Article title: Predictors for Difficult Laryngeal Exposure in Suspension Laryngoscopy: A Systematic Review and Meta-Analysis

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Highlight:

Investigation of critical predictors for difficult laryngeal exposure in suspension laryngoscopy.

Carefully retrieve and screen over 1000 studies from various databases and registers.

Strict adherence to guidelines for Meta-analysis and well-described methodology.

ABSTRACT

Objectives/Hypothesis: Many researchers have investigated parameters that could independently predict difficult laryngeal exposure (DLE) in suspension laryngoscopy; however, inconsistent results and conclusions have been reported in previous studies. We conducted a meta-analysis of the existing literature to determine the parameters that are significant for a standardized preoperative DLE prediction system.

Methods: The literature was retrieved systematically from PubMed, Embase, Web of Science, China national knowledge infrastructure (CNKI), and Wangfang until October 2022. In eligible studies, data were extracted and analyzed using the R language, and effective measures were odds ratios with 95% confidence intervals (CIs) for dichotomous variables and mean differences (MD) with 95% CIs for continuous variables.

Results: The search yielded 1574 studies, of which eighteen involving 2263 patients were included. Pooled analysis demonstrated that patients with DLE during microsurgery are often men (OR =1.73, 95% CI = [1.16, 2.57]); older age (MD = 5.47 years, 95% CI = [2.44, 8.51]); high body mass index (BMI; MD = 1.19Kg/m^2, 95% CI = [0.33, 2.05]); bullnecked (MD =2.50cm, 95% CI = [1.56, 3.44]); limited mouth opening (MD = -0.52cm, 95% CI = [-0.88, -0.15]); limited neck flexibility (MD = -

10.05cm, 95% CI = [-14.10,-6.00]); specific anatomical characteristics; and modified Mallampati's index or test (OR = 3.37, 95% CI = [2.07, 5.48]).

Conclusions: Our study made a comprehensive and systematic analysis of The DLE relevant factors. Gender, age, body mass index(BMI), neck circumference (NC), modified Mallampati's index(MMI), inter-incisor gap(IIG), hyoid-mental distance (HMD), thyroid-mental distance (TMD), sterno-mental distance (SMD), and flexion-extension angle were eventually identified as highly correlated factors for DLE.

Key Words: difficult laryngeal exposure, suspension laryngoscopy, anterior commission, microlaryngoscopy.

INTRODUCTION

Suspension laryngoscopy is a widely used technique in laryngeal surgery to assist surgeons with clear exposure and visualization of the larynx. Laryngeal lesions such as vocal nodules, vocal cord polyps, papilloma of the larynx, and laryngeal carcinoma in the early clinical stage can be completely removed under suspension microlaryngoscopy. Fully exposing the larynx structure, especially the anterior commissure (AC), is important for the success of microlaryngosurgery.

Up till now, there is no consensus regarding the definition and grading of difficult laryngeal exposure (DLE). Indeed, a full visual of the anterior commissure under an adult normal-sized laryngoscope was identified as the non-DLE case [1], as well as the cases only with posterior commissure or epiglottis exposure, were defined as DLE [2]. The debate on the definition of DLE has focused on two issues: first, whether the anterior commission exposure requires external laryngeal counter pressure[3, 4]; second, the exposure limitation on the vocal cord should be defined at the first third part or the last third part[5-7]. Though the definition varies, researchers strive to identify potential factors to predict DLE. The available evidence has demonstrated the role of numerous parameters in the prediction of DLE in clinical settings; however, inconsistent results and conclusions have been reported in previous studies. Hsiung[8] pointed out that increased body mass index (BMI) is not a predictor of DLE, while Pinar [2] found a statistically significant difference in BMI between patients with and without DLE. Patients' different postures also cause differences in anthropometric parameters, such as the neutral position and the full neck extension position [2, 8]. Therefore, a comprehensive evaluation of diverse parameters in patients to precisely identify DLE is a key determinant for eventual satisfactory surgery.

MATERIALS AND METHODS

Following the preferred reporting items for systematic reviews and meta-analysis guidelines [9], we performed a meta-analysis of studies that comprehensively compared the parameters between patients with and without DLE. The methodology followed the principles of the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy.

Eligibility Criteria

According to the population, intervention, comparison, outcomes, and study design framework, the inclusion criteria were as follows: 1) patients undergoing suspension laryngoscopy owing to benign or malignant laryngeal lesions; 2) no comparison intervention; 3) comparison of patients with DLE with those without DLE in various parameters including age, BMI, sex, physical examination data and so on; and 4)secure records and ascertainment of laryngeal exposure situation as the outcome. 5) prospective or retrospective case-control studies. The exclusion criteria were as follows: 1) review articles, case reports, case series, letters, editorials, comments, and conferences; 2) lack of explicit DLE definition; and 3) insufficient patient information and raw data.

Information Sources and Search Strategy

A systematic electronic literature search was performed on common databases, including PubMed, Embase, Web of Science, China national knowledge infrastructure (CNKI), and Wangfang, until October 2022. To improve the sensitivity of the search strategy, we used the terms “suspension laryngoscopy,” “microsurgery,” “microlaryngoscopy”, “microscopic,” “laryngeal exposure,” “difficult laryngoscopy”, “predict,” and “factor” as either keywords or MeSH terms. The search strategies were modified for each database as presented in Supplementary Table 1. Bibliographies of the retrieved studies were manually checked for additional eligible studies. Only published studies were included in the present meta-analysis.

Selection and Collection Process

Two reviewers independently screened the retrieved records; based on the inclusion and exclusion criteria, eligibility of the studies was decided. In case of any conflict, the decision of the senior authors was accepted. Data compatible with the outcome and detailed information about the experimental design of each study were manually extracted from the included studies by a reviewer and checked by another. The extracted data were divided into three parts: 1) literature information including the first author, publication date, sample size, and publication journal; 2) study methodology: research type, statistical method, the definition of DLE, representativeness of the cases, ascertainment of DLE and non-DLE groups; 3) investigated parameters: general parameters including age, sex, BMI, and physical examination parameters including neck circumference (NC), neck flexion-extension angle/atlanto-occipital extension, inter-incisor gap (IIG), hyoid-mental distance (HMD), thyroid-mental distance (TMD), sterno-mental distance (SMD), vertical thyroid-mental distance (VTMD), horizontal thyroid-mental distance (HTMD), thyroid-mental angle

(TMA), modified Mallampati's index or test (MMI/MMT),[10] and modified Cormack–Lehane scoring (MCLS) [11]. Details were listed in Table 2 and Table 3 in the Supplement.

Assessment

Utilizing the Newcastle-Ottawa Scale (NOS) [12], two reviewers screened and scored all potential studies. For case-control studies, the star system was used to perform a semi-quantitative assessment of study quality, in which studies with six or more stars were defined as high quality with less selection, performance, detection, and attrition bias. According to the number and features of the included studies, publication bias was evaluated using Egger's and Begg's tests. These analysis were presented in Table 4 in the Supplement.

Statistical Analysis

Review Manager 5.4 (Nordic Cochrane Center, Cochrane Collaboration, Copenhagen, Denmark) and R language (R version 4.0.2, meta24, and forest plot 25 package) were used as recommended software for meta-analysis. The different effect measures used in the presentation of results to evaluate the analysis outcome were as follows: odds ratio with 95% confidence intervals (CIs) for dichotomous variables, and mean difference with 95% CIs for continuous variables. The synthesis of results was performed by two reviewers depending on the characteristics of the enrolled parameters in each study. Missing summary statistics were eliminated, and data conversion was used for better synthesis, such as the transition between data of the fully open mouth and inter incisor gap. According to the respective DLE definition, we divided studies into 4 categories as A, B, C, and D for subgroup analysis to control the bias due to different methods of ascertainment for laryngeal exposure. The extent of statistical heterogeneity was evaluated using the Chi-square test and I-square test within and between subgroups resulting in the different models used, the random effect model for high heterogeneity ($P < 1$, $I^2 > 50\%$) and fixed-effect model for the contrary [13]. The leave-one-out method was used for sensitivity analysis and the publish bias was evaluated by Egger's and Begg's test. . Details of subgroups were listed in Table 5 in the Supplement.

RESULTS

Study Selection

A total of 1574 pieces of literature were retrieved using the designed research strategies: 270 from the PubMed database, 522 from the Web of Science database, 356 from the Embase database, 256 from the CNKI database, and 170 from the Wangfang database. After removing 400 duplicates, the remaining 1174 were primarily screened based on the reference type, title, keywords, and abstract. Fifty-two studies with available full texts were evaluated qualitatively and quantitatively, of which nineteen studies defined DLE identically or similarly. A study was excluded for identical data with another study included. Finally, eighteen studies that presented the mean value and standard difference of each parameter between the DLE and non-DLE groups were included after a comprehensive evaluation. A flow diagram describing the detailed process of literature retrieval, screening, and synthesis is illustrated in Figure 1.

Study Characteristics

In the eighteen studies, 704 patients were defined as DLE, and 1559 were non-DLE. All these patients, who came from different countries including China, India [1], Tunisia [14], and Turkey [2], eventually underwent microlaryngosurgery. The most common parameters in these studies were age, sex, and BMI successively. The physical examination parameters pooled from each study were NC, neck flexion-extension angle, IIG, HMD, TMD, SMD, VTMD, HTMD, TMA, MMI, and MCLS. These anatomical parameters are illustrated in supplementary figure 1. All studies received at least six stars on the NOS, most of which were broadly similar in three domains: selection of participants, comparability of study groups, and outcome ascertainment. A summary of the characteristics of all studies is presented in Table 1 and supplementary table 3.

Results of Syntheses

Evidence was found that DLE was more likely to occur in male (OR = 1.73, 95% CI = [1.16, 2.57], I^2 = 65%, *P* = 0.007). Twelve studies involving 822 males and 806 females supported the significant difference except three studies. Seven studies reported the age distribution among patients, including 310 with DLE and 537 without DLE. Study heterogeneity (*P* = 0.003, I^2 = 70%) determined the random-effects model used for analysis. Pooled data revealed that patients with DLE were older than those without DLE (MD = 5.47 years, 95% CI = [2.44, 8.51], *P* = 0.0004). Another general parameter found to be relevant to laryngeal exposure was BMI. We analyzed all available BMI data in eight studies using a random-effects model (*P* < 0.0001, I^2 = 78%). There was a statistically significant difference in BMI between the two groups

(MD = 1.19 Kg/m^2, 95% CI = [0.33, 2.05], *P* = 0.007). General information is shown in Figure 3.

A pooled meta-analysis indicated that the DLE group had a significantly longer NC than the non-DLE group by 2.50 cm (MD = 2.50cm, 95% CI = [1.56, 3.44], I^2 = 73%, *P* < 0.00001) which supported by all subgroup analysis results. A significantly shorter IIG was found in the DLE group than in the non-DLE group (MD = -0.52cm, 95% CI = [-0.88, -0.15], I^2 = 95%, *P* = 0.005) in six studies, while the subgroup C indicated no statistical difference. The flexion-extension angle was mentioned in five studies, which showed an apparently smaller angle in patients with DLE (MD = -10.05cm, 95% CI = [-14.10, -6.00], I^2 = 90%, *P* < 0.00001) than in those without DLE. With regard to HMD, we assessed the difference in both the neutral (MD = -0.23cm, 95% CI = [-0.35, -0.12], *P* < 0.0001) and full extension positions (MD = -0.46cm, 95% CI = [-0.70, -0.22], *P* = 0.0002). The heterogeneity of HMD in the neutral position (I^2 = 0%, *P* = 0.74)was far smaller than the other one (I^2 = 83%, *P* < 0.0001), and the heterogeneity between or within subgroups as well. Similar to HMD, TMD was measured in the neutral position (MD = -0.54cm, 95% CI = [-0.91, -0.17], I^2 = 87%, *P* = 0.004) and full extension position (MD = -1.09cm, 95% CI = [-1.32, -0.86], I^2 = 68%, *P* < 0.00001), which was shorter in the DLE group than in the non-DLE group, according to seven studies. In four studies, the horizontal and vertical components of the TMD in both neutral and full extension positions were also measured; however, no statistical difference was detected in the above four parameters. SMD was significantly different only in the full extension position (MD = -1.85cm, 95% CI = [-2.05, -1.65], I^2 = 47%, P < 0.00001) and not in the neutral position (MD = -0.23cm, 95% CI= [-0.46, 0.01], I^2 = 0%, P = 0.06). All the synthesized results of the anatomical characteristics are illustrated in Figures 3 and 4.

