



# VOICE CONDITION FOLLOWING SHORT-TERM ENDOTRACHEAL INTUBATION IN HEAD AND NECK SURGERY: STUDY PROTOCOL FOR CLINICAL TRIAL

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**SUMMARY** – Endotracheal intubation is an airway management procedure commonly performed under general anesthesia. It is linked with postoperative voice changes. The incidence and reasons of hoarseness and vocal cord injury are not very well investigated, especially after short-term anesthesia and intubation in head and neck surgery. The aim of the study is to identify the causes of voice changes after short endotracheal anesthesia in head and neck surgery. The study will include patients scheduled for head and neck surgery under general anesthesia with endotracheal intubation up to 3 hours. There will be 3 groups of patients, as follows: thyroid surgery, non-thyroid surgery, and control group undergoing surgery outside head and neck. Videostroboscopy will be recorded before and after surgery. Further diagnostic workup will include voice status; subjective voice self-analysis; perceptive and objective acoustic voice analysis at 4 time points (preoperatively, postoperative day 2, 2 weeks and 1 month after surgery). Endotracheal intubation is a safe method of airway management although it can temporarily alter a patient's voice quality. It is not known how much of this is the result of anesthesia, general condition of the patient, or surgery. This trial is expected to shed some light on this issue.

**Key words:** *Endotracheal intubation; General anesthesia; Head and neck surgery; Voice changes*

## Introduction

Disorders of phonation, swallowing and breathing are possible as a result of endotracheal intubation, regardless of the type of the surgery performed. These disorders are usually caused by injuries of the pharynx and/or larynx (mucosal laceration, hematoma, dislocation of the cricoarytenoid joint, etc.)<sup>1</sup>. The reasons for the occurrence of such disorders can be found in inap-

propriate choice of endotracheal tube, general condition of the patient, position of the head during surgery, demographic characteristic of the patient, as well as the type and duration of the operation<sup>2</sup>. While the consequences of prolonged intubation on the larynx and trachea, and consecutively on the breathing and phonation, have been well researched, there are only few studies conducted to identify the consequences of short-term intubation<sup>3,4</sup>. Also, it is well documented that short-term intubation can cause hoarseness and injury of the larynx<sup>4</sup>. There are very few studies of the repercussions of endotracheal intubation during head and neck surgery, in which the head of the patient is in a specific position, with often adaptation during the

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operation. Features of head and neck operations also are collisions of the surgeon and the anesthesiologist. Also, some head and neck operations, such as thyroid gland surgery, carry a risk of postoperative voice and swallowing disorder that is not related to endotracheal intubation but to the operation itself. Hoarseness can appear after thyroid gland operations in 16%–87% of patients, without evident laryngeal or recurrent laryngeal nerve injury<sup>5-7</sup>. Accurate etiology of hoarseness in these patients, which significantly disrupts the quality of life, has not been identified yet<sup>8</sup>. Therefore, it is essential to explore the impact of short-term endotracheal intubation during head and neck surgery on voice characteristics and to determine the extent to which changes in voice characteristics are caused by endotracheal intubation, surgical procedure itself, or demographic features of the patient.

## Materials and Methods

### *Study design*

A prospective cohort clinical trial will be conducted at the Department of Otolaryngology and Head and Neck Surgery, Phoniatic Reference Center, Zagreb University Hospital Center. Inclusion criteria for the study will be age between 18 and 70 years, normal preoperative voice status, and normal laryngeal status. All patients will be informed on the procedures to be performed and will sign informed consent form to participate in the research.

Exclusion criteria will be history of previous head and neck operation or radiotherapy and patients scheduled for head and neck operation that can alter acoustic characteristics of the voice (surgery of the nasal cavity, ear surgery, laryngeal surgery, jaw surgery). Patients with preoperatively diagnosed pathologic vocal cord findings (nodules, polyps, vocal cord paralysis), as well as patients with postoperative injuries of the vocal cords, recurrent and superior laryngeal nerve, patients with laryngopharyngeal reflux, and patients in whom postoperative evaluation of the voice cannot be performed due to uncooperativeness will also be excluded from the study.

All eligible patients will be divided into three groups, as follows: patients scheduled for thyroid gland surgery; patients scheduled for some other type of head and neck operation that does not fall to exclusion criteria (parotidectomy, extirpation of congenital neck

cyst, etc.); and control group including patients scheduled for operation other than the head and neck region. All operations will be performed by experienced operators with more than 100 annual procedures.

### *Anesthesiology protocol*

All included patients will be operated under general endotracheal anesthesia provided by skillful anesthesiologists with more than 250 general anesthesia procedures annually, or supervised by an airway expert. All patients will be intubated after induction with sufentanil, propofol and neuromuscular relaxation with rocuronium, with soft tip Rüsch® Cuffed Reinforced Endotracheal Tubes (ET). These wire-reinforced tubes feature smooth tip and high-volume, low-pressure cuffs. The size of the ET internal diameter (ID) is left to the anesthesiologist's choice. The choice between direct laryngoscopy with Macintosh blade and videolaryngoscopy is up to the anesthesia provider. Anesthesia will be maintained with inhalational anesthetic sevoflurane, with or without supplemental remifentanyl infusion. After neuromuscular reversion, all patients will be extubated in the operating room.

