

REVIEW

Predictive parameters of difficult intubation in thyroid surgery: a meta-analysis

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ABSTRACT

INTRODUCTION: Airway management is a fundamental goal for the anesthesiologist. The rate of difficult laryngoscopy in patients undergoing thyroid surgery ranges from 6.8% to 9.6%. An accurate and detailed preoperative evaluation of the airway seems to be a promising tool to predict a potentially difficult airway management. We aimed to identify possible risk factors and physical findings that predict difficult intubation in thyroid surgery.

EVIDENCE ACQUISITION: MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) were analyzed, and the reference lists from the retrieved articles and previous reviews were searched for additional studies. Difficult intubation was defined as Cormack and Lehane grade ≥ 3 or Intubation Difficulty Scale score >5 by direct laryngoscopy. Studies that used advanced airway devices or ultrasound-based airway management were excluded. Gender, Mallampati Score, interincisor gap, thyromental distance, body mass index, tracheal deviation, histology, mediastinal goiter, mandibular protrusion, neck circumference and neck movement were evaluated. Qualitative analysis has been conducted in case of insufficient data for an appropriate meta-analysis.

EVIDENCE SYNTHESIS: Eight studies that evaluated the accuracy of clinical findings for identifying difficult intubation in thyroid patients were reviewed (5853 patients). Two authors independently screened articles, extracted data and assessed risk of bias. 7.21% [95% CI: 6.57-7.91%] of patients undergoing thyroid surgery were difficult to intubate. The physical examination findings that best predicted a difficult intubation included Mallampati Score ≥ 3 (positive odds ratio 4.75 [95% CI: 2.22-10.12]); shorter thyromental distance thresholds ranging from <6.5 - <6 cm; OR 3.64 [95% CI: 1.9-7.01]); 'low' interincisor gap, defined as a critical distance between incisors (ranging from <3.5 - <4.4 cm; odds ratio 2.57 [95% CI: 1.83-3.62]); presence of tracheal deviation (positive odds ratio, 2.06 [95% CI: 1.58-2.69]); Body Mass Index >30 kg/m² (odds ratio 1.95 [95% CI: 1.20-3.15]) and males (odds ratio 1.54 [95% CI: 1.21-1.95]). Histological examination positive for cancer didn't increase the risk for difficult intubation. For mediastinal goiter, mandibular protrusion, neck circumference and neck mobility only a qualitative analysis was performed.

CONCLUSIONS: In thyroid patients, the presence of high Mallampati Score, shorter thyromental distance, interincisor gap, tracheal deviation (the unique thyroid pathology linked parameter), obesity and male gender were risk factors for difficult intubation. However, all these significant parameters should be used in preoperative assessment to anticipate difficult intubation in thyroid surgery.

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KEY WORDS: Systematic review; Meta-analysis; Intubation, intratracheal; Thyroidectomy.

Introduction

Airway management is a fundamental goal for the anesthesiologists; inappropriate management of the airway remains the single largest class of injury in the American Society of Anes-

thesiology Closed Claims Study.¹ A meta-analysis found that the overall incidence of difficult intubation (DI) for normal patients is 6.2% [95% CI: 4.6-8.3%] (excluding obstetric patients 3.1% [95% CI: 1.7-5.5%] and patients with obesity 15.8% [95% CI: 14.3-17.5%]).² In addition, the

rate of difficult laryngoscopy has been estimated between 6.8% to 9.6% during thyroid surgery.^{3, 4}

An accurate and detailed preoperative evaluation of the airway seems to be a promising tool to predict a potentially difficult airway management.⁵ Many factors, actually used in clinical practice, have been found to be associated with DI but more studies are necessary to define the real predictive value of each parameter (*i.e.* Body Mass Index, goiter, tracheal deviation, cancer etc.) in case of thyroid pathology.

The goal of this meta-analysis is to identify the factors potentially correlated to DI in thyroid surgery, examining both classic predictors (*i.e.* Body Mass Index, Mallampati Score) and thyroid pathology linked parameters (*i.e.* thyroid cancer, mediastinal goiter and tracheal deviation).