There were different kinds of DLE or difficult intubation (DI)-associated evaluation indices, including visual analog score, Mallampati's index, MMI/MMT, MCLS, and Yamamoto index, as possible predictors investigated by various studies. Based on the available data, we analyzed the two most common indices, MMI and MCLS. We found a higher risk of worse MMI index in patients with DLE than in those without DLE (OR = 3.37, 95% CI = [2.07, 5.48], I^2 = 70%, P < 0.0001) from twelve studies. However, the synthesized results of the MCLS demonstrated no statistical differences. The results of the evaluation index are shown in Figure 5. Studies with different DLE definitions sometimes indicated different conclusions in subgroup analysis, however these results were meaningless for the test for subgroup difference is negative (all P>0.05). The results of sensitivity analysis and publication bias are summarized in Supplementary Table 1. Egger's and Begg's tests indicated that there was no obvious publication bias in eligible studies (all P > 0.05). The results of all positive parameters were validated by leave-one-out method.

DISCUSSION

Our study was a concise and comprehensive meta-analysis of prospective and controlled studies that aimed to identify the instructive and predictive parameters of DLE in suspension laryngoscopy. With the ascertainment of laryngeal exposure and related patient parameters, ten independent parameters were determined as powerful predictors of DLE including gender, age, BMI, MMI, NC, IIG, neck flexion-extension angle, HMD, TMD, and SMD. The synthesized results indicated that it was more challenging to ensure a complete and clear laryngeal exposure during microsurgery in patients who were older, obese, bullnecked, with limited mouth opening and neck joint movements, shorter anatomical distance, and with specific MMI.

Among the general parameters, gender, BMI, and age displayed statistical significance in our meta-analysis, which was consistent with previous studies. Clinical observation showed that male had a high rate of short, thick, stiff and muscular neck, obesity, macroglossia, and extension limitations of the cervical spine, but opposite in female[15] [16] [17] High levels of adiposity may impair muscle activation, leading to the functional limitation. Hekiert et al. [5] suggested that obese individuals were 6.5 times more likely to experience DLE than those without obesity. Obesity relevant DLE was always correlated with decreased oxygen saturation, limited jaw mobility, a narrow upper airway and increased muscle size [18-21]. Another positive parameter, age, was closely related to BMI: older patients tended to have a higher percentage of body fat. Additionally, upper airway dimensions such as oropharyngeal junction, maximum pharyngeal area, and pharyngeal volume decreased with age[22]. Several studies pointed out that though the elderly person was more likely to have smaller tongue size due to the degeneration of the tongue muscle fiber size and number[23, 24], they still suffered a DLE situation with other disadvantages like obesity, thick and stiff neck, degeneration of joint and muscle function[8, 15, 17, 20].

In terms of anatomical characteristics, the neck circumference (NC) and neck flexion-extension angle showed obvious discrepancies between the non-DLE and DLE groups. Paul et al. [1] concluded that patients with a NC of more than 34.25 cm were four times more likely to have difficult laryngoscopy. Inter-incisor gap (IIG) is another vital observational index related to DLE. A sufficient wide mouth opening is important for transoral laryngoscopy; therefore, a gum elastic bougie was sometimes used when patients encountered DLE. The absence of teeth broadens the mouth space and expands the IIG. some researchers found that the chance of DLE increases progressively in patients with different dental statuses: edentulous; partially edentulous, normal teeth, and prominent teeth. [4, 25, 26] Considering the various anatomical distances, a slight difference in each parameter in one dimension could result in a significant discrepancy in the three-dimensional structure of the pharyngeal space. To some extent, the investigated parameters, such as TMD, HMD, and SMD, could together determine the aforementioned upper airway dimensions. We classified and counted physical measurement data in the neutral and Boyce-Jackson sniffing positions (the head and neck into full extension), which made laryngeal exposure easier by the placement of sniffing positions [27]. Except for HTMD, the MD of all parameters increased in the sniffing/full extension position compared with the neutral position, which validated the reliability of the synthesized data. Regarding the anatomical characteristics, high heterogeneity could be attributed to measuring bias in addition to the aforementioned factors, particularly for IIG (I^2 = 95%) and flexion-extension angle (I^2 = 92%), which are difficult to be measured precisely as other parameters.

It is also important to note that well-known parameters of difficult endotracheal intubation were also included in our study. MMI, a relatively simple grading system to predict DI, was found to be a strong predictor of DLE. Merah et al. [28] pointed out that MMI was an optimal single predictor with sensitivity, specificity, and positive predictive values of 61.5%, 98.4%, and 57.1%, respectively. MCLS, closely associated with MMI, was a negative result that was investigated in three studies. Regarding MMI (I^2 = 70%) and MCLS (I^2 = 97%), defined by subjective judgment, visual errors are also unavoidable. Furthermore, direct rigid laryngoscopy and microlaryngoscopy have been used to expose the laryngeal cavity in some studies [1, 8]. The size, resolution, focal length, and aperture of the two types of laryngoscopies may determine laryngeal exposure. Unlike anesthesia intubation, even subtle differences in vocal fold exposure could affect DLE grading.

So far, there is no preoperative prediction system to date that uses objective parameters for DLE. Schmitt et al. [29] pointed out that the ratio of height to thyromental distance had a great predictive value, which indicated that we could further investigate the difference value and ratio of existing parameters, and incorporate novel proposed parameters such as mandibular tori [30] and percentage of the glottic opening [31]. Wajekar et al. [19] also found that the combination of the upper lip bite test, MMI, and TMD had the highest specificity with an acceptable sensitivity to predict DI. Kharrat et al. [14] used lateral X-ray films to evaluate anatomical characteristics instead of physical measurements. In addition, various studies have used computed tomography, radiographs, and ultrasound to predict difficult airways [31]. Many studies [1, 2, 5, 8, 32] conducted multivariate logistic regression analysis to control the interaction of parameters. Three studies [2, 5, 6] conducted correlation analysis between parameters and DLE. In addition, several studies [1, 6, 8, 32] have defined the cut-off values of specific parameters and performed receiver operating characteristic analysis to identify useful screening tests for DLE. Furthermore, Piazza et al. [4] established a standardized preoperative assessment protocol known as laryngoscore in 2014, which included 11 parameters, and Arjun et al. [3] and Tirelli et al. [33] conducted external validation of it. In 2019, Incandela et al. [34] then proposed a mini-version of laryngoscore comprised of three parameters: interincisors gap, thyromental distance, and upper jaw dental status. Our analysis results indicate that there is significant statistic difference in age, neck circumference, TMD and SMD in full extension, which should be included in DLE predict system. And the scale score proportion should be customed according to the predictive performance of different parameters. Furthermore, we propose the preoperative prediction system should not only estimate the incidence of DLE but also recommend the optimum surgery approach and laryngoscope model for the individual patient based on the datasets of specific parameters in the future. Larger long-term follow-up studies should be conducted to explore the optimal treatment for DLE and related complications.

In this study, we observed that different study groups had inconsistent definitions of DLE. Therefore, the literature was divided by definition into four subgroups (supplementary table 6) for analysis. The results indicated that the heterogeneity within different DLE definition subgroups was different, but the heterogeneity between subgroups was mostly low, indicating that the difference in DLE classification definition had a limited impact on the group results (see supplementary figure 2-13).

We conducted the first meta-analysis to identify the reliable predictors for DLE according to the standard guidelines, which encompasses over 2000 cases from 4 countries. Rigorous literature quality control eliminates potential bias and ensures the reliability of the results. Subgroup, sensitivity, and publication bias analysis were used to test heterogeneity and validate our conclusion. We found 12 valuable parameters for DLE prediction to help surgeons better deal with DLE in clinical practice. Nevertheless, the present meta-analysis has several limitations. First, inevitable biases existed in our study process; for example, potential bias in the DLE definition might have resulted in the obscure division of the experimental and control groups. The surgeon's experience affects the chance of DLE in clinical practice. Paul mentioned senior surgeons provided guidance in part of the difficult microlaryngosurgery of the participants in his study.[1] But none of the 18 included studies proposed addressing to control this confounding factor. Furthermore, most studies chose hospital controls, which comprised patients with different laryngeal lesions rather than the normal population, which inevitably led to increased selection bias risk. Additionally, a NOS star system was used to evaluate the risk of bias, and most studies obtained six or seven stars instead of eight or more, indicating that the study design and performance should still be optimized. Second, the high heterogeneity of some parameters impaired the credibility of the results. We did not conduct meta regression and owing to inadequate data, study features, and study numbers. Finally, most studies lacked long-term follow-up to observe the related complications in patients with DLE.

CONCLUSION

Reasonable assessment of DLE can help the surgeon prepare alternative surgical plan and instruments in advance, which reduce the chance of surgery failure and related complications. Our study made a comprehensive and systematic analysis of the factors that cause DLE. Gender, age, BMI, NC, MMI, IIG, HMD, TMD, SMD, and flexion-extension angle were confirmed as predictors of DLE, which should be paid more attention during microsurgery.

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Table1 title: Summary of Characteristics of 18 Studies Included.

Legend: (DLE=difficult laryngeal exposure; NOS= the Newcastle-Ottawa Scale)

LIST OF LEGENDS

Fig.1 Flow diagram of article screening for systemic review.

Fig.2 Forest plot demonstrating the discrepancy of general parameters including gender, age and BMI between DLE group and non-DLE group. (DLE= difficult laryngeal exposure; SD= standard deviation; IV= inverse variance; M-H= Mantel Haenszel; CI= confidence interval.)

Fig.3 Forest plot demonstrating the discrepancy of anatomical characteristics including neck circumference, interincisors gap, and flexion-extension angle between DLE group and non-DLE group. (DLE= difficult laryngeal exposure; SD= standard deviation; IV= inverse variance; CI= confidence interval.)

Fig.4 Forest plot demonstrating the discrepancy of anatomical characteristics including hyoid-mental distance (HMD), thyroid-mental distance (TMD), and sterno-mental distance (SMD) between DLE group and non-DLE group. (DLE= difficult laryngeal exposure; SD= standard deviation; IV= inverse variance; CI= confidence interval.)

Fig.5 Forest plot demonstrating the discrepancy of Modified Mallampati's Index (MMI) between DLE group and non-DLE group. (DLE= difficult laryngeal exposure; SD= standard deviation; IV= inverse variance; M-H= Mantel Haenszel; CI= confidence interval.)

Supplementary table 1 title: Research algorithm for each database.

Supplementary table 2 title: Raw data composited of dichotomous and continuous variables collected from included studies

Supplementary table 3 title: Aggregation of the general information of included studies.

Supplementary table 4 title: Aggregation of the detailed NOS score of included studies. ✯: obtaining one point on the Newcastle-Ottawa Scale (NOS).

Supplementary table 5 title: The results of sensitive analysis and publication bias. BMI: body mass index; MMI: Modified Mallampati's Index; IIG: Interincisors gap; HMD: hyoid-mental distance; TMD: thyroid-mental distance; SMD: sterno-mental distance.

Supplementary table 6 title: The grade of subgroups according to the DLE definition. The data of age, BMI, and MMI are included in the overall analysis rather than subgroup analysis, as being insufficient to be transferred and aggregated.

Supplementary figure 1: Illustration of anatomical parameters including HMD, TMD, SMD, VTMD, HTMD, and TMA. A: HMD; B: TMD; C: SMD D: VTMD; E: HTMD.

Supplementary figure 2-13 title: Summary of forest plots with subgroup analysis of all twelve positive parameters.

