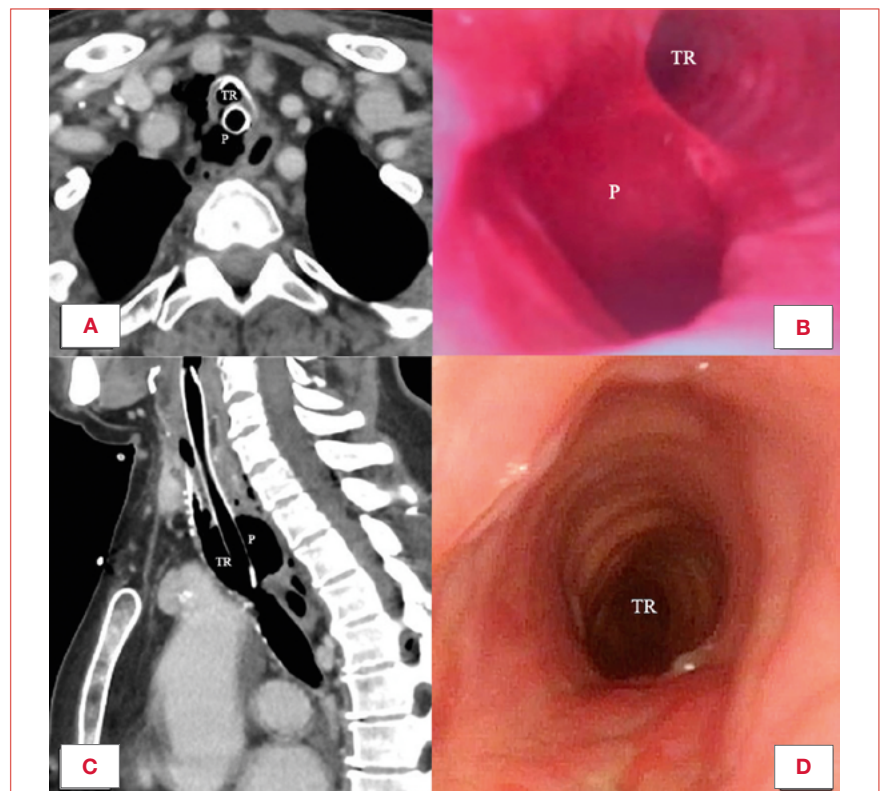


Traumatic lesions of the cervical trachea: conservative or surgical treatment? A systematic review

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Cover figure. Axial (A) and sagittal (C) computed tomography images of a 75-year-old woman showing traumatic injury of the pars membranacea of the cervical trachea following orotracheal intubation for elective gynaecologic surgery. Endoscopic view of the perforation (B). Patient underwent primary emergent surgical repair by circumferential tracheal opening in between the sixth and seventh tracheal rings, trans-tracheal closure of the posterior tear by a double-layered vertical suture, followed by tracheo-tracheal anastomosis and immediate extubation without tracheostomy. Postoperative result at 30 days after surgery (D). TR: tracheal lumen; P: perforation.

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Summary

Traumatic lesions of the cervical trachea are rare but critical conditions potentially resulting either from blunt, penetrating, or iatrogenic injuries. These traumatic events pose challenges in airway management due to their life-threatening nature and need for rapid decision-making. Choice of treatment – conservative *versus* surgical – depends on injury dynamics, features of the traumatic lesion, and patient-related factors. This systematic review, conducted following PRISMA guidelines on 211 studies involving 509 patients, evaluates management strategies, focusing on indications for conservative *versus* surgical approaches and differences between adults and children. Surgical treatment was preferred for penetrating and severe blunt traumas, while conservative management, such as distal intubation, was used for small, superficial lesions. Surgical indications included tears > 20 mm, significant subcutaneous emphysema, and ventilation failure. Treatment should be

individualised based on lesion characteristics and patient factors. Surgery remains essential for severe cases, while conservative approaches are viable in selected scenarios, especially in children.

Keywords: cervical tracheal trauma, blunt tracheal trauma, penetrating tracheal trauma, treatment

Introduction

Airway injuries involving the cervical trachea represent a rare but potentially life-threatening occurrence, which may result from either external or endoluminal traumas. The first scenario can be due to penetrating or blunt trauma, while the latter can be the consequence of intubation manoeuvres, long-lasting invasive ventilation, surgical interventions, and - especially in the pediatric population - foreign body ingestion¹. The incidence of tracheal injuries ranges between 0.5 and 2% after blunt trauma², growing to 3-6% in penetrating injuries³.

