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Evaluation of the Cutaneous-Epiglottic Distance Obtained by Ultrasound in Predicting Difficult Laryngoscopy in AdultPatients: An Observational Study

Tese apresentada à Faculdade de Medicina, Universidade Estadual Paulista "Júlio de Mesquita Filho", Campus de Botucatu, obtenção do título de Doutor em Anestesiologia

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Coorientador: Rodrigo Leal Alves

1. Via Aérea. 2. Laringoscopia. 3. Ultrassonografia. 4. Epiglote. 5. Intubação traqueal. I. Título.

Impacto da Pesquisa

A pesquisa realizada tem o mérito de poder avaliar de modo seguro e com maior acurácia um preditor de possível dificuldade de laringoscopia e intubação orotraqueal.

Cada vez mais os critérios e medidas para assistir o paciente de modo mais seguro tem sido utilizados na prática diária.

Esse estudo mostra uma possibilidade de aumentar ainda mais a qualidade e segurança oferecida aos pacientes submetidos a anestesia geral sob intubação orotraqueal, implementando um dado a mais para o reconhecimento de dificuldade inesperada durante o manuseio da via aérea.

UNIVERSIDADE ESTADUAL PAULISTA

Câmpus de Botucatu

ATA DA DEFESA PÚBLICA DA TESE DE DOUTORADO DE LUÍS HENRIQUE CANGIANI, DISCENTE DO PROGRAMA DE PÓS-GRADUAÇÃO EM ANESTESIOLOGIA, DA FACULDADE DEMEDICINA - CÂMPUS DE BOTUCATU.

Aos 29 dias do mês de outubro do ano de 2024, às 09:00 horas, por meio de Videoconferência, realizou-se a defesa de TESE DE DOUTORADO de LUÍS HENRIQUE CANGIANI, intitulada **Evaluation of the performance of the cutaneous-epiglottic distance obtained by ultrasound in predicting difficult laryngoscopy in adult patients: an observational study**. A Comissão Examinadora foi constituida pelos seguintes membros: Profa. Dra. LAIS HELENA NAVARRO E LIMA (Orientador(a) - Participação Virtual) do(a) Depto. de Especialidades Cirúrgicas e Anestesiologia / FM/Botucatu - Unesp, Profa. Dra. NORMA SUELI PINHEIRO MODOLO (Participação Virtual) do(a) Depto. de Especialidades Cirúrgicas e Anestesiologia / FM/Botucatu - Unesp, Profa. Dra. REGINA HELENA GARCIA MARTINS (Participação Virtual) do(a) Depto. de

Especialidades Cirúrgicas e Anestesiologia / FM/Botucatu - Unesp, Profa. Dra. VANESSA HENRIQUES CARVALHO (Participação Virtual) do(a) Depto. de Anestesiologia / FCM/Campinas - Unicamp, Profa. Dra. MARIA ANGELA TARDELLI (Participação Virtual)

do(a) Depto. de Cirurgia / EPM/São Paulo - Unifesp. Após a exposição pelo doutorando e arguição pelos membros da Comissão Examinadora que participaram do ato, de formapresencial e/ou virtual, o discente recebeu o conceito final: Aprovado. Nada

mais havendo, foi lavrada a presente ata, que após lida e aprovada, foi assinada pelo(a) Presidente(a) da Comissão Examinadora.

Profa. Dra. LAIS HELENA NAVARRO E LIMA

Dedicatória

Dedico minha tese de doutorado a minha esposa Marília, minha filha Carolina e meus pais Luiz e Sonia que sempre me apoiaram e estimularam minha caminhada para a conquista desse honroso título

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O caminho para chegar ao título de Doutor é difícil. Sem ajuda não seria possível. Minha esposa Marília e minha filha Carolina ajudaram a me sustentar dando a mimamor e carinho e possibilitaram que esse projeto se tornasse real cuidando da vida dafamília enquanto eu me dedicava aos estudos. Meu maior exemplo na vida e na carreira de anestesiologista, meu pai Luiz Cangiani, devo a ele grande parte do que sou como médico, como pessoa e como pai. Minha mãe fiel apoiadora e torcedora para o sucesso. Meus orientadores Profa Dra Lais Helena Navarro e Lima e Prof Dr Rodrigo Leal Alves que se empenharam e me cobraram na hora certa para que eu pudesse chegar a esse sonhado título. Todos os demais professores e amigos na UNESP, em especial Profa, Dra Norma Modolo, Prof Dr Leandro Braz e Prof Dr Paulo Nascimento que me ajudaram nas disciplinas, no projeto com críticas esugestões sempre muito positivas. Aos membros da banca da defesa de doutorado Profa Dra Vanessa Carvalho, Profa Dra Rosangela e Profa Dra Mariangela Tardelli, e todos os que me ajudaram durante toda a longa trajetória para chegar até aqui. Também não poderia esquecer dos co-autores da publicação meus amigos Dr GlenioMizubuti e Dr Rodrigo Lima

