatre setting in South Africa and with

appropriate training and expertize, this bedside tool has the potential for more widespread uptake and may be a more accurate means of determining endotracheal tube size in children.

Introduction

The accurate estimation of tracheal diameter to select an appropriately sized endotracheal tube (ETT) is imperative in the pediatric population as it keeps airway instrumentation to a minimum, reduces the number of ETT exchanges and the time to intubation, thereby reducing the risk of complications [1, 2]. The intubation of a pediatric patient is also challenging due to anatomical differences between a pediatric and adult airway [1, 2]. Furthermore, during direct laryngoscopy, the narrowest portion of the pediatric airway cannot be visualized [1, 2].

Point of care ultrasound has become frequently utilized in clinical medicine. Ultrasound (US) has been shown to be a reliable, safe, pain free, non-invasive, portable bedside tool capable of providing real time data [3-5]. Ultrasound can be used to measure the column of air at the level of the cricoid cartilage to predict an appropriately sized ETT in the pediatric population, this is known as the subglottic diameter [4, 5]. The current gold standard for the measurement of subglottic diameter is magnetic resonance imagining (MRI), but the routine use of MRI is not practical due to cost and feasibility [3, 6]. The accuracy of US in measuring subglottic diameter has been shown to be comparable to MRI, and the technique is easily learnt by non-experienced physicians [3, 6].

The use of US for the estimation of ETT size in the pediatric population is a reproducible and accurate method of ETT size estimation when compared to several conventional methods based on physical characteristics including age, weight, height and the width of the fifth finger [4-16]. The most widely used conventional method is age-based formulae [7]. Examples are of these are the Modified Coles [17] and Khine formula [18].

Conventional methods have been shown to lack accuracy and consistency in estimating an appropriate ETT size [6, 7, 18]. This is because these methods have not been validated across different population groups and variations in airway diameter cannot be determined based on a single physical characteristic [6, 7].

No investigations have been done evaluating the use of US for the estimation of ETT size in the South African pediatric population. Knowledge of this is important due to the complications which may occur with the use of an incorrectly sized ETT. If too small, there will be increased resistance to gas flow, risk of aspiration, insufficient ventilation, leakage of anaesthetic volatile agents into the theatre environment and inaccurate end tidal carbon dioxide and gas monitoring [6, 15]. If too large, airway trauma, resulting in laryngeal edema, stridor, local ischemia, ulceration of the tracheal mucosa, granulation tissue formation, scar formation and subglottic stenosis may occur [6, 15].

The aim of this study was to compare the accuracy of ETT size estimation using airway US to the local convention, of using age-based formula in the South African pediatric population. The objectives were to describe subglottic diameter using airway US, describe the size of ETT needed using age-based formulae, describe the incidence of leak and compare the accuracy of airway US versus age-based formulae. The secondary objectives were to describe the type of ETT used, describe re-intubation frequency and to describe cuff pressures in cases where cuffed ETTs were used.

Methods

This study was a prospective, observational study. The study population included pediatric patients presenting for elective surgery at Chris Hani Baragwanath Academic Hospital (CHBAH) situated in Soweto, Johannesburg, Gauteng, South Africa. It is a tertiary public hospital, with approximately 3200 beds and is a teaching hospital affiliated to the University of the Witwatersrand. CHBAH caters to a large, diverse population group providing services to the impoverished, patients living in urban areas and those referred from other provinces due to a lack of access to tertiary health care.

Ethics approval was granted by the Wits Human Research Ethics Committee (Medical) (Reference R14/49) and permission granted by the CHBAH Medical Advisory Committee. The study was registered and approved on the National Health Research Data base (reference: GP 202201 065).

Consecutive convenience sampling was used. The inclusion criteria were patients aged two to 12 years, presenting for elective surgery requiring general anesthesia and intubation with an ETT and American Society of Anesthesiologists (ASA) physical status I to III patients. The exclusion criteria were patients requiring a rapid sequence induction, ASA physical status IV or more, an anticipated difficult airway, a haemodynamically unstable patient and lesions, deformities or previous procedures which may have influenced US assessment of the airway.

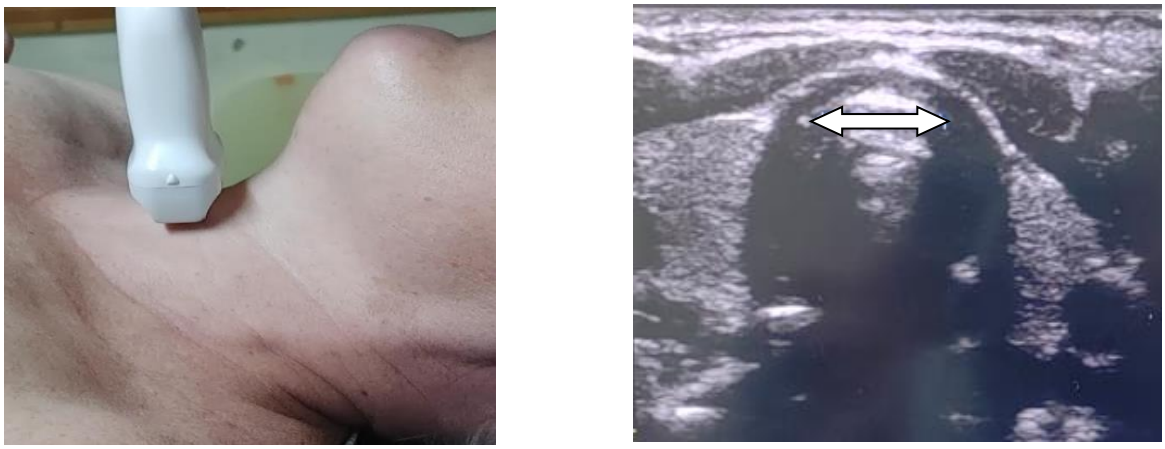
In all cases, in person, written informed consent was obtained from the caregivers of the patients as well as written assent from the patients where appropriate, based on the child's maturity and understanding of the study, prior to arrival in theatre. In situations when understanding due to a language barrier was a concern, a translator was used.

The sample size was determined using accuracy of ETT size estimation as the primary variable for each method. Altun et al [9] found airway US correlated with the best fit ETT in 88% of pediatric patients where an age-based formula was 48% accurate. Pearson's chi-squared test, with alpha value = 0.05, power = 90%, delta = 40%, P1 = 48% and P2 = 88%, gave a sample size of 54 patients (27 patients per group).

Patients were allocated to one of two groups, in chronological order of presenting to theatre. In group one, the age-based method was used to calculate ETT size. The modified Coles formula (age in years/4 + 4) [17] was used for uncuffed ETTs and the Khine's formula (age in years/4 + 3) [18] for cuffed ETTs. In group two the US method was used to measure the subglottic transverse diameter for ETT size selection. The decision of the type of ETT used was made by the attending anesthetist.

No data on the use of premedication was collected as administration was at the discretion of the attending anesthetist. The patient was placed supine on the theatre bed and standard ASA monitors applied. Pre-oxygenation with 100% oxygen was done prior to induction. Induction of general anaesthesia was performed (either an inhalational or intravenous induction). Intravenous access was then obtained for those receiving an inhalational induction. Apnoea was then induced, with either propofol, an opioid or neuromuscular blocking agent (NMBA). Once apnoeic, bag mask ventilation was commenced.

All US measurements were done by the principal researcher, with the patient supine and head in the neutral position. A linear US probe (Vivid™ *Iq*, GE Healthcare), frequency four to 10 MHz, in high resolution B mode was used. The US probe was placed transversely on the midline of the anterior portion of the neck (Figure 1A). Firstly, the vocal cords were visualized, and the probe was moved caudally to identify the cricoid cartilage, this avoided confusion between the cricoid cartilage and the first tracheal ring [11]. Once the cricoid cartilage was identified, bag mask ventilation was briefly stopped, this prevented changes in airway diameter during ventilation [6]. The adjustable pressure–limiting (APL) valve was set to 10 cmH_20 maintaining patency of the trachea [4]. The subglottic diameter was then measured at the level of the cricoid cartilage, shown in Figure 1B, defined as the diameter of the hyperechoic air shadow transmitted at the level of the cricoid cartilage [4, 9, 14]. This measurement was correlated to the closest outer diameter (≤ 0.3 mm) of the ETT which was used for intubation [12].



A B

Figure 1: A: Placement of the Ultrasound probe, B: Ultrasound image at the level of the cricoid cartilage. Arrow indicating the measurement of the subglottic diameter, the acoustic air shadow emitted at this level.

In all patients a standardized leak test was performed to assess the appropriateness of the size ETT selected [9, 19]. The patient's head was placed in the neutral position and a fresh gas flow of 5 l/min was set [19]. The APL valve was set to 25 cmH_2O and the circuit pressure was allowed to increase gradually, this prevented barotrauma [19]. An audible leak was listened for with a stethoscope over the skin in the midline of the anterior larynx. The APL valve was then adjusted to 10 cmH_2O and an audible leak listened for [9].

The presence of a leak was classified as: large (a leak present at a pressure ≤ 10 cmH_2O), indicating the ETT was too small; appropriate (a leak present between 10 and 25 cmH_2O) indicating the ETT was appropriately sized, or no leak (a leak absent at pressure of 25 cmH_2O) indicating the ETT was too large. If the ETT was unable to be passed through the cords, it was considered too be too large [9]. The appropriateness of the ETT size was then communicated to the attending anesthetist with an appropriate recommendation.

Where cuffed ETTs were used, cuff pressures were measured using a Rusch® Endotest™ cuff pressure manometer and recorded. Cuff pressures were adjusted to an appropriate range (20 - 25 cmH_2O) in all patients where needed [20]. Patients received standard post-operative monitoring. Thirty minutes post operatively, patients were assessed for features of airway injury (hoarseness of the voice, stridor) and features of difficulty of breathing (tracheal tug, nasal alar flaring, accessory muscle use) [14].

