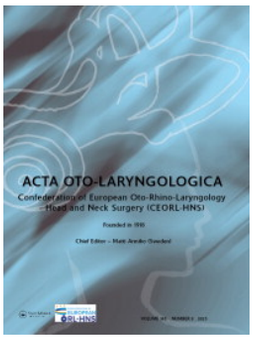

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RESEARCH ARTICLE

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A descriptive study on laryngotracheal stenosis in the Northern Sweden

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ABSTRACT

Background: We have in a retrospective design used laryngotracheal stenosis (LTS) classification to describe stenotic subsites and through international classification of disease (ICD-10) codes its diagnostic origins. The diagnostic challenge posed by varied etiologies can lead to treatment delays, in potentially life-threatening conditions

Aims/objectives: The purpose of this study is to explore and ascertain the etiological and anatomical distribution of LTS to reduce misdiagnosis and as such delayed access to adequate treatment

Material and methods: The included cases were consecutively recruited between 1999 and 2019, all labeled with relevant ICD-10 codes for the research question in combination with medical records for evaluation of its accuracy. The primary outcome was the causes, and anatomical locations of LTS.

Results: A total of 1441 records were screened, with 1071 cases meeting the inclusion criteria. The most common cause was unilateral vocal fold immobility, followed by glottic cancer. Benign causes were more prevalent than malignant ones, with glottic-level stenoses being most frequent.

Conclusion and significance: Unilateral vocal fold immobility is the most prevalent cause of LTS in our material. These findings can enhance diagnostic efficiency by increasing clinical awareness of common etiologies.

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Laryngotracheal stenosis; diagnostic errors; subglottic stenosis; unilateral vocal fold immobility

Introduction

Laryngotracheal stenosis (LTS) comprises a wide array of different conditions that require precise preoperative assessment and classification to improve comparison of different therapeutic modalities. LTS are potentially life threatening due to obstruction of the airway at different anatomical subsites and different origins. The inability to breathe has a major impact on quality of life besides being life-threatening if left untreated [1,2]. Asthma is the most common cause of diagnostic failure and misclassification, with a reported delay in LTS diagnostics of up to >18 months [3]. In addition to posing a danger to the patient a diagnostic delay also affects healthcare costs [1,4]. There are no healthcare economic reports available for the general term LTS representing a continuum of disease that can be stratified into different anatomical subsites in the larynx: (i) supraglottic, (ii) glottic, and (iii) subglottic and/or the trachea. Using subglottic stenosis (SGS) as one cause of LTS there is a reported annual financial healthcare burden comparable to COPD and diabetes mellitus [5,6].

European Laryngological Society (ELS) proposed a five-step endoscopic airway assessment and a standardized reporting system to better differentiate fresh, incipient from mature, cricotrachial LTSs, simple one-level from complex multilevel LTSs and finally 'healthy' from 'severely morbid' patients [7]. We have used the LTS to describe affected airway subsites in the larynx and trachea in relation to international classification of disease (ICD-10) diagnostic codes and comorbidities as defined by the age-adjusted Charlson Comorbidity Index (ACCI) [1]. The Myer-Cotton airway grading system describes the degree of narrowing as a percentage of the expected functional airway: Grade less than 50% airway obstruction; Grade II 51–70%; Grade III 71–99% and Grade IV to no detectable lumen [2,8]. Grade 2 reflects in most cases persistent dyspnoeic symptoms [2,9]. LTS can also be stratified into acquired or congenital subgroups [10]. Idiopathic SGS (iSGS) is an acquired benign LTS condition with a fibrotic progressive airway obstruction, without cure and a recurrent need of surgical treatment. iSGS predominantly affects women between the third and fifth decades of life [9,11]. Other benign conditions embraced under the LTS umbrella are tracheo-laryngomalacia, vocal fold immobility, secondary airway lesions such as airway trauma (intubation) and infection (HPV in recurrent respiratory papillomatosis) and finally systemic diseases [1,2,10,12,13].