The following data will be obtained on every patient: age, sex, occupation, height, weight, body mass index, smoking/no smoking habits, previous diseases, regular therapy, duration of operation, size of the endotracheal tube/laryngeal mask used during operation, intubation technique, number of attempts during intubation, Mallampati score, and types of anesthetics used during operation.

### *Voice analysis*

In all patients, voice analysis will be performed 4 times, i.e., the day before surgery, on postoperative day 2 and postoperative day 14, and one month after the surgery. Videostroboscopy, objective, subjective and perceptive voice assessment will be performed on the first two occasions, and objective, subjective and perceptive voice assessment on the next two occasions (Table 1).

*Videostroboscopy (VS)* is the most widely used tool for vocal fold vibration evaluation and it is considered the gold standard in today's clinical practice. The VS images are obtained by reconstructing images within different phases of different vocal cord cycles due to frequency difference between phonation frequency and source of light frequency. Therefore, images are perceived as consecutive images in the same period. VS

Table 1. Time table of methods

	Before surgery	Postoperative day 2	2 weeks after surgery	1 month after surgery
Videostroboscopy	•	•		
Objective Voice Analysis = Acoustic Voice Analysis	•	•	•	•
Perceptive Voice Analysis = GRBAS score	•	•	•	•
Subjective Voice Self-analysis = Voice Handicap Index	•	•	•	•

enables evaluation of vocal fold amplitude, symmetry and vocal cycle phases during phonation<sup>9</sup>.

**Objective voice assessment** is performed *via* acoustic analysis of the voice. It will be performed in the acoustic laboratory of the Phoniatic Center using the LingWAVES SLP Suite Pro VPR (WEVOSYS medical technology GmbH, Germany). The sound signal will be collected using a microphone that is fixed at a distance of 30 centimeters from the mouth of the subject and placed at an angle of 45°. Then the recorded sound signal will be converted from analog sound waves to digital form using LingWaves software. Digital document will be stored on a computer (256MB RAM sound card, 500 GB free hard disk space) running Windows® 10.

### Voice Acoustic Analysis Protocol

In this study, three speech samples will be collected for each patient and 5 seconds of the middle part of the second phonation signal will be taken for analysis. Acoustic voice analysis shows the following data: fundamental frequency, intensity, *jitter*, *shimmer* and maximal phonation time.

Fundamental frequency is defined as the voice pitch and is measured in Hertz (Hz). Average voice pitch in women is 220-225 Hz, in men 100-150 Hz, and in children around 300 Hz<sup>2</sup>. Intensity is defined as the volume of the voice; it is measured in decibels (dB) and the average intensity is 60 dB. *Jitter* indicates perturbations of the vocal cord vibrations in the fundamental frequency; it is measured in percentages (%) and is considered regular in the range from 0 to 0.5%. *Shimmer* gives information on vibration perturbations in intensity, it is measured in percentages (%) and is

considered normal in the range from 0 to 5%. Maximal phonation time is measured in seconds (s) during habitual phonation<sup>12</sup>.

For perceptive voice assessment, we will use GRBAS scale. It is an auditive-perceptive scale which evaluates voice quality on several parameters: G - Grade, R - Roughness, B - Breathiness, A - Asthenia, and S - Strain. Each of the mentioned parameters is scored on a scale from 0 to 3, where 0 indicates no deviation, 1 indicates slight deviation, 2 moderate deviation, and 3 marked deviation from a normal voice. The reliability of the results on the GRBAS scale is dependent on the examiner and there can be significant variability among different examiners<sup>13</sup>. For subjective self-assessment of the voice, the Voice Handicap Index (VHI) will be used<sup>14</sup>. VHI consists of 30 questions that measure three factors: functional component (10 questions), emotional component (10 questions), and physical component (10 questions). Functional component contains statements that examine the impact of voice problems on daily activities; emotional component examines emotions related to voice disorders; and physical component consists of items about one's own perception of voice characteristics. The answers offered range from 0 to 4, where 0 represents the answer never and 4 the answer always. The scale has been translated into Croatian and represents a reliable measure of self-assessment of the impact of voice quality on the quality of life<sup>15</sup>. The voice status will collect all history and demographic data, as well as the patient's habits and voice status.

### Data analysis

Statistical analysis will include descriptive analysis and nonparametric Wilcoxon Signed Ranks Test. In all statistical tests, the level of statistical significance

will be set at 95% ( $p < 0.05$ ). While conducting the study, ethical principles and the Declaration of Helsinki principles will be respected. All personal data on the respondents will be stored and processed in electronic form and the project manager and his associates are obliged to fully comply with the prescribed procedures for protection of personal data. Respondents will be entered into our databases by the initials of their first and last names and using a special code. Their medical documentation will be reviewed only by the project manager and his associates, and the name of the subject will never be revealed to third parties.

