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ORIGINAL ARTICLE

Surgical treatment is effective in severe cases of exercise-induced laryngeal obstruction: A follow-up study

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Abstract

Conclusions: Surgery is an effective treatment in severe cases of supraglottic exercise-induced laryngeal obstruction (E-ILO). Conservatively treated subjects and subjects tested negative for E-ILO, who still experience breathing problems 1–3 years after diagnosis, tend to adjust their physical activity to a greater extent than surgically treated subjects. **Objective:** To investigate how symptoms and level of physical activity change over time in patients with E-ILO who have undergone surgery, patients with E-ILO treated conservatively and patients who tested negative for laryngeal obstruction at continuous laryngoscopy exercise-test (CLE-test). **Methods:** Patients referred for exercise-induced breathing difficulties answered questionnaires at diagnostic CLE-test and at follow-up. Questions regarded exercise-induced breathing problems, current physical activity level, and medical history of asthma and perennial allergy. **Results:** Out of 84 invited subjects, 59 (70%) answered both questionnaires. Surgically treated subjects had less breathing problems at follow-up compared with conservatively treated subjects and subjects who tested negative ($p < 0.001$). None of the surgically treated subjects were less physically active or had changed sport due to exercise-induced dyspnoea, whereas 41.7% of the conservatively treated subjects had made such adjustments ($p < 0.001$).

Keywords: Laryngoplasty, exercise-induced dyspnoea, vocal cord dysfunction, physical activity, E-ILO

Introduction

Exercise-induced breathing problems can be caused by many different medical conditions and through various pathophysiological mechanisms [1–3]. Exercise-induced laryngeal obstructions (E-ILO) are such conditions where different anatomical structures in the larynx cause airway obstruction at the supraglottic or glottic level or both. E-ILO is diagnosed by continuous laryngoscopy exercise-test (CLE-test) [4] and type and severity can be assessed according to the CLE-score [5]. E-ILO is often diagnosed in young, physically active persons [6], and experience of breathing problems during exercise might lead to an unwanted decrease in physical activity and reduced health benefits [7].

There is no pharmacological treatment for E-ILO. Glottic obstruction, in the literature often called vocal cord dysfunction, has traditionally been treated by speech-pathologists [8,9]. Inspiratory muscle training has been shown to lead to abduction in healthy subjects [10] and to be successful in one case report with exercise-induced paradoxical vocal fold motion [11]. Inspiratory muscle training has not yet been tested in controlled studies.

Severe supraglottic obstruction, i.e. a grade 2 or 3 in the validated CLE-score, can, unlike glottic obstruction, be treated with laryngoplasty [12,13]. Since surgery always involves potential risks, it is important to identify the subjects who would benefit from an operation and to evaluate the treatment.

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Little is still known about the natural course of E-ILO. Only one study has been published previously, where it was found that exercise induced dyspnoea generally decreased in both surgically and conservatively treated subjects [14].

In the present study, the aims were to evaluate if surgery is an effective treatment in severe cases of supraglottic E-ILO regarding exercise-induced self-reported symptoms, and to investigate to which extent subjects with breathing problems suggestive of E-ILO had adjusted their physical activity level due to breathing difficulties during exercise.

Materials and methods

The study was performed as an observational, longitudinal follow-up study of a cohort of 84 consecutively CLE-tested patients, retrospectively comparing answers to a questionnaire at diagnostic CLE-test with a questionnaire at follow up. During a 4-year period, 69 females and 15 males were referred to the Department of Otorhinolaryngology for exercise-induced dyspnoea. To diagnose or rule out E-ILO the patients underwent a CLE-test on a treadmill (Master Fitness T590; Master Fitness, Guangzhou, China) [4] and were instructed to run until breathing problems forced them to stop or until exhaustion. The pulse was continuously monitored (T31, Polar, Oulu, Finland) to ensure that the subject reached at least 90% of expected maximum heart rate [15]. The larynx was filmed via a fiberoptic laryngoscope (Olympus ENF-P3, Southend-on Sea, UK). Immediately after the test two experienced laryngologists made a joint assessment of the larynx findings and a scoring according to the CLE-score method [5].