Evidence acquisition

A review protocol was written before conducting this study and published on a prospective register of systematic reviews, PROSPERO, with identifier CRD42019129472 (available online for consultation) on May 28, 2019. We performed a meta-analysis of the medical literature following the PRISMA Statement Guidelines (Preferred Reporting Items for Systematic Reviews and Meta-analyses)⁶ for the identification, screening, and inclusion of articles (Figure 1).⁶

Search strategy

The searches were performed on May 31st 2019 in the following databases: MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL). To reduce publication bias, the ongoing trials at ClinicalTrials.gov and the proceedings from the American Society of Anesthesiologists annual meetings over the last five years were also retrieved. The search strategy used was (“difficult intubation” or “difficult laryngoscopy” or “difficult airway” or “difficult airway management”) and (thyroid or thyroidectomy or goiter or goitre or “thyroid surgery”). We did not apply any restrictions on publication type, status and year of publication in our search. We also checked the reference lists of included studies. Each citation was reviewed in duplicate by two of the reviewers, with full-text retrieval

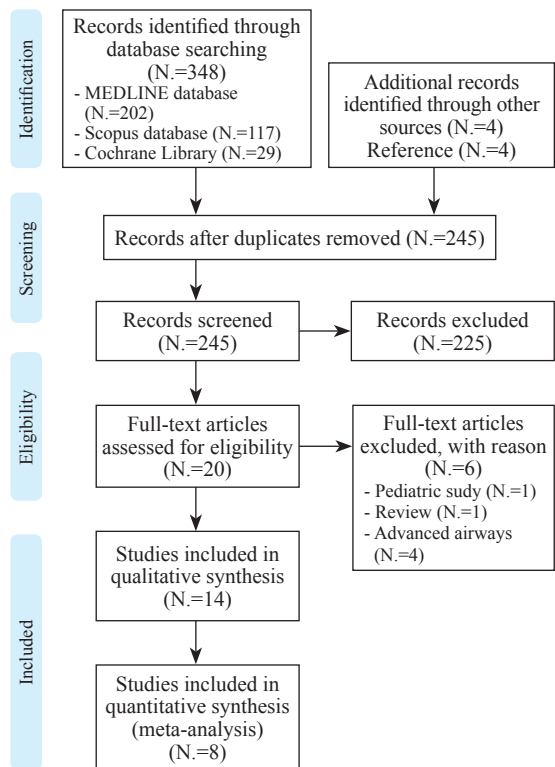


Figure 1.—PRISMA flowchart.⁶

of any citation that either reviewer considered potentially relevant for assessing risk factors or clinical tests that predict difficult intubation.

Study selection

The two reviewers (AB and ADC) independently assessed the full text of each retrieved citation. The following criteria were used for study inclusion: 1) cohort studies with more than 20 participants or randomized controlled studies with more than 20 participants; 2) population of adult patients aged 18 years or older undergoing thyroid surgery; 3) intervention of endotracheal intubation performed by direct laryngoscopy; 4) outcomes of difficult laryngoscopy or endotracheal intubation that was measured in the same manner for all patients in each individual study. We excluded studies that were not written in English or Italian, review articles, case reports, or if we were not able to extract relevant data. Studies that used advanced airway devices (*i.e.*, videolaryngoscopy) or ultrasound-based airway assessment for endotracheal intubation also were excluded.

Data retrieval

After identifying those studies that met our inclusion criteria and determining whether additional data were missing, a request about the potential risk factors affecting DI (*i.e.* gender, Mallampati Score etc.) was sent by mail to the corresponding author of the study. If no response was received from the corresponding author after our initial request, after a week, a second request was sent.

Quality assessment

The two authors who performed searching and data extraction then independently read all included non-randomized comparative studies and evaluated the quality using the Newcastle-Ottawa Scale (NOS). The following three items were assessed: selection, comparability and outcome. A study can be awarded a maximum of one star for each numbered item with the “selection” and “outcome” categories. A maximum of two stars can be given for “comparability.” The total score of the NOS ranged from zero to nine. Studies scoring <4 points was considered to be of low quality.⁷

Quality of evidence assessment

The quality in prognosis studies (QUIPS) tool is an important instrument to assess the study quality and risk of bias. It consists of several prompting items categorized into six domains, and each domain is judged on a three-grade scale (low, moderate or high risk of bias).⁸ High bias occurs when the relationship between prognostic factors and the outcome is very likely to be different for participants and eligible nonparticipants. Moderate bias occurs when the relationship between prognostic factors and outcome may be different for participants and eligible nonparticipants. Low bias occurs when the relationship between prognostic factors and outcome is unlikely to be different for participants and eligible nonparticipants.