Me lembro de uma imagem mostrada em uma das aulas em que um caminho muito tortuoso e com várias escapatórias foi mostrada. Logo em seguida, a pergunta do professor foi clara... Alguém vai desistir? Agora é a hora! Um silêncio tomou a sala... ninguém desistiu, mas confesso que por várias vezes exitei e pensei em não concluir. Conseguiterminar por enorme incentivo dos meus orientadores, da minha esposa, da minha filha e dos meus pais. Meus sinceros agradecimentos e lembranças eternas. Lembranças que ficarão eternizadas nessa tese que foi desenvolvida e aprimorada por todos.

RESUMO

Introdução: A ultrassonografia (US) surgiu recentemente como um método simples, não invasivo e seguro para avaliação rápida das vias aéreas à beira do leito. O objetivo do estudo foi verificar o desempenho da distância cutâneo-epiglótica (DCE) medida por US na predição de laringoscopia direta difícil (definida como graus 3-4 de Cormack-Lehane). Também avaliamos a associação potencial entre CED, sexo, índice de massa corporal (IMC) do paciente e as associações independentes entre CED e aumento das chances para graus 3-4 de Cormack-Lehane (desfechos secundários).

Métodos: Foram incluídos pacientes com idade entre 18 e 70 anos submetidos a cirurgias eletivas sob anestesia geral com intubação traqueal. Foram excluídos aqueles com IMC >35 kg/m^2 e/ou história prévia de intubação traqueal difícil. A DCE foi medida com os pacientes anestesiados e antes da intubação traqueal. Foram registrados os seguintes dados: idade, sexo, IMC, tipo de cirurgia e número de tentativas até sucesso da intubação traqueal. A análise da curva Receiver Operator Characteristic (ROC) foi realizada para avaliar a relevância clínica do DCE. Análises secundárias compararam a associação entre DCE e IMC em pacientes com graus 1-2 de Cormack-Lehane versus aqueles com graus 3-4. A relação entre DCE e IMC foi avaliada por meio de regressão logística linear e binária múltipla, considerando DCE (em milímetros) e IMC como covariável para prever os graus 3-4 de Cormack-Lehane como desfecho dicotômico. A significância estatística foi fixada em $p<0,05$.

Resultados: A análise discriminatória da curva ROC revelou área sob a

curva de 0,899 (IC 95% = 0,836 a 0,963; p<0,001). O ponto de corte máximo do DCE determinado pelo índice de Youden foi de 25,6 mm. DCE e IMC foram positivamente correlacionados. A regressão logística binária demonstrou um aumento independente na razão de chances (OR) para laringoscopia difícil (OR para CED = 1,81, IC 95% = 1,35 a 2,41; IMC = 1,30, IC 95% =1,05 a 1,59).

Conclusão: O DCE medido com US tem uma alta capacidade discriminatória para prever a visualização da glote de Cormack-Lehane inferior (graus 1-2) e superior (graus 3-4) durante a laringoscopia direta. Além disso, o DCE foi positivamente correlacionado com o IMC noaumento das chances de laringoscopia difícil.

Palavras-chave: Via aérea; Epiglote; Laringoscopia; Intubação traqueal; Ultrassonografia.

ABSTRACT

Background: Ultrasound (US) has recently emerged as a simple, noninvasive, and safe method for rapid bedside airway assessment. We aimed to verify the performance of the US-measured cutaneous-epiglottic distance (CED) in predicting difficult direct laryngoscopy (defined as Cormack-Lehane grades 3-4). We also evaluated the potential association between CED, sex, patient's body mass index (BMI), and the independent associations between CED and increased odds for Cormack-Lehane grades 3-4 (secondary outcomes).

Methods: Patients aged 18-70 years scheduled for elective surgeries under general anesthesia with tracheal intubation were included. Those with a BMI >35 kg/m^2 and/or previous history of difficult tracheal intubation were excluded. CED was measured with patients anesthetizedand before tracheal intubation. The following data were recorded: age, sex, BMI, type of surgery, and number of attempts until successful tracheal intubation. Receiver operator characteristic (ROC) curve analysis was performed to assess the CED's clinical relevance. Secondary analyses compared the association between CED and BMI in patients with Cormack-Lehane grades 1-2 versus those with grades 3-4. The relationship between CED and BMI was assessed using multiple linear and binary logistic regression considering CED (in millimeters) and BMI as a covariate for predicting Cormack-Lehane grades 3-4 as a dichotomous outcome. Statistical significance was set at $p<0.05$.