LIST OF ABBREVIATIONS

DLE:difficult laryngeal exposure; NC:neck circumference; IIG:inter-incisor gap HMD:hyoid-mental distance; TMD:thyroid-mental distance; SMD: sterno-mental distance; VTMD: vertical thyroid-mental distance; HTMD: horizontal thyroid-mental distance; TMA: thyroid-mental angle; MMI/MMT: modified Mallampati's index or test; MCLS: modified Cormack–Lehane scoring; M-H= Mantel Haenszel

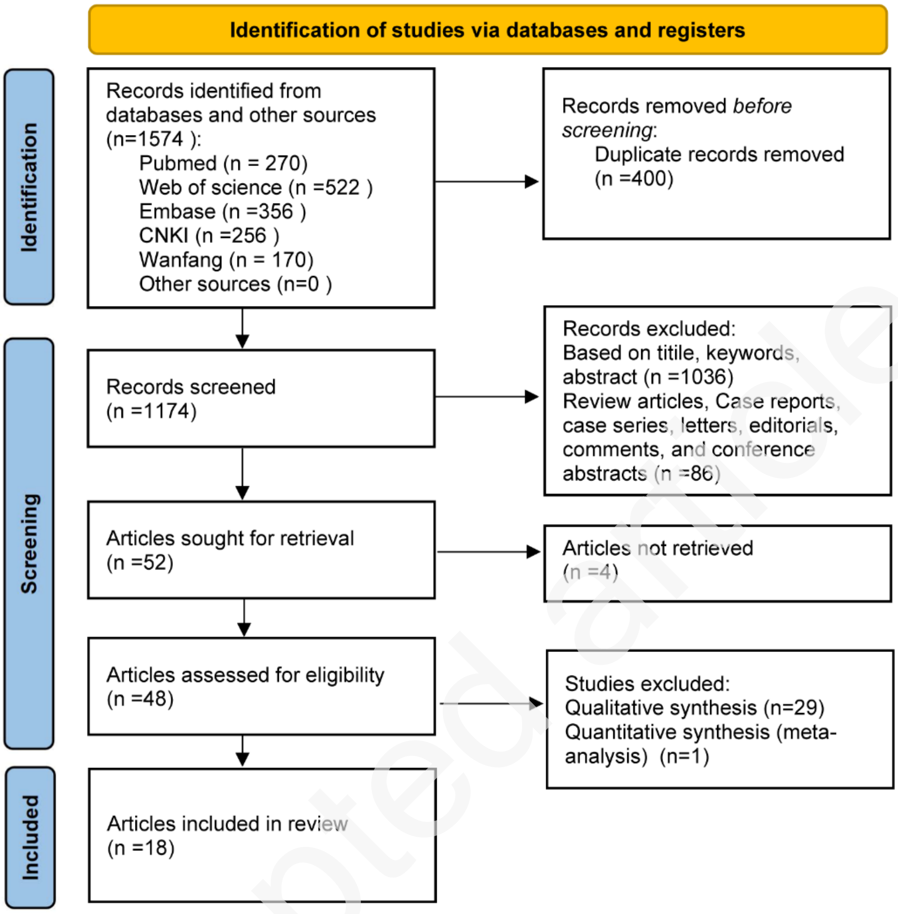
Table 1.

Table 1 Summary of Characteristics of 18 Studies Included					
Author/year	Type of analysis	Parameter amount	DLE patient quantity	Non-DLE patient quantity	NOS stars
Meng 2010	prospective	10	7	46	7
Wang 2012	prospective	11	20	69	7
Sun 2015	prospective	9	64	93	7
Wang 2015	prospective	8	81	206	7
Huang 2016	prospective	12	6	52	7
Ma 2016	prospective	18	22	40	7
Paul 2016	prospective	11	31	86	7
Jin 2016	prospective	10	35	158	7
Li 2017	prospective	14	35	55	7
Pinar 2009	prospective	11	22	71	7
Liu 2021	prospective	11	52	98	7
Liu 2022	prospective	7	22	73	7
Chen 2019	retrospective	11	63	121	6
Cheng 2020	prospective	13	97	113	7
Hsiung 2004	Prospective	9	19	37	6

Wei 2018	prospective	7	32	46	7
Wang 2021	prospective	12	37	141	6
Kharrat 2022	prospective	16	19	62	7

DLE=difficult laryngeal exposure; NOS= the Newcastle-Ottawa Scale

Fig. 1



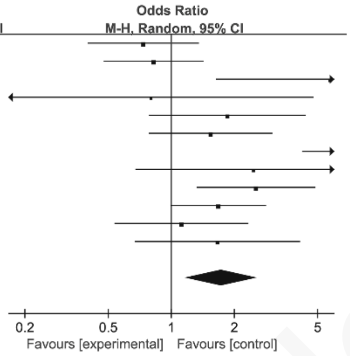
Identification of studies via databases and registers
Identification
Screening
Included
Records identified from databases and other sources (n=1574):
Pubmed (n = 270)
Web of science (n =522)
Embase (n =356)
CNKI (n =256)
Wanfang (n = 170)
Other sources (n=0)
Records removed *before screening*:
Duplicate records removed (n =400)
Records screened (n =1174)
Records excluded:
Based on titile, keywords, abstract (n =1036)
Review articles, Case reports, case series, letters, editorials, comments, and conference abstracts (n =86)
Articles sought for retrieval (n =52)
Articles not retrieved (n =4)
Articles assessed for eligibility (n =48)
Studies excluded:
Qualitative synthesis (n=29)
Quantitative synthesis (meta-analysis) (n=1)
Articles included in review (n =18)

Fig. 2

GENDER

Study or Subgroup	DLE Events	DLE Total	NON-DLE Events	NON-DLE Total	Weight	Odds Ratio M-H, Random, 95% CI
Chen 2019	29	63	65	121	10.6%	0.73 [0.40, 1.35]
Cheng 2020	40	97	52	113	11.1%	0.82 [0.48, 1.42]
Hsiung 2004	10	19	6	37	5.8%	5.74 [1.64, 20.14]
Huang 2016	2	6	20	52	3.6%	0.80 [0.13, 4.78]
Li 2017	18	35	20	55	8.5%	1.85 [0.78, 4.38]
Liu 2021	30	52	46	98	10.0%	1.54 [0.78, 3.04]
Ma 2016	16	22	6	40	5.7%	15.11 [4.21, 54.25]
Paul 2016	28	31	68	86	5.6%	2.47 [0.67, 9.06]
Sun 2015	38	64	34	93	10.2%	2.54 [1.32, 4.87]
Wang 2015	50	81	101	206	11.3%	1.68 [0.99, 2.83]
Wang 2021	22	37	80	141	9.5%	1.12 [0.54, 2.33]
Wei 2018	19	32	22	47	8.1%	1.66 [0.67, 4.12]
Total (95% CI)		**539**		**1089**	**100.0%**	**1.73 [1.16, 2.57]**
Total events	302		520			

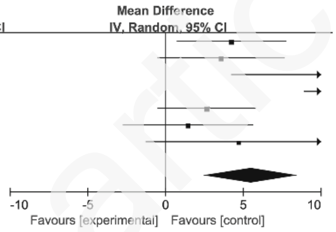
Heterogeneity: Tau² = 0.29; Chi² = 31.40, df = 11 (P = 0.0010); I² = 65%
Test for overall effect: Z = 2.70 (P = 0.007)



AGE

Study or Subgroup	DLE Mean	DLE SD	DLE Total	NON-DLE Mean	NON-DLE SD	NON-DLE Total	Weight	Mean Difference IV, Random, 95% CI
Chen 2019	45.62	12.07	63	41.38	10.54	121	16.5%	4.24 [0.72, 7.76]
Cheng 2020	48.73	16.07	97	45.16	13.95	113	15.3%	3.57 [-0.53, 7.67]
Hsiung 2004	51.3	11	19	41	11	37	11.4%	10.30 [4.22, 16.38]
Li 2017	50.43	13.41	35	36.27	10.61	55	13.0%	14.16 [8.91, 19.41]
Liu 2021	44.41	8.62	52	41.76	10.79	98	17.2%	2.65 [-0.52, 5.82]
Liu 2022	43.12	8.35	22	41.68	10.15	73	15.1%	1.44 [-2.75, 5.63]
Ma 2016	45.25	12.37	22	40.55	9.73	40	11.6%	4.70 [-1.28, 10.68]
Total (95% CI)			**310**			**537**	**100.0%**	**5.47 [2.44, 8.51]**

Heterogeneity: Tau² = 11.37; Chi² = 19.99, df = 6 (P = 0.003); I² = 70%
Test for overall effect: Z = 3.53 (P = 0.0004)



BMI

Study or Subgroup	DLE Mean	DLE SD	DLE Total	NON-DLE Mean	NON-DLE SD	NON-DLE Total	Weight	Mean Difference IV, Random, 95% CI
Chen 2019	23.85	3.94	63	23.17	2.05	121	13.4%	0.68 [-0.36, 1.72]
Cheng 2020	24.18	3.02	97	23.59	2.65	113	14.7%	0.59 [-0.18, 1.36]
Hsiung 2004	23.6	2.4	19	22.7	3.3	37	11.0%	0.90 [-0.61, 2.41]
Li 2017	23.9	4.72	35	23.09	1.73	55	10.4%	0.81 [-0.82, 2.44]
Liu 2021	27.64	3.21	52	24.04	1.69	98	13.9%	3.60 [2.67, 4.53]
Liu 2022	26.56	2	22	25.64	2.57	73	13.5%	0.92 [-0.10, 1.94]
Ma 2016	24.36	1.86	22	24.01	2.58	40	13.0%	0.35 [-0.77, 1.47]
Paul 2016	23.91	4.34	31	22.36	3.8	86	10.0%	1.55 [-0.18, 3.28]
Total (95% CI)			**341**			**623**	**100.0%**	**1.19 [0.33, 2.05]**

Heterogeneity: Tau² = 1.15; Chi² = 31.72, df = 7 (P < 0.0001); I² = 78%
Test for overall effect: Z = 2.71 (P = 0.007)

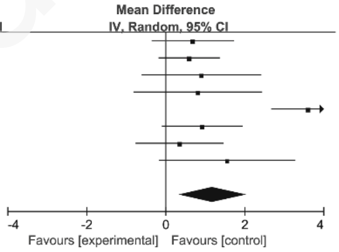
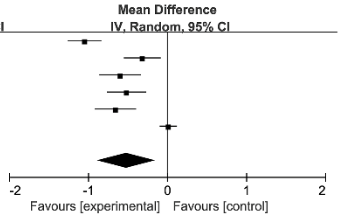


Fig. 3

INTERINCISORS GAP

Study or Subgroup	DLE Mean	DLE SD	DLE Total	NON-DLE Mean	NON-DLE SD	NON-DLE Total	Weight	Mean Difference IV, Random, 95% CI
Chen 2019	3.76	0.72	63	4.81	0.65	121	16.8%	-1.05 [-1.26, -0.84]
Cheng 2020	3.81	0.74	97	4.13	0.98	113	16.6%	-0.32 [-0.55, -0.09]
Huang 2016	3.7	0.3	6	4.3	0.4	52	16.3%	-0.60 [-0.86, -0.34]
Jin 2016	3.96	0.68	35	4.48	0.65	158	16.5%	-0.52 [-0.77, -0.27]
Li 2017	3.81	0.63	35	4.47	0.6	55	16.3%	-0.66 [-0.92, -0.40]
Liu 2021	4.04	0.35	52	4.03	0.27	98	17.5%	0.01 [-0.10, 0.12]
Total (95% CI)			**288**			**597**	**100.0%**	**-0.52 [-0.88, -0.15]**

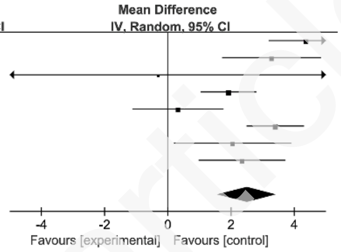
Heterogeneity: Tau² = 0.19; Chi² = 93.91, df = 5 (P < 0.00001); I² = 95%
Test for overall effect: Z = 2.79 (P = 0.005)



NECK CIRCUMFERENCE

Study or Subgroup	DLE Mean	DLE SD	DLE Total	NON-DLE Mean	NON-DLE SD	NON-DLE Total	Weight	Mean Difference IV, Random, 95% CI
Chen 2019	42.98	3.75	63	38.61	4.13	121	14.7%	4.37 [3.19, 5.55]
Cheng 2020	39.85	6.26	97	36.57	5.13	113	12.5%	3.28 [1.72, 4.84]
Huang 2016	46.8	6.5	6	47.1	8.9	52	2.3%	-0.30 [-6.04, 5.44]
Jin 2016	39.57	2.34	35	37.65	2.73	158	16.4%	1.92 [1.04, 2.80]
Li 2017	33.09	4.09	35	32.77	1.86	55	13.2%	0.32 [-1.12, 1.76]
Liu 2021	41.26	3.17	52	37.86	1.46	98	16.3%	3.40 [2.49, 4.31]
Liu 2022	41.36	3.98	22	39.31	3.67	73	10.9%	2.05 [0.19, 3.91]
Paul 2016	37.86	3.26	31	35.51	3.58	86	13.6%	2.35 [0.98, 3.72]
Total (95% CI)			**341**			**756**	**100.0%**	**2.50 [1.56, 3.44]**

Heterogeneity: Tau² = 1.19; Chi² = 25.61, df = 7 (P = 0.0006); I² = 73%
Test for overall effect: Z = 5.22 (P < 0.00001)



FLEXION-EXTENSION ANGLE

Study or Subgroup	DLE Mean	DLE SD	DLE Total	NON-DLE Mean	NON-DLE SD	NON-DLE Total	Weight	Mean Difference IV, Random, 95% CI
Chen 2019	94.05	5.34	63	107.49	10.31	121	21.5%	-13.44 [-15.70, -11.18]
Cheng 2020	97.56	6.89	97	102.37	9.1	113	21.6%	-4.81 [-6.98, -2.64]
Huang 2016	26.3	5.6	6	34.6	9.2	52	16.8%	-8.30 [-13.43, -3.17]
Li 2017	93.29	5.59	35	108.36	12.19	55	19.3%	-15.07 [-18.79, -11.35]
Liu 2021	92.19	7.09	52	100.96	9.7	98	20.8%	-8.77 [-11.49, -6.05]
Total (95% CI)			**253**			**439**	**100.0%**	**-10.05 [-14.10, -6.00]**