The data was analysed using GraphPad Prism® software [version 9.5.1 (733)]. Descriptive statistics were used. Categorical data was described with frequencies and percentages. Comparisons were done with the Fisher's exact test. Continuous variables were described using means and standard deviations. Comparison of the continuous variables between the two groups was done using the Mann-Whitney U test and the accuracy of the two methods compared using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 54 patients were included in the study. The demographic data is summarized in Table 1. There was no difference between the two groups with regards to age, sex, weight, and height.

The mean subglottic diameter measured in the US method group was 7.23 mm ± 1.08. There was a significant difference in the mean ETT size estimated between the two groups. The mean ETT size for the age-based group was 4.20 ± 0.68 and the mean ETT size for the US group 5.30 ± 0.85 ($p < 0.0001$).

Table 1: Demographic data

Demographic variable:	Age-based method	US method
Age (yr)*	4.74 ± 2.71	6.26 ± 3.16
Weight (kg)*	17.23 ± 7.76	22.04 ± 9.52
Height (m)*	1.07 ± 0.19	1.18 ± 0.23
Male: *n* (%)	16 (59.26)	20 (74.07)
Female: *n* (%)	11 (40.74)	7 (25.93)

*Data presented as mean ± SD, yr = years, kg = kilograms, m = metres, *n* = number of patients, % = percentage of patients

The US method was statistically more accurate than the age-based method (p=0.0011) in estimating appropriate ETT size. The US method estimated an appropriate ETT size in 20 out of 27 participants (74.07%), with an estimated ETT size being too small in four out of 27 patients (14.81%) and too large in three out of 27 patients (11.11%), whilst the age-based method estimated an appropriate ETT size in only eight out of 27 patients (29.63%), with an estimated ETT size being too small in 17 out of 27 patients (62.96%) and too large in two out of 27 patients (7.41%). This is shown in Figure 2.

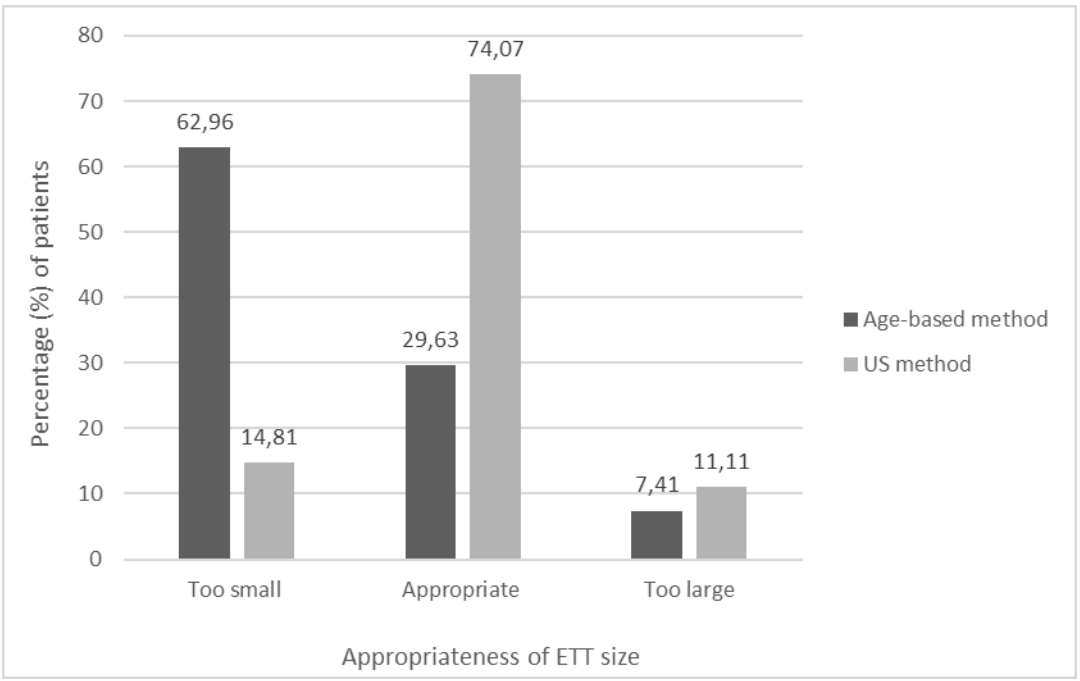


Figure 2: The accuracy of ETT size estimation.

In all cases, a cuffed ETT was selected for intubation. The reintubation frequency was higher in the age-based group with five patients (18.52%) being reintubated.

One patient was reintubated with a half size smaller ETT and four patients with a half size larger ETT, compared to the reintubation frequency in the US group with only three patients being reintubated with a half size smaller ETT (11.11%).

Table 2 shows the data of the measured ETT cuff pressures of the two groups. There was no difference between the mean ETT cuff pressure in the age-based group (15.20 mmHg ± 10.50) and the US group (17.64 mmHg ± 8.43) (p = 0.24). In both groups most patients had underinflated ETT cuffs. The ETT cuff was not inflated in seven patients (two in the age-based group and five in the US group).

Table 2: ETT cuff pressures

ETT cuff pressure	Age-based method	US method
Mean ETT cuff pressure (cmH_20) *	15.20 (± 10.50)	17.64 (± 8.43)
Appropriate (pressure 20 – 25 cmH_20): *n* (%)	2 (7.41)	5 (18.52)
Overinflated (pressure > 25 cmH_20): *n* (%)	5 (18.54)	3 (11.1)
Underinflated (pressure < 20 cmH_20): *n* (%)	20 (74.07)	19 (70.37)

*Data presented as mean ± SD, cmH_20 = centimetres of water, *n* = number of patients,

% = percentage of patients

Analysis of the different methods of apnoea showed that a combination of propofol and an opioid was the most frequent method used in the study (44.44% of patients in the age-based group and 59.26% in the US group) with a NMBA being the second (37.04% of patients in the age-based group and 40.74% of patients in the US group). In the age-based group propofol was used as a single agent in 14.81% of patients and an opioid alone in 3.70% of patients. Propofol or an opioid as a single agent was not used in any of the patients in the US group.

At the 30 minute post operative follow up, two patients in the age-based group were excluded from follow up, due to remaining intubated post operatively. In the age-based group, four patients showed features of difficulty breathing, whilst in the US group, two patients showed these features. One of which was post-operative coughing which responded to adrenaline nebulisation. The other patients responded

to airway suctioning of blood and secretions. The type of surgical procedure performed in all these cases involved trauma to the airway.

Discussion

The results from this study demonstrate that the US method is more accurate than the age-based method when used for ETT size selection. The US method had an accuracy of 74.07% compared to 29.63% with the age-based method, a marked difference of 44.44%. This is in keeping with results found in other studies [5-15]. It is interesting to note that the accuracy of the US method in this study, while high, was not as high as in some studies [6, 7]. Reasons for this may be that this study had a different study population with no previous data on the accuracy of the US method in the South African pediatric population, and the fact that US is an operator dependant technique [3]. Whilst the low accuracy of the age-based formula can possibly be attributed to the type of formula used and due to its non-validation in South African patients.

Systematic reviews by Gupta et al [6] and Saravia et al [7] show that the US method is superior compared to conventionally used age-based formulae for the estimation of ETT size. The US method has been shown to have a mean accuracy of 86%, which was even higher when cuffed ETTs were used (92%). The accuracy of results with the US method do range widely from 48% to 100% [7]. The accuracy of age-based formulae is reported to be lower (mean accuracy of 54%), with studies showing an even wider range of accuracy (24% to 95%). The mean accuracy of age-based formulae for cuffed ETTS is reported at 56% [7]. The studies included in these reviews were conducted in diverse locations including resource limited settings, suggesting the US method may be useful in the South African setting, as has been shown in this study [6, 7].

Ekor et al [10] and Elshazly et al [14] conducted similar studies in Africa and the US method showed high accuracy in appropriate ETT size estimation (98% and 92% respectively), with the age-based formula used in both studies being less accurate (66% and 68% respectively) [10, 14].

This study found the US group to have a mean subglottic diameter of 7.23mm ± 1.08, with a mean ETT size of 5.30 ± 0.85. This was larger than the mean in the age-based group (4.20 ± 0.68). This differed from other studies where age-based

formulae tend to estimate a larger size ETT size [15]. The use of different age-based formulae among studies, as well as the patient population may account for this [6, 7].

This study directly converted the measured subglottic diameter to the closest outer diameter of an ETT, which was correlated to an appropriate ETT size based on the internal diameter reading. This has been shown to be simple yet accurate when compared to studies where the subglottic diameter was measured and an ETT size was calculated using a complicated formula [8-11, 14-16]. The relationship between the inner diameter and outer diameter of ETTs is known to vary between different brands. The use of a single physical parameter such as an age-based formula to predict ETT size will yield varying results as these methods make a prediction based on internal diameter readings [9, 15]. A possible advantage of using US is that it provides a measurement of subglottic diameter which can accommodate for this variation [9, 13].

In general, the US method tended to underestimate ETT size with an incidence of 14.81%, a trend found in other studies [7], and overestimated 11.11% of the time. It is thought that the US method may underestimate ETT size due to technical considerations. The subglottic anteroposterior diameter of the trachea is longer than the transverse diameter but cannot be measured with US as the acoustic air shadow emitted by the cricoid cartilage prevents its visualization for measurement [1]. A slight underestimation of ETT size could be beneficial though, with the use of cuffed ETTs, as it allows for accommodation of the extra bulk of the cuff [1].