Statistical analysis

Published data with mean and standard deviation were entered as continuous variables, while published data with the presence or absence of difficult intubation were entered as dichotomous variables. For continuous variable outcomes, the weighted mean difference (WMD) and 95%

CI were calculated. An outcome subgroup analysis for both Cormack-Lehane (CL) and Intubation Difficulty Scale (IDS) was performed to explain the heterogeneity across studies.

In order to determine the risk factors affecting difficult intubation, gender, Mallampati Score (MS), interincisor gap (IG) (defined as the distance between superior and inferior incisors), thyromental distance (TM) (measured from the thyroid notch to the tip of the jaw with the head extended), body mass index (BMI), tracheal deviation (TD), histology (Hist), mediastinal goiter (MG), mandibular protrusion (MP), neck circumference (NC) and neck movement (NM) were considered and the meta-analysis was performed using RevMan version 5.3 (Foundation for Statistical Computing, Vienna, Austria).

The confidence interval was established at 95%, and $P < 0.05$ was considered to be statistically significant. For the assessment of study heterogeneity, the χ^2 distribution and I^2 statistic were used (we considered I^2 values as follows: minimal: <25%, moderate: 25% to 50%, or high: >50%). If a moderate or high level of heterogeneity was noted, squared Pearson residual Baujat plot and *r* student diagnostic tests were undertaken to identify outlier studies for consideration of exclusion. Sensitivity was also assessed by leave-one-out analysis. We excluded studies with an *r* student *z*-value higher than two, and the effect size recalculated in the absence of these studies.^{9, 10}

Evidence synthesis

Study selection

We summed up the results of bibliographic search in Figure 1. It shows the PRISMA diagram indicating the number of papers included and excluded at each stage. In our bibliographic search we identified 348 articles. After removal of duplicate studies, the search retrieved 245 articles that were retrieved for further examination after inspecting titles and abstracts. After reviewing these, 20 full-text articles^{3, 4, 11-28} were assessed for eligibility and six were excluded (one pediatric trial, one review and four studies based on advanced airway devices for tracheal intubation or surgical items).²³⁻²⁸ A total of 14 studies entered the qualitative analysis^{3, 4, 11-22} but

six of them were excluded because we were not able to extract relevant data.^{16, 18-22} Therefore, eight studies, including a total of 5853 patients, were considered in the final quantitative analysis.^{3, 4, 11-15, 17}

Data retrieval

Three authors replied to our query. However, only one author¹⁴ provided us the missing data about gender, Mallampati Score, IG etc.

Study characteristics

Table I compiles the included studies' characteristics.^{3, 4, 11-15, 17}

When considering the eligible studies alone,

the overall proportion of difficult intubation in patients undergoing thyroid surgery was 7.21% [95% CI: 6.57-7.91%].

DI was defined as a CL grade ≥ 3 ²⁹ in three studies^{3, 4, 15} and as an IDS Score >5 ³⁰ in five studies.^{11-14, 17}

With regards to quality assessment, five studies were recorded as "good quality" (NOS equals to 6)^{3, 4, 11, 12, 14} and only three recorded a 'fair quality' (NOS 5).^{13, 15, 17} Specifically, Meco *et al.*¹³ recorded only two stars in the 'selection' domain because the authors enrolled only females; while Kalezić *et al.*¹⁵ and Mallat *et al.*¹⁷ recorded only one star in outcome categories because their assessment outcome was very poor. In detail, the aim of the first study¹⁵ was to

TABLE I.—Overview of included studies' characteristics and quality assessment.