Heterogeneity: Tau² = 18.54; Chi² = 38.77, df = 4 (P < 0.00001); I² = 90%
Test for overall effect: Z = 4.87 (P < 0.00001)

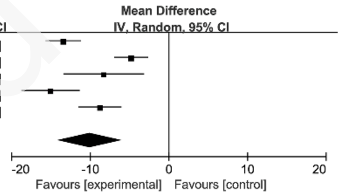
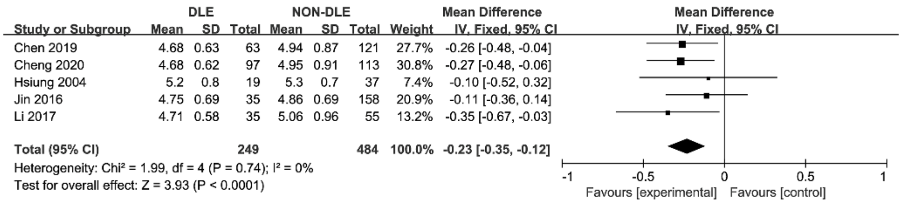
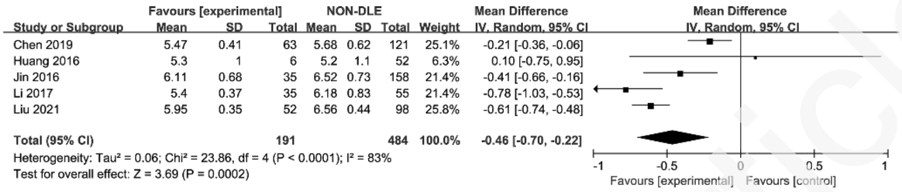


Fig. 4

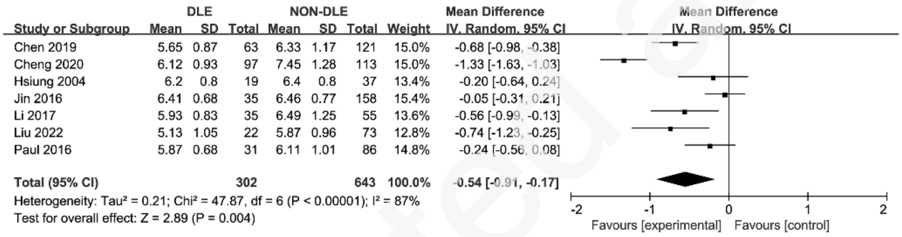
HMD IN NEUTRAL POSITION



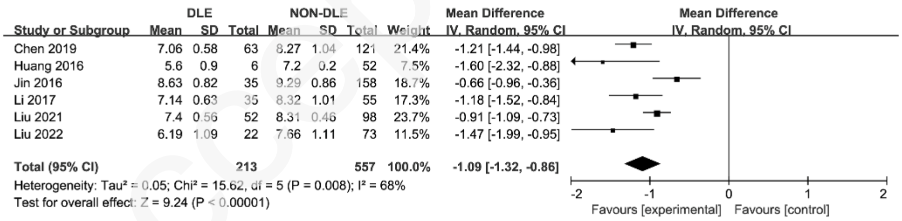
HMD IN FULL EXTENSION



TMD IN NEUTRAL POSITION



TMD IN FULL EXTENSION



SMD IN FULL EXTENSION

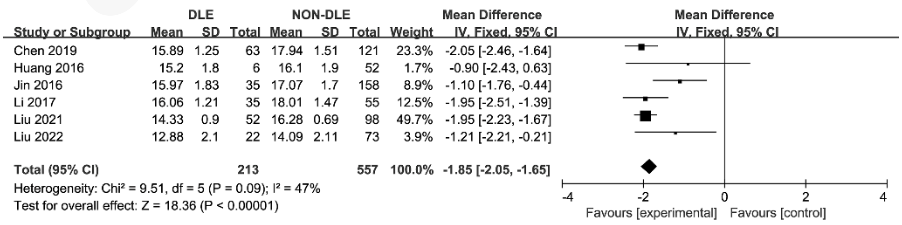


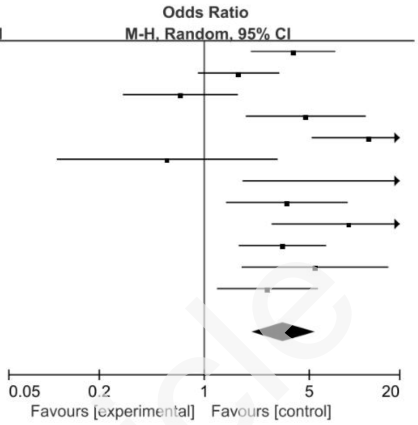
Fig. 5

MMI

Study or Subgroup	DLE Events	DLE Total	NON-DLE Events	NON-DLE Total	Weight	Odds Ratio M-H, Random, 95% CI
Chen 2019	43	63	43	121	10.6%	3.90 [2.04, 7.46]
Cheng 2020	76	97	77	113	10.7%	1.69 [0.91, 3.16]
Kharrat 2022	12	59	14	52	9.1%	0.69 [0.29, 1.67]
Li 2017	25	35	19	55	8.9%	4.74 [1.89, 11.89]
Liu 2021	29	52	9	98	9.2%	12.47 [5.19, 29.98]
Ma 2016	2	22	6	40	5.1%	0.57 [0.10, 3.08]
Meng 2010	7	7	14	46	2.3%	33.62 [1.80, 628.92]
Paul 2016	12	31	13	86	8.8%	3.55 [1.40, 9.02]
Pinar 2009	10	22	6	72	7.4%	9.17 [2.80, 29.96]
Sun 2015	36	64	26	93	10.5%	3.31 [1.70, 6.48]
Wang 2012	9	20	9	69	7.7%	5.45 [1.77, 16.81]
Wang 2021	15	37	29	141	9.8%	2.63 [1.22, 5.70]
Total (95% CI)		**509**		**986**	**100.0%**	**3.37 [2.07, 5.48]**
Total events	276		265			

Heterogeneity: $Tau^2 = 0.48$; $Chi^2 = 36.54$, df = 11 (P = 0.0001); $I^2 = 70\%$

Test for overall effect: Z = 4.88 (P < 0.00001)



Supplementary table1

Research algorithm for each database

Database	Research algorithm
Pubmed	#1 Search: microsurgery[MeSH Terms] OR microscopy[MeSH Terms] OR laryngoscopy[MeSH Terms] #2 Search: laryngoscop*[Title/Abstract] OR laryngoscopic surgical procedure*[Title/Abstract] OR surgery laryngoscopic[Title/Abstract] OR laryngoscopic surger*[Title/Abstract] OR microlaryngoscopy[Title/Abstract] OR suspension laryngoscop*[Title/Abstract] #3 #1 OR #2 #4 Search: predic*[Title/Abstract] OR factor[Title/Abstract] OR preoperative*[Title/Abstract] #5 Search: laryngeal exposure[Title/Abstract] OR difficult laryngoscopy[Title/Abstract] #6 #3 AND #4 AND #5
Embase	#1 'suspension laryngoscopy'/exp OR 'microsurgery'/exp OR 'microscopy'/exp OR 'laryngoscopy'/exp OR 'microlaryngoscopy'/exp #2 'laryngoscopic surgical procedure':ab,ti OR 'surgery laryngoscopic':ab,ti OR 'laryngoscopic surger*':ab,ti #3 #1 OR #2 #4 factor*:ab,ti OR predict*:ab,ti OR preoperative*:ab,ti #5 'laryngeal exposure':ab,ti OR 'difficult laryngoscopy':ab,ti #6 #3 AND #4 AND #5

Web of science	#1 TS=(microsurgery OR microscopy OR laryngoscopy) #2 (TS=(microsurgery OR microscopy OR laryngoscopy)) AND TS=(laryngoscop* OR laryngoscopic surgical procedure* OR surgery laryngoscopic OR laryngoscopic surger* OR microlaryngoscopy OR suspension laryngoscop*) #3 #1 OR #2 #4 TS=(predic*OR factor OR preoperative*) #5 TS=(laryngeal exposure OR difficult laryngoscopy) #6 #3 AND #4 AND #5
Wanfang	SUB:（(suspension microlaryngoscopy) or SUB:(suspension laryngoscopy) or SUB:(microlaryngoscopic surgery）） and SUB:（(exposure) or (difficult laryngoscopy）） and （ SUB:(predict) or SUB:(relate) or(influence))
CNKI	TKA=('microlaryngoscopic surgery ' + ' suspension laryngoscopy' + ' laryngeal exposure ') AND TKA='predict' +'relate' +‘influence’ AND TKA=‘exposure’+‘difficult laryngocopy’

Supplementary table 2

Raw data composited of dichotomous and continuous variables collected from included studies

1. Modified Cormack–Lehane scoring>=3						
Study	Events-DLE	Total-DLE	Events-non DLE	Total-non DLE		
Li 2017	13	35	2	55		
Paul 2016	13	31	75	86		
Kharrat 2022	16	19	3	52		
2.Gender=male						
study	Events-DLE	Total-DLE	Events-non DLE	Total-non DLE		
Chen 2019	29	63	65	121		
Cheng 2020	40	97	52	113		
Hsiung 2004	10	19	6	37		
Li 2017	18	35	20	55		
Liu 2021	30	52	46	98		
Paul 2016	28	31	68	86		
Huang 2016	2	6	20	52		
Sun 2015	38	64	34	93		
Wang 2015	50	81	101	206		
Ma 2016	16	22	6	40		

Wei 2018	19	32	22	47		
Wang 2021	22	37	80	141		
3.Vertical thyroid-mental distance in neutral position						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Cheng 2020	4.49	0.82	97	5.05	0.9	113
Hsiung 2004	3.5	0.7	19	3.7	1	37
Jin 2016	4.81	1	35	4.71	0.95	158
Li 2017	3	0.94	35	3.04	0.75	55
4.Vertical thyroid-mental distance in full extension						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Jin 2016	7.77	1.14	35	8.11	1.06	158
Li 2017	5.3	0.85	35	6.42	1.23	55
5.Horizontal thyroid-mental distance in neutral position						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Cheng 2020	5.65	0.74	97	5.99	1.02	113
Jin 2016	5.15	1.12	35	4.99	0.95	158
Li 2017	5.39	0.59	35	6.17	0.89	55
6.Horizontal thyroid-mental distance in full extension						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE

Jin 2016	2.68	0.67	35	2.74	0.84	158
Li 2017	4.17	0.58	35	4.25	0.73	55
7.Sterno-mental distance in neutral position						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Chen 2019	13.38	1.82	63	13.61	1.63	121
Cheng 2020	13.49	0.74	97	14.03	2.15	113
Jin 2016	11.14	1.45	35	11.01	1.35	158
Li 2017	13.44	1.74	35	13.55	1.58	55
Liu 2022	11.24	1.87	22	11.54	1.97	73
Paul 2016	12.62	1.93	31	12.65	1.6	86
8.Thyroid-mental angle						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Chen 2019	109.84	5.34	63	107.52	5.68	121
Cheng 2020	114.57	7.24	97	123.62	8.15	113
Hsiung 2004	139.5	8.6	19	118.8	11.4	37
Jin 2016	121.29	8.87	35	134.29	8.38	158
Li 2017	111.85	5.15	35	107.01	6.05	55
9.Age						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE

Chen 2019	45.62	12.07	63	41.38	10.54	121
Cheng 2020	48.73	16.07	97	45.16	13.95	113
Hsiung 2004	51.3	11	19	41	11	37
Li 2017	50.43	13.41	35	36.27	10.61	55
Liu 2021	44.41	8.62	52	41.76	10.79	98
Liu 2022	43.12	8.35	22	41.68	10.15	73
Ma 2016	45.25	12.37	22	40.55	9.73	40
10.Body mass index						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Chen 2019	23.85	3.94	63	23.17	2.05	121
Cheng 2020	24.18	3.02	97	23.59	2.65	113
Hsiung 2004	23.6	2.4	19	22.7	3.3	37
Li 2017	23.9	4.72	35	23.09	1.73	55
Liu 2021	27.64	3.21	52	24.04	1.69	98
Liu 2022	26.56	2	22	25.64	2.57	73
Paul 2016	23.91	4.34	31	22.36	3.8	86
Ma 2016	24.36	1.86	22	24.01	2.58	40
11.Modified Mallampati's index>=3						
study	Events-DLE	Total-DLE	Events-non DLE	Total-non DLE		