The management and treatment of these patients is challenging both for the specific anatomical conditions, potentially altered by the trauma itself, and for the quick decision-making process required by such a situation. Clinical presentation and symptoms may vary between spontaneous breath and severe respiratory distress, with patient's symptoms depending not only on the extent of injury, but also on the presence of concomitant lesions to other organs, such as the oesophagus, cervical spine, and major neck and/or thoracic vessels⁴. The first step of the management is always to secure a safe airway (A-management) to allow ventilation without further compromising the laryngotracheal framework. The decision between conservative and surgical treatments should be then discussed considering the patient's clinical conditions, extent of tracheal damage, and involvement of other structures. Given the challenges in documenting tracheal injuries, stemming from the intrinsic rarity of the condition and its elevated mortality, the literature is lacking specific guidelines and clear indications about whether to proceed with conservative or surgical treatment, and under which circumstances.

Our work finds its place within this context, with the goal of performing a systematic review of the literature on management of traumatic lesions of the cervical trachea, specifically addressing airway management, indications for treatment, and outcomes, aiming to fill the gap in knowledge.

Materials and methods

Objectives

The primary objective was to define the management and treatment of cervical tracheal trauma, with particular focus on the indications of conservative *versus* surgical approach-

es. A further objective was to define potential differences in treatment strategies between the adult and paediatric populations (defined as younger than 18 years).

Search strategy

This systematic review follows the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) recommendations. The query “(cervical OR neck) AND trachea* AND (rupture OR laceration OR injury OR trauma OR transection)” was used to make a comprehensive search on PubMed, Scopus, and Web of Science.

Selection criteria

We considered only papers published from January 1st, 2000 to August 26th, 2024, sorted by English language. Book chapters, non-human or autoptical studies, and purely thoracic tracheal traumas were excluded, as well as articles missing sufficient information on both traumatic event and management. All titles and abstracts were screened and full text obtained for selected publications.

Data extraction

Data entry and analysis were carried out and a dedicated database was built. For each study demographic features (age, gender), dynamics of trauma (blunt, penetrating, iatrogenic, spontaneous, foreign body, or resulting from childbirth), clinical presentation (respiratory distress), tracheal wound features (location, size), management (conservative, surgical), and related outcomes were collected.

Lesion size was reported according to its cranio-caudal extension. Conservative management was defined as clinical observation, intubation, and tracheal stent placement, while surgical treatment included tracheotomy, cervical drainage, and airway repair.

Results

The initial search returned 4,783 records. After identification and screening, a total of 211 full text articles, both case series (Tab. I) and case reports⁵⁻¹⁷⁶ involving 509 patients, were included in the present review (Fig. 1).

Demographics

The main features of the population are listed in Table II, the majority consisting of adult males, with a mean age of 31 years.

Table I. Case series (n = 40) included in the present systematic review (n = 338 patients).