Study	Design	Outcome	N. patients	Gender	MS	IG	TM	BMI	TD	Hist	MG	MP	NC	NM	NOS Score [^]
Amathieu (2006) ¹¹	Cohort	IDS	324	a	a	a	a	a	a	a	a	a		a	Selection *** Comparability * Outcome/Exposure ** <i>Good quality</i>
Bouggad (2004) ¹²	Cohort	IDS	320	a	a	a	a		a	a		a		a	Selection *** Comparability * Outcome/Exposure ** <i>Good quality</i>
De Cassai (2019) ⁴	Cohort	Cormack	500	a	a	a/b	a/b	a/b	a	a	a	a	a/b	a	Selection *** Comparability * Outcome/Exposure ** <i>Good quality</i>
Kalezić (2009) ¹⁵	Cohort	Cormack	2000	a						a					Selection *** Comparability * Outcome/Exposure * <i>Fair quality</i>
Kalezić (2016) ³	Cohort	Cormack	2379	a	a	a	a	a	a	a		a	a	a	Selection *** Comparability * Outcome/Exposure ** <i>Good quality</i>
Mallat (2010) ¹⁷	Cohort	IDS	80	a				b							Selection *** Comparability * Outcome/Exposure * <i>Fair quality</i>
Meco (2015) ¹³	Cohort	IDS	50	a	a		a			a			a	a	Selection ** Comparability * Outcome/Exposure ** <i>Fair quality</i>
Tutuncu (2018) ¹⁴	Cohort	IDS	200	a	a	a	a	a/b	a	a	a	a	a	a	Selection *** Comparability * Outcome/Exposure ** <i>Good quality</i>

IDS: Intubation Difficulty Scale; MS: Mallampati Score; IG: interincisor gap; TM: thyromental distance; BMI: Body Mass Index; TD: tracheal deviation; Hist: histology; MG: mediastinal goiter; MP: mandibular protrusion; NC: neck circumference; NM: neck movement; a: dicotomiche b: medie; NOS: Newcastle-Ottawa Scale.

[^]*Good quality*: 3 or 4 stars (*) in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome domain; *Fair quality*: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain; *Poor quality*: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 1 or 1 star in outcome/exposure domain.

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TABLE II.—Risk of bias of the included studies based on the QUIPS tool.

Study	Study participation	Study attrition	Prognostic factor measurement	Study confounding	Outcome measurement	Statistical analysis and reporting
Amathieu (2006) ¹¹	Green	Green	Green	Yellow	Green	Green
Bouggad (2004) ¹²	Green	Green	Green	Yellow	Yellow	Yellow
De Cassai (2019) ⁴	Green	Green	Green	Green	Green	Green
Kalezic (2009) ¹⁵	Green	Yellow	Yellow	Green	Yellow	Yellow
Kalezic (2016) ³	Green	Green	Green	Green	Green	Green
Mallat (2010) ¹⁷	Green	Yellow	Yellow	Green	Yellow	Yellow
Meco (2015) ¹³	Yellow	Yellow	Green	Red	Yellow	Green
Tutuncu (2018) ¹⁴	Green	Green	Green	Yellow	Green	Green

Authors' judgment about each risk of bias item for each included study. High risk of bias (red): The relationship between the PF and outcome is very likely to be different for participants and eligible nonparticipants. Moderate risk of bias (yellow): The relationship between the PF and outcome may be different for participants and eligible nonparticipants. Low risk of bias (green): The relationship between the PF and outcome is unlikely to be different for participants and eligible nonparticipants.

evaluate the incidence of DI in thyroid surgery and to assess possible correlation of DI with sex and primary diagnosis. So, no data were available about the risk factors for DI under consideration in this meta-analysis; while Mallat *et al.*¹⁷ reported their findings only as median and 25th-75th percentiles (except for gender and BMI).

With respect to risk of bias (Table II),^{3, 4, 11-15, 17} the most part of the considered studies recorded low or moderate risks (green or yellow circle) about study participation, study attrition, outcome

and statistical analysis and reporting.^{3, 4, 11, 12, 14-17} One study solely had a high risk of bias because only females were enrolled ('study confounding', red circle).¹³

Risk factors of DI

Gender

As shown in Figure 2A, compared with women, men were more difficult to intubate (positive OR, 1.54 [95% CI: 1.21-1.95], P<0.001). Specifically,