Chen 2019	43	63	43	121		
Cheng 2020	76	97	77	113		
Li 2017	25	35	19	55		
Liu 2021	29	52	9	98		
Paul 2016	12	31	13	86		
Kharrat 2022	12	19	14	52		
Meng 2010	7	7	14	46		
Wang 2012	9	20	5	69		
Sun 2015	36	64	26	93		
Ma 2016	2	22	6	40		
Wang 2021	15	37	29	141		
12.Inter-incisor gap						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Chen 2019	3.76	0.72	63	4.81	0.65	121
Cheng 2020	3.81	0.74	97	4.13	0.98	113
Jin 2016	3.96	0.68	35	4.48	0.65	158
Li 2017	3.81	0.63	35	4.47	0.6	55
Liu 2021	4.04	0.35	52	4.03	0.27	98
Huang 2016	3.7	0.3	6	4.3	0.4	52
13.Flexion-extension angle						

study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Chen 2019	94.05	5.34	63	107.49	10.31	121
Cheng 2020	97.56	6.89	97	102.37	9.1	113
Li 2017	93.29	5.59	35	108.36	12.19	55
Liu 2021	92.19	7.09	52	100.96	9.7	98
Huang 2016	26.3	5.6	6	34.6	9.2	52
14.Hyoid-mental distance in neutral position						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Chen 2019	4.68	0.63	63	4.94	0.87	121
Cheng 2020	4.68	0.62	97	4.95	0.91	113
Hsiung 2004	5.2	0.8	19	5.3	0.7	37
Jin 2016	4.75	0.69	35	4.86	0.69	158
Li 2017	4.71	0.58	35	5.06	0.96	55
15.Hyoid-mental distance in full extension						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Chen 2019	5.47	0.41	63	5.68	0.62	121
Jin 2016	6.11	0.68	35	6.52	0.73	158
Li 2017	5.4	0.37	35	6.18	0.83	55
Liu 2021	5.95	0.35	52	6.56	0.44	98

Huang 2016	5.3	1	6	5.2	1.1	52
16.Thyroid-mental distance in neutral position						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Chen 2019	5.65	0.87	63	6.33	1.17	121
Cheng 2020	6.12	0.93	97	7.45	1.28	113
Hsiung 2004	6.2	0.8	19	6.4	0.8	37
Jin 2016	6.41	0.68	35	6.46	0.77	158
Li 2017	5.93	0.83	35	6.49	1.25	55
Liu 2022	5.13	1.05	22	5.87	0.96	73
Paul 2016	5.87	0.68	31	6.11	1.01	86
17.Thyroid-mental distance in full extension						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Chen 2019	7.06	0.58	63	8.27	1.04	121
Jin 2016	8.63	0.82	35	9.29	0.86	158
Li 2017	7.14	0.63	35	8.32	1.01	55
Liu 2021	7.4	0.56	52	8.31	0.46	98
Liu 2022	6.19	1.09	22	7.66	1.11	73
Huang 2016	5.6	0.9	6	7.2	1.2	52
18.Sterno-mental distance in full extension						

study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Chen 2019	15.89	1.25	63	17.94	1.51	121
Jin 2016	15.97	1.83	35	17.07	1.7	158
Li 2017	16.06	1.21	35	18.01	1.47	55
Liu 2021	14.33	0.9	52	16.28	0.69	98
Liu 2022	12.88	2.1	22	14.09	2.11	73
Huang 2016	15.2	1.8	6	16.1	1.9	52
19.Neck circumference						
study	Mean-DLE	SD-DLE	Total-DLE	Mean-non DLE	SD-non DLE	Total-non DLE
Chen 2019	15.89	1.25	63	17.94	1.51	121
Jin 2016	15.97	1.83	35	17.07	1.7	158
Li 2017	16.06	1.21	35	18.01	1.47	55
Liu 2021	14.33	0.9	52	16.28	0.69	98
Liu 2022	12.88	2.1	22	14.09	2.11	73
Huang 2016	15.2	1.8	6	16.1	1.9	52

Events: number of people with the particular event. Total: number of all patients in different groups. SD: standard deviation. DLE: difficult laryngeal exposure.

Supplementary table 3

Aggregation of the general information of included studies

Study/Collection period	Location	Subject (male/female)	Age	Incidence rate of DLE	Type of disease	Type of anesthesia	Laryngoscope Model
Meng,2010(1) 2006.05-2006.10	Department of ENT in Guangzhou First People's Hospital, Guangzhou, China	21/32	20-50(Me=30)	13.21%		Midazolam 1-2mg/Kg Atracurium0.25-0.5mg/kg or Vicuronium bromide 0.04-0.08mg/kg Fentanyl 2-4 mg/kg Isopropylphenol 1-2mg/Kg Succinylcholine 1-2mg/Kg	

Wang,2012(2) 2010.10-2011-12	The Third Xiangya Hospital, Central South University, China	50/39	43.12±1.63	22.47%		Midazolam 5-10 mg/Kg Fentanyl 2 to 4 mg/kg Isoproterenol 1-2 mg/kg Rocuronium bromide 0.6-1.2 mg/kg		
Sun,2015(3) 2012.05-2013.05	Department of ENT in the Affiliated Hospital of Inner Mongolia Medical University, China	82/75	14-71(46.064±11.69)	40.76%	Vocal fold polyp-157 Vocal cord nodule-12 Vocal fold cyst-2 Amyloidosis of the vocal cords-2 Vocal cord nerve schwannoma tumor-1			

Wang,2015(4) 2013.01-2015.03	Department of ENT in Tangshan Xiehe hospital, Tangshan,China	154/133	21~74	28.22%	Vocal fold polyp Vocal cord leukoplakia Vocal fold cyst Early laryngeal carcinoma.	Midazolam 1-2mg/Kg Sufentanil 0.2-0.4μg/Kg Propofol2-3mg/Kg Rocuronium bromide 0.6-1.2mg/Kg	
Huang,2016(5) 2013.10-2015.09	Department of ENT in Shekou Hospital, Shenzhen, China	22/36	29-71(46.5±13.4)	10.34%	Vocal fold polyp-53 Vocal fold cyst-4 Early laryngeal carcinoma-1		
Ma,2016(6) 2013.10-2015.08	Department of ENT in Zhongshan hospital, Xiamen	22/40	16-69(Me=40)	35.48%	Vocal fold polyp-42 Vocal fold cyst-8 Reinke's edema-4 Sulcus of the vocal	Endotracheal tube (diameter 5.5-6.0mm) The degree of muscle relaxation	8588BV,Karl Storz GmbH&Co (Outer diameter 28mm, inner diameter 17mm)

	University, Xiamen, China				folds-2 Vocal cord granulation-2 Laryngeal papilloma-2 Vocal fold closure Incomplete-2	reached TOF=0 and PTF<20	8590JA,Karl Storz GmbH&Co (Outer diameter 25mm, inner diameter 12mm)
Pual,2016(7) 2007.08-2009.07	Department of ENT in Christian Medical College, Vellore, India	96/21		26.49%	Vocal polyps Malignancy of the vocal cords Vocal cyst		Storz laryngoscope Anterior commissure scope for DLE patient
Jin,2016(8) 2013.05-2014.12	Department of ENT, The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou 310009, China	67/126	22-80 (47.8±11.2）	18.61%	Vocal fold polyp-190 Laryngeal carcinoma-2 Vocal cord leukoplakia-1	Propofol 1.5-2.5 mg/kg Dexmedetomidine 0.8-1 μg /kg Rocuronium bromide 5-10 μg/kg	Laryngoscope tube(ZC502.002) Laryngoscope holder(502.003) Hangzhou Nanyu medical instrument corporation

						Sufentanil 0.1-0.5 μg/kg	
Li,2017(9) 2014.10-2015.05	Department of ENT, the First People's Hospital of Foshan, China	35/52	14-61 (41.78±13.42)	38.88%	Vocal fold polyp-44 Vocal cord nodule-28 Vocal fold cyst-11 Vocal process granuloma-2 Vocal cord leukoplakia-5		Storz laryngoscope
Pinar,2009(10) 2005.01-2006.10	Otolaryngology Department, Ataturk Training and Research Hospital, Izmir, Turkey	79/14	22-85 (52.70±13.01)	23.65%	Vocal fold nodules or polyps Premalignant or malignant lesions of the larynx or hypopharynx Cysts of the supraglottis	Intubated with an endotracheal tube (5.5 or 6.0 mm in diameter) under general anesthesia and	8580B and 8585D, Karl Storz GmbH&Co, Germany

					Intracordal cysts Reinke's edema Large intubation granulomas	muscle relaxation.	
Liu,2021(11) **2020.01-2021.01**	Department of Otolaryngology, Jiangsu Taizhou People's Hospital, Jiangsu, Taizhou 225300, China	76/74	21-75 (44.33±10.63)	34.66%	Vocal fold polyp Vocal cord leukoplakia Vocal fold cyst Early laryngeal carcinoma Vocal fold papilloma Vocal fold granulomas		Same model laryngoscope
Liu, 2022(12) **2019.04-2020.10**	Department of Otorhinolaryngology, Tongren Hospital, Shanghai Jiao Tong University School of	73/22	16-69(42.0 ± 9.7)	23.15%	Vocal fold nodules or polyps Premalignant or malignant lesions ofthe larynx or	Intubated with an endotracheal tube (5.5 or6.0 mm in diameter) under general	8575KA, Karl Storz, Germany

	Medicine, No. 1111 Xianxia Road, Shanghai 200336, China				hypopharynx Cysts of the supraglottis Intracordal cysts Reinke's edema large intubation granulomas.	anesthesia and muscle relaxation.	
Chen,2019(13) 2016.01-2017.05	Wuhan University School of Basic Medical Sciences,Wuhan 430000,China	94/90	21-68 (45.43±11.06)	34.23%	Vocal fold polyp-86 Vocal cord nodule-58 Vocal fold cyst-28 Vocal process granuloma-7 Vocal cord leukoplakia-4		
Cheng,2020(14) 2017.05-2018.10	Department of Otolaryngology, Meizhou People's	77/133	21-71 (46.83±14.07）	44.09%	Vocal fold polyp-104 Vocal cord		Laryngoscope ZC, Hangzhou Nanyu

	Hospital, Meizhou Hospital Affiliated to Sun Yat-sen University, Meizhou, Guangdong 514031, China				nodule-53 Vocal fold cyst-38 Reinke's edema-15		medical instrument corporation
Hsiung,2004(15) 2002.01-2002.09	Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O.C.	16/40		33.92%	Patients with dysphonia undergoing microlaryngoscopic surgery	Intubated with an endotracheal tube (5.5 or 5.5 mm in diameter) under general anesthesia	Anterior commissure laryngoscope (8580B, 8585D, Karl Storz, GmbH & Co, Culver, CA or 10338501, 10338602,10338503, Nagashima Medical Instrument Co., Tokyo, Japan) and holder

							device(8675 or 10338400)
Wei,2018(16) 2016.09-2017.09	Department of ENT,the Third People's Hospital of Huizhou City, Guangdong Province, Huizhou 516002,China	41/38	14-71 (46.05±11.65)	41.02%	Vocal fold polyp-77 Vocal cord nodule-6 Vocal fold cyst-1 Amyloidosis of the vocal cords-1 Vocal cord nerve schwannoma tumor-1		
Wang,2021(17) 2016.10-2019-6	The First People's Hospital of Zhumadian City ,Zhumadian	102/76	20-69 (44.5 4 ± 1 3.6 0)	20.78%	Early laryngeal cancer patients undergoing microlaryngoscopic surgery		

	463000, Henan, China						
Kharrat,2022(18) 2021.01-2021.11	Department of Otorhinolaryngology, Habib Bourguiba Hospital, Sfax, Tunisia			23.45%	Patients with benign or malignant lesions of the larynx undergoing microlaryngoscopic surgery	Intubated with the smallest possible endotracheal tube	

Supplementary table 4

Aggregation of the detailed NOS score of included studies.