According to ELS classification of LTS the terminology is afflicted with a benign condition, however stenotic anatomical subsites may have its origin in a primary malignant lesion [14], or secondary lesion to treatments. Notably, primary malignant causes are excluded in most reviews. As with its cause, definitive management of LTS has remained

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elusive, however always with the goal to preserve airway, voice, and swallowing function [2,14,15].

This study aims to assess the cause and location of LTS based on ICD-10 codes and concurrent medical records for cases presenting over a 20-year period. The study outcome could play a key part in and serve as a database for further studies. Our hypothesis is that our outcome could possibly have an impact on reducing diagnostic failures and as such provide the patients with relevant treatments targeting the LTS.

Material and methods

Ethical approval

This study was performed adhering to the principles of the 1964 Declaration of Helsinki and its later amendments. The study was approved by the Swedish Ethical Review Authority, approval number nr; 2020-00253 (2020-04-14). We confirm that the study was reported according to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) recommendations.

Study design

Retrospective descriptive, observational.

Participant recruitment

All patients visiting the Department of Otorhinolaryngology, University Hospital of Umeå/Västerbotten, a tertiary referral center between January 1999 and December 2019 labeled with the selected ICD-10 codes were evaluated for inclusion. The research cases were identified with ICD-10 codes comprising the upper airway at the LTS level: dyspnea, on exertion (R060), dyspnea while resting, stridor (R061), SGS (J398), supraglottic cancer (C321), subglottic cancer (C322), bilateral vocal fold immobility (J380C), unilateral vocal fold immobility (J380B), benign laryngeal tumor (D141), laryngocele (congenital) (Q313), and respiratory recurrent papilloma (D141A). Also, additional admission, glottic cancer (C320), post-surgical SGS (J955). Glottal laryngeal cancer TNM classification T2–T4 is defined by a reduced vocal cord mobility on the affected side, thus with an impact on the upper airway. T1 glottic laryngeal cancer is described without vocal fold immobility but still is included since even a smaller tumor can affect the airway by mucus formation or tumor mass. An intentionally broad inclusion was used to capture as many cases with LTS as possible without affecting the outcome with confounding factors of impact. Due to the retrospective study design, no further prospective and objective methods could be used to confirm diagnosis.

Study population/demographic data are provided in Table 1.

Age was defined as age at first visit. In case of diagnosis before 1999, age at first visit within the time frame was used. Comorbidity evaluation was performed using the ACCI [16]. Smoking status was documented as non-smoker, former smoker, smoker, and unknown. Smoking was defined as life consumption of >100 cigarettes. Former smokers were interpreted by life consumption of >100 cigarettes and cessation up until first visit. Former smoker and current smokers together were expressed as 'ever smokers'. Unknown was used when no information was found in the medical journal.

Malignant cause was classified if this diagnosis was confirmed at a microscopic level. Vocal fold immobility without macroscopic obstructive lesions was classified as benign. Vocal fold immobility was stated as an absence of abduction and adduction in relation to the midline, thus including vocal fold paralysis as well as cricoarytenoid joint ankylosis.

Gastroesophageal reflux (GERD) was based on self-reported data and/or medical treatment.

Laryngomalacia was not included. For this study, SGS was defined as a fibrous soft tissue stenosis at the level of the cricoid cartilage within the larynx.

Exclusion criteria are shown in Figure 1. Patients with no upper airway compromise at the LTS level were excluded and considered as misdiagnosed, as well as patients with pathology of the pharynx.

The ICD diagnosis code was corrected in case of initial misregistration. The diagnostic testing supported a high exclusion rate in cases labeled with dyspnea (R060), where only 1% (2/205) were included further as LTS. Eight percent (6/77) of cases labeled with R061 (subjective symptoms without objective pathology) were included, both conditions are heterogenous and as such easily misdiagnosed.

Statistical method

All statistics analysis was performed with SPSS version 27 (IBM Corp. Released 2020. IBM SPSS Statistics for Windows version 27.0. Armonk, NY). Mean and median values were calculated. Descriptive analysis was presented as frequencies and cross-tabulations with multiple categories. Identifying differences between groups and significance testing was performed using a p value < 0.05, and with a two-sample z test.

