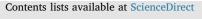
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Videolaryngoscopy versus direct laryngoscopy for nasotracheal intubation: A systematic review and meta-analysis of randomised controlled trials^{\star}



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ABSTRACT

Study objective: Nasotracheal intubation (NTI) is a common practice in the oral and maxillofacial surgeries. A systematic review and meta-analysis was performed to determine whether videolaryngoscopy (VL) compared with direct laryngoscopy (DL) can lead to better outcomes for NTI in adult surgical patients. *Measurements:* Only randomised controlled trials comparing VL and DL for NTI were included. The primary

Measurements: Only randomised controlled trials comparing VL and DL for N11 were included. The primary outcome was overall success rate and the second outcomes were first-attempt success rate, intubation time, rate of Cormack and Lehane classification 1, rate of Magill Forceps used, rate of postoperative sore throat, and ease of intubation.

Main results: Fourteen studies with 20 comparisons (n = 1052) were included in quantitative synthesis. The overall success rate was similar between two groups (RR, 1.03; p = 0.14; moderate-quality evidence). VL was associated with a higher first-attempt success rate (RR 1.09; p = 0.04; low-quality evidence), a shorten intubation time (MD-6.72 s; p = 0.0001; low-quality evidence), a higher rate of Cormack and Lehane classification 1 (RR, 2.11; p < 0.01; high-quality evidence), a less use of the Magill forceps (RR, 0.11; p < 0.01; high-quality evidence), a less use of the Magill forceps (RR, 0.11; p < 0.01; high-quality evidence). Subgroup analysis based on whether with a difficult airway showed higher overall success (p < 0.01) and first-attempt success rates with VL (p = 0.04) in patients with difficult airways; however, these benefits was not shown in patients with a normal airway (p > 0.05); Subgroup analysis based on operators' experience showed that success rate did not differ between groups (p > 0.05), but intubation time was shortened by more than 50s by non-experienced operators (p < 0.05). Subgroup analysis based on different devices used showed that only non-integrated VL led to a shorter intubation time (p < 0.05).

Conclusions: The use of VL does not increase the overall success rate of NTI in adult patients with general anesthesia, but it improves the first-attempt success rate and laryngeal visualization, and shortens the intubation time. VL is particularly beneficial for patients with difficult airways.

1. Introduction

Nasotracheal intubation (NTI) is a practice used commonly in the oral and maxillofacial surgeries to secure airway safety and provide a favorable operation field. It can also be employed in patients with suspicious cervical instability or severe spine degeneration with limited mouth opening and minimum spine mobility [1–7]. The NTI with direct laryngoscopy (DL) is most common in clinical practice, but it usually

requires additional maneuvers such as the external laryngeal pressure or the assistant of the Magill forceps. Even a poor laryngeal visualization by DL can result in difficult or failed NTI [3].

Videolaryngoscopy (VL) has been used for orotracheal intubation (OTI) in the patients with normal and difficult airways. It has been reported that VL can provide an improved laryngeal visualization as well as an increased intubation success rate, especially for patients with difficult airways and novice operators [8–11]. For NTI, it has been

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demonstrated a higher success rate by using VL in observational studies [12,13]. Case series on extremely difficult airways recommended the use of VL for NTI [14–16]. A systematic review performed in 2013 showed that VL can provide a higher success rate and a shorter intubation time of NTI compared with the Macintosh DL [17]. However, two previous randomised controlled trials (RCTs) before 2013 [18,19] and two recent RCTs [20,21] comparing VL and DL for NTI are not included in this systematic review. Thus, this systematic review and meta-analysis of randomised RCTs was performed to determine whether the use of VL could improve the NTI outcomes such as overall and first-attempt success rates in adult surgical patients undergoing general anesthesia compared with DL. Our review has been registered at PROSPERO (http://www.crd.york.ac.uk/PROSPERO) and the registration number is: CRD42018086468.

2. Materials and methods

The PRISMA guidelines were followed [22]. The Cochrane Central Register of Controlled Trials (CENTRAL; 2017, Issue 9), PubMed (1946 to February 15th, 2018), EMBASE (1974 to February 15th, 2018), and ScienceDirect (1997 to February 15th, 2018) were searched. The search strategies of the four electronic databases were provided in the Supplemental data [23]. Study authors were mailed for literature without full-text or other useful information. Studies that have not been fully published (e.g. conference abstract) or studies without full-text were excluded. The reference lists of all eligible trials and reviews were screened for additional citations. No language restriction was imposed.

Only RCTs comparing the VL and DL for NTI in adult (age > 18 years old) surgical patients requiring general anesthesia were included. Manikin study, cadaver study, simulated study, and observational study were excluded. Patients with chronic suppurative sinusitis, midface instability, suspected basilar skull fracture, coagulopathy, or limited mouth opening (< 3 cm) were excluded. Patients in the intervention group used a VL and patients in the control group used a DL. Optimizing maneuvers such as rotation of the nasal tube, cuff inflation to elevate the tip of the tube, external laryngeal pressure, or use of stylet and the Magill forceps, could be initiated at the discretion of the operators.

The Primary outcome was overall success rate. The secondary outcomes were first-attempt success rate, intubation time (from advancement of nasal tube into nostril until the appearance of a capnography curve or from the blade passing the incisors until passage of the nasal tube was completed, according to the original authors' definitions), rate of Cormack and Lehane classification 1, rate of the Magill forceps used, rate of postoperative sore throat (moderate and severe, assessed during hospitalization), and ease of intubation.

The titles and abstracts were independently screened by two study authors (J.J.; D.X.M.). After retrieving the full-texts of any potentially relevant studies, their eligibility was determined. Any disagreements between the two review authors were resolved by discussion with other authors until a consensus was obtained. A PRISMA flow diagram was completed to record the selection process in sufficient detail [24].

Data was extracted by two review authors (J.J. and D.X.M.). For continuous data, mean, standard deviation (SD), and sample size were extracted. Data like median and interquartile range that could not be used directly were converted to mean and SD by using formula provided in the Cochrane handbook [23]. For the dichotomous variables, the number of events occurred, and sample size were extracted. For the studies with more than two comparisons under same grouping method according to different situations, each situation was considered as a single comparison and thus two or more comparisons with equational sample size were created. Although a unit-of-analysis error would occur accordingly, this could facilitate the investigation of heterogeneity and subgroup analyses [23]. Any disagreement on data extraction was resolved by discussion with a third author (F.S.X.) until a consensus was reached. The study author of the original report was contacted for important missing statistics. For the participants missing due to dropout, if "missing at random", analysis was performed based on the available data, if not, an available case analysis was performed, and the potential bias was discussed in discussion section. If a study did not mention withdrawals, no drop-out was assumed [23].