Results: Discriminatory ROC curve analysis revealed an area under the curve of 0.899 (95%CI = 0.836 to 0.963; $p <0.001$). The maximum CED cut-off point determined by the Youdenindex was 25.6 mm. CED and BMI were

positively correlated. Binary logistic regression demonstrated an independent increase in the odds ratio (OR) for difficult laryngoscopy (OR for CED = 1.81, 95% CI = 1.35 to 2.41; BMI = 1.30, 95% CI = 1.05 to 1.59).

Conclusion: CED measured with US has a high discriminatory capability for predicting lower (grades 1-2) and higher (grades 3-4) Cormack-Lehane glottis visualization during direct laryngoscopy. Additionally, CED was positively correlated with BMI in increasing the odds of difficult laryngoscopy.

Keywords: Airway; Epiglottis; Laryngoscopy; Tracheal intubation; Ultrasonography.

Sumário

1. Evaluation of the Cutaneous-Epiglottic Distance Obtained by Ultrasound in Predicting Difficult Laryngoscopy in Adult Patients: An Observational Study

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Ethics Approval: This investigation was approved by the UNESP – Faculdade de Medicina de Botucatu Research Ethics Committee (Protocol 4.961.886) and was registered in the Brazilian Registry of Clinical Trials (U1111-1275-1120). Written patient consent was obtained as appropriate,

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1.1 CREDIT AUTHOR STATEMENT:

Luis Henrique Cangiani: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Project administration, Writing – original draft, Writing – Review, edit and approval of final manuscript.

Rodrigo Leal Alves Salvador: Conceptualization, Methodology, Investigation, Data curation, Project administration, Writing – original draft, Writing – Review, edit and approval of final manuscript

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Rodrigo Moreira e Lima: Writing – Review, edit and approval of final manuscript.

Lais Helena Navarro e Lima: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Project administration, Writing – original draft, Writing – Review, edit and approval of final manuscript.
All authors reviewed and edited the manuscript with important intellectual contributions and approved the final version for submission for publication.

Critical and potentially fatal situations, such as ‘cannot intubate, cannot oxygenate,’ are estimated to occur in one of every 1000 elective surgeries and one of every 250 rapid sequence intubations [1]. Proper preoperative evaluation can help manage a difficult airway; therefore, preoperative airway assessment is paramount for reducing potentially related risks.

Bedside tests and measurements, such as the Mallampati classification, thyromental distance, sternomental distance, neck circumference, and interincisor distance, are routinely used in clinical practice to predict difficult tracheal intubation [2,3]. However, when used independently, most standard tests have limited predictive value, particularly in patients with no evidence of increased risk for difficult airway and in whom challenging situations may occur [2,4,5]. Concerning the easiness of airway manipulation, according to the Cormack-Lehane visualization classification, patients with Cormack-Lehane grades 1 or 2 are considered easy to intubate, while those with grades 3 or 4 are considered difficult [1,6]. However, this classification is only possible with direct visualization during laryngoscopy. Therefore, an index that can accurately predict difficult intubation scenarios *before* performing a laryngoscopy is needed.

The use of ultrasound (US) in operating rooms and emergency care has been increasing because it is simple and harmless [4,7,8]. Previous studies have found that difficult airway cases are associated with longer cutaneous-epiglottic distances (CED) as measured by US [9]. Although this measurement provided good predictive results, there is limited information regarding the optimal cut-off point to make it reliable for routine clinical practice [10]. We, therefore, aimed to verify the predictive capability of US-measured CED to identify patients who are potentially difficult to intubate (defined as Cormack-Lehane grades 3-4) with direct laryngoscopy. Secondarily, we evaluated potential correlations between CED, sex, patient’s body mass index (BMI), and independent associations between CED and increased odds for Cormack-Lehane grades 3-4.

3. MATERIALS AND METHODS

The study was approved by the Research Ethics Committee of the Faculdade de Medicina de Botucatu – UNESP (protocol 4.961.886) in September 2021 and registered in the Brazilian Registry of Clinical Trials (U1111-1275-1120) in August 2022. This report followed the Standards for Reporting of Diagnostic Accuracy Studies protocol [11]. Patients aged between 18 and 70 years who were scheduled for elective surgery under general anesthesia and tracheal intubation at the Centro Médico Campinas Foundation Hospital in Brazil were included. Patients with a BMI >35 kg/m^2 and those with a previous history of difficult intubation and/or any difficult airway predictors (thyromental distance, sternomental distance, reduced mouth opening, upper lip bite test, or other tests) were excluded. Patients in whom adequate US measurement was impossible due to technical reasons (radiotherapy or surgery of the neck, goiter, soft tissues masses), incorrectly recorded data, or those who had difficulty with bag-mask ventilation after induction of general anesthesia and required alternative means of tracheal intubation other than direct laryngoscopy were excluded.

