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Laryngeal Injury and Upper Airway Symptoms after Oral Endotracheal Intubation with Mechanical Ventilation During Critical Care: A Systematic Review

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Abstract

Objective: To systematically review the symptoms and types of laryngeal injuries resulting from endotracheal intubation in mechanically ventilated patients in the intensive care unit (ICU).

Data Sources: PubMed, Embase, CINAHL, and Cochrane Library from database inception to September 2017.

Study Selection: Studies of adult patients who were endotracheally intubated with mechanical ventilation in the ICU and completed post-extubation laryngeal examinations with either direct or indirect visualization.

Data Extraction: Independent, double-data extraction and risk of bias assessment followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Risk of bias assessment followed the Cochrane Collaboration's criteria.

Data Synthesis: Nine studies (7 cohort, 2 cross-sectional) representing 775 patients met eligibility criteria. The mean (standard deviation; 95% confidence interval) duration of intubation was 8.2 (6.0; 7.7–8.7) days. A high prevalence (83%) of laryngeal injury was found. Many of these were mild injuries, although moderate to severe injuries occurred in 13%–31% of patients

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across studies. The most frequently occurring clinical symptoms reported post-extubation were dysphonia (76%), pain (76%), hoarseness (63%), and dysphagia (49%) across studies.

Conclusions: Laryngeal injury from intubation is common in the ICU setting. Guidelines for laryngeal assessment and post-extubation surveillance do not exist. A systematic approach to more robust investigations could increase knowledge of the association between particular injuries and corresponding functional impairments, improving understanding of both time course and prognosis for resolution of injury. Our findings identify targets for future research and highlight the long-known, but understudied, clinical outcomes from endotracheal intubation with mechanical ventilation in ICU.

Keywords

endotracheal intubation; intensive care; larynx; voice; deglutition

INTRODUCTION

Globally, there are 13–20 million critically ill patients intubated in intensive care units (ICU) annually.¹ Similar to many medical treatments, the iatrogenic effects of intubation have potential for acute and chronic symptoms, and both short- and long-term harms requiring further medical care that extends beyond ICU discharge.

Patient complaints frequently include hoarseness, loss of voice, throat clearing, sore throat, and vocal fatigue post-extubation.^{2–4} Laryngeal injuries from intubation during surgery are believed to be confined to minor injuries.^{5–7} By comparison, critically ill patients intubated in ICU generally experience longer intubation resulting in laryngeal injuries that are more prevalent, potentially more severe, frequently overlooked, and often result in voice dysfunction (i.e., dysphonia) and/or swallowing dysfunction (i.e., dysphagia).^{8–15} Despite potentially serious injury, laryngeal evaluations are often delayed, occurring only if symptoms persist 1 week,^{16–18} sometimes as long as 1–3 months.^{19–21} This delay results, in part, from the absence of guidelines establishing standard practices for post-extubation assessment. Patients with these injuries, therefore, experience increased risk for both medical sequelae (e.g., post-intubation stenosis with delayed presentation^{22,23}) and prolonged functional handicap (e.g., chronic dysphonia,²⁴ chronic dysphagia²⁵).

The purposes of this systematic review are to: (1) evaluate the nature and severity of laryngeal injury after endotracheal intubation in ICU patients and (2) identify areas of inquiry for mitigation strategies and future intervention. We focused on prospective studies with post-extubation laryngoscopic assessment of laryngeal injury.

MATERIALS AND METHODS

Literature Search

A clinical informationist (C.P.) developed and executed the search strategy in the electronic bibliographic databases PubMed, Embase, CINAHL, and Cochrane Library from inception to April 2016, with two updates in March and September 2017 (eAppendix 1). The searches were limited to the English language and created using controlled vocabulary, such as

Medical Subject Headings, Emtree terms, and CINAHL headings, in combination with keywords for the concepts of intubation, visualization techniques, and injury where appropriate. Efforts were made to exclude pediatric-focused research by excluding specific pediatric-related terms from the titles only and a filter was applied to exclude animal-only research. A research filter was applied based on the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE, sensitivity and precision-maximizing version²⁶ with additions for other types of clinical studies.