The risk of bias for each eligible study was independently assessed by two review authors (J.J. and D.X.M.) by using the "Risk of bias" assessment tool of the Cochrane Handbook [23], and a "Risk of bias" summary figure was generated by using Review Manager (RevMan 5.3; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). If all seven domains were assigned to "low risk" of bias, the study was classified as "low risk"; if one or more domains were assigned to "unclear risk" of bias, the study was classified as "unclear risk"; if one or more domains were assigned to "high risk" of bias, the study was classified as "high risk" [23]. The criteria of the GRADE system (study limitations, consistency of effect, imprecision, indirectness, and publication bias) were used to assess the quality of evidence associated with all outcomes [25,26]. Then a "Grade evidence profile" table was developed by using the GRADE software (www.guidelinedevelopment. org) to rate these outcomes as high, moderate, low, or very low quality. The quality of evidence was downgraded by one or two level when serious or very serious deficiencies were considered in these criteria.

Both weighted mean difference (WMD) and 95% confidence interval (CI) were used for continuous data. Both relative risk (RR) and 95% CI were used for dichotomous data. P < 0.05 was considered statistically significant. Review Manager was used to perform the pooled analysis for the outcomes from more than one study. A Chi-squared test with the I^2 statistic (with statistical significance set at the level of two-tailed 0.10) was used to describe the percentage of the total variance across studies from heterogeneity rather than from chance. If I^2 is < 40%, namely there is no statistical heterogeneity among studies, and a fixed-effect model is used; otherwise, a random-effects model is used. For the results that could not be analyzed via meta-analysis, only a qualitative systematic review was planned.

Before pooled analysis, clinical and methodological heterogeneity was considered. In the presence of statistical heterogeneity ($l^2 > 40\%$) or an indication of clinical heterogeneity, subgroup analysis was planned for primary outcome and two secondary outcomes (first-attempt success rate and intubation time) according to following possible heterogeneous factors: whether with a difficult airway; operator' s experience: experienced or inexperienced (according to the judgments of study authors); different devices: VL with an integrated channel like Airtraq, VL with a standard blade like C-MAC, or VL with an angled blade like Glidescope [27]. Sensitivity analysis was planned to explore other potential sources of heterogeneity if necessary. Reporting bias was also assessed by using funnel plot if the result of primary outcome was from at least 10 trials [28].

3. Results

Using search strategy, a total of 103 papers were identified. Of them, 82 were excluded during title and abstract screening due to duplicates and being irrelevant to our research question. Twenty-one studies were selected for full text assessment using inclusion and exclusion criteria. Seven studies were further removed because of awake intubation [29], different grouping methods [30], no external video [31], no full-text [32], and non-RCTs [12,14,33]. Among the remaining 14 studies [6,18–21,34–42], 6 had 2 comparisons [6,20,35,39,41,42], thus, 14 studies with 20 comparisons (n = 1052) were eventually included in the review for data extraction. Authors from 7 studies were contacted for unpublished data and detailed information on study design [19–21,36,38,39,42], only 2 of them replied [19,39]. The process of selection of studies is shown in Fig. 1.

The characteristics of included studies are listed in Table 1. Of the 14 included studies, 12 were carried out in the dental, maxillofacial, or

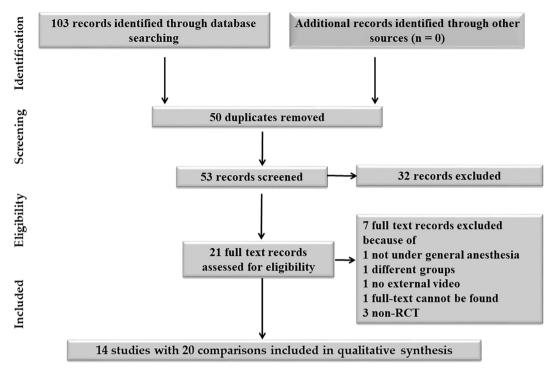


Fig. 1. Flow chart of included and excluded studies.

neck surgeries, one in the spine surgery [38], and one did not report the type of surgery [36]. The NTI was performed by inexperienced operators in 3 studies [36,37,40] and by the experienced operators in the remaining studies. Of 20 comparisons, 2 were carried out in the patients with difficult airways [34,41]. Six comparisons used the VLs with integrated channel blades (Airtraq [36] or Pentax AWS [20,35,39,42]), 2 used the VLs with standard blades (McGrath MAC [39] or C-MAC [34]), and 12 used the VLs with angled blades (Glidescope [6,18–20,35,37,38,40], McGrath [21] or Airtraq without an integrated channel [6,41]).

Detailed description regarding the risk of bias of the included studies is shown in Fig. 2 and summarized in Table S1. The overall risk of bias of the included studies was low or unclear. Of those, 4 could be classified as "low risk" studies [18,19,34,37] and 2 as "high risk" studies [6,42]. The funnel plot obtained from primary outcome with its visually symmetrical distribution qualitatively indicated a low risk of publication bias (Fig. S1). The GRADE system showed that the quality of most evidences was high or moderate, and the quality of evidence was downgraded manly due to inconsistency from moderate or high level of heterogeneity. The results of the evidence of outcomes were listed in Table 2.

All included studies reported the overall success rate. Pooled analysis showed no significant difference in the overall success rate between VL and DL (RR, 1.03; 95%CI, 0.99–1.07; n = 1052; p = 0.14; $I^2 = 66\%$; moderate-quality evidence) (Fig. 3). Subgroup analysis according to whether with difficult airways showed a higher overall success rate in patients with difficult airway when using VL than when using DL (3 studies; RR, 1.29; n = 260; p < 0.01; $I^2 = 36\%$; high-quality evidence). No difference was shown in patients with a normal airway (11 studies with 17 comparisons; RR, 1.00; n = 792; p = 0.74; $I^2 = 0\%$; high-quality evidence). Subgroup analyses based on operators' experience and different devices showed no differences in the overall success rate among all subgroups (p > 0.05) (Figs. S2–S4).