All scans were performed by an expert airway ultrasonographer (LHC). CED was measured using a high-frequency (6–13 MHz) linear US transducer in the axial/transverse position, in the region surrounding the thyroid cartilage, as described by Kundra et al [4]. The epiglottis was visualized as a hypoechoic semi-curvilinear structure in the midline with its anterior border delineated by the hyperechoic pre-epiglottic space and its posterior border by a bright air-mucosal interface corresponding to the air column in the airway. Once the image was obtained, a measurement line was drawn (with minimal pressure on the US probe) from the skin to the epiglottis (CED, in millimeters). All CED measurements were taken with the patients lying supine in the “sniffing” position. All US images were deemed adequate and CED measurements took an average of 180 seconds per patient. Figure 1 illustrates airway US images and their respective CED measurements.

All CED measurements took place immediately after induction of general anesthesia (GA) such that the patient's head was not repositioned between the measurement and tracheal intubation. Induction of GA was achieved with midazolam, fentanyl or remifentanil, propofol

and rocuronium. Patients were kept hemodynamically stable, in an adequate anesthesia plane and ventilated under a facial mask with 100% oxygen before tracheal intubation. Direct laryngoscopy with appropriately sized Macintosh blades was performed by an experienced anesthesiologist after confirming the absence of muscular response (train-of-four of zero). The Cormack-Lehane classification was assessed in the first attempt as follows: grade 1 = full view of the glottis; grade 2 = partial view of the glottis and/or arytenoid cartilages visualized; grade 3 = only the epiglottis visualized; and grade 4 = neither the glottis nor the epiglottis visualized.

The same anesthesiologist performed up to three attempts at intubation under direct laryngoscopy. In exceptional circumstances of inability to intubate after the third attempt, a more experienced anesthesiologist, if available, was permitted one additional attempt. If, for any reason, tracheal intubation was not possible under direct laryngoscopy, alternative means such as videolaryngoscopy, flexible fiberoptic scope, optic stylet, and/or surgical airway kit were available at the discretion of the attending anesthesiologist.

Statistical Analysis

A descriptive analysis of the study population was performed, and the following data were analyzed: age, sex, weight, height, BMI, type of surgery, and number of attempts required for tracheal intubation.

To evaluate the clinical relevance of CED as a predictor of difficult tracheal intubation, a receiver operator characteristic (ROC) curve analysis was performed, and the sample size calculation considered a 25% prevalence of Cormack-Lehane grades 3-4 in a mixed surgical population [10]. For practical clinical discriminatory capability, we assumed that an area under the ROC curve (AUC-ROC) of at least 0.85 would be required to be proven by the evaluated method, and that 100 individuals would provide a width of 0.2 around this area, within a 95% confidence interval (CI).

Categorical variables were expressed as absolute and relative frequencies, and continuous variables were expressed as mean and standard deviation, as the Shapiro-Wilk test and histogram analysis showed a near-normal distribution.

The ROC curve was constructed by plotting the true positive rates (sensitivity) on the Y-axis and the false positive rates (1 – specificity) on the X-axis, and the optimal cut-off point was defined by the highest Youden index, in which the sum of the sensitivity and specificity is maximized. The p-value for the AUC-ROC was evaluated under the null hypothesis of an area of 0.5, which denotes a 50/50 probability of either a true or false-positive result for detecting potentially difficult airways.

Secondary analyses were performed using the independent Student's t-test to compare the difference between CED in patients with Cormack-Lehane grades 1-2 versus those with grades 3-4. The relationship between CED and BMI was assessed using multiple linear regression, with sex as a covariate.

Binary logistic regression was also performed, relating the CED results in millimeters and the patients' BMI as covariates for predicting Cormack-Lehane 3-4 as a dichotomous outcome, since both covariates showed a positive correlation between them.

A p-value <0.05 was considered statistically significant.

4. RESULTS

This study included 100 patients whose assessments were conducted between November 2023 and May 2024. Table 1 presents the demographic data of the study population. The average age of the patients involved in the study was 47.6 ± 14.2 years, 54% were male, and the average BMI was 26.4 ± 3.7 kg/m^2. We identified 24 patients with Cormack-Lehane grades 3-4 among the 100 participants. Tracheal intubation was performed on the first attempt in 86% of the cases, and all patients were successfully intubated using direct laryngoscopy.