	Authors	Population	No. of cases	Aetiology	Management
1	Liu et al. ¹⁹⁵	Adults	5	Ventilation	Surgical
2	Da Silva Costa et al. ¹⁸⁶	Adults	2	Intubation	Surgical
3	Cassada et al. ¹⁹⁶	Adults	9	Penetrating (7), blunt (2)	Surgical (8), death (1)
4	Almasi et al. ¹⁹⁷	Adults and children	2	Blunt	Surgical
5	Ehab Hussein et al. ³⁸	Adults	4	Intubation	Surgical
6	Evermann et al. ¹⁹⁸	Adults and children	26	Intubation (19), foreign body (7)	Surgical
7	Dong Ye et al. ¹⁹⁹	Adults	17	Blunt	Surgical
8	Wu et al. ²⁰⁰	Adults and children	7	Blunt	Surgical
9	Cunningham et al. ²⁰¹	Children	2	Intubation	Conservative
10	Han et al. ¹⁸⁵	Adults	2	Surgery	Conservative
11	Elbadan et al. ²⁰²	Adults	23	Blunt	Surgical
12	Bin Pervez et al. ²⁰³	Adults	12	Penetrating (3), blunt (3), intubation (6)	Surgical
13	Herrmann et al. ¹⁹¹	Adults	50	Surgery	Surgical
14	Mubarak et al. ²⁰⁴	Adults	50	Blunt (35), penetrating (15)	Surgical
15	Frost et al. ²⁰⁵	Adults	2	Intubation, surgery	Conservative
16	Bowley et al. ¹⁸⁸	Adults and children	2	Blunt	Surgical
17	Yalçın et al. ²⁰⁶	Children	6	Foreign body (4), surgery (2)	Conservative (1), surgical (5)
18	Duval et al. ¹⁸¹	Children	5	Blunt	Conservative
19	Chandra et al. ¹⁹²	Adults and children	10	Foreign body (4), blunt (3), surgery (2), penetrating (1)	Surgical
20	Li et al. ²⁰⁷	Children	6	Penetrating	Surgical
21	Carbognani et al. ²⁰⁸	Adults	6	Intubation	Conservative (2), surgical (4)
22	Hsu et al. ²⁰⁹	Children	8	Blunt (2), intubation (4), surgery (1), ventilation (1)	Conservative (4), surgical (4)
23	Guo et al. ²¹⁰	Adults	2	Foreign body	Conservative
24	Corsten et al. ²¹¹	Children	2	Blunt	Surgical
25	Lyons et al. ¹⁸⁹	Adults and children	22	Penetrating	Conservative (1), surgical (21)
26	Aerni et al. ²¹²	Adults	2	Surgery	Surgical
27	Kaintura et al. ¹⁹³	Adults	5	Blunt	Surgical
28	Łochowski et al. ²¹³	Adults	6	Penetrating	Surgical
29	Janni et al. ¹⁸⁷	Adults	3	Intubation	Surgical
30	Mazita et al. ²¹⁴	Adults	2	Blunt	Surgical
31	Gómez-Caro Andrés et al. ²¹⁵	Adults and children	9	Intubation	Conservative (8), surgical (1)
32	Mahieu et al. ²¹⁶	Children	4	Intubation (2), Birth (2)	Conservative (1), surgical (3)
33	Pan et al. ²¹⁷	Adults and children	2	Penetrating	Surgical
34	Sippel et al. ¹⁸²	Adults	2	Intubation	Conservative
35	Atalay et al. ²¹⁸	Adults	2	Intubation	Conservative (1), surgical (1)
36	Seidl et al. ²¹⁹	Children	2	Foreign body	Surgical
37	Wood et al. ¹⁸³	Children	7	Blunt (1), intubation (5), dilatation (1)	Conservative (6), surgical (1)
38	Leoncini et al. ¹⁹⁰	Adults	7	Penetrating (2), blunt (2), intubation (3)	Conservative (5), surgical (2)
39	Borowski et al. ²²⁰	Adults	2	Blunt	Surgical
40	Huang et al. ¹⁹⁴	Adults	2	Penetrating	Conservative

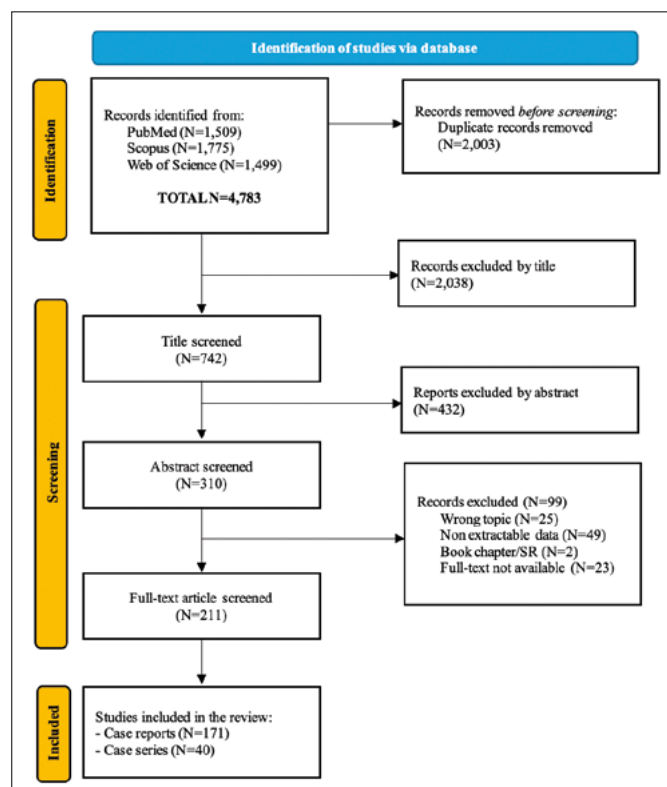


Figure 1. Flow chart according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) recommendations.