The methodology in this study, differed from others as not all inappropriately sized ETTs were exchanged. The decision to exchange an inappropriately sized ETT was at the discretion of the attending anaesthetist and not the role of the principal researcher. However, recommendations were communicated to the attending anaesthetist with all patients regarding the appropriateness of ETT size. The standardized leak test was used to determine accuracy of ETT selection and reintubation for a best fit ETT was not mandated in the study design. Despite this, the incidence of reintubation was lower in the US group (11.11%) compared to the age-based group (18.52%) which is in keeping with other studies, possibly reducing the risk of airway complications [8-10, 12, 14]. As not all cases were reintubated in this study, where ETTs were incorrectly sized, the ETT cuff was inflated if found to be too

small, to overcome the leak. Four of the five over-sized ETTs in both groups were exchanged for a half size smaller. All reintubations in the US group were due to the attending anesthetist not being able to pass the originally selected ETT through the vocal cords. This may be explained by increased muscular tone of the vocal cords due to the non-routine use of NMBAs, possibly influencing the accuracy of the method or due to the fact that US can directly over or under measure the subglottic diameter [9, 11].

A preference for cuffed ETTs among anesthetists in our institution was noted for pediatric patients over the age of two. Available literature shows varied preference among different institutions [7, 21]. Historically uncuffed ETTs were favoured due to concerns of tracheal mucosal damage caused by the pressure of the cuff, but the development of new micro-cuff ETTs has addressed this concern [1, 21, 22]. The benefits of using cuffed ETTs are that they allow for the use of lower fresh gas flow rates, with less use of inhalational agents allowing for economical anesthesia delivery. The seal created by the cuff reduces air pollution, lowers the incidence in of reintubation and improves ventilation and end tidal gas monitoring [1, 18, 22]. Disadvantages include cost, a smaller internal diameter ETT needs to be used causing increased work of breathing due to higher resistance to airflow, with a higher chance of ETT obstruction and difficulty in suctioning. It is important to remember that tracheal mucosa damage may still occur from the cuff [1, 21].

There was no difference in mean ETT cuff pressures between the two groups in the study. The incidence of ETT cuff overinflation was low in each group with the majority of ETT cuffs being under inflated. Only 7.41% in the age-based group and 18.52% in the US group had appropriately inflated ETT cuffs. Underinflation of the ETT cuff may increase risk of aspiration and hypoventilation, however routine cuff pressure monitoring is complicated and currently not available in our theatre setting, with little data available on cuff pressure recommendations in pediatric patients [1, 21, 22].

Based on the above, the US method is a reliable and reproducible method of ETT size estimation in the pediatric population presenting for elective surgery in a resource limited setting. A more accurate estimation of ETT size in theatre will result in reduced airway instrumentation, economical use of equipment and theatre time

with a reduction in airway complications. This will result in possible long term economic benefits.

Due to time constraints and the sampling method used, this study had a small sample size, however, this was comparable to the sample sizes used in several other studies [10,14,16]. An avenue for further research would be to investigate this in the wider South African population. Blinding in this study was not possible due to theatre staff constraints, which is a possible source of bias and different ETT brands had to be used. A NMBA was not used in all patients. This may have influenced the accuracy of the leak test and US method. The standardized use of NMBAs would have limited the number of patients enrolled in the study as most pediatric surgical cases did not warrant NMBA use and added to this, with the absence of nerve stimulators leading to concerns of residual paralysis, the study design opted to allow the attending anaesthetist to decide on their use and to not interfere with their practise. This study was not able to assess for post operative airway complications as where this was detected, the surgical procedure performed was known to cause trauma to the airway, thus it was not possible to ascertain whether it was from the intubation or the surgical procedure itself. The duration of US examination was not measured in this study; however, literature does show that the US method may prolong time to intubation [14]. Further research is needed in the South African setting to elucidate what effect operator experience and available resources have on time to intubation with the US method. This study did not assess the role of airway US in emergency cases and can only be applied to elective cases.

Conclusion

Ultrasound is a more accurate predictor of appropriate ETT size in the pediatric population compared to a conventional age-based formula. The use of ultrasound for the estimation of ETT size is a non-invasive, accurate, reproducible technique with potential for long-term cost saving and reduced complications. Ultrasound is becoming readily accessible in the theatre setting in South Africa and with appropriate training and expertise, this bedside tool has the potential for more widespread uptake and may be a more accurate means of determining endotracheal tube size in children.

What is already known about this topic?

Studies show that US is superior to conventional age-based methods when estimating ETT size in pediatric patients across diverse backgrounds.

What new information this paper adds

This study contributes to the expanding body of evidence that US is feasible and a better estimate of appropriate ETT size in the South African pediatric population. It is a useful bedside tool which can be used in a resource limited setting.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Funding statement

No funding was needed or received for the conduction of this study.

Conflict of interest disclosure

There are no conflicts of interest to declare.

Ethics approval statement

Ethics approval was granted by the Wits Human Research Ethics Committee (Medical) (Reference R14/49) and permission granted by the CHBAH Medical Advisory Committee.

Patient consent statement

Written informed consent was obtained from the caregivers of the patients as well as written assent from the patients where appropriate.

Clinical Trial registration

This trail was registered with The National Health Research Database: GP 202201 065

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Section 4: Proposal

The use of ultrasound compared to an age-based formula to estimate endotracheal tube size in an academic hospital

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4.1 Introduction

Anaesthetists need to be proficient in the skill of airway management (1, 2). A knowledge of airway anatomy, physiology, and pathology is needed as they have implications on an anaesthetist's ability to secure it (1).

General anaesthesia with an endotracheal tube (ETT) is the preferred anaesthetic technique in paediatric patients (3, 4). However, intubation of paediatric patients remains challenging due to anatomical differences between a paediatric and adult airway (1).

There are anatomical differences between an adult and paediatric airway which become less prominent with increasing age (3, 5). The paediatric patient's head is larger relative to their body size, with a prominent occiput and short neck (3, 5). They have a larger tongue, shorter mandible and the larynx is more cephalic with a longer, stiffer, U-shaped epiglottis, that sits at a 45-degree angle from the anterior laryngeal wall (3, 5). The vocal cords are angled in an anterior-inferior to a posterior-superior position (5). The mucous membranes consist of ciliated columnar epithelium which is loosely attached by submucosa tissue and is prone to oedema formation (3). These differences predisposed them to airway obstruction and difficult laryngoscopy. The cricoid ring is the narrowest portion of the paediatric airway compared to the glottic opening in adults making the airway funnel shaped (3, 5). During direct laryngoscopy one is unable to view the narrowest point of the paediatric airway (3).

During laryngoscopy patients are rendered apnoeic. Paediatric patients are prone to rapid desaturation, hypoxaemia, and hypercapnia during periods of apnoea (1, 6). Prolonged intubation attempts may also result in awareness, laryngospasm, and bronchospasm (7).

Complications may also occur due to the use of an incorrectly sized ETT. If too small, there will be increased resistance to gas flow, risk of aspiration, insufficient ventilation, leakage of anaesthetic volatile agents into the theatre environment and inaccurate end tidal carbon dioxide and gas monitoring (8-10). If too large it can cause significant airway trauma, resulting in laryngeal oedema, stridor, local ischaemia, ulceration of the tracheal mucosa, granulation tissue formation, scar formation and subglottic stenosis (11-14). These result in increased resistance to

airflow and work of breathing. Repeat laryngoscopies and intubation attempts exacerbate this (1).

An accurate estimation of tracheal diameter to select an appropriate ETT size prior to laryngoscopy would keep airway instrumentation to a minimum, reduce the number of ETT exchanges, and reduce the risk of the complications mentioned above (7, 14-16).

Different methods based on physical characteristics are available to determine the size ETT needed for paediatric patients (17). These are based on age (18, 19), height (20, 21), and the width of the fifth finger (22).

Age-based formulae

Two age-based formulae frequently utilised are the modified Coles formula and the Khine's formula (18, 19). The Modified Coles formula (age in years/4 + 4) is used for uncuffed ETTs, adapted from Cole in 1957 (6, 18). The Khine's formula (age in years/4 + 3) (19) was developed for use with cuffed ETTs. It was adapted from the Modified Coles formula, to select a smaller internal diameter ETT, which accommodates the extra space needed for the cuff (19). These methods of ETT size selection are recommended in texts (6) but little data is available on the validation of these formulae (22).

Height-based formulae

The Broselow tape is a colour coded length-based tape which correlates a paediatric patient's height and weight to medical instructions such as drug dosages and equipment size, including the size of ETT needed for intubation (20). It is recommended by the Advanced Trauma Life Support (23) and Pediatric Life Support (24) and is used globally (20). It was validated on American and European paediatric patients (21). However, these showed an appropriate ETT size was only selected 77% of the time in American (25) and 55% in European children (20). It appeared to be more accurate than age-based formula (20, 25). Other height-based formula are available but have not been validated (21).

Width of the fifth finger

There is another method endorsed by the Pediatric Life support (24) and Advanced Trauma Life Support (23). An ETT is selected by choosing the closest in diameter to that of the 5th digit. This is done by holding an ETT over the finger (22). There is little data available on the validation of this method (22).

These methods have been shown to lack accuracy (4, 7, 26-31). Some were developed and only validated on patients from western populations (20). These methods are not able to factor in differences seen in growth, development, and organ size in different populations for various reasons such as genetic, socio-economic, and environmental factors making them likely to be inaccurate (27, 29). The application of these methods can also be subjective (22).

Literature shows age-based formulae tend to over-estimate ETT size (7, 27). This has clinical implications as an ETT that is too big may cause complications (11-14).

Recently another method of ETT size selection has been investigated. This involves directly measuring the diameter of a paediatric patient's trachea using airway ultrasound (US).

Tracheal diameter can be measured pre-intubation to select the most appropriate ETT size for intubation (29, 32). There are multiple methods available to visualise tracheal diameter which include:

- Direct visualisation measurements: Direct laryngoscopy and video-assisted devices.
- Semi-direct visualisation measurement: Magnetic resonance imaging, Computer tomography, X-ray, and US (1, 29)

Ultrasound has become more readily utilised in clinical medicine due to several advantages. It is a reliable, safe, pain free, non-invasive, more readily available, portable bedside tool, and provides real time data (31).

Ultrasound use in paediatric anaesthesia has shown numerous benefits and has multiple applications (33). It has use in pain control via regional techniques, vascular access, pulmonary imaging, haemodynamic monitoring and as an adjunct to detect

cardiac dysfunction (33). Abdominal US imaging can also assess fasting status and aspiration risk, nasogastric tube placement and peri-operative bowel motility (33).