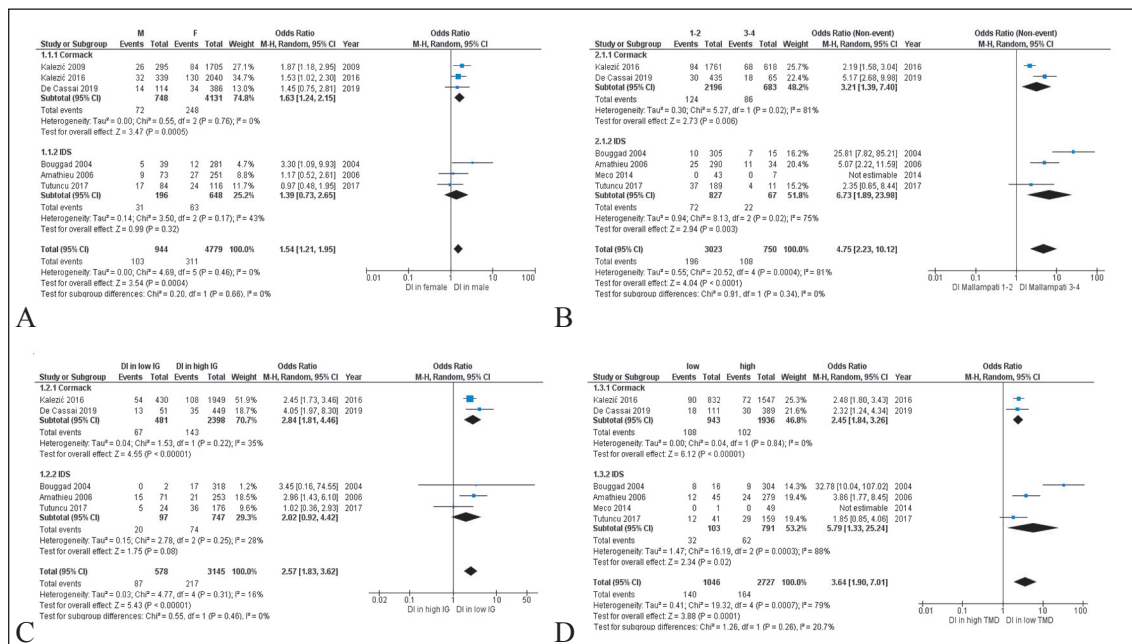


Figure 2.—Forest plot of the odds-ratio of difficult intubation in thyroid patients. A) Random-effect forest plot for gender; B) random-effect forest plot for Mallampati Score; C) random-effect forest plot for interincisor gap; D) random-effect forest plot for thyromental distance.

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six studies were analyzed. Three were based on CL grade ($I^2=0\%$)^{3, 4, 15} and three based on IDS ($I^2=43\%$)^{11, 12, 14}. The overall heterogeneity was $I^2=0\%$ ^{3, 4, 11-15}

Mallampati

The Mallampati Score was the most frequently assessed clinical test in our analysis. A Mallampati score ≥ 3 had strong accuracy for predicting DI (OR, 4.75 [95% CI: 2.22-10.12], $P<0.001$), both when CL grade was ≥ 3 ($I^2=81\%$)^{3, 4} or when IDS was >5 ($I^2=75\%$)¹¹⁻¹⁴. However, there was high heterogeneity across the studies ($I^2=81\%$) (Figure 2B).

Interincisor gap

A short IG was defined as a critical distance <4 cm in four studies^{4, 11, 12, 14} or as a distance <3.5 cm in females and <4.4 cm in males in one study.³ Conventionally, we defined two groups called “low” IG and “high” IG, and patients with a low IG had a risk of DI almost three times higher than the other group (positive OR, 2.57 [95% CI: 1.83-3.62], $P<0.001$). In detail, two studies analyzed CL grade^{3, 4} ($I^2=35\%$), while three IDS ($I^2=28\%$)^{11, 12, 14}. The overall heterogeneity was 16% (Figure 2C).

Thyromental distance

A shorter TM distance (thresholds ranging from <6.5 - <6 cm) increased the likelihood of DI (positive OR, 3.64 [95% CI 1.90-7.01], $P<0.001$). Two studies were based on CL grade ($I^2=0\%$)^{3, 4} and four IDS ($I^2=88\%$)¹¹⁻¹⁴. The overall heterogeneity was $I^2=79\%$ (Figure 2D).

BMI

Obesity, defined as a BMI >30 kg/m², was a valid predictor of DI (positive OR, 1.95 [95% CI 1.20-3.15], $P<0.001$). Two studies were based on CL Score ($I^2=0\%$)^{3, 4} and two on IDS ($I^2=53\%$)^{11, 14}. The final heterogeneity was $I^2=53\%$ (Figure 3A).^{3, 4, 11, 12, 14, 15}

Tracheal deviation

As shown in Figure 3B, the presence of TD had valid accuracy for predicting a DI (OR, 2.06 [95% CI 1.58-2.69], $P<0.001$, $I^2=0\%$). Specifically,

two studies considered CL grade ($I^2=19\%$)^{3, 4} and three IDS ($I^2=0\%$)^{10, 11, 13}

Histology

A positive histology for malignant cancer did not increase the risk of DI ($P=0.21$). Three studies were considered CL grade ($I^2=7\%$)^{3, 4, 15} and four investigations were based on IDS ($I^2=94\%$)¹¹⁻¹⁴ and the overall heterogeneity was $I^2=89\%$ (Figure 3C).