Twelve studies with 16 comparisons reported the first-attempt success rate. Pooled analysis showed a higher first-attempt success rate with VL than with DL (RR, 1.09; 95%CI, 1.00–1.17; n = 930; p = 0.04; $I^2 = 84\%$; low-quality evidence). Subgroup analysis according to

whether with difficult airways showed a higher first-attempt success rate in patients with difficult airways when using VL than when using DL (3 studies; RR, 1.30; n = 260; p = 0.04; $I^2 = 63\%$; moderate-quality evidence, Fig. 4). No difference was shown in patients with a normal airway (10 studies with 13 comparisons; RR, 1.03; n = 670; p = 0.24; $I^2 = 63\%$; moderate-quality evidence). Subgroup analysis based on operators' experience showed no differences in the first-attempt success rate between experienced or inexperienced operators (p > 0.05). Subgroup analysis based on different devices found a higher first-attempt success rate when using VL with standard blades (2 studies; RR, 1.14; n = 130; p = 0.02; $I^2 = 0\%$; high-quality evidence). However, one of 2 studies included in this subgroup, which had a larger sample size than the other one, was performed in patients with difficult airways [34]. Thus, the difference between groups might probably originate from this study rather than from the device used (Figs. S5–S7).

All included studies reported the intubation time with different definitions (Table 1). Pooled analysis showed a significant difference in the intubation time between VL and DL (MD, -6.72; 95%CI, -10.17 to -3.26; n = 1012; p < 0.05; $I^2 = 74\%$; low-quality evidence, Fig. 5). This significant difference was shown in all but one subgroup (p < 0.05). Furthermore, subgroup analyses showed that intubation time was similar in two groups when using the VLs with integrated channel blades (MD, -2.69; 95%CI, -9.95-4.58; n = 220; p < 0.05; $I^2 = 74\%$; low-quality evidence), but it was reduced by more than 50s when using VL by inexperienced operators (MD, -50.95; 95%CI, -92.22 to -9.68; n = 119; p < 0.05; $I^2 = 75\%$; low-quality evidence) (Figs. S8–S10).

Six studies with 8 comparisons reported the rate of Cormack and Lehane classification 1, 8 studies with 10 comparisons reported the rate of the Magill forceps used, and 3 studies with 5 comparisons reported the rate of postoperative moderate and severe sore throat. Pooled analysis showed a lower rate the Magill forceps used (RR, 0.11; n = 485; p < 0.01; $I^2 = 14\%$; high-quality evidence) (Fig. S11) and a lower incidence of postoperative sore throat when using VL (RR, 0.50; n = 234; p = 0.03; $I^2 = 0\%$; high-quality evidence) (Fig. S12). More patients could be classified as Cormack and Lehane classification 1 when using VL (RR, 2.11; n = 759; p < 0.01; $I^2 = 78\%$; high-quality

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Table 1	Characteristics of the fourteen inclu	

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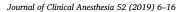
Studies	п	Types of surgery	Studied devices	Inclusive criteria	Exclusive criteria	Operators' experience	Definition of failed intubation	Definition of one attempt	Definition of intubation time
Hazarika 2018 [34]	100	Head and neck cancer	C-MAC and ML	ASA I–III, aged 20–70 yrs., El- Ganzouri risk index 1 ~ ≤7	ASA IV, mouth opening < 2.5 cm, difficult mask ventilation	Experienced	$SpO_2 < 90\%$ at any time; after 3 attempts	If intubation is still unsuccessful after using all accessory maneuvers; withdrawal of laryposcope from the mouth at anv time	From introduction of laryngoscope into mouth to appearance of 3 consecutive capnographs
Hirabayashi 2009 [35]	20	Unclear	Airtraq and ML	Adults	Not specified	Inexperienced	Not specified	Not specified	From interruption of mask ventilation to connecting the nasal tube to an anesthesia cirrle
Hirabayshi 2013 [36]	60	Dental or oral	Pentax-AWS, GVL and ML	Adults with a normal airway	Not specified	Experienced	Not specified	Not specified	From interruption of mask ventilation to connecting the nasal tube to an anesthesia circle
Jones 2008 [36]	69	Dental or maxillofacial	GVL and ML	≥ 18 yrs.	Known difficult airways and need for RSI	Inexperienced (majority)	If intubation attempt took longer than 150 s	If laryngoscope was removed from the mouth	From removal of mask to appearance of 3 consecutive capnographs
Kwak 2015 [21]	70	Oral and maxillofacial	GVL and ML	20–60 yrs., ASA I or II, and with an expected normal airway	Suspected difficult airways, cervical spine injury, bleeding tendency, and need for RSI	Experienced	Needing > one attempt to achieve successful intubation	Intubation time $> 150 s$ or SpO ₂ $< 95\%$	From insertion of nasal tube through the nostril to the detection of EtCO ₂
Li 2007 [19]	40	Plastic	GVL and ML	ASA I - II, 18–50 yrs	Cardiovascular diseases, reactive airways, or predicted difficult airways, and taking the medication that have an effect on blood pressure or heart rate	Experienced	Not specified	Not specified	From termination of mask ventilation to restarting of ventilation via the nasal tube
Mont 2012 [41]	200	Maxillo facial	Airtraq (without channel) and ML	Difficult nasal intubation predictors or expected easy airway	ASA 4, need for RSI, suspected reduced tolerance for apnea, and mouth opening < 1.5 cm	Experienced	If alternative device was attempted	Inability to achieve a view of at least grade 3, or inability to advance the nasal tube into the trachea with all optimizing maneuvers, or $SpO_2 < 90\%$	Time between opening of the mouth and inflation of cuff of nasal tube
Puchner 2011 [6]	62	Dental or maxillofacial	Airtraq (without channel), GVL and ML	ASA I or II, 18–80 yrs	Predicted difficult airways, or history of Experienced bleeding	Experienced	Severe bleeding, > 3 attempts, or intubation time > 2 min	Not specified	From insertion of blade to the final tube position
Sato 2017 [39]	60	Oral	McGrath MAC, Pentax-AWS, and ML	ASA I-II, 20-70 yrs	Rhinostenosis, and predicted difficult intubation	Experienced	Not specified	Not specified	From the nasal tube passed through the nasal cavity to the initiation of ventilation via the nasal tube
Shimada 2010 [40]	40	Dental or oral	GVL and ML	Adults	Not specified	Inexperienced	Not specified	Not specified	From interruption of mask ventilation to connecting the nasal tube to an anesthesia circle.
Suzuki 2012 [42]	06	Orthodontia	Pentax-AWS indirect, Pentax- AWS direct, and ML	ASA I-II, > 18 yrs	Cervical spine injury, difficult airway, gastroesophageal reflux disease, or body mass index > 35 kg/m ²	Experienced	If nasal tube could not be placed at an ideal depth by 2 attempts	$SpO_2 < 95\%$ or obstructed view by fogging or secretions	From the blade passing the incisors to passage of the nasal tube into the trachea
Tseng 2017 [20]	108	Oro- maxillofacial	GVL, Pentax AWS, and ML	ASA I or II, 20–65 yrs	Limited mouth opening < 3 cm, a history of difficult intubation, cervical spine instability, chronic suppurative sinusitis, and contraindications to nasal intubation	Experienced	Not specified	Not specified	Nasal tube advanced from oropharynx into trachea and removal of the scope form oral cavity
Xu 2014 [38]	60	Spine	GVL and ML	ASA I-II, 23–59 yrs	Risk of aspiration	Experienced	> 3 attempts	Intubation time > 60s or removal and reposition of laryngoscope	From insertion of the device into the mouth to passage of nasal tube via the glottis
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Studies	и	Types of surgery	Studied devices	Studied devices Inclusive criteria	Exclusive criteria	Operators' experience	Definition of failed intubation	Definition of one attempt	Definition of intubation time
Xue 2008 [18] 76 Plastic	76	Plastic	GVL and ML ASA I, adults	ASA I, adults	Reactive airway disease, predicted difficult airways, gastroesophageal reflux, morbid obesity, diabetes mellitus, hypertension and cardiovascular diseases.	Experienced	Needing > one attempt to achieve successful intubation	Needing $>$ one attempt SpO ₂ $<$ 95% due to prolonged to achieve successful intubation time intubation	From termination of mask ventilation to restarting of ventilation via the nasal tube