Study/Collection period	**Definition of DLE and non-DLE**	**Representativeness of the cases of the cases**	**Selection of Controls**	**Definition of controls**	**Comparability on the basis of the design**	**Ascertainment of exposure**	**Same method of ascertainment for cases and controls**	**Non-Response rate**
Meng,2010(1) 2006.05-2006.10	Adequate and based on Cormack–Lehane scoring with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó

Wang,2012(2) 2010.10-2011-12	Adequate and based on Cormack–Lehane scoring with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó
Sun,2015(3) 2012.05-2013.05	Adequate and based on Cormack–Lehane scoring with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó

Wang,2015(4) 2013.01-2015.03	Adequate and based on Cormack–Lehane scoring with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó
Huang,2016(5) 2013.10-2015.09	Adequate and refer to Hsiung,2004 with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó

Ma,2016(6) 2013.10-2015.08	Adequate and refer to Piazza,2014 with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó
Pual,2016 (7) 2007.08-2009.07	A defined grading system with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó

Jin,2016(8) 2013.05-2014.12	Adequate and based on Cormack–Lehane scoring with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó
Li,2017(9) 2014.10-2015.05	Adequate and refer to Roh,2005 with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó

Pinar,2009(10) 2005.01-2006.10	A defined grading system with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó
Liu,2021(11) 2020.01-2021.01	Adequate and based on Cormack–Lehane scoring with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó

Liu, 2022(12) 2019.04-2020.10	Adequate and based on Cormack–Lehane scoring with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó
Chen,2019(13) 2016.01-2017.05	Cormack–Lehane scoring with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Retrospective surveys and records not blinded to case/control status	Same rate for both groups ó

Cheng,2020(14) 2017.05-2018.10	Adequate and based on Cormack–Lehane scoring with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó
Hsiung,2004(15) 2002.01-2002.09	A defined grading system with independent validation ó	Unrepresentative sample with defined period of time, area, group of hospitals	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure with confounders like type of disease ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó

Wei,2018(16) 2016.09-2017.09	Adequate and based on Cormack–Lehane scoring with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó
Wang,2021(17) 2016.10-2019-6	Adequate and based on Cormack–Lehane scoring with independent validation ó	Unrepresentative sample with defined period of time, area, group of hospitals	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure with confounders like type of disease ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó

Kharrat,2022(18) 2021.01-2021.11	A defined grading system with independent validation ó	Random sample with defined period of time, area, group of hospitals ó	Hospital controls	First occurrence of outcome both in cases and controls ó	Study control for laryngeal exposure without any additional factors ó	Secure records of physical examination ó	Secure records where blind to case/control status ó	Same rate for both groups ó

☆: one point in Newcastle-Scale obtaining the Ottawa (NOS).

Supplementary table 5

The results of sensitive analysis and publication bias

Factors	Participants	I^2	Model	OR/MD[95%CI]	OR/MD Fluctuation	95%CI Fluctuation	Egger(P value)	Begg(P value)
Age	847	70%	R	5.47[2.44,8.51]	[3.830,6.210]	[1.903,9.733]	0.1189	0.1765
Gender	1628	65%	R	1.73[1.16,2.57]	[1.473,1.896]	[1.069,2.851]	0.09023	0.1702
BMI	964	78%	R	1.19[0.33,2.05]	[0.726,1.312]	[0.203,2.289]	0.8758	0.3223
MMI	1495	70%	R	3.37[2.07,5.48]	[3.328,4.347]	[2.254,6.688]	0.352	0.2429
IIG	885	95%	R	-0.52[-0.88,-0.15]	[-0.633-0.407]	[-1.001, 0.076]	0.05706	0.3476
Flexion-extension angle	692	90%	R	-10.05[-14.10,-6.00]	[-11.577, -8.857]	[-15.747, -4.531]	0.6893	0.6242
HMD in neutral position	733	0%	F	-0.23[-0.35,-0.12]	[-0.264, -0.214]	[-0.394, -0.076]	0.6414	0.6242

HMD in full extension	675	83%	R	-0.46[-0.70,-0.22]	[-0.568, -0.373]	[-0.772, -0.085]	0.8322	0.3272
TMD in neutral position	945	87%	R	-0.54[-0.91,-0.17]	[-0.633, -0.391]	[-1.019, -0.077]	0.8145	0.6523
TMD in full extension	770	68%	R	-1.09[-1.32,-0.86]	[-1.164, -1.031]	[-1.452, -0.782]	0.2748	0.573
SMD in full extension	770	47%	F	-1.85[-2.05,-1.65]	[-1.923, -1.612]	[-2.135, -1.151]	0.07428	0.1885
Neck circumference	1097	73%	R	2.50[1.56,3.44]	[2.204, 2.866]	[1.228, 3.696]	0.5213	0.4579

BMI： body mass index; MMI: Modified Mallampati's Index; IIG: interincisors gap; HMD: hyoid-mental distance; TMD: thyroid-mental distance; SMD: sterno-mental distance.

Supplementary table 6

The grade of subgroups according to the DLE definition.

		Non-DLE group		**DLE group**		
	Study	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Position**
A	**Meng2010, Wang2012 Sun2015, Wang2015 Jin 2016, Li2017 Cheng2020, Wang2021 Wei2018**	Completely exposure vocal folds area and anterior commissure under suspension laryngoscopy	Partial view of vocal cords with the anterior commissure seen only with external pressure.	Nonvisualization of the anterior commissure even with external compression	The vocal folds and epiglottis are not exposed and only the soft palate is visible	Non mentioned
	Paul2016	Full view of vocal cords	Partial view of vocal cords with the anterior commissure seen only with external pressure.	Nonvisualization of the anterior commissure even with external compression	Visualization of only posterior 1/3 of the vocal cords	Classic Boyce Jackson sniffing position.
B	**Ma 2016**	The anterior commissure exposed in the sniffing position, with large laryngoscopes and	The anterior commissure exposed in the sniffing position, with large laryngoscopes and	The anterior commissure exposed in the sniffing position, with small laryngoscopes and	Exposure of laryngeal view limited to the posterior third or less of the vocal cord in the sniffing position,	Sniffing position

		no external laryngeal pressure	external laryngeal pressure	external laryngeal pressure	with small laryngoscopes and external laryngeal pressure	
	Pinar2009,Hsiung2004, Kharrat2022	The others were defined as non-DLE groups.		Exposure of laryngeal view limited to the posterior third or less of the vocal cord in the sniffing position, with small laryngoscopes and external laryngeal pressure		Flexion-extension/classic sniffing or/Boyce-Jackson position
C	**Liu2021,Chen2019**	Full view of vocal cords	Partial view of vocal cords or posterior commissure	Visualization of only epiglottis	Nonvisualization of epiglottis and vocal cords	Neutral position

D	**Liu2022**	Patients with full view of the vocal cords or simply without exposure of anterior commissure after external manual compression		The others were defined as non-DLE groups.		Sniffifing position
	Huang2016	Full view of vocal cords with or without external compression	Simply non visualization of anterior commissure with external compression	Visualization of only posterior 2/3 of the vocal cords with external compression	Visualization of only posterior 1/3 of the vocal cords with external compression	Boyce-Jackson position

The data of age, BMI, and MMI are included in the overall analysis rather than subgroup analysis, as being insufficient to be transferred and aggregated.

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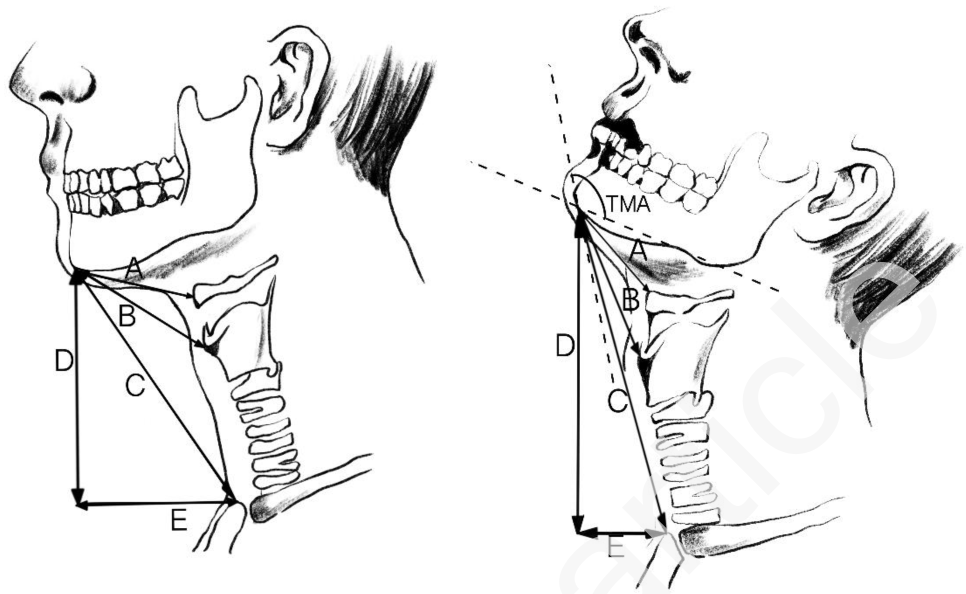
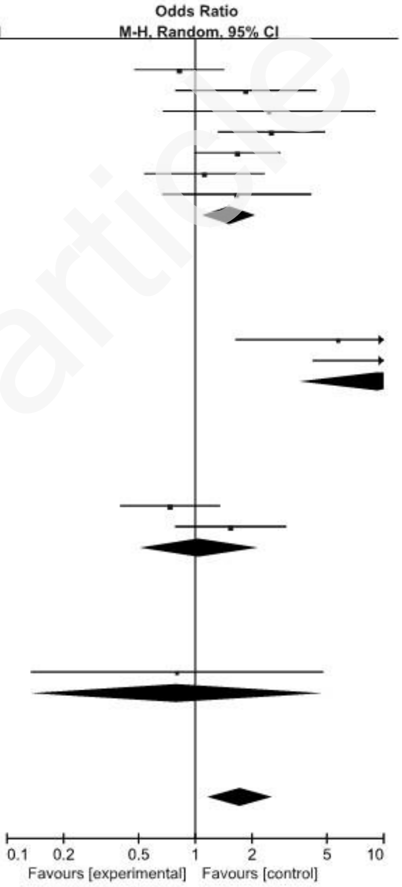
Supplementary figure 1.



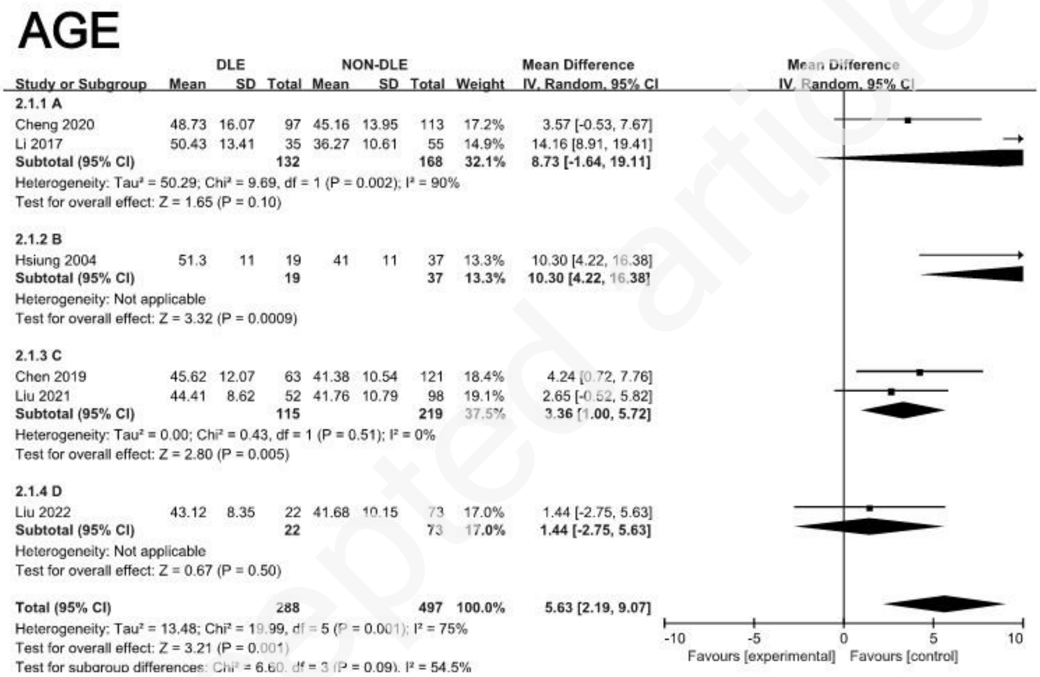
Supplementary figure 2.