Forty-seven subjects were diagnosed with E-ILO and 37 tested negative for the diagnosis. All subjects diagnosed with E-ILO were thoroughly informed about the condition. They were informed that E-ILO is benign, and that the larynx normalizes when they stop exercising. We also discussed the time factor, depending on whether the diagnosis was supraglottic or glottic E-ILO, as supraglottic obstruction tends to normalize in only a few minutes, while glottic obstruction often seem to last longer. In addition, all subjects received instructions about breathing techniques to use during exercise, which might reduce symptoms [9]. All E-ILO subjects were invited to contact the investigating doctors by phone 2 months after the CLE-test for a follow-up report on the effect of breathing exercises. If breathing exercises were not sufficient, possible future improvement by surgery and whether they were interested in surgical treatment or not were discussed with subjects diagnosed with severe supraglottic E-ILO. Out of

27 subjects with supraglottic E-ILO where surgical treatment was discussed on these grounds, 15 underwent laryngoplasty with reduction of the mucosa of the aryepiglottic folds [12].

At the same visit as the CLE-test was performed, all subjects answered a questionnaire about breathing difficulties during exercise focusing on severity of breathing problems, sporting habits, current physical activity level, and current asthma and/or perennial allergies. To rate symptom severity of breathing problems during exercise, a visual analogue score (VAS) ranging from 0 (no breathing problems) to 10 (worst possible breathing problems) was used.

A follow-up questionnaire (Table I) was sent to all subjects 1–3 years after the diagnostic CLE-test. The subjects were again asked to rate their current symptom severity by VAS and to fill in the same questionnaire. In addition the follow-up questionnaire comprised questions about whether the subject had changed physical activity level and/or type of sport. If that was the case, they were asked to specify whether the changes were due to breathing problems or not. If the adolescent was under 18 years old, the questionnaire was sent to the guardian and they were asked to answer it together with the adolescent.

The responders were categorized as subjects with E-ILO who had undergone surgery, patients with E-ILO treated conservatively and patients who tested negative for laryngeal obstruction. A schematic overview of the study design, participants, and drop-outs are presented in (Figure 1).

Statistical analysis

Kruskal-Wallis test (non-parametrical ANOVA) was used to analyze if there was any difference between the three groups regarding symptom severity. If the result of the Kruskal-Wallis test was significant ($p < 0.05$) Mann-Whitney U-tests were performed to compare groups two-by-two. Fisher's exact test was used to compare adjusted physical activity level between surgically treated and conservatively treated E-ILO subjects. A p -value < 0.05 was regarded as statistically significant. SAS software version 9.3 (SAS Institute, Cary, NC, USA) was used for statistical analyses.

Results

Time between the diagnostic CLE-test and the follow-up questionnaire was on average 17.6 (10–36) months (median (interquartile range)). The overall response rate was 70%. In all three groups, more females than males answered the follow-up questionnaire, 77% of invited females compared to 40% of males. A higher proportion, 76%, of those tested

Table I. Follow-up questionnaire.

Symptoms of breathing difficulties during exercise

Since examination with the CLE-test: Do you have less symptoms than before/as many symptoms as before/more symptoms than before?

Physical activity

Are you less active than before/as physically active as before/more active than before?

Are you less active because of breathing difficulties?

What sport do you practice?

Have you changed sport since the CLE-test?

Have you changed sport because of breathing difficulties?

Asthma and/or perennial allergy

Do you have physician diagnosed asthma and/or perennial allergy?