Aetiology

The majority of traumas were due to blunt ($n = 220$, 43.2%) and penetrating ($n = 97$, 19.1%) events. Iatrogenic and other types of lesions were reported with lesser incidence. Details are outlined in Table III.

Respiratory distress and first management

At the onset, signs and symptoms of respiratory distress were documented in 153 patients (30.1%). In addition, 83 patients (16.3%) were reported to have airway patency al-

ready secured by tracheotomy or intubation at the time of diagnosis. In case of respiratory distress after the traumatic event, the majority of patients were managed directly in the hospital where they were subsequently treated ($n = 91$, 60%). In other, usually more severe cases, patients were initially managed in field ($n = 28$, 18%) or local hospitals ($n = 23$, 15%) before being transferred to the referral centre. In a small percentage of cases, the airway was not managed as an emergency, but restored along with trauma treatment ($n = 5$, 3.3%), while in a few cases the patient was already intubated ($n = 3$, 1.9%) or on extracorporeal membrane oxygenation ($n = 1$, 0.7%). Airway management in case of respiratory distress is outlined in Table IV.

Management

The data compares conservative, surgical, and tracheotomy approaches across the paediatric and adult populations. In the paediatric group ($n = 105$), conservative methods were described in 34 cases (32.3%), surgical interventions in 64 (61%), and tracheotomy alone in 7 (6.7%). Among the adult population ($n = 378$), conservative management accounted for 47 cases (12.4%), while surgical approaches were 315 (83.3%), and tracheotomy alone was performed in 15 cases (3.9%). Additionally, there were 26 surgical cases in which patient's age was not specified. One patient died shortly after the diagnosis.

Among 81 patients treated conservatively, 36 (44.4%) underwent exclusive clinical monitoring ($n = 23$, 48.9% adults and $n = 13$, 38.2% children), while 27 (33.3%) were intubated ($n = 9$, 19.1% adults and $n = 18$, 52.9% children). In the adult series, 6 patients (7.4%) underwent tracheal stent placement only. These data were not available in 12 cases. In the conservatively treated group, the mean lesion length was 18.1 mm, while among the patients treated with exclusive clinical monitoring the average lesion size was 15 mm in both populations. Intubated children presented lesions with an average size of 13.6 mm, while in adults the average lesion size was 25.2 mm.

Table II. Demographic features of the entire study population, including case series and case reports ($n = 509$).

	Adults	Children	NA	Total
Males	233	61	4	298 (58.6%)
Females	92	44	22	158 (31%)
NA	53	-	-	53 (10.4%)
Total	378 (74.1%)	105 (20.8%)	26 (5.1%)	509
Age, yrs, mean (range)	40.9 (18-92)	8.3 (0-17)	65.7	31

NA: not available.

Table III. Aetiology of tracheal injuries (n = 509).

Etiology			Adults (n = 378)	Children (n = 105)	NA (n = 26)
Blunt trauma	194	38.1%	143 (37.9%)	51 (48.6%)	-
Penetrating trauma	98	19.3%	85 (22.4%)	13 (12.4%)	-
Iatrogenic trauma: surgery	82	16.1%	77 (20.4%)	5 (4.8%)	-
Iatrogenic trauma: intubation	80	15.7%	45 (11.9%)	16 (15.2%)	19 (73.1%)
Iatrogenic trauma: ventilation	18	3.5%	16 (4.2%)	2 (1.9%)	-
Foreign body	16	3.1%	5 (1.3%)	4 (3.8%)	7 (26.9%)
Iatrogenic trauma: dilatation	11	2.2%	3 (0.8%)	8 (7.6%)	-
Spontaneous	8	1.6%	4 (1.1%)	4 (3.8%)	-
Childbirth	2	0.4%	-	2 (1.9%)	-

NA: not available.

Table IV. Airway management.