Mediastinal goiter

Mediastinal goiter was evaluated only in three studies and their outcome assessment was very different.^{4, 11, 14} As such, a meta-analysis was not performed.

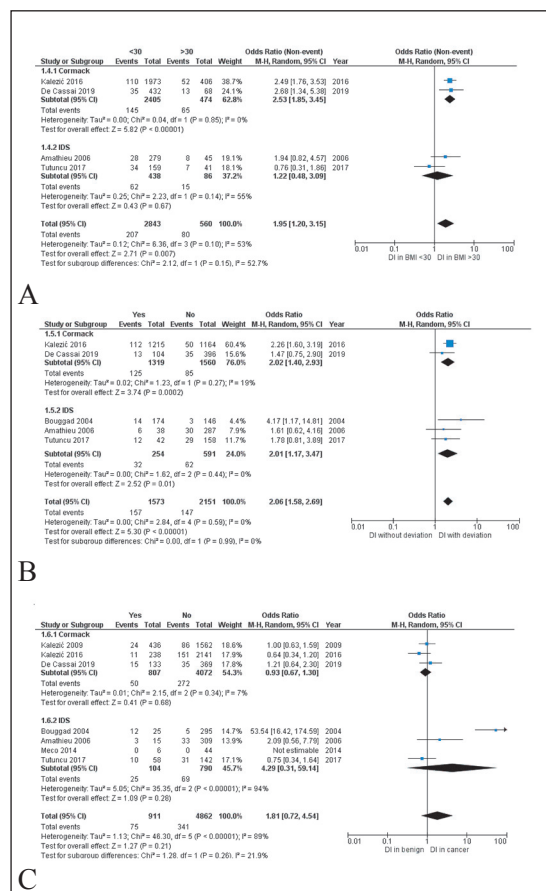


Figure 3.—Forest plot of the odds-ratio of difficult intubation in thyroid patients. A) Random-effect forest plot for Body Mass Index; B) random-effect forest plot for tracheal deviation (predictive factor related to thyroid pathology); C) random-effect forest plot for histology (predictive factor related to thyroid pathology).

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Mandibular protrusion

Mandibular protrusion had heterogeneous definitions and for this reason we were not able to perform a meta-analysis.

Neck circumference

Evaluation of neck circumference had heterogeneous definition ranging from “impression” of short and large neck,¹¹ to numeric evaluation (<40 cm, <39.5 cm, <43 cm),^{4, 14, 17} to classification in three categories (<25 cm, 25-30 cm, >30 cm).³ Although these heterogeneous conditions prevent us from performing a meta-analysis, we have to highlight that all studies found significant correlation between a larger neck circumference and difficult intubation.

Neck movement

Neck mobility reduction was defined as a movement ranging from less than 80^{3, 11, 13, 17} to less than 90 degrees.^{4, 12} However, the comparability of data was difficult because the method of measurement was not clearly stated in each study. So, we decided not to perform a quantitative synthesis of this variable given the heterogeneous endpoint.

Discussion

This is the first meta-analysis specifically focused on DI predictors in patients undergoing thyroid surgery, examining both classic predictors (*i.e.* Body Mass Index, Mallampati Score)^{1, 2} and thyroid pathology linked parameters (*i.e.* thyroid cancer, mediastinal goiter and tracheal deviation).

The main results of this meta-analysis suggest the possibility to anticipate a DI in thyroid surgery when Mallampati Score (MS) is above 3, thyromental distance (TM) is short (usually defined as less than 6.5 cm) and interincisor gap (IG) is below 4.4 cm. Specifically, MS estimates the size of the tongue relative to the oral cavity and this test assesses not only pharyngeal structure but also head and neck mobility. However, in our analysis MS recorded a high heterogeneity ($I^2 > 50\%$) limiting its diagnostic value in clinical practice.