Airway US is used in the peri-intubation period (34). US technology and quality has improved which previously hampered its use for airway procedures (33). There is growing evidence for the use of airway US in the paediatric population (33). It is used as a pre-screening intubation tool for difficult laryngoscopy, selection of ETT size, confirmation of ETT placement and depth, and to detect laryngeal mask airway malrotation. It assists in procedure guidance for percutaneous cricothyroidotomy, percutaneous dilatational tracheostomy and airway nerve blocks (33-35). Airway US can be used to measure the column of air at the level of the cricoid cartilage to predict an appropriately sized ETT prior to intubation (7, 31, 32).

Lakhal et al. (32) demonstrated that US is comparable in accuracy to magnetic resonance imaging when measuring the diameter of the air column at the level of the cricoid cartilage. A non-experienced physician was able to accurately measure subglottic diameter after just 15 airway US procedures being performed before data collection (32). Other studies reiterate that airway US is an easy skill to learn. A study in Canada found physicians were able to accurately detect ETT placement with 98% sensitivity and 100% specificity after one tutorial and two practice attempts (36). Another study done in Turkey showed that after a one hour course and one live demonstration, anaesthesia registrars with no prior experience had an overall success rate in correct ETT size determination of 77.5%. There was some variability in achieving competency in this skill (37).

Several studies have been conducted comparing the use of the airway US method to the conventional methods of ETT size selection to determine which is more accurate in selecting the most appropriate ETT in paediatric patients. Results from these show that the airway US method of ETT size selection is more accurate than conventional methods in selecting an appropriately size ETT prior to intubation (4, 7, 26-31).

There are two types of ETT type available for use, which are cuffed and uncuffed ETTs.

There are advantages to the use of either ETT type

Uncuffed ETTs have a larger internal diameter which decreases resistance to airflow, lowers work of breathing, allows for easier suctioning, causes less trauma to airway mucosa, and cost less than cuffed ETTs (19).

Cuffed ETTs allow for lower fresh gas flow rates, less use of inhalational agents for economical anaesthesia delivery, reduced air pollution, reduced number of laryngoscopies and intubation attempts, improved ventilation and end tidal gas monitoring (19, 38-40).

There are disadvantages to the use of either ETT type

Uncuffed ETTs have a higher incidence of re-intubation which leads to a higher incidence of complications (41, 42), oversized tubes can cause airway injury, air leak which can cause ventilation difficulties and atelectasis. There is environmental contamination of anaesthesia gases, risk of aspiration and micro-aspiration and inaccurate end tidal gas concentration measurement (41).

Cuffed ETTs are costly. A smaller internal diameter ETT needs to be used causing increased work of breathing due to higher resistance to airflow, higher chance of ETT obstruction and difficulty in suctioning. They are more complicated to use, require additional monitoring cuff pressure and are prone to inappropriate placement due to variations in design and lack of appropriate depth markers. Tracheal mucosa damage may still occur from the cuff (41).

ETT cuff pressure monitoring in theatre is not routine practice (43). Tracheal injury caused by an overinflated ETT cuff is related to the absolute pressure of the ETT cuff and duration of exposure to this pressure. The former contributing more, but tracheal mucosal injury can also occur within 15 minutes of exposure to a high pressure ETT cuff (44).

Endotracheal tube cuff pressures are a dynamic process and are affected by body temperature, head position, movement, depth of anaesthesia, neuromuscular blockade, and the use of nitrous oxide (41, 45).

Currently, guidelines for optimal ETT cuff pressure ranges are not available in paediatric patients (44). It is suggested that ETT cuff pressures in adults be kept less than 20 - 30 cmH_20 (45). In normotensive adults, tracheal mucosal blood flow becomes compromised at pressures of 30 cmH_20 and completely occluded at

pressures of 50 cmH_20 (46). No studies have been conducted on paediatric patients and the actual value is unknown, but mucosal capillary pressures may be lower (41, 44). The 2015 American Heart Association Pediatric Life Support guidelines have suggested a pressure range of 20 - 25 cmH_20 in children under 9 years old (47).

Anaesthetists use free inflation techniques to inflate the cuffs of ETTs which have been shown to be unreliable (41, 44, 48, 49). Measuring cuff pressure is a definitive method for keeping pressures in an acceptable range. ETT cuff pressure measurement is done by attaching a manometer to the pilot balloon of the ETT via a 3 way stop-cock (50). This allows for the cuff pressure to be recorded and adjusted appropriately, yet these are not routinely available in theatres (41, 45, 50).

An appropriately sized ETT can be determined using the leak test (6, 51, 52). The leak test is performed by intubating a paediatric patient with an ETT. The fresh gas flow rate is set to 5 litres/min, the patient is positioned supine, head neutral in the sniffing position (53). A pressure of 25 cmH_20 is applied to the breathing bag. An audible air leak around the ETT is listened for by placing a stethoscope over the skin of the larynx (52). If a leak is present the ETT is said to be appropriately sized and if no audible leak is detected the ETT is too large and should be exchanged. It was found that 50% of patients who developed post intubation croup (described as any feature of airway obstruction i.e., hoarseness, stridor or sternal retraction) did not have a leak around their ETT at a pressure of 25 cmH_2O (51).

This method does have limitations (45). Factors which may influence the pressure at which a leak occurs include head position, the degree of neuromuscular blockade, the depth of the ETT and the inspiratory flow rate. There has also been significant inter-observer difference noted when conducting the leak test (54). There are currently no suitable alternatives method available to determine clinically appropriate ETT size (26, 53).

Determining the size of the narrowest portion of a paediatric patient's airway to select the most clinically appropriately sized ETT remains a challenge for anaesthetists. An inappropriately sized ETT can result in complications which may cause significant morbidity to paediatric patients presenting to theatre (8-14). Conventional methods of ETT size selection lack accuracy and visualisation of the trachea with US has been shown to be a better alternative (4, 7, 26-31).

4.2 Problem statement

The anatomical differences between an adult and paediatric patient's airway makes the accurate estimation of ETT size prior to intubation in paediatric patient a challenge (1, 3, 5, 45).

An incorrectly sized ETT results in repeat laryngoscopies, wastage of equipment and has complications which have been shown to increase morbidity in this population group (8-12, 14-16).

There are different methods of ETT size estimation based on physical characteristics which lack accuracy when applied to individual paediatric patients due to variations in their growth, development, and physical characteristics (17, 20, 22, 25, 29).

Ultrasound is becoming a more readily available tool in anaesthesiology and familiarity in its application is increasing (29, 33-35). Ultrasound may offer better accuracy in the estimation of ETT size prior to laryngoscopy by providing a measurement of subglottic diameter, allowing for an individualised approach for ETT size selection in paediatric patients (4, 7, 26-31).

4.3 Aim

The aim of this study is to compare the accuracy of ETT size estimation using airway US to conventional age-based formula in South African paediatric patients.

4.4 Objectives

The primary objectives of this study are to:

- Describe subglottic diameter using airway US.
- Describe the size of ETT needed using age-based formulae.
- Describe the incidence of leak.
- Compare the accuracy of airway US vs age-based formulae.

The secondary objectives of this study are to:

- Describe the type ETT type used.
- Describe re-intubation frequency.

- Describe cuff pressures in cases where cuffed ETTs were used.

4.5 Research assumptions

In this study the following definitions will be used:

Anaesthetist: A qualified doctor working in the Department of Anaesthesia, including consultants, registrars, and medical officers.

Registrar: A qualified medical doctor who is enrolled in a training post for 4 years with the aim of specialising in field of anaesthesia.

Consultant: A qualified medical doctor who has completed a registrar program and is a specialist in the field of anaesthesia.

Paediatric patient: A patient presenting to theatre for a surgical procedure aged less than 12 years.

Caregiver: The person responsible for providing long term, day to day care for the child. They may exercise the parental right to consent to a medical examination or treatment of the child in terms of the Children's Act, 38 0f 2005 (55).

Intubation: The insertion of an ETT into the trachea for ventilation.

Laryngoscopy: A visual examination of the larynx to obtain a view of the glottis and vocal cords.

Air leak test: Test performed where an audible air leak is auscultated for at a circuit pressure of 25cmH_20 and 10cmH_20, to determine if an ETT is an appropriate size or not (14).

Age-based formula: A calculation based on a paediatric patients age in years used to estimate the internal diameter size of ETT needed for intubation. In this study the modified Coles formula (age/4 + 4) will be used to calculate the internal diameter for uncuffed ETTs (18). The Khine's formula (age/4 + 3) will be used to calculate the internal diameter for cuffed ETTs (19).

Ultrasound machine: An imaging device which transmits high-frequency sound waves, which reflect off body structures. A computer receives the waves and uses them to create an imagine which can be used to view organs and structures.

Subglottic diameter: The diameter of the acoustic air shadow transmitted by the cricoid cartilage, when viewed with an ultrasound machine. This correlates to the diameter of the trachea at this level of the airway.

Accuracy: Is the degree of closeness of measurements of a quantity to that quantity's actual value. In this study a standard leak test (52) will be used to determine the accuracy of ETT size selection based on either the US or age-based method. The appropriate size being based on the presence of an air leak between a specific air pressure range.

4.6 Demarcation of the study field

The study will be conducted in the theatre complex of Chris Hani Baragwanath Academic Hospital (CHBAH) situated at 6 Chris Hani Road, Diepkloof, Johannesburg, South Africa. The Anaesthetic department is affiliated with the University of the Witwatersrand. On average 2500 paediatric surgeries are done annually in this complex with 2760 performed in 2020.

4.7 Ethical considerations

For this study to be conducted, ethical approval will be obtained prior to the commencement of the study from the Wits Human Research Ethics Committee (Medical). Additional permission to proceed with the study will be obtained from the Postgraduate Committee of the University of the Witwatersrand. Permission will also be sought from the CHBAH Medical Advisory Committee (Appendix 1) and the Head of Department of Anaesthesia of CHBAH to conduct the study in the CHBAH theatre complex (Appendix 2).