Selection Criteria

Included studies assessed adult (≥ 18 years old) patients employing either direct (e.g., line of sight) or indirect (e.g., mirror, flexible endoscopy) visualization of the larynx and reported sufficient laryngeal injury data (e.g., frequencies, nature). Exclusion criteria included: (1) non-English language, (2) case studies and retrospective study designs, (3) patients <18 years old, (4) pre-existing laryngeal injury/disease, (5) patients with surgical interventions that have inherent risk of recurrent laryngeal nerve injury (e.g., neck surgeries, thoracic surgeries), (6) gray literature,²⁷ and (7) non-focal, neurologically impaired patient populations in whom neurologic injury may have made assignment of post-intubation dysphonia and dysphagia to laryngeal injury difficult (e.g., stroke).

Data Extraction/Risk of Bias Assessment

Search strategy results were imported to an online platform (Covidence: www.covidence.org, Melbourne, Australia) for independent review. Two authors (B.B., E.J.) independently screened articles by title, abstract, and full text. Disagreements were refereed by a third author (M.B.B.). Six authors (L.M.A., M.B.B., G.C., E.J., M.J.L., V.P.) completed independent, double-data extraction and risk of bias assessment for accepted articles. Risk of bias assessment followed the Cochrane Collaboration's criteria,²⁸ with each risk parameter judged as *low*-, *unknown*-, or *high-risk*. Disagreements were settled by consensus. Authors were contacted to provide missing information as needed. A meta-analysis was judged to be inappropriate due to substantial heterogeneity of study methods for the accepted articles.^{29,30}

A 4-point grading rubric was used to classify laryngeal injuries, guided by previous publications.^{14,31,32} The rubric was developed via consensus by 5 authors: 3 laryngologists (L.M.A., S.R.B., A.T.H.), an emergency physician (M.J.L.), and a speech-language pathologist (M.B.B.). Prevalence was calculated as the total number of patients observed with each injury or symptom divided by the total number of patients analyzed across studies analyzing these outcomes, omitting studies that did not analyze a particular outcome and patients that did not meet criteria. All outcomes were assessed post-extubation. Across studies, terminology describing voice quality was inconsistent. For purposes of prevalence, we report *dysphonia* and *hoarseness* separately using the terms relevant to each article, but we group these symptoms of laryngeal injury as “voice dysfunction” in our discussion.

RESULTS

Search Results

There were 4530 publications identified from the 4 databases and other sources as part of a larger systematic review on laryngeal injury. Screening by title and abstract resulted in 126 full-text reviews. Of these, 9 studies from 5 countries were accepted with the focus on laryngeal injury from oral endotracheal intubation in mechanically ventilated ICU patients (Figure 1). These 9 studies comprised 7 cohort studies (663 patients)^{33–39} and 2 cross-sectional studies (112 patients),^{40,41} totaling 775 patients (Table 1).

Clinical Presentation

Eight studies had laryngeal injury after oral intubation as the primary objective,^{34–37,40} whereas one study had frequency of dysphagia post-extubation as its primary objective.⁴¹ Patients' mean (SD; 95% confidence interval [95%CI]) age was 53.4 (7.0; 52.8–54.0) years across the 8 (89%) studies reporting age.^{33–38,40,41} Diagnoses included cardiac,^{38,41} medical,^{33,34,36,38–41} mixed medical-surgical,⁴⁰ oncological,^{38,41} surgical,^{39–41} non-neurological trauma,⁴¹ and unclear/unstated diagnoses.^{35,37,41} Whereas 6 (67%) studies reported endotracheal tube (ETT) size,^{33–36,40,41} only 1 (11%) study distinguished ETT size between the sexes, with most females receiving a 7.0 mm inner diameter (range: 6.5–7.0 mm) compared with most males receiving an 8.0 mm inner diameter (range: 7.5–8 mm).³⁴ Two (22%) studies reported ETT manufacturer.^{33,36} Across 7 (78%) studies, the calculated mean (SD; 95%CI) duration of intubation was 8.2 (6.0; 7.7–8.7) days.^{33,34,36–38,40,41} One (11%) study reported median duration of 4 days, but without any measure of variability³⁵ and one study reported 3 groups with ranges of intubation duration without summary statistics³⁹ (Table 1).