Results

Study population

A total of 1441 consecutive medical journals were screened, 1071 cases met the inclusion criteria. Participants in the study were categorized by anatomical subsites as LTS and ICD-10 diagnostic codes received at hospital admission. The study population is summarized in Table 1 and Figure 2. Glottic airway comprise was the most prevalent stenosis location (77%, 824/1071). In the stratified study population, unilateral vocal fold immobility was the most common diagnosis presenting with a higher comorbidity score compared to the benign group in total, 31% (151/489) with severe ACCI (>5) compared to 15% (44/302) in the benign group. The second most common LTS cause was glottic cancer. Benign origin 74% (791/1071) was on an aggregated level more prevalent than malignant causes 26% (280/1071), the

Table 1. Study population and patient characteristics.

Diagnosis	Frequency in percentage in brackets quota (x/xx)	Co-morbidity None Mild 1–2 Moderate 3–4 Severe >5	Ever smoker
Overall upper airway stenosis, age at first visit	Males mean years 59.75 (median 64) Females mean years 58,5 (median 61)		
Overall upper airway stenosis, gender	Males 58.3% (624/1071) Females 41.7% (447/1071)		
C320, glottic cancer	18.8% (201/1071)	None 0% (0/201) Mild 5% (10/201) Moderate 46.8% (94/201) Severe 48.3% (97/201)	Non-smoker 17.9% (36/201) Smoker 80.6% (162/201) Unknown 1.5% (3/201)
C321, supraglottic malignancy	6.3% (68/1071)	None 0% (0/68) Mild 59% (4/68) Moderate 41.2% (28/68) Severe 52.9% (36/68)	Non-smoker 7.4% (5/68) Smoker 91.2% (62/68) Unknown 1.5% (1/68)
C322, subglottic malignancy	0.9% (10/1071)	None 0 % (0/10) Mild 20% (2/10) Moderate 40% (4/10) Severe 40% (4/10)	Non-smoker 20% (2/10) Smoker 80% (8/10) Unknown 0% (0/10)
D141, benign tumor in larynx	4.8% (51/1071)	None 23.5% (12/51) Mild 47.1% (24/51) Moderate 7.8% (4/51) Severe 21.6% (11/51)	Non-smoker 45.1% (23/51) Smoker 49.0% (25/51) Unknown 5.9% (3/51)
D141A, recurrent respiratory papillomatosis	9.2% (99/1071)	None 66.7% (66/99) Mild 23.2% (23/99) Moderate 8.1% (8/99) Severe 2.0% (2/99)	Non-smoker 75.8% (75/99) Smoker 24.2% (24/99) Unknown 0% (0/99)
J380B, unilateral vocal fold immobility	45.7% (489/1071)	None 16.0% (78/489) Mild 24.3% (119/489) Moderate 28.8% (141/489) Severe 30.9% (151/489)	Non-smoker 40.9% (200/489) Smoker 26.0% (127/489) Unknown 33.1% (161/489)
J380C, bilateral vocal fold immobility	5.1% (55/1071)	None 10.9% (6/55) Mild 12.7% (7/55) Moderate 41.8% (23/55) Severe 34.5% (19/55)	Non-smoker 49.1% (27/55) Smoker 23.6 (13/55) Unknown 27.3% (15/55)
J398, other specified diagnosis in upper airway e.g. fibrous subglottic stenosis	7.5% (80/1071)	None 43.8% (35/80) Mild 22.5% (18/80) Moderate 20.0% (16/80) Severe 13.8% (11/80)	Non-smoker 58.8% (47/80) Smoker 16.3% (13/80) Unknown 25.0% (20/80)
Q313, laryngocele	0.5% (5/1071)	None 20% (1/5) Mild 20% (1/5) Moderate 40% (2/5) Severe 20% (1/5)	Non-smoker 40% (2/5) Smoker 40% (2/5) Unknown 20% 1/5)
In total benign cause	73.9% (791/1071)	None 25.3 (200/791) Mild 25% (198/791 Moderate 25% (198/791) Severe 24.7% (195/791)	Non-smoker 47.9% (379/791) Smoker 26.2% (207/791) Unknown 25.9 (205/791)
In total malignant cause	26.1 % (280/1071)	None 0% (0/280) Mild 5.4% (15/280) Moderate 44.6% (125/280) Severe 50.0% (140/280)	Non-smoker 15.4% (43/280) Smoker 82.5% (231/280) Unknown 2.1% (6/280)