Figure 2 shows the distribution of patients according to the Cormack-Lehane classification and the respective mean CED values in a violin plot, indicating that patients with Cormack-Lehane grades 3-4 presented longer distances than those with grades 1-2.

The only patient who was intubated after the third attempt was a 68-year-old female with a BMI of 22.3 kg/m^2. In this case, the CED was 26.9 mm, and the Cormack-Lehane score was 4.

Discriminatory ROC curve analysis showed an AUC of 0.899 with a p-value of <0.001 (null hypothesis of an AUC of 0.5), as shown in Figure 3. This confirms the CED's excellent discriminatory capability for predicting Cormack-Lehane grades 3-4 on direct laryngoscopy. The maximum cut-off point determined by the Youden index was 25.6 mm. Values equal to or above this threshold showed a detection rate of 76 out of 100 patients with potentially difficult laryngoscopy, with false positives in 1 out of 10 individuals.

Figure 4 shows that CED and BMI were positively correlated, and that sex did not significantly affect this interaction. The binary logistic regression results in Table 2 demonstrate an independent increase in the OR for difficult laryngoscopy with each additional point increase in CED and BMI. In the specific case of the US measurement, a nearly 80% increase in the odds of Cormack-Lehane grades 3-4 was observed for each millimeter increase in distance.

5. DISCUSSION

Advances and greater access to equipment and airway management techniques have contributed to reduce the risks associated with unanticipated difficult airways [5,8,12-15]. The results of our study suggest that US-measured CED may help predict Cormack-Lehane grades 3-4 prior to direct laryngoscopy in adult patients without other classic predictors of difficult airway. Notably, since the patients included in this study had no predictors of difficult airway the CED measurement was performed after induction of GA, thereby mimicking situations in which the anesthesiologist may be surprised by an unanticipated difficult airway.

Assessment of the airway using anatomical predictors such as mouth opening, tongue thickness, and hyomental distance is limited to external visualization. US can be useful for identifying potentially difficult airways by assessing the thickness of soft tissues and the inner aspects of the submandibular and neck areas [1,16-19].

Multiple US-guided measurements have recently gained relevance in the specialized literature, such as the distance from skin to the hyoid bone, the relationship between the pre-epiglottic space (distance from the skin to the epiglottis) and the sub-epiglottic space (from the epiglottis to the anterior commissure) [20], evaluation of the angle formed between the glottis and the epiglottis, and calculation of the ratio between the hyomental distance with the head in neutral position vs. extension [21], among others. It has also been noted that combining these measurements with the Mallampati score may further enhance predictive accuracy [21-25].

In a prospective observational study, Falcetta et al. attempted to determine the correlation between the sonographic measurements of anterior cervical soft tissue thickness and Cormack-Lehane grade on direct laryngoscopy in 301 patients without predictors of difficult airway [25]. Pre-epiglottic area of 5.04 cm^2 (sensitivity=85%; specificity = 88%) and mean CED of 25.4 mm (sensitivity = 82%; specificity = 91%) were considered good predictors for diagnosing patients with Cormack-Lehane grade ≥ 2b [20], the latter being similar to (and therefore corroborated by) the results (25.6 mm) found in the present

investigation.

Similarly, a recent systematic review and meta-analysis (N=1812 from 10 studies) focused on the ability of US to predict difficult laryngoscopy in patients without significant clinical/anatomical predictors demonstrated a high accuracy for CED in predicting difficult laryngoscopy with an AUC-ROC of 0.87 (95%CI 0.84–0.90) [25]. As expected, CED was higher in patients with higher Cormack-Lehane grades [25]. Once again, our findings corroborate the systematic review results, with a CED AUC-ROC of 0.899 for detecting patients with Cormack-Lehane grades 3-4. Interestingly, the authors suggest that, despite its excellent sensitivity and specificity, CED is probably most useful when its result is negative [25]. In such cases, the probability of an easy laryngoscopy is approximately 95-97% [25]. This is due to the low prevalence (ranging from 10-20%) of patients with difficult laryngoscopy in the studied populations. A positive CED result suggests approximately 30-50% probability that the patient will indeed present difficulty to be intubated [25].

Although these (and several other) studies have documented CED as a predictor of difficult laryngoscopy, the ideal cut-off points and potential interactions with other factors, such as sex and BMI remain undetermined.

As expected, CED showed a positive correlation with BMI, which was not influenced by sex, as adipose tissue accumulates in the submandibular region somewhat evenly in both men and women. Despite this positive correlation, any increase in CED or BMI was independently associated with greater odds of worse glottic visualization during laryngoscopy [18].