Similar results were obtained for TM. It is considered a valid indicator of mandibular space, reflecting whether displacement of the tongue by the laryngoscope blade will be easy or difficult;

but, as shown in the overall population,^{1, 2} the methods of measurements (from inside or outside the mentum) and test thresholds (cutoff points varied from 6 to 6.5 cm) should be standardized, both possible reasons of high heterogeneity, as reported in our results.

Considering IG, we calculated an OR of 2.57, with a low heterogeneity, in patients with “lower” gap, which means limited movements of the temporo-mandibular joint and reduced exposure of the larynx. A previous multivariate analysis, conducted in adults without thyroid pathology,^{31, 32} confirmed our findings, even if some authors still disagree about the real prognostic value of this parameter.²

In addition, we found that the odds of DI increases moderately when BMI is higher than 30 kg/m² and in males.¹ Specifically, obesity is a recognized risk factor of DI also in the overall population, with an incidence around 15.8%.² Both mask ventilation and laryngoscopy could be potentially challenging. The reasons are related to shorter safe apnea time, altered lung mechanics, and increased risk of gastroesophageal reflux disease.³³ So, suitable techniques for minimizing risks and length of time of hypoventilation during induction, intubation and recovery must be adopted and planned in advance.³³

About mandibular protrusion (MP), its definition was heterogeneous and we were not able to perform a meta-analysis. Amathieu *et al.*¹¹ found that an appearance of a retrognathic midface and prognathic mandibular profile correlate with a difficult intubation (<0.001). In another study Kalezic *et al.*³ classified mandibular protrusion in three classes (absent, moderate and significant) and found a higher incidence of difficult intubation in the presence of mandibular protrusion (<0.001). However, three other studies found that a protruding or receding mandible,¹² the inability to prognath⁴ or mandibular protrusion¹⁴ were not correlated with difficult intubation.

In addition, a qualitative analysis suggests that larger neck circumference (NC)^{3, 4, 11, 14, 17} and reduced neck movements (NM)^{11, 12} correlate with DI.

Focusing on the risk factors that are unique linked to thyroid surgery (*i.e.* TD, Hist, MG), the presence of tracheal deviation (TD) correlates to a twice higher risk of DI, even if it could be defined a “subglottic” parameter. Specifically, we

can speculate two different reasons for this finding: one affecting the glottic plane directly and the other indirectly. Firstly, tracheal deviation occurs with larger goiter. A larger goiter could potentially dislocate the glottic plane laterally causing a worse view of epiglottis at direct laryngoscopy. Secondly, a larger goiter is usually correlated with a larger NC, a recognized risk factor of difficult intubation. In fact, all the studies included in this meta-analysis showed significant correlation between a larger neck circumference and difficult airway management, even if heterogeneous conditions prevented us to perform a quantitative analysis.

About Hist, a positive histology for malignant cancer did not increase the risk of DI (p 0.21); while mediastinal goiter (MG) was evaluated only in three studies and their outcome assessment was very different,^{4, 11, 14} so we were not able to perform a valid meta-analysis. However, Amathieu *et al.*¹¹ solely found a meaningful correlation between mediastinal goiter and DI.

Further investigations are necessary to assess the real probability of difficult intubation in the case of patients affected by thyroid pathology. In addition, it's important to understand if the presence of TD is the unique risk factor, linked to thyroid pathology, really significant in this specific clinical setting.

In fact, patients undergoing thyroid surgery are wrongly considered at higher risk of difficult intubation; but, according to our findings, the rate of difficult airway management in case of thyroid pathology is even lower (7.21% [95% CI: 6.57-7.91%]) than the incidence in standard population (10% [95% CI: 8.2-12%]).³⁴ This meta-analysis shows that there are not specific predictive parameters of difficult intubation exclusively linked to thyroid surgery, except for tracheal deviation. It means that the risk of difficult intubation, in this specific subgroup of patients, is comparable to that in the overall population and it should be stratified using the same tools available for standard population.

New technologies, such as ultrasound probes³⁵ and videolaryngoscope,³⁶ are making a great difference in airway management in last decades. We strongly believe that these technologies will radically modify the way to predict and plan potential difficult intubations.