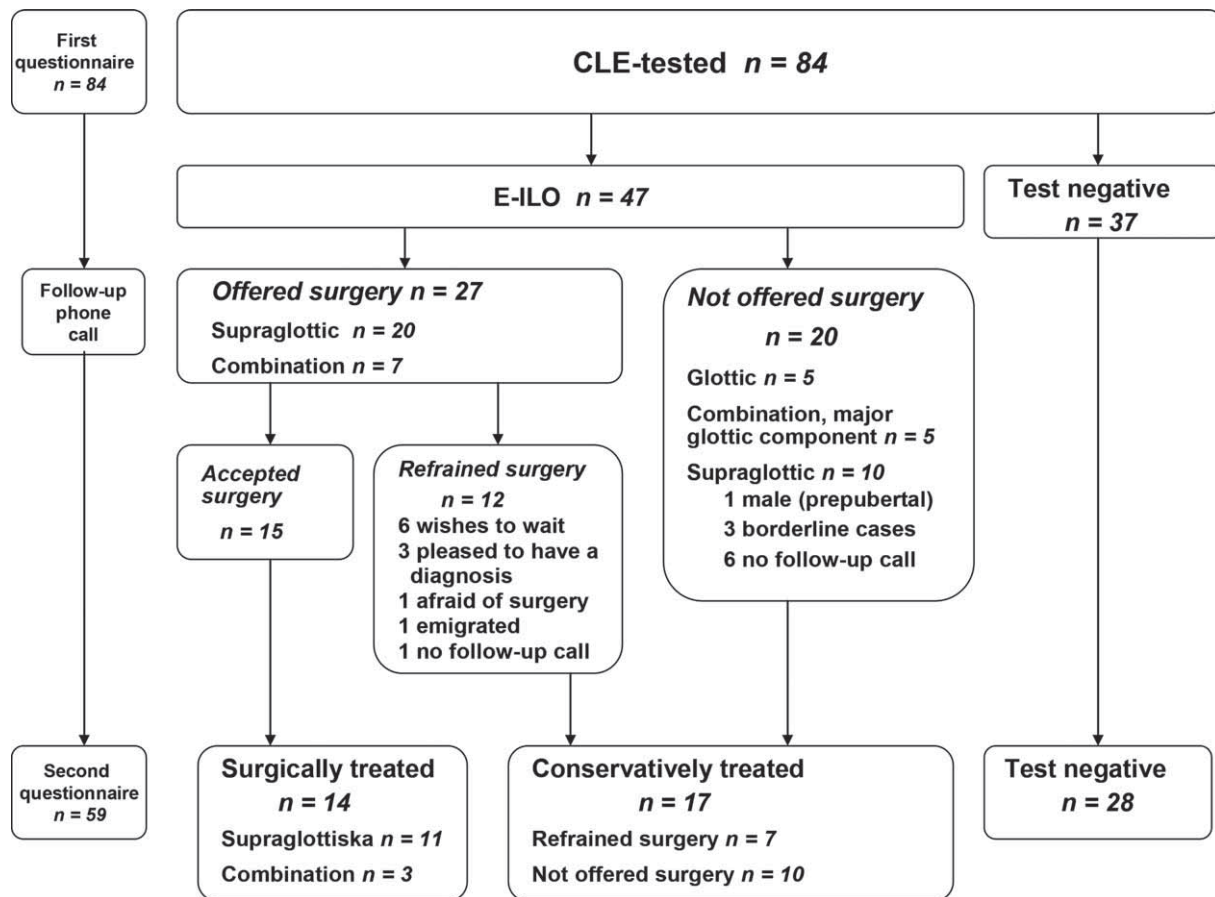


Figure 1. Overview of participants and drop-outs. E-ILO subtypes, number of patients who were offered surgery and how many who refrained surgery are presented for each group.

negative for laryngeal obstruction responded, compared to subjects with E-ILO, where 66% returned the questionnaire.

Among responders diagnosed with E-ILO, a majority, 71%, had an obstruction at the supraglottic level. A glottic obstruction was observed in 10% of the responding subjects and obstruction at both levels in 19%. There were 11 subjects with supraglottic obstructions and three subjects with a combination of glottic and supraglottic obstruction in both the

surgically treated and the conservatively treated E-ILO groups. Subject sample characteristics are presented in Table II.

Symptom severity assessed by VAS

None of the surgically treated subjects reported increased breathing problems at follow-up. Assessed by the change in VAS from diagnosis to follow-up (Δ -VAS), the surgically treated reported significantly

Table II. Demographic data and characteristics of the invited subjects and of the responders at follow-up.