GENDER

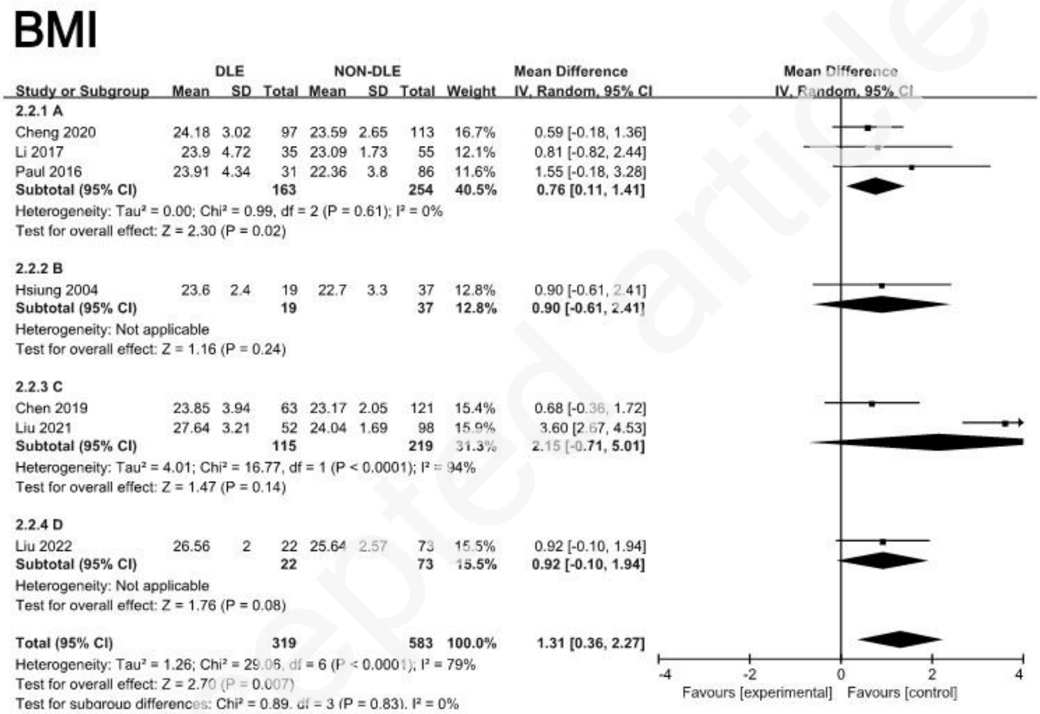
Study or Subgroup	DLE Events	DLE Total	NON-DLE Events	NON-DLE Total	Weight	Odds Ratio M-H, Random, 95% CI
2.12.1 A						
Cheng 2020	40	97	52	113	11.1%	0.82 [0.48, 1.42]
Li 2017	18	35	20	55	8.5%	1.85 [0.78, 4.38]
Paul 2016	28	31	68	86	5.6%	2.47 [0.67, 9.06]
Sun 2015	38	64	34	93	10.2%	2.54 [1.32, 4.87]
Wang 2015	50	81	101	206	11.3%	1.68 [0.99, 2.83]
Wang 2021	22	37	80	141	9.5%	1.12 [0.54, 2.33]
Wei 2018	19	32	22	47	8.1%	1.66 [0.67, 4.12]
Subtotal (95% CI)		**377**		**741**	**64.3%**	**1.51 [1.09, 2.11]**
Total events	215		377			
Heterogeneity: Tau² = 0.06; Chi² = 8.71, df = 6 (P = 0.19); I² = 31%						
Test for overall effect: Z = 2.46 (P = 0.01)						
2.12.2 B						
Hsiung 2004	10	19	6	37	5.8%	5.74 [1.64, 20.14]
Ma 2016	16	22	6	40	5.7%	15.11 [4.21, 54.25]
Subtotal (95% CI)		**41**		**77**	**11.6%**	**9.24 [3.58, 23.86]**
Total events	26		12			
Heterogeneity: Tau² = 0.05; Chi² = 1.12, df = 1 (P = 0.29); I² = 11%						
Test for overall effect: Z = 4.60 (P < 0.00001)						
2.12.3 C						
Chen 2019	29	63	65	121	10.6%	0.73 [0.40, 1.35]
Liu 2021	30	52	46	98	10.0%	1.54 [0.78, 3.04]
Subtotal (95% CI)		**115**		**219**	**20.5%**	**1.05 [0.51, 2.17]**
Total events	59		111			
Heterogeneity: Tau² = 0.17; Chi² = 2.53, df = 1 (P = 0.11); I² = 60%						
Test for overall effect: Z = 0.13 (P = 0.90)						
2.12.4 D						
Huang 2016	2	6	20	52	3.6%	0.80 [0.13, 4.78]
Subtotal (95% CI)		**6**		**52**	**3.6%**	**0.80 [0.13, 4.78]**
Total events	2		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.24 (P = 0.81)						
Total (95% CI)		**539**		**1089**	**100.0%**	**1.73 [1.16, 2.57]**
Total events	302		520			
Heterogeneity: Tau² = 0.29; Chi² = 31.40, df = 11 (P = 0.0010); I² = 65%						
Test for overall effect: Z = 2.70 (P = 0.007)						
Test for subgroup differences: Chi² = 15.07, df = 3 (P = 0.002), I² = 80.1%						



Supplementary figure 3.



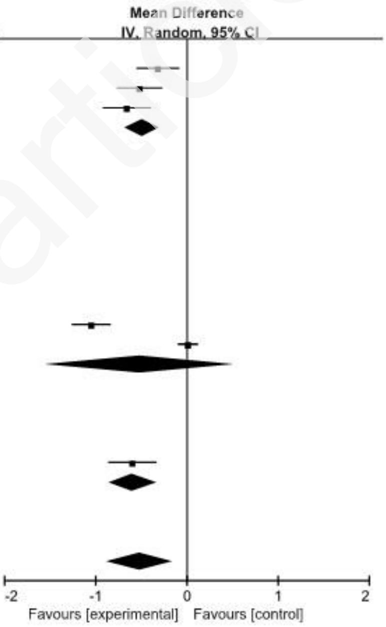
Supplementary figure 4.



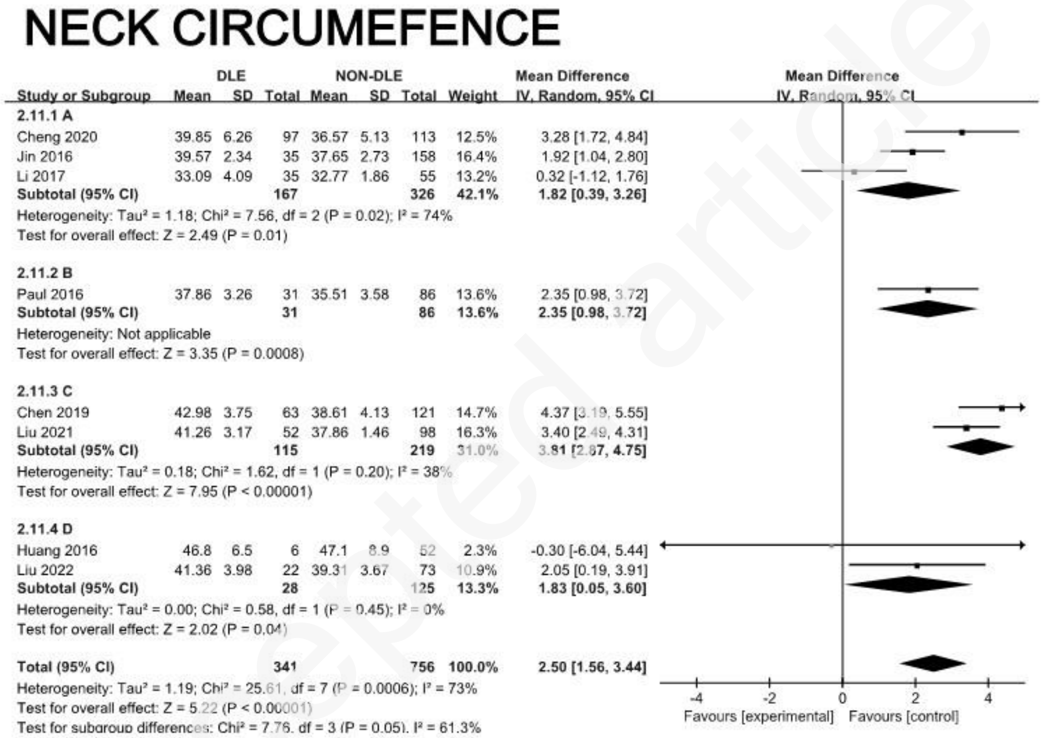
Supplementary figure 5.

IIG

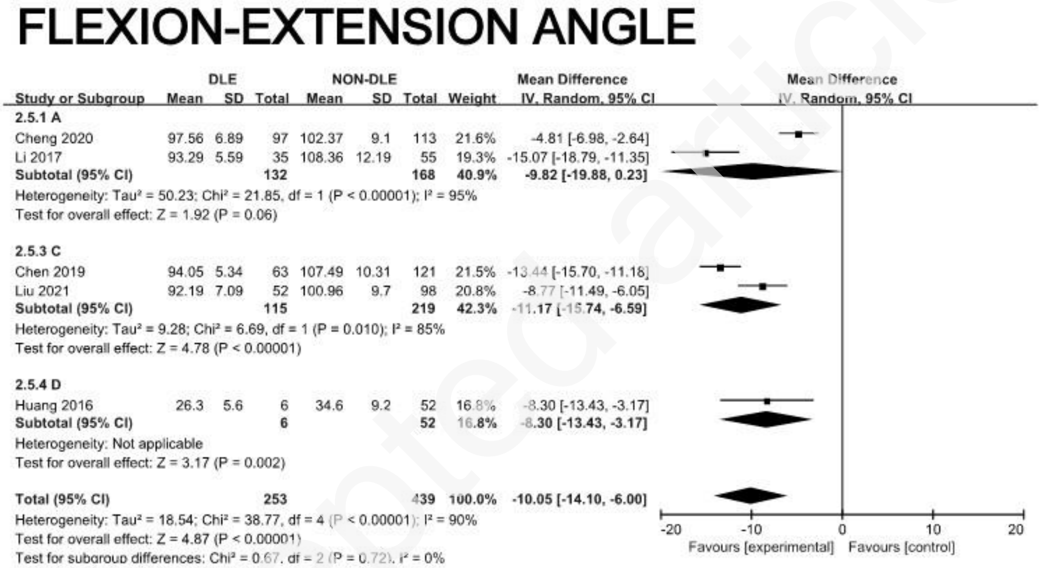
Study or Subgroup	DLE Mean	DLE SD	DLE Total	NON-DLE Mean	NON-DLE SD	NON-DLE Total	Weight	Mean Difference IV, Random, 95% CI
2.4.1 A								
Cheng 2020	3.81	0.74	97	4.13	0.98	113	16.6%	-0.32 [-0.55, -0.09]
Jin 2016	3.96	0.68	35	4.48	0.65	158	16.5%	-0.52 [-0.77, -0.27]
Li 2017	3.81	0.63	35	4.47	0.6	55	16.3%	-0.66 [-0.92, -0.40]
Subtotal (95% CI)			**167**			**326**	**49.4%**	**-0.49 [-0.69, -0.30]**
Heterogeneity: Tau² = 0.01; Chi² = 3.71, df = 2 (P = 0.16); I² = 46%								
Test for overall effect: Z = 4.97 (P < 0.00001)								
2.4.2 B								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
2.4.3 C								
Chen 2019	3.76	0.72	63	4.81	0.65	121	16.8%	-1.05 [-1.26, -0.84]
Liu 2021	4.04	0.35	52	4.03	0.27	98	17.5%	0.01 [-0.10, 0.12]
Subtotal (95% CI)			**115**			**219**	**34.3%**	**-0.52 [-1.55, 0.52]**
Heterogeneity: Tau² = 0.55; Chi² = 75.82, df = 1 (P < 0.00001); I² = 99%								
Test for overall effect: Z = 0.97 (P = 0.33)								
2.4.4 D								
Huang 2016	3.7	0.3	6	4.3	0.4	52	16.3%	-0.60 [-0.86, -0.34]
Subtotal (95% CI)			**6**			**52**	**16.3%**	**-0.60 [-0.86, -0.34]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.46 (P < 0.00001)								
Total (95% CI)			**288**			**597**	**100.0%**	**-0.52 [-0.88, -0.15]**
Heterogeneity: Tau² = 0.19; Chi² = 93.91, df = 5 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 2.79 (P = 0.005)								
Test for subgroup differences: Chi² = 0.41, df = 2 (P = 0.81), I² = 0%								



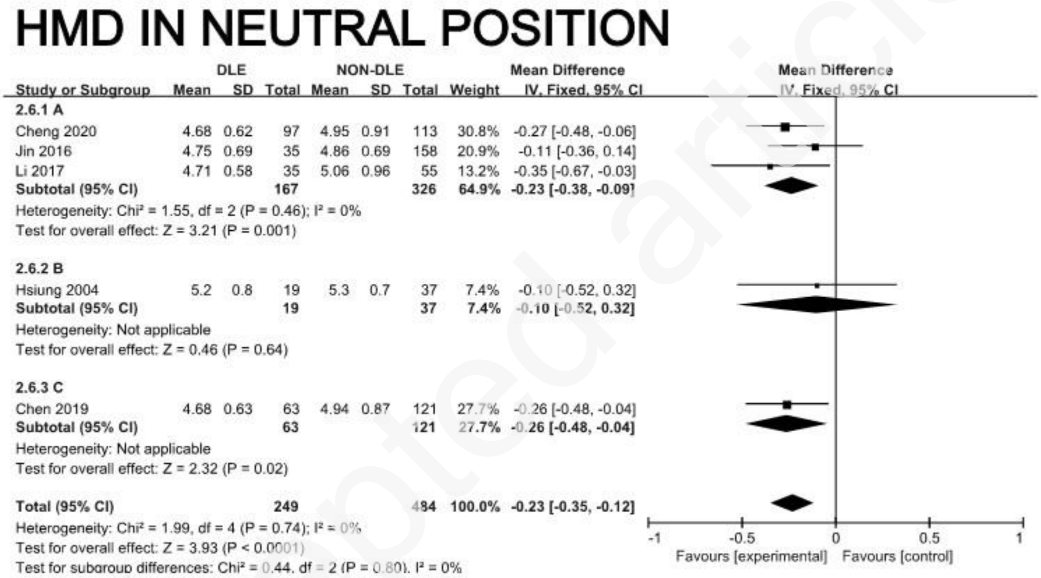
Supplementary figure 6.