Our analysis showed that a higher Youden index was obtained with a CED of 25.6 mm, which represents the point of optimal trade-off between true and false positive results. Considering this cut-off point, a positive test (equal or higher value) would increase the basal (*a priori*) chance of difficult laryngoscopy by 7.6 times (likelihood positive ratio). With an incidence rate of 27.9%, as observed in our sample, this translates into a positive predictive value of 74% and a negative predictive value of 91%.

Failure to recognize a problematic airway can be dangerous in clinical practice.

Anesthesiologists should approach patients with positive test results cautiously, such as by using videolaryngoscopy, as some of these cases will indeed present difficulties. Being overzealous in this setting may be prudent [25]. Therefore, determining the ideal cut-off point is not as straightforward as univariate comparisons of CED and other population variables, even though the observed AUC-ROC was clinically significant [10].

Owing to the inherent risks associated with difficult airways and the potential for catastrophic results, one might argue that it is better to increase the detection rate, even at the expense of a higher false-positive rate. For example, reducing the cut-off point to 23.35 mm would detect 92% of patients with Cormack-Lehane grades 3-4, with a negative predictive value close to 96%. However, this would also mean that approximately 30% of the patients with lower visualization grades would have values equal to or higher than this threshold, with an unavoidable reduction in the positive predictive value to 54.9%.

The cut-off values for CED considered predictive of difficult laryngoscopy and found in previous studies [10,21-23] range from 25.4 mm to 27.5 mm, with an AUC-ROC of 0.693 to 0.903, which may be explained in part by differences in ethnicity and other population characteristics. Our results not only corroborate those findings, but further extend the current knowledge by showing that with each millimeter increase in CED, the odds of Cormack-Lehane grade 3-4 on direct laryngoscopy increased by approximately 80%.

This study has limitations: (i) since studied patients had no predictors of difficult laryngoscopy, CED measurements took place *after* induction of anesthesia and muscle relaxation; nevertheless, it would have been beneficial to also assess the CED's predictive capability in (spontaneously breathing) patients *before* anesthesia induction which we intend to study in a follow-up investigation; (ii) this was a single-center investigation that did not include patients with known markers of difficult airway (e.g., limited mouth opening/neck extension) which would have likely increased the incidence of Cormack-Lehane grades 3-4; (iii) there is a tendency for videolaryngoscopy to become the standard technique for tracheal intubation, particularly in patients with suspected difficult airways, and the classic predictors of difficulty in direct laryngoscopy may not apply in this context; (iv) due to the exploratory

nature of our secondary objectives and the absence of specific sample size calculations or correction methods used for multiple comparisons, our results should be interpreted cautiously. Type II errors may occur with an unspecified probability in situations where there are no significant differences, and higher chances of type I errors are expected due to the family-wise error rate. Therefore, the Bonferroni correction suggests that the p-value threshold for statistical significance should be 0.016 for our secondary outcomes; (v) adequate training is necessary for one to accurately measure CED [26] which also requires adequate patient ("sniffing") positioning; and (vi) should oxygen desaturation occur following induction of GA, measures to re-establish adequate oxygenation must take precedence over CED measurement.

In conclusion, US-measured CED has a high discriminatory capability at predicting lower (grades 1-2) and higher (grades 3-4) Cormack-Lehane visualization during direct laryngoscopy. This suggests that CED can be a valuable tool for identifying patients with potentially difficult airways and challenging management. Additionally, our results indicate a positive correlation between CED and BMI, with increasing BMI independently associated with a higher chance of difficult intubation. No significant differences were found when evaluating the correlation between patient sex and CED.

6. REFERENCES

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7. TABLES

Table 1. Demographic data, type of surgery, Cormack-Lehane classification, and frequency of tracheal intubation attempts.

Variable	Value
Age*	47.6 ± 14.2 years
Sex†	
Male	54 (54%)
Female	46 (46%)
Weight*	76.2 ±14.6 kg
Height*	169.7 ± 9.3 cm
BMI	26.4 ± 3.7 kg/m^2
Cormack-Lehane grade†	
1 or 2	62 (72.1%)
3 or 4	24 (27.9%)
Frequency of intubation attempts†	
1	86 (86%)
2	8 (8%)
3	5 (5%)
4‡	1 (1%)
Type of surgery†	
Abdominal	34 (34%)
Orthopedic	30 (30%)
Ear, nose, and throat	15 (15%)
Neurosurgery	12 (12%)
Urologic	3 (3%)
Thoracic	3 (3%)
Cardiac	3 (3%)

*Values expressed in mean ± standard deviation.
†Values expressed as absolute and relative frequencies.
‡Three attempts by the same anesthesiologist with an additional attempt by a more experienced specialist.