	Total	E-ILO (surgically treated)	E-ILO (conservatively treated)	Tested negative
<i>Invited population</i>				
Subjects, <i>n</i>	84	15	32	37
Females/males	69/15	15/0	25/7	29/8
<i>Follow-up</i>				
Response rate, %	70.2	93.3	53.1	75.7
Subjects, <i>n</i>	59	14	17	28
Females/males	53/6	14/0	15/2	24/4
Age at diagnosis, years, median (Q1 to Q3*)	16.5 (15.0–17.6)	16.3 (15.3–16.8)	16.3 (14.0–17.5)	17.3 (15.5–19.3)
Follow-up time from CLE-test, months, mean	17.6	18.8	16.8	17.5
Follow-up time from surgery, months, median (Q1 to Q3*)	—	11.5 (7.3–19.3)	—	—
<i>Sub-types, n</i>				
Glottic	3	—	3	—
Supraglottic	22	11	11	—
Combination	6	3	3	—

*Q1, First quartile; Q3, Third quartile.

Table III. Severity of breathing symptoms during exercise scored on visual analogue scale VAS at diagnosis and at follow-up. Change in VAS (Δ -VAS), presented as median (Q1 to Q3).

	Median (Q1 to Q3)			<i>p</i> -value*			
	E-ILO surgically treated	E-ILO conservatively treated	Tested negative	Surg vs Cons vs neg	Surg vs Cons	Cons vs neg	Surg vs neg
At diagnosis	8.2 (7.7 to 10.0)	7.5 (6.6 to 8.4)	7.6 (5.8 to 8.1)	—	—	—	—
At follow-up	3.8 (1.4 to 7.7)	7.7 (7.0 to 8.2)	6.8 (5.2 to 7.9)	—	—	—	—
Δ -VAS	-4.5 (-6.1 to -1.8)	-0.0 (-0.9 to 1.3)	-0.8 (-2.9 to 0.2)	< 0.001	< 0.001	0.084	0.003

**p*-value from Kruskal–Wallis and Mann–Whitney U-tests.

Q1, First quartile; Q3, Third quartile.

less breathing problems than the other groups. There was a statistically significant difference between the surgically and the conservatively treated subjects. No difference was seen between conservatively treated and subjects who tested negative (Table III). The responses concerning current activity levels are presented in Table IV.

Activity level relative to severity of breathing problems

Among surgically treated subjects, nobody stated breathing problems to be the cause of decreased physical activity, even though one third of the subjects in this group reported a lower level of activity at follow-up compared to the level at the time of the CLE-test. In the group of conservatively treated E-ILO subjects 41.2% reported that they were less active or had adjusted their activity level, i.e. changed

what sport they practiced, due to breathing difficulties during exercise. The difference between these two groups was statistically significant ($p < 0.001$).

Types of sports practiced in the study population

Among the participants, 20 different sport activities were represented. Many patients practiced more than one sport, but they all declared one main sport. Among E-ILO positive subjects, both surgically treated (57.1%) and conservatively treated (58.8%), endurance sports (such as football, running, swimming, cross country skiing) were more common than interval sports (e.g. floor ball, handball, ice hockey) or other sports which contain both endurance and interval training (e.g. riding, dancing). Among subjects tested negative, this difference could not be distinguished (Table IV).

Table IV. Data from follow-up questionnaire presenting symptom severity, activity level, practiced sports, and prevalence of asthma and/or perennial allergy.

	E-ILO Surgically treated (n = 14)	E-ILO Conservatively treated (n = 17)	Tested negative (n = 28)
<i>Symptom severity at follow-up</i>			
Less symptoms, n (%)	11 (78.6)	3 (17.6)	12 (42.9)
Symptoms unchanged, n (%)	3 (21.4)	12 (70.6)	14 (50)
More symptoms, n (%)	0	2 (11.8)	2 (7.1)
<i>Activity level at follow-up</i>			
Less active or adjusted activity because of breathing problems, n (%)	0	7 (41.2)	7 (25)
Less active other causes, n (%)	5 (35.7)	2 (11.8)	7 (25)
As active as before, n (%)	5 (35.7)	3 (17.6)	8 (28.6)
More active, n (%)	4 (28.6)	5 (29.4)	6 (21.4)
<i>Practiced sports</i>			
Endurance sports, n (%)	8 (57.1)	10 (58.8)	10 (35.7)
Interval sports, n (%)	2 (14.3)	3 (17.6)	8 (28.6)
Other sports, n (%)	3 (21.4)	2 (11.8)	6 (21.4)
Not active, n (%)	1 (7.1)	2 (11.8)	3 (10.7)
Missing answers, n (%)	0	0	1 (3.4)
Changed sport because of breathing problems, n (%)	0	4 (23.5)	2 (7.1)
<i>Asthma or perennial allergy</i>			
Reported asthma or perennial allergy, n (%)	2 (14.3)	3 (17.6)	8 (28.6)