Neither method of ETT size selection will pose any additional risk to the patients participating in the study. The age-based method is a current method used in anaesthetic practice and the US method is non-invasive, requiring the placement of an US probe on the anterior portion of the skin of the neck.

Written informed consent will be obtained from the caregiver of each patient prior to inclusion in the study. Assent will be obtained from the child participating in the study where possible (Appendix 5). This will be done prior to the patient being in theatre.

The details of the study will be explained to the caregiver and the child. An information sheet will be provided for the caregiver's reference (Appendix 3). The caregiver providing consent for participation in the study will sign a separate consent form (Appendix 4).

Patient confidentiality and anonymity will be maintained during the study. Participants will be randomly allocated to one of two groups and assigned a study number. A separate sheet will be kept with participants information assigned to each study number.

The raw data collected will only be accessible to the researcher and supervisors of this study. The raw data collected will be kept securely until the youngest participants twenty-first birthday. All consent forms and data collection sheets will be kept in a locked cupboard for this duration.

Conduction of this study will be in accordance with the principles of the Declaration of Helsinki (56) and the South African Guidelines for Good Clinical Practice (57).

4.8 Data collection

4.8.1 Study design

The design of a study refers to a set of methods, or a framework used to analyse data on variables related to an identified research problem (58). This study will be conducted as a prospective, observational study.

A prospective study is where the outcomes of a group of participants has not occurred at the start of the study. The participants in the study are followed over a period to assess particular outcomes (58).

An observational study is a study where participants are observed, and certain outcomes are measured. No attempt is made to affect the outcome (58).

4.8.2 Study population

The study population will be patients presenting for surgery at the CHBAH theatre complex, aged two to 12 years, requiring a general anaesthetic and endotracheal intubation for elective surgical procedures.

4.8.3 Study sample

4.8.3.1 Sample method

This study will use consecutive convenience sampling. Consecutive sampling is the attempt by the researcher to include all available subjects in the study sample with convenience sampling referring to the use of the of the most readily available subjects (58).

Paediatric patients presenting to the CHBAH theatre complex for surgical procedures requiring intubation will be the population sample for this study. An attempt will be made to include all these patients presenting to theatre. All patients booked on elective lists in the relevant paediatric theatres who meet the inclusion criteria will be approached to participate in this study.

4.8.3.2 Sample size

The sample size for this study was determined using the results of a similar study conducted using accuracy of ETT size estimation as the primary variable for each method. Altun et al (27) found airway US correlated with the best fit ETT in 88% of paediatric patients where an age-based formula was 48% accurate. These results were used to determine a sample size for this study using the Pearson's chi-squared test. The following values were assumed: alpha value of 0.05, power of 90%, delta (difference) value of 40%, P1: 48% and P2 88%. From this a sample size of 54 patients (27 patients per group) was calculated.

4.8.3.3 Inclusion and exclusion criteria

The inclusion criteria of this study are:

- Paediatric patients aged two to 12 years.
- Patients presenting for elective surgery requiring intubation with an ETT.
- American Society of Anaesthesiology (ASA) physical status I to III patients.

The exclusion criteria of this study are:

- Patients requiring rapid sequence induction.
- ASA physical status IV.
- Patients with an anticipated difficult airway.

- Haemodynamically unstable patient.
- Patients with lesions, deformities, or previous procedures of the airway which may influence US assessment of the airway. These include patients with laryngeal and tracheal deformities, pathology such masses or growths, previous tracheostomy, and history of tracheal surgery.

4.9 Collection of data

Written consent will be obtained prior to the patient being in theatre. Patients will be allocated to one of two groups.

Group 1: Age-based method for ETT size selection.

Group 2: US method for ETT size selection.

The patients will be allocated to a group. The assignment of patients to a group will be done prior to the patients being in theatre, in order of presentation to theatre. Patients one to 27 will be allocated to group one and patients 28 to 54 will be allocated to group two.

The patient will be taken to the theatre and premedication will be administered at the discretion of the attending anaesthetist. The patient will be placed on the theatre bed and standard ASA monitors (electrocardiogram, pulse oximeter and non-invasive blood pressure) will be applied.

Induction of general anaesthesia will be performed, and the method of induction used will be at the discretion of the attending anaesthetist. A facemask with 100% oxygen will be applied during induction. Once induced the caregiver will be asked to leave the theatre room. Intravenous access will be obtained. Apnoea will be induced at the discretion of the attending anaesthetist with either an induction agent, neuromuscular blocking agent or opioid. Once the patient is apnoeic bag mask ventilation will be commenced.

In group one, an age-based formula will be used to determine ETT size needed for intubation. The modified Coles formula (age in years/4 + 4) (18) will be used in cases where uncuffed ETTs are used and the Khine's formula (age in years/4 + 3) (19) will be used in cases where cuffed ETTs are used. The type of ETT used will be at the

discretion of the attending anaesthetist. In this group the ETT size calculated will be predetermined prior to induction.

In group two, the subglottic transverse diameter will be measured with US. All US measurements will be done by the principal researcher for the duration of the study. This will be done using a linear US probe, in brightness mode. Whilst bag mask ventilation continues, the patient will be placed supine with the head in neutral position. The US probe will be placed transversely on the midline of the anterior portion of the neck and the vocal cords visualised. It will then be moved caudally to identify the cricoid cartilage. Once identified, bag mask ventilation will then be stopped briefly (this prevents changes in airway diameter during ventilation). The adjustable pressure–limiting (APL) valve will be set to 10 mmHg to maintain patency of the airways by producing a continuous airway pressure (26). The subglottic diameter will then be measured at the level of the cricoid cartilage. The subglottic airway diameter is defined as the diameter of the hyperechoic air shadow transmitted at the level of the cricoid cartilage (26-28). This measurement in millimetres will be correlated to the closest outer diameter of ETT to determine size of ETT needed for intubation, regardless of the type of ETT (cuffed or uncuffed) used (29). The patient will be intubated and placement of the ETT will be confirmed using conventional methods.

To determine if the ETT is appropriately sized, a leak test will be performed by the principal researcher. The ETT will be attached to a closed circuit. The patients head will be placed in the neutral position for the test. The anaesthesia machine will be placed on manual ventilation mode. A fresh gas flow of 5 L/min will be set. The APL valve will be set to 25 cmH_2O and the pressure allowed to rise slowly and prevent barotrauma from occurring (14, 52). This pressure will be confirmed using the anaesthetic machine airway pressure sensor. An audible leak will be listened for with a stethoscope over the skin in the midline of the anterior larynx. The APL valve will then be set to 10 cmH_2O and an audible leak listened for (7, 27, 30). The presence of a leak will be classified as:

- Large leak: a leak detected a pressure less than or equal to 10 cmH_2O
- Appropriate leak: a leaked present between 10 and 25 cmH_2O
- No leak: no leak present at pressure of 25 cmH_2O

The presence of a large leak indicates the ETT selected is too small. The presence of an appropriate leak indicates the ETT selected is appropriate. If the ETT cannot be passed through the glottis or no leak is present the ETT is too large.

The appropriateness of ETT size will be communicated to the attending anaesthetist. If an ETT is too small, recommendation of exchanging it 0.5 size bigger will be made or cuff be inflated in cases where cuffed tubes are used. If the ETT is too large, recommendation of exchanging ETT 0.5 size smaller will be made. This decision will be at the discretion of the attending anaesthetist.

In cases where cuffed ETT are used, cuff pressures will be measured using a cuff manometer attached to a three way stop-cock and recorded. The pressures will be adjusted to a range of 20 - 25 cmH_2O as required (47).

After the operation the patient will be taken to the post-operative recovery room. Standard post-operative monitoring and observations will be done. After 30 minutes the principal researcher will assess the patient for hoarseness of the voice, stridor and features of difficulty of breathing (tracheal tug, nasal alar flaring, accessory muscle use).

4.10 Data analysis

Data will be collected in theatre using a prepared data collection sheet (Appendix 6) and will be transferred to a Microsoft Excel® spreadsheet before analysis.

In this study, descriptive statistics will be used. The categorical data collected in the study will include age, race, sex, BMI and surgical discipline and procedure. This data will be summarized in tables with the use of frequencies and percentages. The comparison of categorical variables between the two groups will be done with a Fisher's exact test.

The continuous variables in this study with normal distribution will be described using means and standard deviations. A test for normality will be done. Comparison of the continuous variables between the 2 groups will be done using the student t-test if normally distributed variables are present. The Mann-Whitney U test will be used if the variables are not normally distributed. The 95% confidence interval from the

frequency of correct ETT size estimation will be calculated for each group. A p-value of less than 0.05 will be considered statistically significant.

4.11 Significance of the study

Conventional methods of ETT size determination before laryngoscopy in paediatric patients lack accuracy. Age-based calculations have been shown to lack accuracy in different regions of the world, including developing countries (27-29, 31). These formulae have several limitations and cannot factor in differences in individual growth seen in different populations globally (7, 27, 29-31).

The importance of the first attempt being the best attempt at intubation in this population group cannot be underestimated (59, 60). Studies have shown an association with repeat intubation attempts and higher complication rates (61). Paediatric patients also have reduced physiological reserves compared to that of an adult, predisposing them to hypoxaemia and haemodynamic derangements (60).

The US method of ETT size selection may more accurately predict optimal ETT size in this population by providing a non-invasive accurate measurement of the narrowest portion of a paediatric patient's airway, which cannot be assessed during laryngoscopy. This allows for more optimal ETT selection, making the practice of anaesthesia safer by improving first pass success rate of intubation. Another advantage includes reduced wastage of equipment from repeat ETT exchanges, translating into overall cost saving. This is applicable in a resource constrained setting such as South Africa.