Assessment and Diagnosis

Direct visualization via laryngoscope^{38,39} was used in 2 (22%) studies. Indirect visualization as a laryngeal mirror,³⁹ rigid endoscope³⁵ flexible nasoendoscopy,^{34,36,37,39–41} and flexible bronchoscopy was used in 8 (89%) studies (Table 1).³³ Otolaryngologist interpretation of findings was confirmed in 7 (78%) studies.^{34–36,38–41} After extubation, assessment was completed within 6 hours,^{36–38} within 24 hours,^{34,35,39,40} within 72 hours,⁴¹ and at 2 weeks post-extubation.³³

Laryngeal Injury – Signs

The prevalence of post-extubation laryngeal injury across all 4 severity grades is summarized in Table 2. Injuries were inconsistently reported across studies, as seen in the raw data presented in Supplementary Table 1. No laryngeal injury was observed in 17% of patients across the 7 (78%) studies reporting this outcome.^{33–36,38,40,41}

A high prevalence of minor injury and lower prevalence of more severe injury occurred. Many injuries were self-limiting, Grade 1 injuries. Overall, erythema was most frequent, with a prevalence of 82% (252/307 patients),^{35,37,40,41} followed closely by edema with a prevalence of 70% (583/828 patients).^{34–37,40,41} The interarytenoid space, the area through which the ETT passes and remains present *in situ*, had a 95% (106/112 patients) - 96%

(108/112 patients) prevalence of edema and erythema, respectively.^{40,41} Ulcerations, with a 31% (174/524 patients) prevalence, were the most frequently reported moderate (i.e., Grade 2) injury.^{33,34,36–38,40,41} Intubation granulomas/granulation tissue, the only other injury type reported, had a 27% (86/318 patients) prevalence.^{33,35,36,40,41} Vocal fold immobility was the most frequently reported and most common of the severe (i.e., Grade 3) injuries, with a 21% (105/508 patients) prevalence.^{33,34,36,37,40,41} There was a 6% (12/200 patients) prevalence of glottic stenosis³⁹ and 13% (15/112 patients) prevalence of subglottic stenosis.^{40,41} A prevalence of 5% or less for both subglottic mucosa edema³³ and arytenoid(s) dislocation were reported.³⁴

Laryngeal injury prevalence may change with longer durations of intubation. We further analyzed injury findings based on 3 average durations of intubation identified by data generated from this review: (1) <5 days,^{34,35,37} (2) 5–10 days,^{33,36,40,41} and (3) >10 days^{38,39} (Table 2; Supplementary Table 2). There was increased prevalence and increased severity of injury observed in patients intubated 5–10 days compared with those intubated <5 days. Specifically, there was a 37% and 38% increased prevalence of injury in Grades 1 and 2, respectively. Grade 3 had a 125% increase in prevalence between the same two periods. Two studies with durations >10 days^{38,39} reported 3 unique injury types and are unable to be summarized.