Asthma and perennial allergy

At follow-up 28.6% in the group of subjects who tested negative reported asthma, compared to 14.3% in the surgically treated group, and 17.6% in the conservatively treated group (Table IV). Two subjects were unable to answer, since the investigation into whether they had asthma or not was not completed.

Discussion

The group of surgically treated E-ILO-subjects reported decreased breathing problems at follow-up when assessed by change in VAS. In contrast, the conservatively treated and the subjects who tested negative had not improved. In addition, none of the surgically treated reported exercise-induced dyspnoea as a cause of decreased or adjusted physical activity while, among the conservatively treated E-ILO subjects, 41.2% of them reported less activity or adjusted physical activity level due to exercise-induced dyspnoea at follow-up. In this particular sub-group, four subjects out of seven reported that they had adapted to their breathing problems by changing what sport they practiced.

Surgery seems to be an effective treatment for E-ILO as measured by self-reported respiratory symptoms during physical activity. In our study only subjects with severe supraglottic obstruction, objectively scored, combined with a strong subjective sensation of dyspnoea and a high motivation for surgery were operated. Severe obstruction means a grade 2 or 3 on the validated CLE-score [5], caused by the aryepiglottic folds tilting into the laryngeal aperture. Three of the subjects who underwent laryngoplasty had a combination of supraglottic and glottic obstruction. In these cases the supraglottic component was assessed as being the main cause of the obstruction.

Prior to our study, one follow-up study has been published in which surgically and conservatively treated E-ILO subjects, diagnosed with the CLE-test, were investigated. They found that both surgically and conservatively treated subjects reported less symptoms at follow-up [14]. Our results are equivalent concerning surgically treated subjects, but differ regarding the results for conservatively treated subjects. The majority of conservatively treated E-ILO subjects in our study (70.6%) reported no change of symptom severity. One possible explanation for this difference is that in our study we sent follow-up questionnaires not only to supraglottic E-ILO-patients, but also to E-ILO patients with a strict glottic

sub-type or a combination sub-type with a major glottic component.

In the present study, the response rate among conservatively treated E-ILO subjects was 53%, which is considerably lower than among those surgically treated, 93%. The possibility of selection biases must be taken into consideration. However, in the conservatively treated group, the distribution of patients that had been offered surgery but retained, and those who had not been candidates for surgery, did not differ much between responders and non-responders: Among 17 conservatively treated who did answer the follow-up questionnaire, seven had been offered surgery, and 10 had not. Among those who did not answer, five had been offered surgery and 10 had not (Figure 1).

The response rate among those who tested negative is 76%, which is higher than in the conservatively treated group. One can speculate as to whether the lower response rate in the conservatively treated group reflects the fact that they have a diagnosis and have received much information about the condition in contrast to those tested negative whose breathing problems remain unexplained.

All evaluation of treatments may also be influenced by potential biases in terms of positive and negative expectations. When high expectations of the surgical outcome are not met, the relief that anything at all is done can influence both the response rate and the outcome of the responses to our questions. Therefore, it cannot be ruled out that disappointment over having an inoperable sub-type may have affected the result negatively in the conservatively treated group. However, since surgically treated subjects had continued to practice the same sport as they did at time for diagnosis, it appears that the reported decrease of exercise-induced breathing problems in this sub-group is true.

In our study, the number of E-ILO subjects with supraglottic obstruction and a combination of supraglottic and glottic obstruction was equal between the surgically treated and the conservatively treated groups. All E-ILO subjects received the same information about the diagnosis and possible treatments for their specific E-ILO sub-type at diagnostic CLE-test. Why some of the subjects chose surgery and some did not were only asked at the follow-up call 2 months after diagnosis but not investigated further. A limitation of our study is that we, at follow-up, did not specifically ask the conservatively treated why they had not reconsidered surgery if they still had breathing problems, provided that their specific condition was operable.