Table 2. Binary logistic regression for Cormack-Lehane grades 3 or 4 according to the cutaneous-epiglottic distance (mm) and the body mass index (kg/m^2).

Variable	Odds ratio (OR)	OR 95% Confidence Interval	p-value
Cutaneous-epiglottic distance	1.81	1.35–2.41	<0.001
Body mass index	1.30	1.05–1.59	0.014

8. FIGURE CAPTIONS

Figure 1. Airway ultrasound images and respective cutaneous-epiglottic distance (CED) measurements. The epiglottis is outlined (dashed orange line) in panel A.

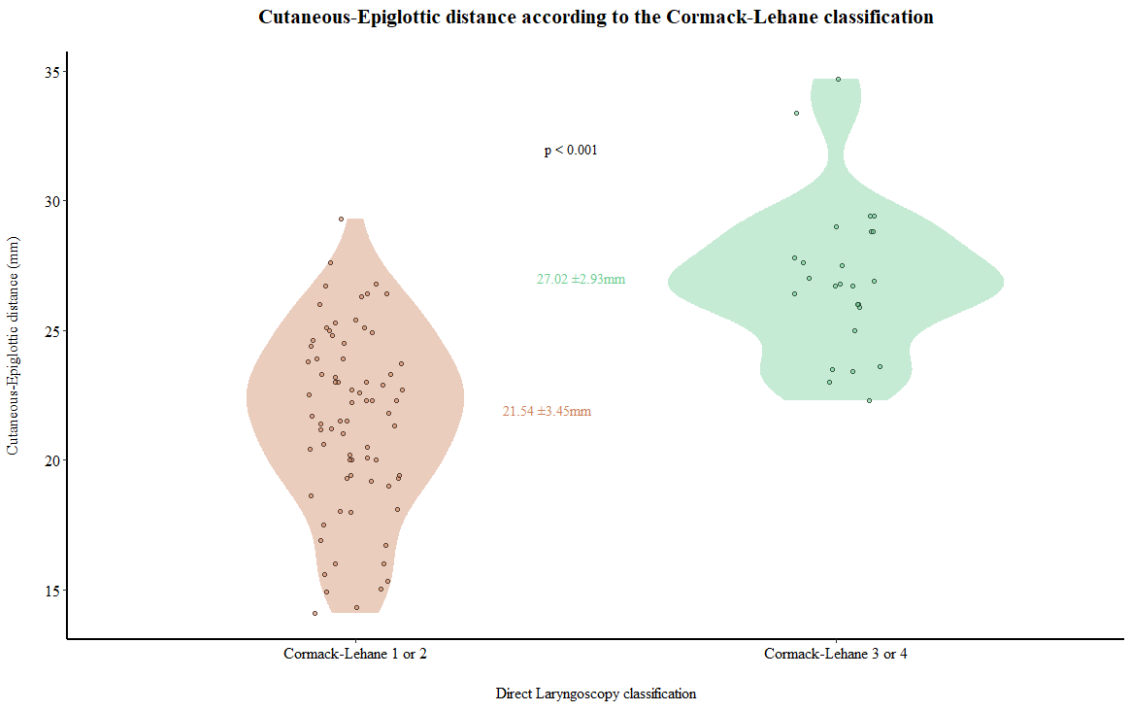

Figure 2. Relationship between the cutaneous-epiglottic distance and the Cormack-Lehane classification with respective means and standard deviations