Delays in post-extubation assessment may also contribute to variability in laryngeal injury prevalence. We identified 4 windows of assessment across studies: (1) 6 hours,^{36–38} (2) 24 hours,^{34,35,39,40} (3) 72 hours,⁴¹ and (4) 2 weeks³³ (Table 3; Supplementary Table 3). Compared with overall prevalence and considering variability in the reporting of data, timing of assessment resulted in little change in laryngeal injury prevalence within grade. This finding suggests that the injuries observed vary little within 3 days post-extubation. One study completed assessments 2-weeks post-extubation and demonstrated 84% prevalence of injury in patients who were intubated a mean of 6.2 days (range: 2–14 days), similar to each of the earlier time points.³³

Laryngeal Injury – Symptoms

Symptoms of laryngeal injury identified after extubation were common (Table 4, Supplementary Tables 1–3), with voice dysfunction (i.e., dysphonia), dysphagia, and pain being the most frequent. Both voice dysfunction (197/260 patients)^{33,34,37} and pain (184/241 patients)^{34,37} had a 76% prevalence. Dysphagia had a prevalence of 49% (157/319 patients).^{33,34,37,41} Laryngeal dyspnea and stridor were least frequent with a prevalence of 23% (48/209 patients)³⁴ and 7% (11/155 patients),^{33,36} respectively.

Methodological quality

Methodological quality is summarized as risk of bias (Supplementary Table 4). All studies provided adequate rationale with clear objectives. Most studies included sufficient subject selection criteria (8/9: 89%) and minimized reporting bias (7/9: 78%). Weaknesses included insufficient information for study replication (3/9: 33%) and appropriate controls for sampling (3/9: 67%), in addition to detection (5/9: 56%), attrition (3/9: 33%), and avoidance (3/9: 33%) biases.

DISCUSSION

This systematic review demonstrates that laryngeal injury is a frequent consequence of intubation and is exacerbated with increased duration, despite considerable variability of study methods, patient populations, and outcomes reporting among the accepted articles. Only a small fraction of patients will emerge from intubation injury-free. Although less severe injuries are more common, Grades 2 and Grade 3 injuries occur with a remarkable frequency of 31% and 13%, respectively. On average, more than twice as many patients will sustain moderate or severe injuries that impact airway, voice, and/or swallowing than will have no injury. Assessments completed within 72 hours of extubation appear to have little effect on outcomes, suggesting that resolution of even less severe injuries extends beyond 3 days.

A necessary first step in managing laryngeal injuries is in determining their presence and severity to facilitate appropriate and individualized management. Management could be coordinated by the ICU team and involve a variety of other disciplines. Treatment might include prescribing glucocorticoids⁴² and anti-reflux medications,⁴³ procedures such as stenosis dilation⁴⁴ and vocal fold medialization by anesthesiology and otolaryngology,^{45,46} therapy by speech-language pathology for voice^{47,48} and swallowing,^{49,50} and other complementary therapies for improving patient function and quality of life.^{51,52}

One finding worth highlighting is that approximately half of all patients experienced dysphagia after extubation and that 1 in 5 patients had vocal fold immobility. It is well-recognized that intubation duration more than 2 days places patients at high risk for both acute and chronic dysphagia^{25,34,41,53,54} that may result in aspiration, possibly leading to aspiration pneumonia or pneumonitis.^{55–59} There are several potential contributing etiologies that might increase aspiration risk in this population, including compromised cognition,⁶⁰ sensory impairment,^{17,61} reduced laryngeal adductor reflex,^{62,63} and reduced strength in muscles involved in swallowing.⁶⁴ Emerging evidence is linking morphological laryngeal injury to aspiration,⁴¹ with an aspiration prevalence of 38%–44% during oral consumption in patients with unilateral vocal fold immobility.^{65,66} Moreover, the risk of pneumonia doubles in patients with unilateral vocal fold paralysis.⁶⁷ Early recognition of vocal fold paralysis may mitigate risks for pneumonia or pneumonitis with a timely vocal fold medialization procedure, for example.^{45,68} Additionally, comprehensive investigation may identify other findings associated with symptoms such as dysphagia, increasing the chances for earlier risk stratification and appropriate management.