4.12 Validity and reliability of the study

Validity is defined as the veracity of the results, in other words, if the study measures what was intended to be measured (62).

Reliability is defined as the reproducibility or consistency of the study's results (62).

The validity and reliability of the study will be ensured by:

a) Appropriate study design
b) Appropriate sample size in consultation with a biostatistician.

c) Using a consistent measure to assess the intervention, in this case a standardised leak test.

d) Statistical analysis done with the assistance of a biostatistician

4.13 Limitations of the study

- Consecutive convenience sampling will be used. This may not be a true reflection of the paediatric population presenting to CHBAH and may result in uneven data sets between each group.
- Blinding in this study is not possible due to theatre staff constraints. This may lead to bias as the principal researcher will be involved in ETT estimation and determining appropriateness of ETT with the leak test.
- Paediatric lists may not run daily, given the Covid-19 pandemic which may lead to longer time needed for data collection.
- A neuromuscular blocking agent might not be used in all patients and may affect muscle tone of the larynx affecting accuracy of the leak test.
- Data collection will be done in several theatres with different anaesthetic machines, and as such the anaesthetic sensors may be calibrated differently.
- Convenience sampling will be used which reflects paediatric patients presenting to CHBAH theatre, this may not be reflective of the South African paediatric population.

4.14 Project outline

Year	**2021**					
Month	**Jul**	**Aug**	**Sept**	**Oct**	**Nov**	**Dec**
Protocol						
Post Graduate Approval						
Ethic Approval						

Year	2022											
Month	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sept**	**Oct**	**Nov**	**Dec**
Data Collection												
Data Analysis												
Submission												

4.15 Financial plan

The cost of printing will be covered by the Department of Anaesthesia.

Description	Price Per Item	Number of pages	Number of copies	Total
Printing Proposal	R 1	30	10	R300
Post Graduate Form	R 1	2	6	R12
Printing Patient information sheets	R1	8	54	R432
Printing consent and assent forms	R1	3	54	R162
Printing research report	R 1	100	4	R400
Total				R1306

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4.17 Appendices

Appendix 1: Request Letter to the Medical Advisory Committee at CHBAH requesting permission to conduct the study at the facility.

Appendix 2: Request letter to the Head of Department of Anaesthesia at CHBAH requesting permission to conduct the study in the department.

Appendix 3: Caregiver/participant information letter for participation in the study.

Appendix 4: Written consent form to participate in the study.

Appendix 5: Assent form to participate in the study.

Appendix 6: Data collection form.

4.17.1 Appendix 1: Letter to the Medical Advisory Committee of Chris Hani Baragwanath Academic Hospital

To: The Medical Advisory Committee of Chris Hani Baragwanath Academic Hospital.

My name is Dr Donovan Heslop, I am currently a registrar in the department of anaesthesiology at Chris Hani Baragwanath Academic Hospital. As part the completion of my specialisation programme I am required to complete a research project for the MMed (Anaes) component of my degree.

Herewith, I would like to ask for your permission to conduct a study in the Department of Anaesthesia titled: The use of ultrasound compared to an age-based formula to estimate endotracheal tube size in an academic hospital. The study involves using point of care ultrasound as a method to estimate endotracheal tube size prior to intubation in paediatric patients. The study will be conducted as a randomised trial and will examine the use of the ultrasound method compared to conventional age-based formulae commonly used in anaesthetic practice to estimate endotracheal tube size in paediatric patients.

All patients will be fully informed about the nature of the study and consented before participation in the study. The study will incur no extra cost to the hospital as ultrasound machines are readily available in theatre and intubations will be done with the current equipment available for all routine anaesthetic procedures in the Chris Hani Baragwanath Academic Hospital theatre complex. This alternative method of endotracheal tube size estimation is safe and there will be no increased risk to patients.

A copy of the protocol to conduct this study is attached for your reference.

I hereby ask you to grant me permission to conduct this study.

Yours sincerely

Dr Donovan Heslop (MP0824259)

Permission granted/not granted by the Medical Advisory Committee of Chris Hani Baragwanath Academic Hospital.

Signed: _____ Date: _____

Official stamp: _____

4.17.2 Appendix 2: Letter to the Head of Department (Anaesthesia) of Chris Hani Baragwanath Academic Hospital

Dear Dr P Mogane.

My name is Dr Donovan Heslop, I am currently a registrar in the department of anaesthesiology at Chris Hani Baragwanath Academic Hospital. As part the completion of my specialisation programme I am required to complete a research project for the MMed (Anaes) component of my degree.

Herewith, I would like to ask for your permission to conduct a study in the Department of Anaesthesia titled: The use of ultrasound compared to an age-based formula to estimate endotracheal tube size in an academic hospital. The study involves using point of care ultrasound as a method to estimate endotracheal tube size prior to intubation in paediatric patients. The study will be conducted as a randomised trial and will examine the use of the ultrasound method compared to conventional age-based formulae commonly used in anaesthetic practice to estimate endotracheal tube size in paediatric patients.

All patients will be fully informed about the nature of the study and consented before participation in the study. The study will incur no extra cost to the hospital as ultrasound machines are readily available in theatre and intubations will be done with the current equipment available for all routine anaesthetic procedures in the Chris Hani Baragwanath Academic Hospital theatre complex. This alternative method of endotracheal tube size estimation is safe and there will be no increased risk to patients.

A copy of the protocol to conduct this study is attached for your reference.

I hereby ask you to grant me permission to conduct this study.

Yours sincerely

Dr Donovan Heslop (MP0824259)

Permission granted/not granted by the Head of department of Anaesthesia Chris Hani Baragwanath Academic Hospital.

Signed: _____ Date: _____

Official stamp: _____

4.17.3 Appendix 3: Study Information Sheet for Participation in the Study.

Study Information Sheet

for Patients Participating in Study

Title of Research: The use of ultrasound compared to an age-based formula to estimate endotracheal tube size in an academic hospital

Principal Researcher: Dr Donovan Heslop

Department: Anaesthesia

Affiliation: University of the Witwatersrand

Supervisors: Dr Cara Redelinghuys

Dr Tristan Leonard

Greetings. We are inviting you to give permission to include your child in a study at Chris Hani Baragwanath Academic Hospital. If you agree to have your child participate in this study and before signing the consent form at the end of this document, it is important that you read the information provided in this document and understand what will happen during the study and the reasons it is being done. This document will give you information about the study we are conducting in Chris Hani Baragwanath Academic Hospital operating theatres. Please read through this information and ask any questions you may have about the study. The principal researcher (Dr Heslop) will explain any information you do not understand. Thank you for taking the time to read this document.

Introduction and Purpose of this study:

The principal researcher and supervisors of this study are doing research on how to improve the safety of a procedure called intubation, which is one of the ways used to make a child sleep for their operation, so that they are not aware of what is going on or experience pain during the operation.

Intubation is done by looking into your child's throat after they are asleep with a device called a laryngoscope (Figure 1) and placing a plastic tube called an endotracheal tube through into your child's breathing pipe (Figure 2). This is done after your child is asleep and they will not be aware it is happening. Intubation allows for anaesthetic medication to be given to your child and keep them asleep for the duration of the operation, to give them oxygen and to protect their lungs from food particles in the stomach.

Figure1: A laryngoscope (1)

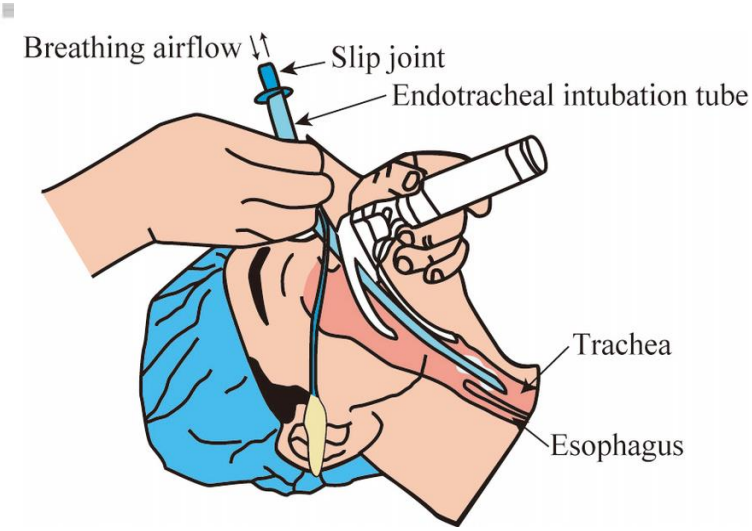

Figure 2: Placing of an endotracheal tube into the windpipe (2)

A calculation is used to decide what size tube a child will need to be intubated with before they are made to sleep for their operation. This calculation uses a child's age to work out the tube size. Deciding which size tube to use in children is more difficult than it is in an adult. It is important to decide the correct size of tube size before trying to intubate a child because if the tube is not the correct size it may be problematic during the operation.

There is a new way in deciding what size tube children need for their operation. We can measure the size of a child's windpipe with a picture created by a device called an ultrasound machine (Figure 3).

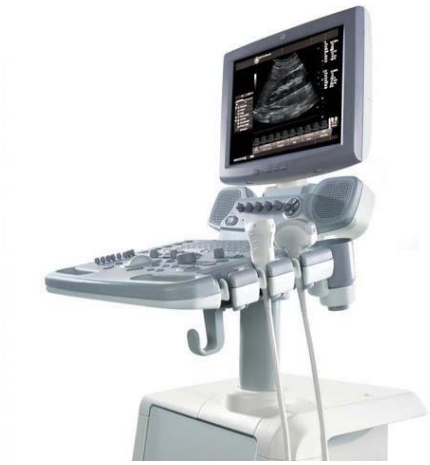

Figure 3: An ultrasound machine (3)

In this study we want to learn if using the ultrasound machine to decide which size tube to use for your child coming to theatre is a better option to the current calculation we use and by inviting you to allow your child to participate in the study, we may be able to improve patient care.