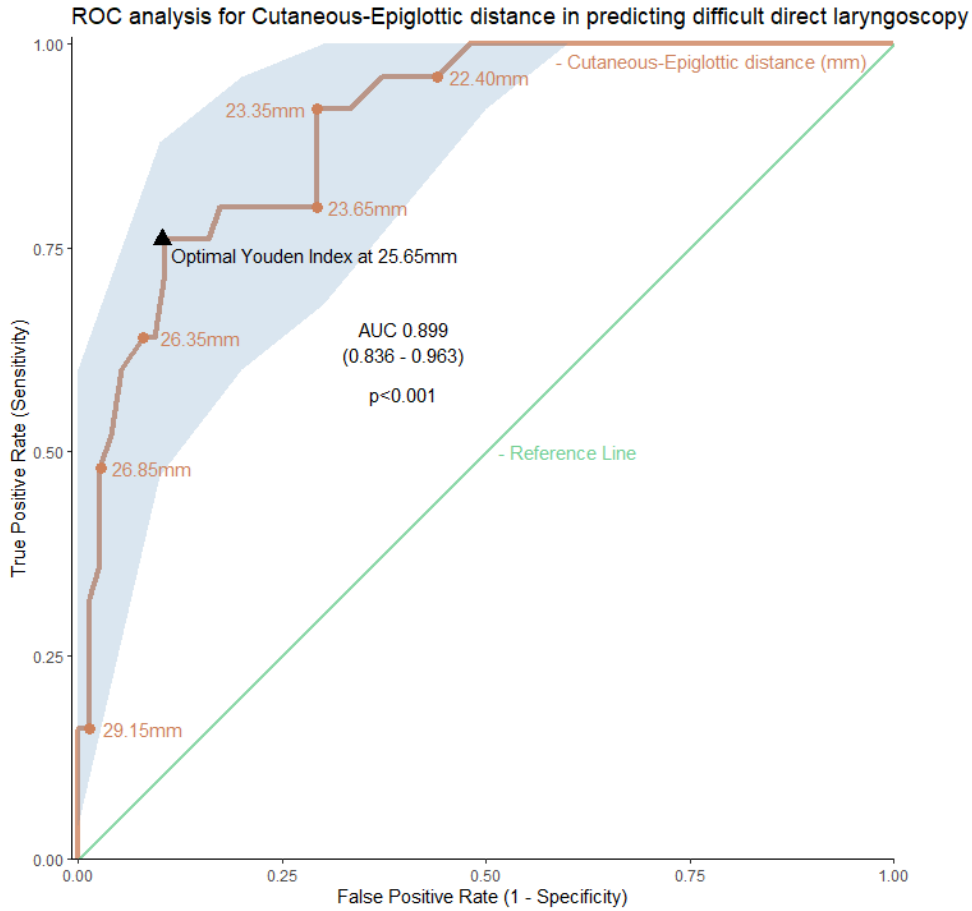

Figure 3. Receiver operator characteristics curve with the area under the curve (AUC) and the 95% confidence interval of the cutaneous-epiglottic distance for prediction of Cormack-Lehane grades 3 or 4.

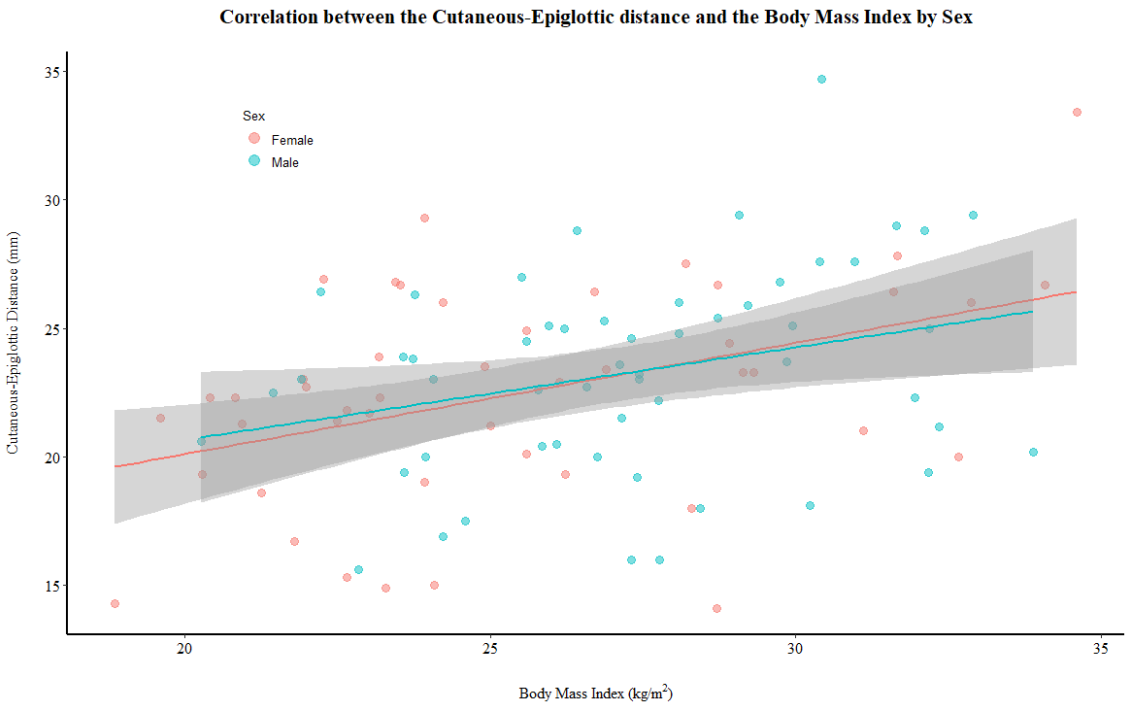

Figure 4. Scatter plot of cutaneous-epiglottic distance and body mass index by sex with respective linear regression lines, p-values, and confidence intervals.