Similar ETT inner diameters (i.e., ETT size) were used across studies, but not all studies reported size and/or manufacturer. This presents 2 issues for attribution of laryngeal injury to ETT size. First, there is no standard for assigning ETT size, but size: (1) reflects *inner* lumen diameter, (2) has no association with *outer* diameter measurement, (3) is similar across manufacturers, and (4) may be considered with therapeutic value (e.g., air volume, pressure, oxygenation)⁶⁹ and instruments use via the ETT (e.g., bronchoscope). The ETT outer diameter: (1) contacts anatomical structures, (2) is associated with occupying space within the larynx/trachea, and (3) is, at least partly, responsible for laryngeal injuries and their symptoms. There is minor (0.5 mm) variability in outer diameter between manufacturers

(i.e., Mallinckrodt,TM Portex, Smiths Medical, Unoflex), each using similar materials. However, MallinckrodtTM currently produces 2 ETTs (i.e., TaperGuardTM Evac, SealGuardTM Evac) that have outer diameters approximately 1 mm larger than other ETTs across sizes and manufacturers.⁷⁰ No conclusions can be made concerning laryngeal injury, ETT size, and/or materials/manufacturing due to the large variability within and between studies. Future studies should report these characteristics to address this concern.

Our findings encourage more routine, timely and consistent use of a laryngeal assessment and dysphagia screening post-extubation, especially in the wake of payment reform and a national focus on patient safety. Hospital-acquired conditions represent a multi-dimensional risk with both cost and exposure dimensions. Aspiration pneumonia and pneumonitis are potentially preventable hospital-acquired conditions that require significant resources, including primary care and specialty physicians,⁷¹ with prevalence as high as 14% in post-extubated ICU patient populations.⁵⁴ Hospital-acquired pneumonia can increase length of stay in the ICU by more than 8 days.⁷² The exposure and costs (financially and in occupancy) associated with such preventable harm represent a strong market, fiscal, and moral case for prevention, or at least early screening, assessment, and treatment. A screening for laryngeal injury is, perhaps, more complicated. Moderate to severe laryngeal injuries may result in more than 2 days and \$6000 in costs with readmission for repair.⁷³ Despite frequent complaints of dysphonia and pain after extubation, identifying which patients are at high risk for moderate to severe laryngeal injury and the best time for assessment is less clear. Moreover, there are no screening tools or published guidelines offering direction on this issue, a large gap in critical care patient populations and their long-term outcomes.⁷⁴

Regardless of which symptom(s) are present, “wait and see” remains the most common approach to identification and management of these injuries,^{17–19} despite nearly 40 years of evidence and recommendations for more timely evaluations.^{15,34,41,75–77} Remarkably, there are no published guidelines for post-extubation assessment of laryngeal injury or dysphagia. The only published guideline concerning post-extubation assessment specifically addresses one symptom—hoarseness.²¹ It states that the laryngoscopic evaluation of patients with both hoarseness and a history of intubation “*may [be completed] at any time*” (p. S14), but “*clinicians should perform laryngoscopy...[with unresolved hoarseness] within 4 weeks or irrespective of duration if a serious underlying cause is suspected*” (p. S15).²¹ Much is left to interpretation from these recommendations because they are made for hoarseness of any etiology, written for ambulatory outpatients instead of at-risk ICU patients, and are not specific to intubation injury. We emphasize that hoarseness may be only one of many symptoms of laryngeal injury. Among the most prevalent symptoms is pain, which may be indicative of serious laryngeal injury. Dysphagia is also highly prevalent with potential for serious consequences soon after extubation.^{8,33,34,36,37,41} Future studies and screening guidelines should consider these other symptoms.

A high risk of bias was observed in >50% of the rating parameters. These results appear to reflect difficulties controlling experimenter biases, specifically: 1) detection bias, 2) attrition bias, avoidance bias, and reporting bias. The 2 cross-sectional studies (both from one lab) included in this review represent a low risk of bias across all parameters.^{40,41} The 7 cohort studies all introduced unknown or high risks of bias.^{33–39} The introduction of these biases

may reflect the dynamic, frequently unpredictable ICU setting combined with data collection across multiple time points. Extra care must be taken to reduce biases through methodological controls with these types of study designs. Clarity in writing for study replication is also concerning. Editorial review, and publication guidelines for clinical studies should strive for improvements in writing clarity and reduction of study biases.