J. Jiang et al.

Abbreviation: yrs., years; GVL, Glidescope videolaryngoscope; ML, Macintosh laryngoscope; ASA, America Society of Anesthesiologist; RST, rapid sequential intubation; EtCO₂, end-tidal CO₂; SpO₂, pulse oxygen saturation.



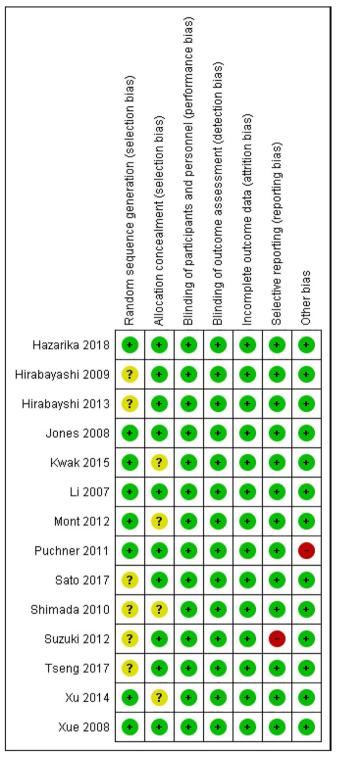


Fig. 2. Risk of bias summary: judgements about each risk of bias item for fourteen included studies. Green, low risk of bias; red, high risk of bias; yellow, unclear risk of bias. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

evidence) (Fig. S13).

Seven studies reported the ease of intubation using different assessment methods. Two studies [37,38] used a 0–100 mm visual analogue scale (0 being 'worst' and 100 'best'), and results were not pooled due to significant heterogeneity; 3 [6,38,42] used the Intubation Difficulty Scale (IDS) score, and one [20] used a modified naso-intubation