Type of Research Intervention:

The study will involve 2 ways of calculating the size of tube needed for your child's operation. The first way will be the calculation using their age will be used to decide what size tube will be needed for their operation. The second way we will use the ultrasound machine (Figure 3) to decide the size of tube needed for their operation. This method is safe and not an invasive or painful procedure. A probe (Figure 4) with gel will be placed on your child's throat to measure the size of their windpipe after they are asleep.

Figure 4: Placing the ultrasound probe on the throat to get a picture of a child's windpipe (4)

Participant selection:

All patients between the ages of 1 and 12 years old, coming to Chris Hani Baragwanath Academic Hospital theatres for a general anaesthetic needing an endotracheal tube during their planned operation are being approached to participate in this study.

Voluntary Participation:

The decision whether to participate in this study or not is entirely your own choice. Your participation is voluntary, and your decision will not affect the quality of service and care you are entitled to receive in theatre for your child's operation. By choosing not to take part in this study, the same routine method of anaesthetic care will be offered for your child's operation. It is important to note that you have the right to change your mind at any time during the research study, even if you agree to have your child participate currently, with no consequences for doing so.

Study Protocol and Procedure:

Participation of your child in this study will not require any extra time by you or your child. There will be no additional cost to you or your child for taking part in the study.

We will place children involved in the study into 2 groups. The group your child will be allocated to will be selected by chance. You will not know which group your child will be placed in.

You will come with your child to theatre if permitted. Your child will be placed on the theatre bed or your lap, which ever they are more comfortable with.

Below is a flow chart (Figure 5) of what will happen during the study:

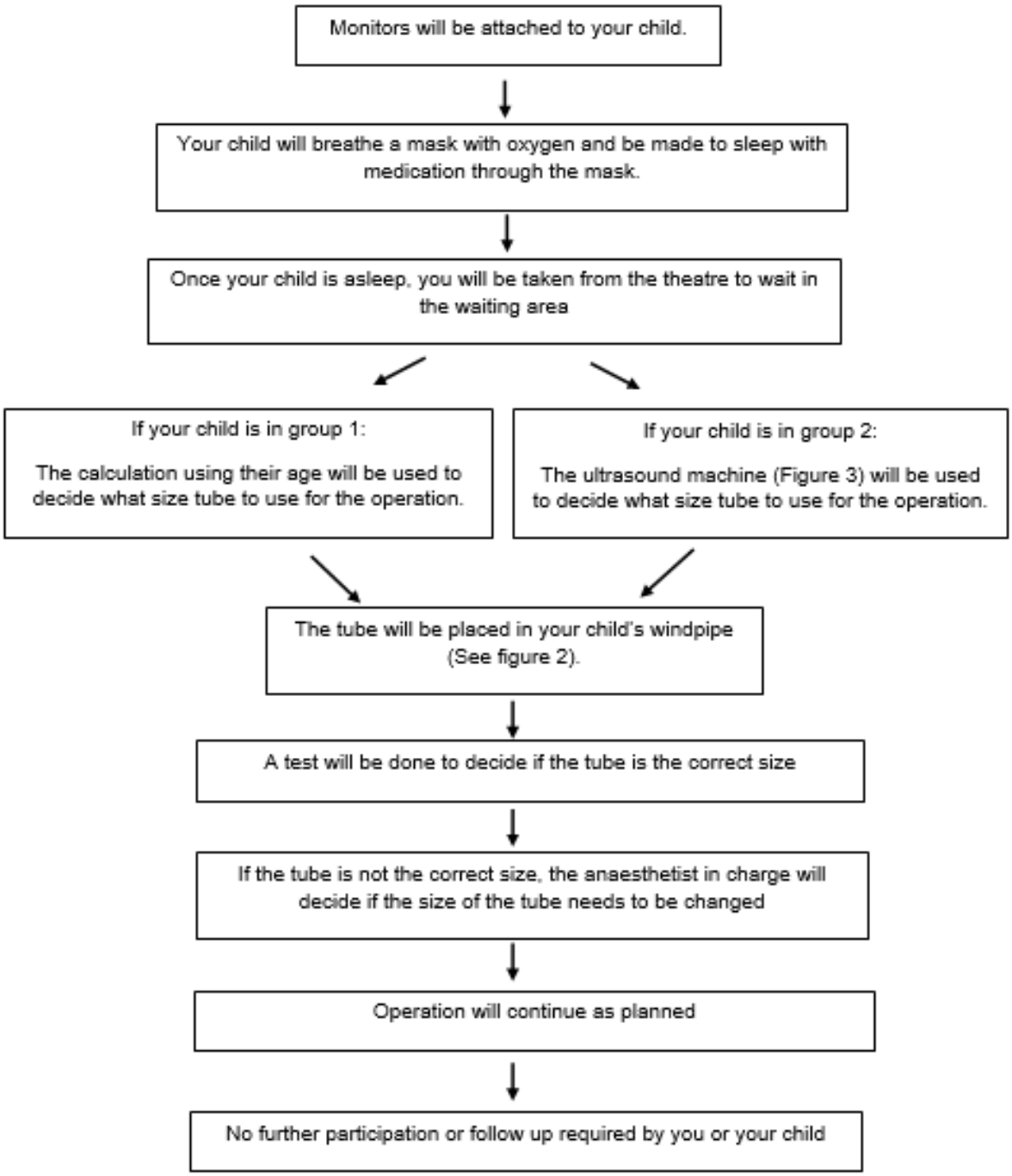

Figure 5: A flow chart of the process of data collection for the study

Risks of being involved in the study:

Participation in this study will not introduce any increased risk to the participants. The risks associated with a routine general anaesthetic for your child's operation will still apply.

Benefits of being in the study:

There may be no direct benefit to your child for participation in this research study. However, your participation in this study may help us find a more accurate method to decide the size of endotracheal tube in children. This may lead to safer anaesthetic practice in the future.

Confidentiality:

All personal information will be treated in the strictest confidence and will only be available to the principal researcher and his supervisors. Your information will not be shared or given to anyone that is not involved in this study. All the data collected will be given a number instead of using your child's name.

The only exceptions to this maybe be in the following circumstances:

- Personal information may be disclosed if required by law.
- The Human Research Ethics Committees of the University of the Witwatersrand may exceptionally require personal data to respond to a formal complaint, or for a compliance audit.
- The South African Health Products Regulatory Authority (SAHPRA), which is the successor body to the South African Medicines Control Council (SAMCC), might conceivably require access to personal data, if investigating a trial.

All data collected during this study will be stored securely for two years if a scientific publication arises from the study and six years if there is no publication. After this, it will be destroyed accordingly.

Right to Refuse or Withdraw from the study:

You do not have to participate in this study if you do not wish to. You may change your decision in taking part in this research at any point, even after giving permission to take part in this research study. The decision you make is your right and will always be respected. No penalty nor change in quality of care will occur if you refuse

to participate in the study. No reason is required for the decision you make. In the event you decide to withdraw from the study, the data which has been collected will be destroyed.

Contact details of researcher/s:

If you need further information about this study at any stage, or would like to report any adverse events or concerns while participating in this study, please contact the principal researcher Dr Donovan Heslop on the telephone number 079 511 9118, or by email on 0700819K@students.wits.ac.za . The contact number for the supervisors of this study is 011 933 9413 and their email addresses are tristan.leonard@wits.ac.za and cara.redelinghuys@wits.ac.za .

If you would like to receive a copy of the results of this study once it is completed, please make it known to the principal researcher and it will be made available to you.

The University of the Witwatersrand Human Research ethics committee (HREC):

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg ("Committee"). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za.

The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za.

Thank you for reading this Study Information Sheet

Figure references:

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4.17.4 Appendix 4: Written consent form to participate in the study

I, _____ have read the above information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I voluntarily agree to have my child participate in this research study.

Print Name of Participant_____

Signature of Participant _____

Date _____

Day/month/year

(If illiterate complete section below)

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Thumb print of participant:

Print name of witness_____

Signature of witness _____

Date _____

Day/month/year

Statement by the researcher/person taking consent:

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands the research being done.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this consent has been provided to the participant.

Print Name of Researcher/person taking the consent _____

Signature of Researcher /person taking the consent _____

Date _____

Day/month/year

4.17.5 Appendix 5: Assent form to participate in the study

Name of the research project:
Using ultrasound compared to age to decide what endotracheal tube size to use in children coming to theatre.

Principal Researcher: Dr Donovan Heslop

Contact No: 079 511 9118

Supervisors: Dr Cara Redelinghuys and Dr Tristan Leonard

Contact No: 011 933 9413

What is research?

Research is something we do to find new knowledge about the way things (and people) work. We use research projects to help us find out more about children and teenagers and the things that affect their lives, their schools, their families, and their health. We do this to try and make the world a better place.

What is this research project all about?

This research is about the size of plastic tubes used to put in the windpipe in children coming to theatre. This is done for many operations. We want to see if a new way of choosing the right size plastic tube is better than the way we do it now.

Why have I been invited to take part in this research study?

You have been invited to take part in this research study because you are coming for an operation at CHBAH.

Who is doing the research?

I am, Dr D Heslop, a doctor and I work at CHBAH. For part of my learning, I need to learn how to do research. I am doing this research project as part of my learning and to try to improve the safety for making children sleep for operations.

What will happen to me in this study?

- You will come to the operating room for your operation.
- You will then lay down on special bed in theatre.

- The doctor will give you a mask to breath with medicine which will make you go to sleep.
- Once you are asleep you will not be aware or have pain for the operation.
- Once you are asleep, we will put a plastic pipe into your windpipe.
- This is so we can give you medicine to keep you asleep for the operation.
- One of two things will happen once you are asleep.
    - I will put the plastic tube in like we normally do

      Or
    - 2. I will put a special piece of equipment onto the front of your neck to see your windpipe before we put the plastic tube in. This equipment is called an ultrasound machine. It does not cause pain or cause any problems to you. It is safe (See Figure 1).
    - After this is done, we will check to see in the plastic pipe is the correct size.
    - Then your operation will carry on like normal.