Limitations

There are three potential limitations noted. First, our search was limited to the English language. We acknowledge that studies from other languages may provide results that are contrary to our findings and conclusions, but we believe this to be unlikely with the robust agreement between studies accepted for review. Second, our data were limited to ICU. Intubation is also performed routinely in emergency medicine and surgical settings. Although emergency medicine settings were not specifically excluded, we are not aware of any studies using laryngoscopy for post-extubation evaluation of these patients. Studies about intubation trauma and laryngeal injury in surgical settings offer a different patient population and considerable differences in intubation duration and were not the focus of this review. Third, after study acceptance, we observed a 19 year gap between three studies published in/before 1987^{33,38,39} and the next study published in 2006.³⁵ Although clinical practice and improved construction of endotracheal tubes during this period may have impacted intubation technique and laryngeal injury, prevalence of injury between these two time periods were similar. Despite these limitations, this systematic review makes a novel contribution toward ongoing research in the area of post-extubation laryngeal injury, and is a call to action for increased awareness of this phenomenon.

CONCLUSIONS

Considering the prevalence of laryngeal injury, dysphonia, and dysphagia and their associated risks for more serious medical complications, practice guidelines are needed for post-extubation screening/assessment in the ICU. Evidence strongly indicates that intubation duration is associated with prevalence and severity of laryngeal injuries. Injuries are frequent and range widely in severity post-extubation. Although mild injuries are more prevalent, moderate to severe injuries occur frequently and require timely clinical attention. Presently, no clinical standards of practice address these potentially serious injuries and there is little evidence in this review to offer direction. Findings suggest new areas for scientific inquiry and highlight long-known and under-identified iatrogenic injury from one of the most common procedures in medicine—endotracheal intubation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

LMA	laryngeal mask airway
RLN	recurrent laryngeal nerve

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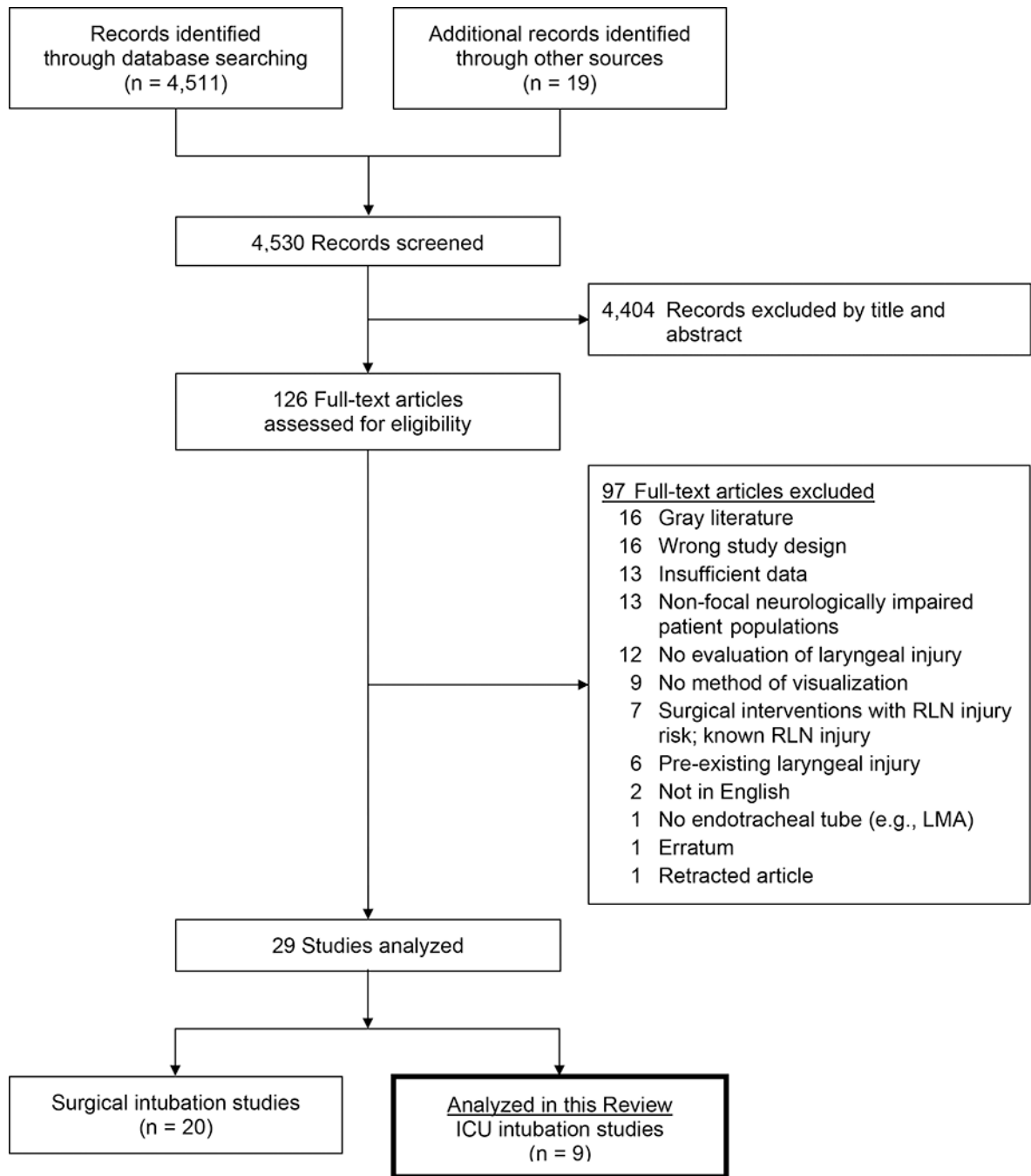