Supplementary figure 7.



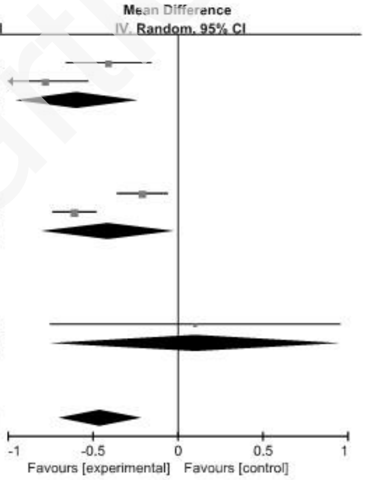
Supplementary figure 8.



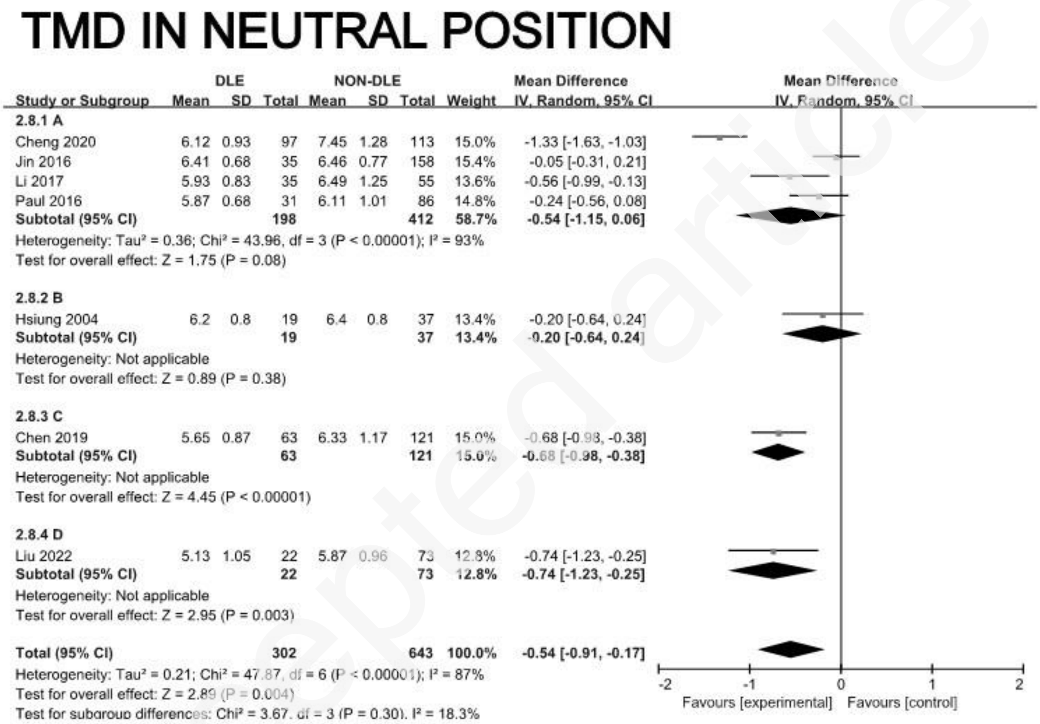
Supplementary figure 9.

HMD IN FULL EXTENSION

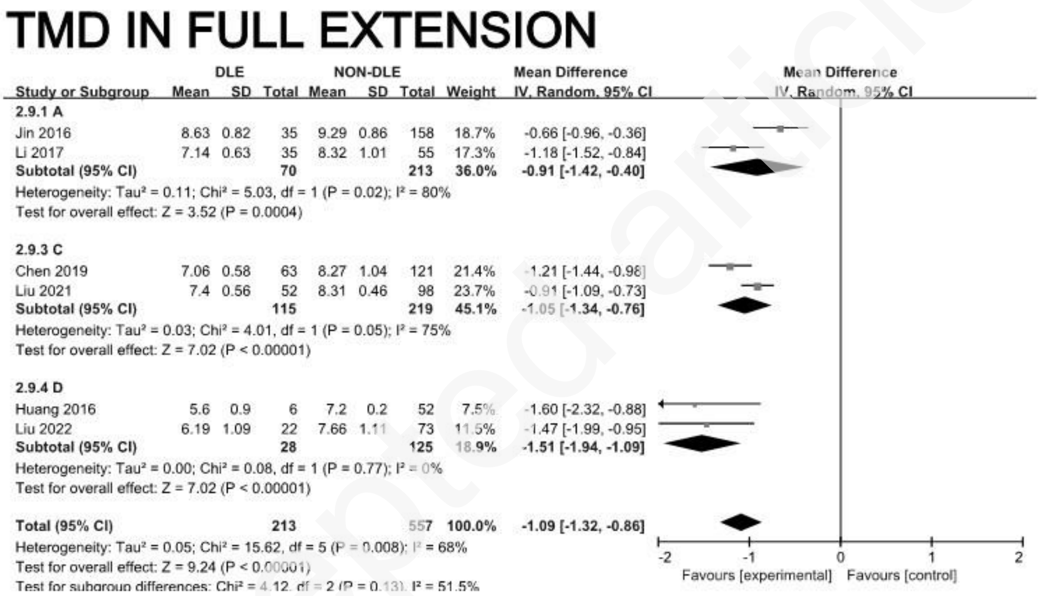
Study or Subgroup	Favours [experimental] Mean	SD	Total	NON-DLE Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.7.1 A								
Jin 2016	6.11	0.68	35	6.52	0.73	158	21.4%	-0.41 [-0.66, -0.16]
Li 2017	5.4	0.37	35	6.18	0.83	55	21.4%	-0.78 [-1.03, -0.53]
Subtotal (95% CI)			**70**			**213**	**42.8%**	**-0.60 [-0.96, -0.23]**
Heterogeneity: Tau² = 0.05; Chi² = 4.15, df = 1 (P = 0.04); I² = 76%								
Test for overall effect: Z = 3.22 (P = 0.001)								
2.7.3 C								
Chen 2019	5.47	0.41	63	5.68	0.62	121	25.1%	-0.21 [-0.36, -0.06]
Liu 2021	5.95	0.35	52	6.56	0.44	98	25.8%	-0.61 [-0.74, -0.48]
Subtotal (95% CI)			**115**			**219**	**50.9%**	**-0.41 [-0.80, -0.02]**
Heterogeneity: Tau² = 0.07; Chi² = 15.72, df = 1 (P < 0.0001); I² = 94%								
Test for overall effect: Z = 2.06 (P = 0.04)								
2.7.4 D								
Huang 2016	5.3	1	6	5.2	1.1	52	6.3%	0.10 [-0.75, 0.95]
Subtotal (95% CI)			**6**			**52**	**6.3%**	**0.10 [-0.75, 0.95]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.23 (P = 0.82)								
Total (95% CI)			**191**			**484**	**100.0%**	**-0.46 [-0.70, -0.22]**
Heterogeneity: Tau² = 0.06; Chi² = 23.86, df = 4 (P < 0.0001); I² = 83%								
Test for overall effect: Z = 3.69 (P = 0.0002)								
Test for subgroup differences: Chi² = 2.24, df = 2 (P = 0.33), I² = 10.8%								



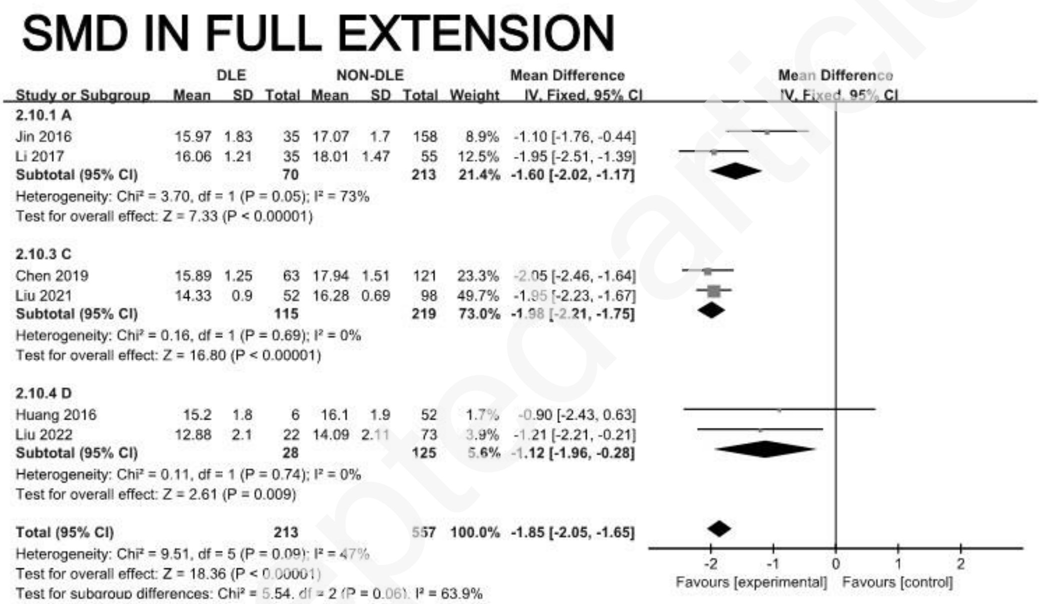
Supplementary figure 10.



Supplementary figure 11.



Supplementary figure 12.



Supplementary figure 13.

MMI

Study or Subgroup	DLE Events	DLE Total	NON-DLE Events	NON-DLE Total	Weight	Odds Ratio M-H, Random, 95% CI
2.3.1 A						
Cheng 2020	76	97	77	113	11.4%	1.69 [0.91, 3.16]
Li 2017	25	35	19	55	9.3%	4.74 [1.89, 11.89]
Meng 2010	7	7	14	46	2.3%	33.62 [1.80, 628.92]
Paul 2016	12	31	13	86	9.3%	3.55 [1.40, 9.02]
Sun 2015	36	64	26	93	11.1%	3.31 [1.70, 6.48]
Wang 2012	9	20	9	69	8.0%	5.45 [1.77, 16.81]
Wang 2021	15	37	29	141	10.4%	2.63 [1.22, 5.70]
Subtotal (95% CI)		**291**		**603**	**61.8%**	**3.16 [2.14, 4.68]**
Total events	180		187			
Heterogeneity: Tau² = 0.07; Chi² = 8.21, df = 6 (P = 0.22); I² = 27%						
Test for overall effect: Z = 5.76 (P < 0.00001)						
2.3.2 B						
Kharrat 2022	12	59	14	52	9.6%	0.69 [0.29, 1.67]
Pinar 2009	10	22	6	72	7.6%	9.17 [2.80, 29.96]
Subtotal (95% CI)		**81**		**124**	**17.3%**	**2.44 [0.19, 30.71]**
Total events	22		20			
Heterogeneity: Tau² = 3.05; Chi² = 11.77, df = 1 (P = 0.0006); I² = 92%						
Test for overall effect: Z = 0.69 (P = 0.49)						
2.3.3 C						
Chen 2019	43	63	43	121	11.3%	3.90 [2.04, 7.46]
Liu 2021	29	52	9	98	9.6%	12.47 [5.19, 29.98]
Subtotal (95% CI)		**115**		**219**	**20.9%**	**6.71 [2.15, 20.89]**
Total events	72		52			
Heterogeneity: Tau² = 0.52; Chi² = 4.36, df = 1 (P = 0.04); I² = 77%						
Test for overall effect: Z = 3.28 (P = 0.001)						
Total (95% CI)		**487**		**946**	**100.0%**	**3.68 [2.27, 5.97]**
Total events	274		259			
Heterogeneity: Tau² = 0.43; Chi² = 32.49, df = 10 (P = 0.0003); I² = 69%						
Test for overall effect: Z = 5.29 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.57, df = 2 (P = 0.46), I² = 0%