	Quality assessment						No of patients	ents	Effect		Quality	Importance
Internet Internet Internet of basic of basic of basicGeneral (0.1) <t< th=""><th>No of Design studies</th><th>Risk of bias</th><th>Inconsistency</th><th>Indirectness</th><th>Imprecision</th><th>Other considerations</th><th>ΛΓ</th><th>DL</th><th>Relative (95% CI)</th><th>Absolute</th><th></th><th></th></t<>	No of Design studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ΛΓ	DL	Relative (95% CI)	Absolute		
Interaction and influction function of the consistency of the constant	Overall success rate 14 th Randomised trials		Serious ^b	No serious indirectness	No serious imprecision	None	582/587 (99.1%)			28 more per 1000 (from 9 fewer to 64 more) 30 more per 1000 (from 10 fewer to 70 more)	⊕⊕⊕O Moderate	Critical
Indicators Indicators Induction 	erall success rate - difficult Randomised trials		No serious inconsistency	No serious indirectness	No serious imprecision	None	126/130 (96.9%)	96/130 (73.8%) 70%	RR 1.29 (1.13 to 1.48)	214 more per 1000 (from 96 more to 354 more) 203 more per 1000 (from 91 more to 336 more)	⊕⊕⊕⊕ High	Critical
all access the - experiment If ye series Note series	erall success rate - easy Randomised trials		No serious inconsistency	No serious indirectness	No serious imprecision	None	456/457 (99.8%)	331/335 (98.8%) 100%		0 fewer per 1000 (from 20 fewer to 20 more) 0 fewer per 1000 (from 20 fewer to 20 more)	⊕⊕⊕⊕ High	Critical
all success rate - inspected inspectioned inspectiod<	erall success rate - experience Randomised trials	d No serious risk of bias	Very serious ^d	No serious indirectness	No serious imprecision	None	518/523 (99%)	365/400 (91.3%) 100%	RR 1.03 (0.99 to 1.08)	27 more per 1000 (from 9 fewer to 73 more) 30 more per 1000 (from 10 fewer to 80 more)	⊕⊕00 Low	Critical
rall success rate - integrated channel No serious No No <td< td=""><td>erall success rate - inexperien Randomised trials</td><td>ced No serious risk of bias</td><td>No serious inconsistency</td><td>No serious indirectness</td><td>No serious imprecision</td><td>None</td><td>64/64 (100%)</td><td>62/65 (95.4%) 95%</td><td>RR 1.03 (0.97 to 1.10)</td><td>29 more per 1000 (from 29 fewer to 95 more) 28 more per 1000 (from 28 fewer to 95 more)</td><td>⊕⊕⊕⊕ High</td><td>Critical</td></td<>	erall success rate - inexperien Randomised trials	ced No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	64/64 (100%)	62/65 (95.4%) 95%	RR 1.03 (0.97 to 1.10)	29 more per 1000 (from 29 fewer to 95 more) 28 more per 1000 (from 28 fewer to 95 more)	⊕⊕⊕⊕ High	Critical
rail success rate - standard blade Randomised trials No serious risk Very serious ^d No serious imprecision No serious (100%) 65.7%) 10.9(1.9) 78 more per 1000 (from 78) 0000 rail success rate - angled blade 0f bias 92% 100%) 66.7%) 10.11) 78 more per 1000 (from 78) 0000 rail success rate - angled blade 100% 83.737 RR 1.04 (0.98) 36 more per 1000 (from 18) 0000 rail success rate - angled blade 100% 09.7% 01.1% 01.1% 0000	erall success rate – integrated Randomised trials	channel No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	143/143 (100%)	77/78 (98.7%) 100%	RR 1.00 (0.96 to 1.05)	10 more per 1000 (from 39 fewer to 49 more) 10 more per 1000 (from 40 fewer to 50 more)	⊕⊕⊕⊕ High	Important
rall success rate – angled blade Randomised trials No serious risk Very serious ^d No serious None 369/374 298/327 RR 1.04 (0.98 36 more per 1000 (from 18 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	erall success rate – standard t Randomised trials	olade No serious risk of bias	Very serious ^d	No serious indirectness	No serious imprecision	None	70/70 (100%)	52/60 (86.7%) 92%	RR 1.09 (0.91 to 1.31)	78 more per 1000 (from 78 fewer to 269 more) 83 more per 1000 (from 83 fewer to 235 more)	⊕⊕00 Low	Important
t-attempt success rate 453/506 340/424 RR 1.09 (1 to 72 more per 1000 (from 0 ΦΦΟΟ Randomised trials No serious risk Very serious ⁴ No serious No serious 0 ΦΘΟ Randomised trials No serious risk Very serious ⁴ No serious No serious 0 ΦΘΟ Randomised trials No serious risk Very serious ⁴ No serious No serious 0 ΦΘΟ Induction Induction Induction Induction Induction 100 (from 0 Randomised trials No serious risk Inductions Induction Induction Induction	rall succes	de No serious risk of bias	Very serious ^d	No serious indirectness	No serious imprecision	None	369/374 (98.7%)	298/327 (91.1%) 100%	RR 1.04 (0.98 to 1.1)	36 more per 1000 (from 18 fewer to 91 more) 40 more per 1000 (from 20 fewer to 100 more)	⊕⊕00 Low	Important
	t-attempt	No serious risk of bias	Very serious ^d	No serious indirectness	No serious imprecision	None	453/506 (89.5%)	340/424 (80.2%) 88.3%	RR 1.09 (1 to 1.17)	72 more per 1000 (from 0 more to 136 more) 79 more per 1000 (from 0 more to 150 more)	⊕⊕00 Low	Critical

Journal of Clinical Anesthesia 52 (2019) 6–16

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First-attempt success rate - difficult

Quality assessment	essment						No of patients	ients	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	٨٢	DL	Relative (95% CI)	Absolute		
m	Randomised trials	No serious risk of bias	Serious ^b	No serious indirectness	No serious imprecision	None	102/130 (78.5%)	77/130 (59.2%) 66%	RR 1.3 (1.01 to 1.68)	178 more per 1000 (from 6 more to 403 more) 198 more per 1000 (from 7 more to 449 more)	⊕⊕⊕O Moderate	Critical
First-attem ₁ 10 ^h	First-attempt success rate – easy 10 ¹ⁱ Randomised trials	No serious risk of bias	Serious ^b	No serious indirectness	No serious imprecision	None	351/376 (93.4%)	263/294 (89.5%) 90%	RR 1.03 (0.98 to 1.09)	27 more per 1000 (from 18 fewer to 81 more) 27 more per 1000 (from 18 fewer to 81 more)	⊕⊕⊕O Moderate	Critical
First-attemJ 9 ^h	First-attempt success rate - experienced 9 ¹¹ Randomised trials No serious risk of bias	rienced No serious risk of bias	Very serious ^d	No serious indirectness	No serious imprecision	None	390/442 (88.2%)	288/359 (80.2%) 88.3%	RR 1.06 (0.98 to 1.15)	48 more per 1000 (from 16 fewer to 120 more) 53 more per 1000 (from 18 fewer to 132 more)	⊕⊕00 Low	Critical
First-attem] 3	First-attempt success rate – inexperienced 3 Randomised trials No seri of bias	success rate – inexperienced Randomised trials No serious risk of bias	Very serious ^d	No serious indirectness	No serious imprecision	None	63/64 (98.4%)	52/65 (80%) 72.5%	RR 1.23 (0.90 to 1.69)	184 more per 1000 (from 80 fewer to 552 more) 167 more per 1000 (from 73 fewer to 500 more)	⊕⊕00 Low	Critical
First-attem] 4 ⁱ	First-attempt success rate – integrated channel blade 4 ⁱ Randomised trials No serious risk N of bias ii	success rate – integrated channel blac Randomised trials No serious risk of bias	de No serious inconsistency	No serious indirectness	No serious imprecision	None	106/123 (86.2%)	56/68 (82.4%) 86.7%	RR 1.06 (0.94 to 1.19)	49 more per 1000 (from 49 fewer to 156 more) 52 more per 1000 (from 52 fewer to 165 more)	00000000000000000000000000000000000000	Important
First-attem] 2	First-attempt success rate – standard blade 2 Randomised trials No serious risk of bias	dard blade No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	68/70 (97.1%)	51/60 (85%) 87%	RR 1.14 (1.02 to 1.27)	119 more per 1000 (from 17 more to 229 more) 122 more per 1000 (from 17	⊕⊕⊕⊕ High	Important
First-attem] 8 ^j	First-attempt success rate – angled blade 8 ¹ Randomised trials No seri of bias	success rate – angled blade Randomised trials No serious risk of bias	Very serious ^d	No serious indirectness	No serious imprecision	None	279/313 (89.1%)	233/296 (78.7%) 91.4%	RR 1.11 (0.98 to 1.25)	more to 235 more) 87 more per 1000 (from 16 fewer to 197 more) 101 more per 1000 (from 18 fewer to 229 more)	⊕⊕00 Low	Important
Time to int 14 ^a	Time to intubation (better indicated by lower values) 14 th Randomised trials No serious risk V of bias	ation (better indicated by lower valu Randomised trials No serious risk of bias	tes) Very serious ^d	No serious indirectness	No serious imprecision	None	583	429	I	MD 6.72 lower (10.17 to 3.26 lower)	⊕⊕00 Low	Important
Time to int 3	Time to intubation - difficult (better indicated by lower values) 3 Randomised trials No serious risk No serious of bias inconsistent	etter indicated by l No serious risk of bias	lower values) No serious inconsistency ^k	No serious indirectness	No serious imprecision	None	127	105	I	MD 13 lower (19.93 to 6.07 lower)	⊕⊕⊕⊕ High	Important
Time to int 12 ^c	Time to intubation - easy (better indicated by lower values) 12 ^c Randomised trials No serious risk Very ser of bias	ation - easy (better indicated by lowe Randomised trials No serious risk of bias	er values) Very serious ^d	No serious indirectness	No serious imprecision	None	456	324	I	MD 5.48 lower (9.23 higher to 1.74 lower)	⊕⊕00 Low	Important
Time to int 11 ^c	Time to intubation - experienced (better indicated by lower values) 11 [°] Randomised trials No serious risk Very serious ^d of bias	ation - experienced (better indicated Randomised trials No serious risk of bias	by lower values) Very serious ^d	No serious indirectness	No serious imprecision	None	519	374	I	MD 5.27 lower (8.31 higher to 2.22 lower)	⊕⊕00 Low	Important
Time to int	Time to intubation - inexperienced (better indicated by lower values)	ced (better indicate	ed by lower values)								(continued	(continued on next page)