## Discussion

According to the literature, appearance of hoarseness after short-term endotracheal intubation can occur in 14.4% to 50% of patients<sup>1,16,17</sup>. These data refer to short-term endotracheal intubation regardless of the type of surgery and part of the human body that was operated on<sup>18</sup>. Voice disorders are expressed in the early postoperative period, which is visible in deviation from normal parameters of acoustic analysis and perceptive and subjective voice analysis<sup>18</sup>. A study by Sørensen *et al.* showed a statistically significant increase in jitter and shimmer values 24–48 hours after surgery<sup>19</sup>. Similar results of jitter and shimmer values with increased VHI-30 values and a significant decrease in F0 values were found by Kayir *et al.*<sup>20</sup>. Voice disorders after thyroidectomy are present very often even in cases where there are no visible injuries to the laryngeal nerve, vocal cords or cricoarytenoid joint<sup>6,7</sup>. These disorders are associated with different factors; longer duration of surgery, larger volume of the operated thyroid gland, female gender and older age are associated with a higher frequency of hoarseness<sup>21–24</sup>. However, how much hoarseness after such operations is due solely to the influence of anesthesia (length of anesthesia, tube size, intubation technique), general condition of the patient (age, sex, comorbidity), and how much of the specifics of thyroid surgery (intense movement of the larynx, resection and stretching of the prelaryngeal musculature) is not known. Finding answer to that question was attempted by Sung *et al.*, who compared the results of voice analysis in patients who underwent thyroidectomy and patients who underwent parotidectomy<sup>6</sup>. They found that the voice symptom scores (VSS) were significantly higher

on postoperative day 1 in both groups and returned to preoperative levels 24 months after thyroidectomy and 1 week after surgery in parotidectomy group (control group). This is the only such study that we have, to the best of our knowledge, found. The fundamental shortcoming of that research was that self-assessment voice scores (VSS) were used and, as the authors stated themselves, that it was an unvalidated questionnaire. Patients who had pathologic values of acoustic analysis parameters preoperatively were also included in the study. There is no study that, like our planned study, included patients with different surgical operations with the intention of finding a link with the causes of hoarseness regardless of the localization of the operation, with emphasis on head and neck operations.

This is particularly important for understanding the origin of these disorders in head and neck operations, where the procedures and work of anesthesiologists and surgeons intersect ('shared airway'). It is also worth emphasizing the conclusion of Brodsky *et al.* meta-analysis of 21 studies and 6140 patients with post-intubation laryngeal injuries and swallowing disorders (pain, coughing, sore throat and hoarseness) that there are no uniform guidelines for assessing hoarseness after surgery and that hoarseness is not a good indicator of laryngeal injury<sup>17</sup>. Finally, postoperative hoarseness can significantly disturb the quality of life, especially for voice professionals whose professional work may be limited for a short or long time, with a danger that these consequences will remain permanent<sup>6</sup>. Therefore, it is important to design guidelines for preoperative assessment and postoperative monitoring of patients after endotracheal intubation, as well as guidelines for the inclusion of patients in speech therapy rehabilitation in case that hoarseness is present for a long period and affects the quality of life.

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## Sažetak

## STANJE GLASA NAKON KRATKOTRAJNE ENDOTRAHEALNE INTUBACIJE U KIRURGIJI GLAVE I VRATA: PROTOKOL ISTRAŽIVANJA ZA KLINIČKI POKUS

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Endotrahealna intubacija je dio rutinskog anesteziološkog postupka tijekom opće anestezije kojoj su svakodnevno podvrgnuti brojni bolesnici. Povezana je s poslijeoperacijskim promjenama glasa. Incidencija i točni razlozi promuklosti i ozljeda glasnica, pogotovo nakon kratkotrajnih anestezija i intubacija, još uvijek nisu razjašnjeni. Cilj ove studije je pronaći uzroke promjena glasa nakon kratke endotrahealne anestezije u operacijama glave i vrata. Ova prospektivna kohortna studija će uključiti bolesnike predviđene za operacije u području glave i vrata u općoj endotrahealnoj anesteziji do 3 sata. Predviđene su 3 skupine bolesnika: operacija štitnjače, operacija u području glave i vrata te kontrolna skupina s operacijom izvan ove regije. Svim uključenim bolesnicima snimit će se videostroboskopija prije i nakon operacije. Slijedi obrada glasa koja će uključiti glasovni status; subjektivnu samoprocjenu glasa; perceptivnu i objektivnu akustičku analizu glasa u 4 vremenske točke: prije operacije, 2. poslijeoperacijski dan, 14. poslijeoperacijski dan i mjesec nakon operacije. Endotrahealna intubacija je sigurna metoda zbrinjavanja dišnog puta, iako dovodi do kratkotrajne promjene kvalitete glasa bolesnika. Koliko su one posljedica isključivo utjecaja anestezije, općeg stanja bolesnika, a koliko samog operativnog zahvata nije poznato. Rezultati ove studije bi mogli ovo razjasniti.

*Ključne riječi: Endotrahealna intubacija; Opća anestezija; Kirurgija glave i vrata; Promjena glasa*