	Field (n = 28)	Local hospital (n = 23)	Referral centre (n = 91)	Total (n = 142)
OT-NT intubation	16 (57.1%)	14 (60.9%)	58 (63.7%)	88 (62%)
Tracheostomy	8 (28.6%)	8 (34.8%)	24 (26.4%)	40 (28.2%)
Wound intubation	4 (14.3%)	1 (4.3%)	7 (7.7%)	12 (8.4%)
ECMO	-	-	2 (2.2%)	2 (1.4%)

OT: orotracheal; NT: nasotracheal; ECMO: extracorporeal membrane oxygenation.

Most of the surgically treated patients underwent airway repair (n = 405, 94.9%), while few patients were only tracheotomised (n = 22, 5.1%). Different types of surgical repair are outlined in Table V.

Among surgically treated patients, the average lesion size was 24.7 mm in adults and 30.5 mm in children, while

patients that received a tracheotomy alone had an average lesion size of 31.6 mm in adults and 21.7 mm in children. In the computation of the average dimensions, cases of crico-tracheal separation (n = 12 in children and n = 49 in adults) and complete tracheal separation (n = 10 in children and n = 9 in adults) were not considered. All patients

Table V. Different surgical procedures of tracheal repair as reported in the present systematic review.

	Total (n = 405)	Adults (n = 405)	Children (n = 64)	NA (n = 26)
Tracheal repair + (C)TRA	191 (47.2%)	164 (52.1%)	27 (42.9%)	-
Primary closure NOS	158 (39%)	106 (33.7%)	26 (41.2%)	26 (100%)
Endoscopic repair	24 (5.9%)	24 (7.6%)	-	-
Muscle flap alone	13 (3.2%)	11 (3.5%)	2 (3.2%)	-
Laryngotracheal reconstruction	6 (1.5%)	2 (0.6%)	4 (6.3%)	-
Colon interposition	3 (0.8%)	-	3 (4.8%)	-
Total laryngectomy	1 (0.3%)	1 (0.3%)	-	-
Cervical drainage insertion	3 (0.8%)	2 (0.6%)	1 (1.6%)	-
NA	7 (1.5%)	5 (1.6%)	1 (1.6%)	-

(C)TRA: (cricotracheal) resection and anastomosis; NOS: not otherwise specified; NA: not available.

Table VI. Cardillo's classification¹⁸⁵ of tracheal injuries based on the depth of tracheal wall involvement.

Classification	Morphologic description
Level I	Mucosal or submucosal tracheal involvement without mediastinal emphysema and without oesophageal injury
Level II	Tracheal lesion up to the muscular wall with subcutaneous or mediastinal emphysema without oesophageal injury or mediastinitis
Level IIIA	Complete laceration of the tracheal wall with oesophageal or mediastinal soft-tissue hernia without oesophageal injury or mediastinitis
Level IIIB	Any laceration of the tracheal wall with oesophageal injury or mediastinitis

with this type of trauma, however, underwent surgical treatment.

Overall, after surgical treatment, an endotracheal stent was applied in 21 cases (5.2%): 6 after primary closure (5.7%) in the adult population, in 12 cases after tracheo-tracheal or laryngo-tracheal anastomosis (n = 8 adults, 4.8% and n = 4 children, 14.8%), 2 cases after laryngo-tracheal reconstruction in children (50%), and after local muscle flap suture in an adult (9%).

In 17 cases (4.2%) the use of muscular flap was reported in association with tracheal repair: 8 cases (n = 5 adults and n = 3 children) after tracheal wound closure, and 9 (n = 5 adults and n = 4 children) as reinforcement of the anastomosis. The muscles used both as support for closure or as a stand-alone repair technique were the prelaryngeal (n = 24, 80%), the sternocleidomastoid (n = 5, 16.7%), and the platysma (n = 1, 3.3%).

In the management of tracheo-oesophageal fistulas, other flaps were used either alone or in combination with muscles as interposition between the oesophagus and trachea: fascia lata (n = 4), colon (n = 3), and a single case of pericardial flap.

Overall, 32% of patients (n = 102 adults and n = 28 children) required tracheostomy after surgery.

Outcomes

Mean follow-up lasted 12.6 months (range, 18 days – 5 years). As a consequence of the trauma, some patients reported unilateral (n = 11, 2.2%) or bilateral (n = 17, 3.3%) vocal cord paralysis.