J. Jiang et al.

Journal of Clinical Anesthesia 52 (2019) 6–16

Table 2 (continued)	ontinued)											
Quality at	Quality assessment						No of patients	ents	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	٨٢	DL	Relative (95% CI)	Absolute		
ю	Randomised trials No serious risk of bias	No serious risk of bias	Very serious ^d	No serious indirectness	No serious imprecision	None	64	55	1	MD 50.95 lower (92.22 higher to 9.68 lower)	⊕⊕00 Low	Important
Time to ir 6 ^e	ntubation - integrated channel blade (better indicat Randomised trials No serious risk Serious ^b of bias	hannel blade (bett No serious risk of bias	Time to intubation - integrated channel blade (better indicated by lower values) 6° Randomised trials No serious risk Serious ^b indi of bias	alues) No serious indirectness	No serious imprecision	None	143	77	I	MD 2.69 lower (9.95 lower to 4.58 higher)	⊕⊕00 Low	Important
Time to ir 2	Time to intubation - standard blade (better indicated by lower values) 2 Randomised trials No serious risk No serious of bias inconsistency	ade (better indicat No serious risk of bias	ed by lower values) No serious inconsistency	No serious indirectness	No serious imprecision	None	55	45	I	MD 9.98 lower (15.19 to 4.76 lower)	⊕⊕⊕⊕ High	Important
Time to ir 10 ^f	Time to intubation - angled blade (better indicated by lower values) 10 ⁶ Randomised trials No serious risk Very serious ^d of bias	e (better indicated No serious risk of bias	l by lower values) Very serious ^d	No serious indirectness	No serious imprecision	None	370	300	I	MD 8.11 lower (12.65 to 3.56 lower)	⊕⊕00 Low	Important
Rate of Co 6	Rate of Cormack and Lehane classification 1 6 Randomised trials No serious risk of bias	ssification 1 No serious risk of bias	No serious inconsistency ^k	No serious indirectness	No serious imprecision	None	290/389 (74.6%)	126/370 (34.1%) 42.5%	RR 2.11 (1.53 to 2.92)	378 more per 1000 (from 180 more to 654 more) 472 more per 1000 (from 225 more to 816 more)	⊕⊕⊕⊕ High	Important
Rate of M 8	Rate of Magill forceps used 8 Randomised trials No serious risk 0f bias	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Very strong association ¹	6/277 (2.2%)	69/208 (33.2%) 20%	RR 0.11 (0.05 to 0.21)	295 fewer per 1000 (from 262 fewer to 315 fewer) 178 fewer per 1000 (from 158 fewer po 190 fewer)	⊕⊕⊕⊕ High	Important
Rate of pc 3	Rate of postoperative sore throat 3 Randomised trials No serious risk of bias	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Strong association ^m	17/143 (11.9%)	22/91 (24.2%) 20%	RR 0.5 (0.27 to 0.93)	121 fewer per 1000 (from 17 fewer to 176 fewer) 100 fewer per 1000 (from 14 fewer to 146 fewer)	⊕⊕⊕⊕ High	Important

^a With 20 comparisons.

13

^b Moderate heterogeneity. ^c With 17 comparisons.

^d Severe heterogeneity.
^e With 7 comparisons.
^f With 11 comparisons.
⁸ With 16 comparisons.
^h With 13 comparisons.

¹ With 5 comparisons. ¹ With 9 comparisons. ^k Since there is appreciable effect, the quality of the evidence may or may not be downgraded for inconsistency. ⁿ RR < 0.2. ^m RR < 0.5.