Figure 1.
Study selection flowchart.

Table 1.

Methods of included studies.

Author/Year	Country	Study Design	Number of patients analyzed ^a	Mean Patient Age (years)	ETT size	Method of Visualization	Duration of Intubation (mean days)
Colton House 2011 ⁴⁰	United States	Cross-sectional	61	56	6.0 – 8.0	Indirect	9
Kastonos 1983 ³³	Spain	Cohort	19	59	7.0 – 9.0	Indirect	6.2
Megarbane 2010 ³⁴	France	Cohort	209	40	6.5 – 8.0	Indirect	1.2
Rangachari 2006 ³⁵	India	Cohort	51	50	7.0 – 8.5	Indirect	4 ^b
Scheel 2016 ⁴¹	United States	Cross-sectional	51	58	7, 8	Indirect	9.4
Tadié 2010 ³⁶	France	Cohort	136	62	6.5 – 8.0	Indirect	6.9
Van der Meer 2010 ³⁷	South Africa	Cohort	32	49	nr	Indirect	4.5
Volpi 1987 ³⁸	United States	Cohort	16	53	nr	Direct	20.3
Whited 1983 ³⁹	United States	Cohort	200	nr	nr	Direct, Indirect	nr

Abbreviations: ETT, endotracheal tube; nr, not reported

^aReflects the number of patients meeting inclusion/exclusion criteria, and therefore analyzed and reported in this systematic review.^bDuration in median days.

Table 2.

Prevalence of laryngeal injury grade by average intubation duration.