latter presented with a higher comorbidity score. Glottic cancer had the highest rate of 'ever smokers' (81% 162/201). There was a predominance of males 58% (624/1071) compared to females 42% (447/1071) except for stenoses at the subglottic level where females predominated 69% (67/97). Malignant cause had a higher rate for males, 81% (227/280), with glottic cancer the highest 89% (169/190).

Discussion

We performed a detailed retrospective epidemiological mapping of 1441 cases of suspected LTS between 1999 and 2019, where 1071 were included in the analysis cohort based on diagnosis. The main findings were that unilateral vocal fold immobility was the most common individual cause, followed by glottic cancer. Also, benign conditions on an aggregated level were more common than malignant ones. In accordance with another report of a cohort with 188 patients [17] and exclusion of malignancies, our findings confirm that LTS at the glottic level is the most common stenotic subsite. Divergent data on the location of LTSs with non-malignant histology have been presented [15] with a predominance of stenosis at a subglottic level. This highlights the need for broad inclusion criteria to reduce the risk of selection bias and confounders of impact affecting the outcome measure and reducing the ability to compare data. A Danish nationwide study confirms glottic cancer to be the most common cause of laryngeal cancer (43%) in the Danish population [18]. We found glottic cancer to be the second most common cause of LTS at 19% (201/1071) pin-pointing the need to include both malign and benign conditions in the descriptive LTS subsite data. The male excess in the malignant subgroup

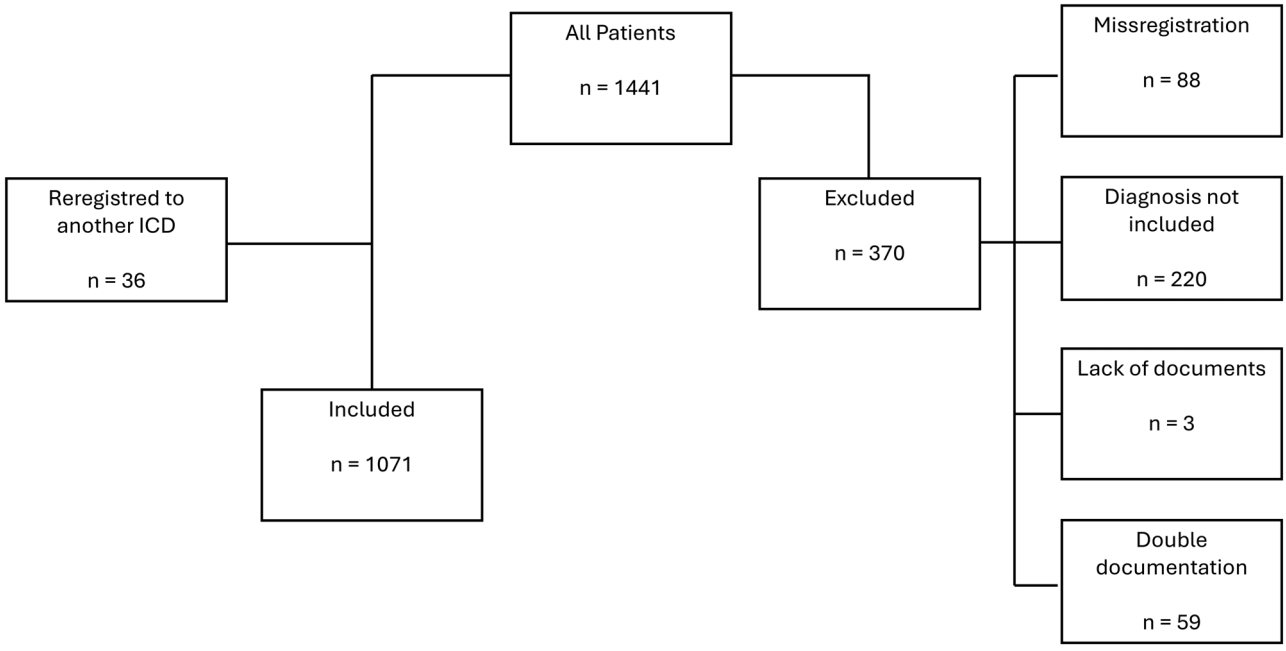

Figure 1. Eligibility criteria, chart of in-, and exclusion.