	VL		DL			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Hazarika 2018	50	50	42	50	4.7%	1.19 [1.05, 1.35]	
Hirabayashi 2009	10	10	9	10	1.7%	1.11 [0.85, 1.44]	
Hirabayshi 2013	20	20	10	10	4.0%	1.00 [0.86, 1.16]	+
Hirabayshi 2013	20	20	10	10	4.0%	1.00 [0.86, 1.16]	
Jones 2008	34	34	33	35	5.8%	1.06 [0.96, 1.17]	
Kwak 2015	35	35	35	35	7.8%	1.00 [0.95, 1.06]	+
Li 2007	20	20	20	20	6.0%	1.00 [0.91, 1.10]	-+-
Mont 2012	47	50	33	50	2.5%	1.42 [1.15, 1.76]	
Mont 2012	50	50	50	50	8.5%	1.00 [0.96, 1.04]	+
Puchner 2011	20	20	10	10	4.0%	1.00 [0.86, 1.16]	
Puchner 2011	20	21	10	11	2.5%	1.05 [0.85, 1.29]	
Sato 2017	20	20	10	10	4.0%	1.00 [0.86, 1.16]	
Sato 2017	20	20	10	10	4.0%	1.00 [0.86, 1.16]	
Shimada 2010	20	20	20	20	6.0%	1.00 [0.91, 1.10]	-+-
Suzuki 2012	30	30	15	15	5.8%	1.00 [0.91, 1.10]	-+-
Suzuki 2012	30	30	15	15	5.8%	1.00 [0.91, 1.10]	-+
Tseng 2017	36	36	18	18	6.5%	1.00 [0.92, 1.09]	-+-
Tseng 2017	33	33	18	18	6.4%	1.00 [0.92, 1.09]	-+-
Xu 2014	29	30	21	30	2.0%	1.38 [1.08, 1.76]	
Xue 2008	38	38	38	38	8.0%	1.00 [0.95, 1.05]	+
Total (95% Cl)		587		465	100.0%	1.03 [0.99, 1.07]	•
Total events	582		427				2
Heterogeneity: Tau ² =		i² = 55		9 (P < I	0.0001): P	² = 66%	
Test for overall effect:							0.5 0.7 1 1.5 2
restrict storal block	- 1.40	v 0.1	,				Favours [DL] Favours [VL]

Fig. 3. Forest plot for the comparison of overall success rate between videolaryngoscopy (VL) and direct laryngoscopy (DL). M-H, Mantel-Haenszel.

	VL		DL			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Hazarika 2018	49	50	42	50	8.4%	1.17 [1.03, 1.33]	-
Hirabayashi 2009	10	10	9	10	4.8%	1.11 [0.85, 1.44]	-
Jones 2008	33	34	32	35	8.7%	1.06 [0.94, 1.19]	+
Kwak 2015	35	35	35	35	10.3%	1.00 [0.95, 1.06]	+
Li 2007	20	20	20	20	9.4%	1.00 [0.91, 1.10]	+
Mont 2012	47	50	33	50	6.1%	1.42 [1.15, 1.76]	
Mont 2012	50	50	50	50	10.6%	1.00 [0.96, 1.04]	+
Sato 2017	19	20	9	10	5.6%	1.06 [0.84, 1.33]	+-
Sato 2017	17	20	9	10	4.6%	0.94 [0.72, 1.25]	
Shimada 2010	20	20	11	20	2.9%	1.78 [1.20, 2.64]	
Suzuki 2012	27	30	13	15	5.6%	1.04 [0.82, 1.31]	
Suzuki 2012	29	30	13	15	6.1%	1.12 [0.90, 1.38]	
Tseng 2017	23	33	12	18	2.9%	1.05 [0.70, 1.55]	
Tseng 2017	30	36	12	18	3.3%	1.25 [0.87, 1.79]	
Xu 2014	6	30	2	30	0.3%	3.00 [0.66, 13.69]	
Xue 2008	38	38	38	38	10.4%	1.00 [0.95, 1.05]	+
Total (95% CI)		506		424	100.0%	1.09 [1.00, 1.17]	•
Total events	453		340				
Heterogeneity: Tau² =	0.01; Ch	i ^z = 91.	79, df = 1	5 (P < (0.00001);	I² = 84%	
Test for overall effect:	Z = 2.05	(P = 0.0)4)				0.1 0.2 0.5 1 2 5 10 Favours [DL] Favours [VL]

Fig. 4. Forest plot for the comparison of first-attempt success rate between videolaryngoscopy (VL) and direct laryngoscopy (DL). M-H, Mantel-Haenszel.

difficulty scale (MNIDS). Punchner et al. [6] also used a numeric rating scale (NRS, 0 being 'easiest' and 10 "the most difficult') to rate difficulties in managing the airway; the ease of intubation was classified as easy or difficult in one study [34]. The above all studies showed a significant difference in the ease of intubation between groups, with VL being superior to DL (p < 0.05). However, one study [21] used a three-level score (easy, moderate, or difficult) to evaluate the ease of intubation, and showed no significant difference between groups (p = 0.32).

4. Discussion

Our study showed that the use of VL did not improve the overall

success rate of NTI; increased overall and first-attempt success rates were only achieved when using VL in patients with difficult airways. This is agreement with the results obtained from the studies regarding OTI [10,43]. In fact, VL has been shown as an effective rescuing method when tracheal intubation with DL is difficult or failure [41,44]. The improved laryngeal visualization with VL should be one of main reasons for increased success rate of NTI in patients with difficult airways. Some of the studies included in our analysis excluded patients with difficult airways. This may be due to ethical considerations, especially when NTI was carried out by inexperienced operators. Furthermore, NTI is mostly used to provide a better surgical field for oral, head and heck operations; only a few of them are specialized for difficult airways. Thus, we do not think that this will restrict the outcomes to a limited group of