However, we decided to exclude these new devices from our protocol for many reasons. Firstly, ultrasound-based methodology is a relatively new technique.³⁵ Viewing retrospectively, none of the papers included in this meta-analysis investigated its use in daily practice. Recent papers, published about the potential role of ultrasound-based airway management to predict difficult direct laryngoscopy, are not focused on thyroid pathology, our first inclusion criteria.³⁵ However, we strongly believe that ultrasound-based airway assessment is a useful, simple, noninvasive bedside tool as an adjunct to clinical methods, but to date, more investigations are necessary to validate its use in clinical practice.

Secondly, video-laryngoscopy is another useful tool to improve glottic view. In many cases, this advance device made easier the glottic plane visualization, and many difficult intubations, defined as $CL \geq 3$, were not anymore. For this reason, we concluded that data derived from direct laryngoscopies or from videolaryngoscopy were not comparable, and including studies based on videolaryngoscopy would raise the heterogeneity of our findings, avoiding us to be conclusive about the investigated variables.

And finally, we would like to highlight the limits of each predictive test previously described, which will always need to be performed properly, especially when considered individually. In addition, we would like to stress the importance of oxygenation during airway management. Neither predictive tests or new devices should cause fixation errors, moving our attention from our first goal: oxygenation.³⁷

Strengths and limitations of the study

Strengths of the meta-analysis include independent screening, study classification and coding, and the risk of bias assessment. The use of meta-analysis increased the precision of the key point estimate, and formal assessment of publication bias has helped to qualify that estimate. To the most part of analyzed studies a low or moderate risk of bias were assigned. Only one study was high in risk of bias, particular concerns study participation (females only), and lack of adjustment for this confounding variable.¹³

We excluded studies focused on advanced

airway devices for endotracheal intubation or ultrasound-based airway management, even if routinely used in 'modern' anesthesia. The aim was to reduce confounders linked to the use of advanced methodologies, valid tools to bypass a potential difficulty but possible source of misleading results. In addition, the definition of difficult intubation could be inappropriate (ie, CL grade ≥ 3 ²⁹ in three studies^{3, 4, 15} and an IDS Score >5 ³⁰ in five studies^{11-14, 17}), because poor visualization is not always associated with difficult intubations especially in the era of videolaryngoscopy.³⁸

Moreover, we investigated a limited number of variables. For example, we did not consider the influence of obstructive sleep apnea, of upper lip bite test or sternomental distance as risk factors of difficult direct laryngoscopy in thyroid subjects. The reason is related to missing data about all these parameters in each reviewed paper, even if these factors have been shown to be potentially linked to higher risk of difficult airway management in standard population.^{34, 39} IG and TM thresholds were heterogeneous across the studies and for this reason we decided to split the population into a high distance and a low distance group. However, we recognize that this is an arbitrary choice and does not permit us to be conclusive about this topic. Heterogeneous endpoints did not permit us to perform meta-analysis on NC and MP and we could perform only a qualitative analysis. However, a meta-analysis is always better than a qualitative analysis and we recognize it as a limit.

Another limitation of this study is the difficulty in retrieving missing data from authors. We recognize that having full data could give more strength to our conclusions.

Another limitation is the choice of the database that is arbitrary and the exclusion of non-English and non-Italian articles.

Conclusions

Prospective cohort studies suggested that $MS \geq 3$, reduced TM distance, low IG significantly increase the likelihood of difficult intubation in thyroid surgery; while the presence of TD (the unique thyroid pathology linked parameter), obesity and males moderately elevate the risk of difficult airway management in this specific clinical setting. In conclusion, we strongly suggest

to use all these significant parameters for a more accurate preoperative assessment with the aim to anticipate difficult intubations and to optimize potentially difficult airways in thyroid surgery.

Key messages

- This is the first meta-analysis specifically focused on DI predictors in patients undergoing thyroid surgery, examining both classic predictors and thyroid pathology linked parameters.
- Our meta-analysis suggests the possibility to anticipate a difficult intubation in thyroid surgery when Mallampati Score is above three, thyromental distance is short (less than 6.5 cm), interincisor gap is below 4.4 cm, BMI is higher than 30 kg/m² and in the presence of tracheal deviation.
- Patients undergoing thyroid surgery are usually considered at higher risk factor for difficult intubation than patients undergoing other surgeries. However, the difficult intubation incidence from this meta-analysis is lower (7.21% [95% CI: 6.57-7.91%]) than in standard population (10% [95% CI: 8.2-12%]).
- There are not specific predictive parameters of difficult airway in thyroid patients, except for tracheal deviation.

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