Figure 1: Putting the ultrasound machine onto your neck to measure your windpipe (1)

Can anything bad happen to me?

There is nothing bad that can happen to you because of being in the study.

Can anything good happen to me?

There is nothing added which will be good for you by being in the study, but by being in the study you may be helping us by making putting children to sleep for an operation safer.

Will anyone know I am in the study?

No one will know you are in the study because we will not use your name. The only people who will know this are the researcher and supervisors of the study.

Who can I talk to about the study?

If you have any questions or want more information on the study, you may contact the researcher or supervisors on the telephone numbers listed above.

What if I do not want to do this?

It is your choice if you want to participate in the study or not. It will not change the care you get in the hospital in any way. If you choose to take part in the study, you may change your mind at any time, and I will remove you information from the study.

Do you understand this research study and are you willing to take part in it?

YES	NO

Has the researcher answered all your questions?

YES	NO

Do you understand that you can STOP being in the study at any time?

YES	NO

_____ _____

Thumb print or Signature of Child Date

Figure reference:

1. Hickman, R. What is a thyroid ultrasound? What to expect when undergoing this test. Thyroid disease. Diagnosis. Very well health [Internet]. Dotdash. 2020. Available from: https://www.verywellhealth.com/thyroid-ultrasound-5074142.

4.17.6 Appendix 6: Data Collection Form

Study number: ___

Age: ___ Gender: ___ Race: ___ ASA status: ___

BMI: ___

Surgical discipline: _____ Procedure: _____

Method used for endotracheal tube size selection (tick appropriate box):

Group 1: Age Based formula: ☐ Group 2: Ultrasound method: ☐

Size of ETT estimated: ____ Subglottic diameter (mm): _____

Size of ETT used: _____ Size of ETT used: _____

Presence of leak (tick appropriate box):

☐ Large leak: a leak detected a pressure less than or equal to 10 cmH_2O

☐ Appropriate leak: a leaked present between 10 and 25 cmH_2O

☐ No leak: no leak present at pressure of 25 cmH_2O

Was the ETT exchanged: Yes ☐ No ☐

If yes: Size smaller ☐ Size larger ☐ Size change: _____

Type of ETT used: Cuffed: ☐ Uncuffed: ☐

If cuffed ETT used: Cuff pressure (mmHg): _____

Post-operative follow-up for complications after extubation (after 30min in recovery room):

Does the patient have (tick appropriate box if present):

Hoarseness of the voice/ croup ☐

Stridor ☐

Features of breathing difficulty ☐

(Nasal alar flaring, inspiratory apnoea, tracheal tug, accessory muscle use)

Section 5: Annexures

5.1 Ethics approval

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research and Innovation)

TO: Dr D Heslop
School of Clinical Medicine
Department of Anaesthesia
Medical School
University

E-mail: Donoheslop@gmail.com

CC: Supervisor: Drs T Leonard and C Redelinghuys
<Tristan.Leonard@hotmail.com>
and <HREC-Medical Research Office@wits.ac.za>

FROM: Mr Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 2022/04/08

REF: R14/49

PROTOCOL NO: **M220228** (This is your ethics application reference number. Please quote it in all enquiries, oral or written, relating to this study.)

PROJECT TITLE: *The use of ultrasound compared to an age-based formula to estimate endotracheal tube size in an academic hospital*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R49 Dr D Heslop

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M220228

NAME: (Principal Investigator) Dr D Heslop

DEPARTMENT: School of Clinical Medicine
Department of Anaesthesia
Medical School
University

PROJECT TITLE: *The use of ultrasound compared to an age-based formula to estimate endotracheal tube size in an academic hospital*

DATE CONSIDERED: 2022/02/25

DECISION: Approved unconditionally

CONDITIONS:

NOTE: If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>

SUPERVISOR: Drs T Leonard and C Redelinghuys

APPROVED BY: Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 2022/04/08

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **February** and therefore reports and re-certification will be due in the month of February each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator

11 | 04 | 2022
Date

5.2 Medical Advisory Committee approval

GAUTENG PROVINCE
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 25th January 2022

TITLE OF PROJECT:

The use of ultrasound compared to an age-based formula to estimate endotracheal tube size in an academic hospital.

UNIVERSITY: Witswatersrand

Principal Investigator: Dr D Heslop

Department: Anaesthesiology

Supervisor : Dr C Redelinghuys

Permission Head Department (where research conducted): Yes

NHRD No GP_202201_065

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Academic Hospital. The CEO / management of Chris Hani Baragwanath Academic Hospital is accordingly informed and the study is subject to:-

- **Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.**
- The Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- The MAC will be informed of any serious adverse events as soon as they occur
- Permission is granted for the duration of the Ethics Committee Approval.

Recommended
(On behalf of the MAC)
Date: 25/01/2022

Approved/Not Approved
Hospital Management
Date: 03/02/2022

5.3 Wits post-graduate studies approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

13 January 2022
Person No: 0700819K
PAG

Dr DC Heslop
Block1 Unit 2, Fish Eagle View
15 C Benacre Lane, Longlake Ext 6
Modderfontein
1609
South Africa

Dear Dr Donovan Heslop

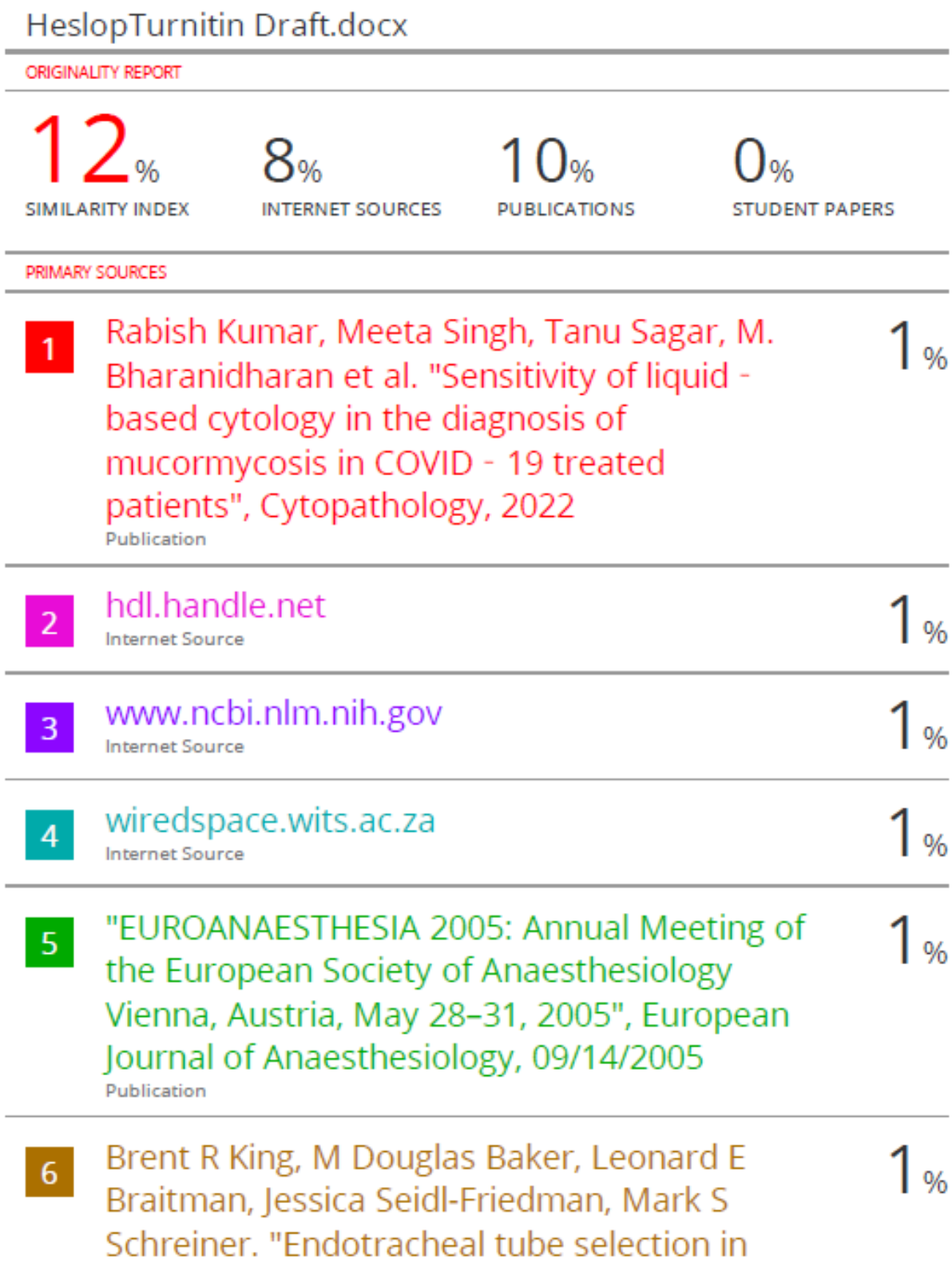
Master of Medicine in Anaesthesia: Approval of Title

We have pleasure in advising that your proposal entitled *The use of ultrasound compared to an age-based formula to estimate endotracheal tube size in an academic hospital* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

5.4 Turnitin report



HeslopTurnitin Draft.docx

ORIGINALITY REPORT

12%	8%	10%	0%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Rabish Kumar, Meeta Singh, Tanu Sagar, M. Bharanidharan et al. "Sensitivity of liquid - based cytology in the diagnosis of mucormycosis in COVID - 19 treated patients", Cytopathology, 2022 Publication	1%
2	hdl.handle.net Internet Source	1%
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5	"EUROANAESTHESIA 2005: Annual Meeting of the European Society of Anaesthesiology Vienna, Austria, May 28–31, 2005", European Journal of Anaesthesiology, 09/14/2005 Publication	1%
6	Brent R King, M Douglas Baker, Leonard E Braitman, Jessica Seidl-Friedman, Mark S Schreiner. "Endotracheal tube selection in	1%