		VL			DL			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Hazarika 2018	39.56	15.65	50	50.34	26.76	42	5.1%	-10.78 [-19.96, -1.60]	+
Hirabayashi 2009	65	24	10	123	70	9	0.5%	-58.00 [-106.09, -9.91]	
Hirabayshi 2013	33	9	20	30	12	10	5.4%	3.00 [-5.42, 11.42]	+
Hirabayshi 2013	37	12	20	30	12	10	5.1%	7.00 [-2.11, 16.11]	
Jones 2008	43.5	20.4	34	66.7	26.7	35	4.3%	-23.20 [-34.39, -12.01]	
Kwak 2015	34.4	13.7	35	44.9	15.6	35	6.0%	-10.50 [-17.38, -3.62]	
Li 2007	49.3	13.7	20	50.7	13.5	20	5.4%	-1.40 [-9.83, 7.03]	-
Mont 2012	45	46	47	77	47	33	2.1%	-32.00 [-52.74, -11.26]	
Mont 2012	31	31	50	34	29	50	4.1%	-3.00 [-14.77, 8.77]	
Puchner 2011	20.1	5.4	20	25.6	7.32	10	6.8%	-5.50 [-10.62, -0.38]	*
Puchner 2011	25.6	6.66	20	25.6	7.32	10	6.7%	0.00 [-5.39, 5.39]	+
Sato 2017	26.8	5.7	20	36.5	8.9	10	6.4%	-9.70 [-15.76, -3.64]	+
Sato 2017	36.4	11	20	36.5	8.9	10	5.9%	-0.10 [-7.43, 7.23]	+
Shimada 2010	54	22	20	141	79	11	0.5%	-87.00 [-134.67, -39.33]	
Suzuki 2012	28	12	30	26	11	15	6.0%	2.00 [-5.03, 9.03]	+
Suzuki 2012	15	5	30	26	11	15	6.5%	-11.00 [-16.85, -5.15]	+
Tseng 2017	32.9	10.5	36	42.7	19.2	18	5.0%	-9.80 [-19.31, -0.29]	
Tseng 2017	38.4	14.4	33	42.7	19.2	18	4.7%	-4.30 [-14.44, 5.84]	
Xu 2014	27.2	5.4	30	38.3	6.2	30	7.5%	-11.10 [-14.04, -8.16]	•
Xue 2008	56	15	38	62	15	38	6.1%	-6.00 [-12.74, 0.74]	
Total (95% CI)			583			429	100.0%	-6.72 [-10.17, -3.26]	•
Heterogeneity: Tau ² =	38 9510	Chi² = 7		f = 19 (F	≺ 0 00	101) [,] P			
Test for overall effect:				(. 0.00	201711	1470		-10050_0_50_100
restron overall effect.	2 - 0.01	v = 0.	0001)						Favours (VL) Favours (DL)

Fig. 5. Forest plot for the comparison of intubation time between videolaryngoscopy (VL) and direct laryngoscopy (DL). IV, inverse variance.

patients. Even if any, our results are also more likely to underestimate rather than overestimate the effect of VL on the outcomes of NTI. Actually, for patients with extremely limited mouth opening and very tricky oral anatomy abnormalities, fiberoptic intubation still has an irreplaceable role in safe airway management. Recently, several case reports have demonstrated that inserting a fibreoptic bronchoscope through the nasal tube under VL may be more effective in complicated airway situations [45–47].

Our analysis showed that the use of VL shortened the intubation time of NTI, which was uniform in all but one subgroup. Especially, the intubation time was shortened by > 50 s when NTI was performed with VL by inexperienced operators. There are several reasons for this. First, an improved laryngeal visualization with VL allows the operators to more quickly target where the nasal tube is being directed. Second, compared with DL, VL creates a more direct route from the nasopharynx to the trachea [48], which can reduce the distortion of the anterior airway and potentially necessitate less nasal tube manipulation. Last, when using VL, the maneuvers to aid the NTI are not applied as much as DL [21,37,39], reducing the time required for these auxiliary maneuvers.

In this analysis, however, the use of VL with an integrated channel blade did not change the intubation time. In this subgroup, all but one study [36] chose the Pentax-AWS. It is suggested that the thick blade of Pentax-AWS and the bulky channel located at the glottic opening may impede the tip of nasal tube to advance through the level of arytenoid cartilages [49]. This undoubtedly will increase the use of auxiliary measures and worsen intubation outcomes. Similarly, a meta-analysis by Hoshijima et al. [50] comparing Pentax AWS and DL for OTI demonstrates that even with a better glottis view, the Pentax AWS does not improve the success rate and intubation time.

Our subgroup analyses also showed that the operators' experience did not result in significant difference in the overall and first-attempt success rates of NTI between groups. This is not agreement with the findings from previous studies regarding OTI with VL, in which VL is associated with better intubation success and faster intubation time for inexperienced operators, but provides no benefit in either of these outcomes with experienced operators [43]. Still, it was noted that patients who were intubated by inexperienced operators might be void of difficult airways. Thus, it is hard to conclude if success rate will be improved when NTI was performed with VL by inexperienced operators in patients with difficult airways. Postoperative sore throat can delay postoperative recovery and reduce patients' satisfaction. In this analysis, the use of VL reduced the incidence of postoperative moderate and severe sore throat. Both improved laryngeal visualization and decreased use of accessory maneuvers with VL can avoid mucosal trauma of the upper airway. Furthermore, the intubation time was shortened with VL, reducing the contact time of device with the airway tissues. In addition, VL exerts a less pressure on the anterior airway structures [37]. All these may be attributable to a decreased risk of postoperative sore throat with VL.

Our analysis has some limitations. First, the included studies had their own research strategies and different endpoint definitions. This will lead to measurement biases on primary and secondary outcomes in our analysis. Second, only 3 studies with a small sample size included inexperienced operators and all 3 studies were performed in patients with a normal airway. Thus, it is unclear whether the use of VL can benefit inexperienced operators, especially for when NTI is performed in patients with difficult airways. Third, blinding was not adopted in most studies. However, most of important endpoints (success rate and intubation time) are robust and patients undergoing general anesthesia are not aware of which group they are assigned to. Moreover, it is impossible for the operators to be unaware of their grouping during the intubation process. Thus, no blinding may not change the main results of this analysis. Last, risk assessment of bias for the 14 included studies showed that only 4 could be classified as "low risk". Most of them did not provide a clear method of random sequence generation used. The quality of some evidences from the GRADE system was low or moderate due to moderate or high level of heterogeneity. Although subgroup analyses have been performed based on potential clinical factors that may produce heterogeneity, there are still heterogeneities within subgroups by other factors, such as study subjects, NTI procedures, auxiliary maneuvers, etc. Thus, the results of our analysis should be interpreted with caution. Further high-quality studies will be needed to determine the exact role of VL in NTI.

Our analysis concludes that the use of VL cannot improve the overall success rate of NTI in adult patients undergoing general anesthesia, but it provides an improved laryngeal visualization, increases the first-attempt success rate, shortens the intubation time, and reduces the occurrence of postoperative sore throat. Furthermore, VL is particularly beneficial for patients with difficult airways. However, further high-quality studies will still be needed to determine the exact role of VL in NTI, especially for when NTI was performed by inexperienced operators in patients with difficult airways.

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Authors' contributions

Study design/planning: F.S.X., J.J.; Study conduct: F.S.X., J.J., B.L., A.S.W., D.X.M.; Data analysis: J.J.; Writing paper: F.S.X., J.J.; Revising paper: all authors.

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