Analysis of treatment outcomes in adults and children revealed distinct patterns across conservative and surgical managements. Among adults, conservative treatment (n = 47) resulted in stenosis in 4.3% and death in 4.3% of cases. In children who underwent conservative treatment (n = 34), a late stenosis occurred in 25.7%. In the population who received tracheotomy alone, among the adult cohort (n = 15), 6.7% died after the event, while in children (n = 7) a late stenosis was observed in 42.9% of cases. Sur-

gical intervention in adults (n = 315) and children (n = 64), was associated to postoperative stenosis in 2.9% and 1.6% of cases, respectively, tracheo-oesophageal fistula in 1.3% of adults, and death rates of 1% in adult and 7.9% in children, respectively.

Subsequent tracheotomy removal was performed in 35 patients (n = 29 adults and n = 6 children), resulting in an overall decannulation rate of 26.9%. Patients in whom decannulation was not possible were those who required prolonged ventilation due to spinal cord injuries, suffering from bilateral vocal cord paralysis or presenting recurrent stenosis.

Among the 22 patients treated with tracheotomy alone, the overall decannulation rate was 63.6% (n = 8 adults and n = 6 children). In the adult population the average decannulation time was 3.1 months (range, 5 days – 1 year), while in children it was 2.5 months (range, 10 days – 6 months).

Discussion

Tracheal trauma is a rare but potentially life-threatening event that must be diagnosed and treated as quick as possible, since time of management and good functional outcomes are strictly linked. The literature lacks a clear consensus on type of management, airway stabilisation method and treatment, in both the paediatric and adult populations. In such a scenario, our systematic review aims to fill a gap in the accumulated evidence, due to the sparse experience that even large, referral centres for airway disease may accumulate in several years of practice.

Demographic features and aetiology

Males are more affected than females both in the paediatric and adult populations¹⁷⁷. Blunt and penetrating traumas still represent the most common causes of tracheal injury, with a prevalence of the former especially in the paediatric population. This trend confirms the general incidence reported in the literature for cervical and laryngeal traumas, in which there is an increasing number of penetrating lesions with

respect to blunt injuries that are probably prevented by the growing use of increasingly safe systems^{178,179}.

Management

There is no consensus regarding initial airway management when laryngo-tracheal trauma is suspected, as clinical presentation depends on the extension of the injury as well as on the complexity of the patient, considering the high probability of lesions in other areas of the body. Furthermore, it is important to balance the need to secure the airway with the possibility of worsening the injury or creating a false path²³.

Our review shows that most of the patients with respiratory distress at the onset were stabilised through orotracheal intubation at the referral centre. This is a safe technique when performed under visual guidance (e.g. flexible bronchoscope) by expert physicians; however, when a quick endotracheal intubation is performed blindly, it may worsen tracheal injury by creating false passages of the tube, dislocating fractured cartilages, or even leading to airway transection³. In our analysis, tracheotomy was used as the first choice for airway stabilisation in patients with respiratory distress in 28% of cases.

Conservative management

The present literature review outlines that conservative treatment can be considered in very specific scenarios, especially in the paediatric population^{59,180}. In this small cohort of patients, in fact, almost half of traumas are represented by contusive neck injury (typically, neck against bicycle handlebars) that may cause small tears in the membranous part of the trachea, without involvement of the oesophagus. If the injury did not cause an immediate airway issue, as a respiratory distress in the most severe cases or an expanding emphysema, conservative treatment can be considered. This often happens with small and/or superficial lesions. In fact, the average dimension of the tracheal tears reported in the cohort of patients who were selected for conservative treatment was 18.1 mm, in accordance with the 20 mm cut-off reported by Mullan et al.⁵⁹.

Conservative treatment includes both invasive (i.e. after tracheal intubation) and non-invasive clinical monitoring. A prolonged intubation with high volume, low pressure endotracheal cuff inflated distally to the site of the injury may facilitate healing process^{128,181-183}. In our review, this treatment strategy was chosen more frequently in children. In the scenario of asymptomatic patients with very superficial iatrogenic injuries (grade I and II according to Cardillo et al.¹⁸⁴) (Tab. VI), invasive ventilation could also be avoided.