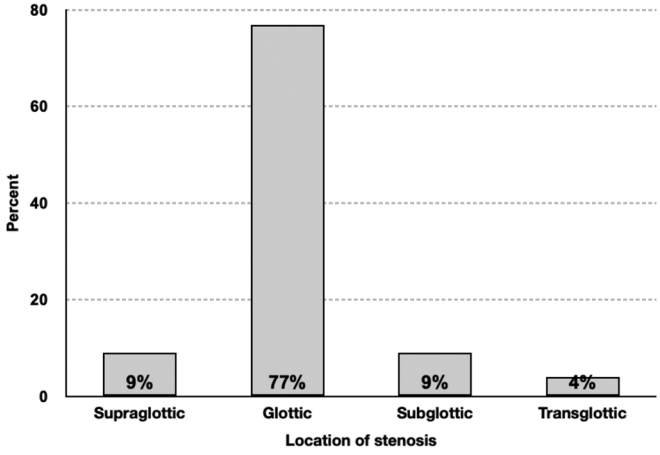

Figure 2. Overall upper airway stenosis location of stenosis.

was like ours, with 82% in the Danish report and 81% in ours [18]. In accordance with our study reporting 72% (201/280) glottic cancer cases out of laryngeal cancer cases in total, the Swedish Head and Neck Cancer Register (2019) [19] reports glottic cancer to represent 71% of laryngeal cancer in Sweden. We observed unilateral vocal fold immobility (paralysis and ankylosis) at 46% (489/1071), and this was the most common cause to benign LTS. Unfortunately, vocal fold immobility is not reported as a causative explanation to LTS on a regular basis [15,17,18]. This may be due to the perception that it does not significantly reduce static cross-sectional area of the airway. In our experience, unilateral vocal fold immobility significantly reduces the glottic airspace. Depending on the level of physical challenge and degree of vocal fold immobility, the functional reduction of the glottic area can have a huge impact on breathing, which is why we included this condition in our study.

We found female gender to be more common than male at the subglottic level. It is known that SGS in general and specifically the idiopathic phenotype is more common in females [2,9]. Including the SGS lesions or not may affect the male/female balance as well as the incidence numbers of subglottic upper airway stenosis. In a retrospective study on SGS, 82% (18/22) were females [12]. These results are confirmed in our findings, reporting 78% (49/63) females [20].

Limitation and strength of the present study

We were unable to find a comparable study including LTS with both malignant and benign causes, which makes comparisons difficult. The strength of our study addressing the prevalence of LTS is the broad inclusion criteria and large sample size. These facts reduce the likelihood of missing relevant diagnoses and supports estimation of relative risks for different conditions causing airway obstruction without hampering outcome data with confounders of impact.

Conclusion

This study presents the prevalence, recognized causes, and comorbidity for LTS in a cohort from the northern part of Sweden. Unilateral vocal fold immobility is the most common cause of LTS, and glottic cancer the second most common.

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Consent to participate

Patients gave their consent for tissue banking and research prior to diagnostic surgery at the Department of Otorhinolaryngology, University Hospital of Umeå.

Author's contribution

ML and AE contributed equally: conceptualization, design, conduct, analysis, and writing the original manuscript draft. AH; analyzing, writing, and reviewing. KO; design conduct, analyzing, writing, reviewing, and editing.

Disclosure statement

The authors report, no competing interests to declare.

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Data availability statement

The data that support the findings of this study are available from the corresponding author AE, upon reasonable request, from other investigators adhering to the European Union General Data Protection Regulation (EU) 2016/679 GDPR.

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