As E-ILO seems to be more common in endurance sports it is interesting to speculate if the mechanism of the supraglottic obstruction is caused by a Bernoulli

effect. The larynx is known as the bottleneck of the airway [6], and the majority of the subjects are females with a relatively narrow larynx. The Bernoulli effect is probably not the explanation of the isolated glottic obstruction which seems more like the paradoxical vocal fold movement or VCD. One can, therefore, speculate that the glottic obstruction during exercise may be a protective laryngeal adductor response in the same way as paradoxical vocal fold movements are triggered by other agents like airborne irritants or gastroesophageal reflux [16]. The protective laryngeal adductor response is preserved during performance of voluntary voice and respiratory tasks such as forced inhalation [17]. Both stimulation with air puffs to the mucosa overlying the arytenoid cartilages and stimulation of mechanoreceptors at that localization have been found to elicit a response of laryngeal adductor muscles [18,19].

Subjects with glottic obstruction participating in the present study only had breathing problems triggered by exercise. Speech therapy with the aim of learning to relax the laryngeal muscles has traditionally been the treatment of choice for vocal cord dysfunction, regardless of trigger factor. Inspiratory muscle training is believed to strengthen the posterior cricoarytenoid muscles, which abducts the vocal cords. A larger laryngeal inlet reduces the airflow resistance, and inspiratory muscle training might, therefore, have an effect both on glottic and supraglottic structures. Overall, however, there have been no major studies evaluating treatment of glottic E-ILO. Based on this, all E-ILO positive subjects in our study, glottic as well as supraglottic sub-types, received the same information about breathing exercises. Whether, and how often, subjects performed these breathing exercises were unfortunately not questions asked in our follow-up questionnaire.

According to our experience, the majority of subjects diagnosed with E-ILO have an isolated supraglottic obstruction. In the combined cases it is sometimes difficult to decide which mechanism is primary, the supraglottic or the glottic obstruction, and therefore one must carefully consider who could benefit from surgery. Another reason not to operate without strong indications is that E-ILO often is diagnosed in young otherwise healthy persons and surgery always involves risks. Maybe changing to an interval sport instead of an endurance sport could be an alternative to surgery. However, in this context it must be understood and accepted that giving up sport activities is seldom an option among these highly motivated adolescents. In this particular age-group, sport activities can be important both in the context of competitions and to get good results, as well as serving a meaningful social function [20]. Motivation can

never be under-estimated. This study hereby raises a question. Even though we see significantly better follow-up results in surgically treated subjects, should surgery be widely recommended? We think it can only be offered in cases with severe supraglottic obstruction, diagnosed by CLE-test, and where there is no glottic component or the glottic component is assessed as being of subordinate importance. We also believe that very young persons, where the larynx is not yet fully grown, should not undergo surgery.

The breathing problems in the group tested negative may have different causes, which, of course, makes a direct comparison between them and E-ILO positive subjects difficult. However, it is interesting that half of those tested negative state that their lower physical activity level is caused by breathing problems. Among the E-ILO positive it is 3.5-times more likely that breathing difficulties is the reason for their decreased physical activity.

The presence of asthma and/or perennial allergy was also requested in our questionnaire. Before referral for a CLE-test, the subjects had been investigated for asthma by the referring doctor, who had referred due to a suspicion of a laryngeal cause of exercise induced problems rather than asthma. A weakness in the current study is that we only analysed the subjective data from the questionnaires, and not the original examination results which were incomplete and heterogeneous. Due to this, and to a small study population, we cannot draw any firm conclusions about differences between groups regarding asthma or allergy, even though higher proportions of these diagnoses were reported among subjects who tested negative in the E-ILO test. However, it does appear likely that the latter group comprises individuals who still suffer from different degrees of exercise-induced asthma.

Conclusion

This study supports that surgery is an effective treatment for severe, well-selected cases of supraglottic exercise-induced laryngeal obstruction. Conservatively treated subjects that still experienced breathing problems during exercise 1–3 years after diagnosis tended to have either adjusted their physical activity level or changed which sport they practiced.

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