Use of a stent as unimodal therapy has been described in exceedingly rare cases, predominantly in patients presenting with a heavily compromised clinical status. Its placement offers a rapid but temporary solution, thus rendering it appropriate for patients unable to withstand an immediate surgical repair and its associated risks^{32,185}. In our personal experience, in fact, tracheal stents might be considered as a temporary solution in order to allow the patient to heal properly in preparation of subsequent surgical procedures, or as a last resort in otherwise untreatable patients.

Surgical management

Surgical treatment appears strongly indicated in patients with extended and/or complete tracheal wall laceration, in which ventilation cannot be safely performed. Patients requiring surgery for lesions of other cervical or thoracic structures (e.g. major vessels), with tracheo-oesophageal fistula, or signs of impending infection, are adequate candidates for surgical repair. In fact, those with penetrating trauma frequently undergo simultaneous surgical treatment of the tracheal lesion during cervical exploration performed to assess and repair other vascular and visceral damages.

In our systematic review, we highlighted that surgical treatment was chosen in cases where the average lesion size was 24.7 mm in adults and 30.5 mm in children, confirming that surgery is preferred over conservative treatment when tracheal tears are larger than 20 mm⁵⁹.

The most reported surgical treatment was represented by primary closure of the tracheal tear through an anterior approach achieved via a circumferential tracheal incision followed by a trans-tracheal repair and (crico-)tracheal anastomosis^{186,187} (Cover figure). This surgical technique was also used in case of complete laryngo-tracheal separation or tracheal rupture involving > 75% of the tracheal circumference^{108,188-190}. For small superficial tears, in selected adult patients, and with the appropriate instrumentation, an endoscopic suture has also been described¹⁹¹.

Few authors described the use of myofascial pedicled flaps (especially from prelaryngeal muscles) as a support/cover for tracheal repair, mainly in case of tracheo-oesophageal fistula¹⁹². There is no consensus in the literature about this technique, which depends mostly on the integrity of muscular tissues after the traumatic event, the size of the lesion, and the surgeon's preferences.

The use of stents after surgical management is debated. In our review, a minority of authors described the use of endotracheal stents (e.g. Montgomery T-tube or Dumon) to prevent tracheal stenosis and facilitate the healing process¹⁹³. Where described, the issues related to the use of

stents, especially T-tubes, are also evident, such as obstruction of the upper limb caused by granulation tissue, tracheal and laryngeal mucosa irritation caused by stent movements, as well as the need for frequent cleaning to prevent secretion drying and subsequent airway blockage¹⁹⁴.

Outcomes

Overall, outcomes assessed in this population were poorly described. According to the available data, a non-negligible number of complications occurred more frequently in conservatively treated patients, particularly children¹⁸³. Despite the limited number of cases documented in the literature, a high incidence of stenosis (42.9%) was also observed in paediatric patients who underwent tracheostomy without subsequent tracheal injury surgical repair. Among those undergoing tracheostomy, the available data in the literature indicate that the overall decannulation rate after surgery was 26.9%.

Study limitations

Heterogeneity represents the main limit of the present review. This is true for the pathology itself, which is heterogeneous by definition, potentially underestimated and underrated by the overall trauma assessment. The heterogeneity can be also attributed to the preference of management among single institutions, specific surgical expertise, and selection bias. Moreover, not all manuscripts adequately reported clinical findings and treatment outcomes.

Conclusions

Despite the rarity of cervical tracheal trauma and the heterogeneity of its presentation, correlated with both different causes and characteristics, our systematic review highlights the importance of a prompt airway management and the pivotal role of a clear treatment strategy. Conservative approach is adequate in the specific scenarios of tracheal tears with a cranio-caudal length < 20 mm and without respiratory issues, especially in children. In all the other clinical scenarios, surgical options should be considered as the first choice. An adequate follow-up of some months appears indicated also when a conservative treatment strategy has been applied, in order to promptly detect post-traumatic late stenosis to be treated by secondary surgical endoscopic and/or open techniques.

Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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Author contributions

CM, DL, CP: study conception and design, critical revision of the article and final approval of the version to be published; CM, DL: articles search and selection, data acquisition and analysis, review drafting; AS: articles search and selection, data acquisition.

Ethical consideration

No formal ethics committee approval was required for this article as it is based on already published clinical data from other studies available in the literature.

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