Injury Grade	All Patients (N ^a = 775) ³³⁻⁴¹ n ^b (%)	Average Intubation Duration			
		<5 Days (N ^a = 342) ^{34,35,37,39} n ^b (%)	5-10 Days (N ^a = 367) ^{33,36,39-41} n ^b (%)	>10 Days (N ^a = 66) ^{38,39} n ^b (%)	
0 No injury present	94/543 (17) ^{33-36,38,40,41}	52/260 (20) ^{34,35}	42/267 (16) ^{33,36,40,41}	0/16 (0) ³⁸	
1 Self-limited, soft tissue (e.g., edema, erythema, hyperplasia, ecchymosis)	835/1135 (74) ^{34-37,40,41}	265/439 (60) ^{34,35,37}	570/696 (82) ^{36,40,41}	-	
2 Hematoma, ulceration, fibrin without glottic narrowing, mass lesion, granulation	260/842 (31) ^{33-38,40,41}	70/292 (24) ^{34,35,37}	174/534 (33) ^{33,36,40,41}	16/16 (100) ³⁸	
3 Stenosis, stenosis with glottic narrowing, hypomobility/immobility of the vocal folds and/or arytenoids complex	137/1048 (13) ^{33,33,34,36,37,39-41}	39/500 (8) ^{34,37,39}	90/498 (18) ^{33,36,39-41}	7/50 (14) ³⁹	

^aN: The total number of subjects across studies.

^bn: The total number of occurrences observed with each injury and within each injury grade divided by the number of possible occurrences. The number of possible occurrences was calculated as the product number of patients evaluated and the number of types of injuries evaluated for each study. Note that each study may not report all injury types. For example, the prevalence of a Grade 1 injury considers all possible injury types (e.g., edema, erythema, hyperplasia, ecchymosis). In the "All Patients" column, the studies reporting each injury type observed 835 occurrences of Grade 1 injury types across 1135 possibilities that they could have occurred, or 74% prevalence of Grade 1 injury.

Table 3.

Prevalence of laryngeal injury grade by timing of assessment post-extubation.

Injury Grade	Timing of Assessment Post-extubation			
	6 Hours (N ^a = 184) ³⁶⁻³⁸ n ^b (%)	24 Hours (N ^a = 521) ^{34,35,39,40} n ^b (%)	72 Hours (N ^a = 51) ⁴¹ n ^b (%)	2 Weeks (N ^a = 19) ³³ n ^b (%)
0 No injury present	36/152 (24) ^{36,38}	52/321 (16) ^{34,35,40}	3/51 (6) ⁴¹	3/19 (16) ³³
1 Self-limited, soft tissue (e.g., edema, erythema, hyperplasia, ecchymosis)	167/264 (63) ^{36,37}	441/616 (72) ^{34,35,40}	227/255 (89) ⁴¹	-
2 Hematoma, ulceration, fibrin without glottic narrowing, mass lesion, granulation	77/320 (24) ³⁶⁻³⁸	122/382 (32) ^{34,35,40}	46/102 (45) ⁴¹	15/38 (39) ³³
3 Stenosis, stenosis with glottic narrowing, hypomobility/immobility of the vocal folds and/or arytenoids complex)	30/168 (18) ^{36,37}	79/740 (11) ^{34,39,40}	26/102 (25) ⁴¹	2/38 (5) ³³

^aN: The total number of subjects across studies.

^bn: The total number of occurrences observed with each injury and within each injury grade divided by the number of possible occurrences. The number of possible occurrences was calculated as the product number of patients evaluated and the number of types of injuries evaluated for each study. Note that each study may not report all injury types. For example, the prevalence of a Grade 1 injury considers all possible injury types (e.g., edema, erythema, hyperplasia, ecchymosis). In the "All Patients" column, the studies reporting each injury type observed 835 occurrences of Grade 1 injury types across 1135 possibilities that they could have occurred, or 74% prevalence of Grade 1 injury.

Table 4.

Prevalence of symptoms reported post-extubation.

Symptoms	Patients, n ^a (%)
Dysphonia (including hoarseness)	197/260 (76) ^{33,34,37}
Pain	184/241 (76) ^{34,37}
Dysphagia	157/319 (49) ^{33,34,37,41}
Laryngeal dyspnea	48/209 (23) ³⁴
Stridor	11/155 (7) ^{33,36}
Overall	597/1184 (50)^{33,34,36,37,41}

^aPrevalence is reported as the total number observed divided by the total number of patients analyzed for each sign/symptom across studies.