OBJECTIVE MORPHOMETRIC ANALYSIS OF DIFFERENT GLOTTIS ENLARGING PROCEDURES AND CLINICAL VALIDATION BY IMAGING, SPIROMETRIC ASSESSMENT AND PHONIATRIC PANEL

Ph.D. Thesis

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ABBREVIATIONS

BVCI	Bilateral Vocal Cord Immobility
BVCP	Bilateral Vocal Cord Palsy
EAAL	Endoscopic Abduction Arytenoid Lateropexy
VCL	Vocal Cord Laterofixation
SELP	Schobel's External Arytenoid Lateropexy
TC	Transverse Cordotomy
AE	Arytenoidectomy
cMAE	Calculated Medial Arytenoidectomy
PEF	Peak Exspiratory Flow
FEV1	Forced Exspiratory Volume in 1 sec
FVC	Forced Vital Capacity
PIF	Peak Ispiratory Flow
HNR	Harmony and Noise Rate
F_0	Pitch frequency

1. INTRODUCTION

In the treatment of bilateral vocal cord immobility (BVCI) it is a great surgical challenge to find the ideal balance between breathing and voicing. Since the mid 20th century there have been surgical innovations such as the tracheotomy, once done purely by open techniques to the common use of minimally invasive endoscopic techniques. Recently, there have been experimental trials to reanimate the neurologically impaired larynx by reinnervation procedures or laryngeal pacing. Additionally, endoscopic glottic aperture enlarging procedures can also be the basis for the treatment of BVCI. The surgical choice should depend on the patient's overall health and the personal voicing needs since the airway achieved is considered inversely proportional with the postoperative voice.

The efficacy of different glottis enlarging techniques cannot be easily compared clinically. Generally, only one procedure can be performed on one patient, and considering the variable anatomical factors and evaluation methods, clinical case series are often statistically insufficient. This results in difficulties in the creation of proper study groups for the meta-analysis.

By assessing the efficacy of different endoscopic procedures, each being performed on the same cadaver larynx, an easier objective comparison would be possible. The glottic area achieved is proportional with the breathing improvement, but voicing effects are a more complex question. One of the most predictive factors is the postoperative angle of the vocal cords at the anterior commissure. Conversely, *Isshiki* described the importance of the integrity, tension, and the mass in paralyzed vocal cord dynamics during phonosurgery. Additionally, studies in the last decades have revealed that vocal cord paralysis is not a static condition. Possible residual motion due to additional or residual innervations, reinnervation, and synkinesis might influence the postoperative voice, especially in larynges with otherwise intact structures.

In our clinic we designed cadaver morphometric studies to provide objective answers to these questions.

In the 100-year-old history of airway stenosis surgery several important works of Hungarian authors *(Rethi, Lichtenberger, Pytel*) are found. In Szeged we have been working in this field since the 1990s, we had several publications in prestigious journals. The

minimally invasive endoscopic arytenoid abduction lateropexy was introduced as a treatment of vocal cord impairment. Over 300 patients were successfully operated.

In previous works our team has already suggested an evaluation panel for the other important aspects of these surgeries, the phoniatric and spirometric outcomes. The efficacy of the procedure can be evaluated by these laryngeal function measuring tests, the pre- and postoperative conditions are easily comparable. Modern, non-invasive high resolution imaging procedures (Computer Tomography, Magnetic Resonance Imaging) may be useful tools for in vivo morphometric analyses.

I have been working in the Department of Otorhinology, Head and Neck Surgery, University of Szeged since 2001. I have joined to the 'airway stenosis surgical team' under the supervision of Professor *Czigner*, Professor *Jóri* and Professor *Rovó*. I took part in several operations of different types of stenosis. One of my main tasks was to perform the pre- and postoperative laryngeal functional examinations for measuring the airway improvement of these surgeries. Our clinic has been paticipated in the development of the Slicer 3D, which is an open source software permits analysis and three dimensional reconstruction of the CT and MRI scans. I have been the member of this group since 2009. This tool provides great opportunity to evaluate the effecacy of different airway stenosis surgical procedures.

2. AIM OF THE THESIS

- Cadaver morphometric studies were performed to compare the efficacy of different glottis enlarging procedures for the treatment of BVCI.
    - The evaluation of glottis enlargement.
    - Proposed phoniatric effect

- In our clinic the minimally invasive endoscopic arytenoid abduction lateropexy was introduced. In 'real patients' the efficacy of this method was measured, the pre- and postoperative status was evaluated.
    - Analysis of the laryngeal configuration. 3d reconstruction of postoperative CT scans.
    - Evaluation of the spirometric results
    - Evaluation of the phoniatrtic results

- Comparison of the results of cadaver and ‘real patients’ studies.

3. METHODS AND SUBJECTS

3.1. SURGICAL ANATOMICAL MORPHOMETRIC STUDIES – COMPARISON OF ENDOSCOPIC GLOTTIS ENLARGING TECHNIQUES ON CADAVER LARYNGES

One-hundred freshly excised cadaver larynges (50 male and 50 female) were analyzed. For a better view of the glottic area the epiglottis and the vestibular folds were removed. Larynges were inserted into a fixation device and secured with three screws along the cricoid cartilage avoiding deformation caused by the screws. The screw positions were always kept constant in each larynx. High-resolution digital photos were taken from a top view by Nikon D60 ® camera fixed onto a tripod. This made possible to take all photos from a constant perspective.

The effect of “simple” suture–based techniques was measured in 60 larynges (30 male and 30 female). First, the normal cadaveric position of the larynges was documented. Then four different suture lateralization maneuvers were performed one by one on the left side on each larynx **(Fig. 3)**. Suture placement was performed according to the techniques described in the literature by typical needle holders and suture materials.

3.1.1. Suture lateralization procedures

1. *Classic vocal cord laterofixation* (VCL-Suture1). The vocal cord is lateralized and fixed by a thread loop inserted at or just anterior to the vocal process. The suture loop was placed according to Lichtenberger’s endo-extralaryngeal concept, which allows for a more precise loop formation around the vocal process.
2. *Modified vocal cord laterofixation* (VCL-Suture2), in which a second suture was inserted anteriorly from the original position.
3. *Endoscopic arytenoid abduction lateropexy* (EAAL). The arytenoid cartilage was rocked into its abducted position and then a suture loop was placed round the vocal process.

These minimally destructive procedures (#'s 1-3) were performed on each larynx. They were taken in a quasi-random sequence (See #4 below for the exception) so that the prior surgical technique would not affect the results. The suture loops were knotted on the outer surface of the thyroid cartilage till maximal lateralization occurred.

4. *Schobel's trans-cervical lateralization procedure* (SELP) exposes the arytenoid body posteriorly. Then it is tilted and fixed laterally by 2-3 horizontal submucosal suture-loops to the posterior margin of thyroid cartilage.

3.1.2. Irreversible resection procedures

Because of the irreversibility of the subsequent procedures, two subgroups were created: the transverse cordectomy (TC) and the total arytenoidectomy (AE). The glottic area created was measured after each surgery on 20-20 cadaver larynges.

5. *Transverse cordectomy* (TC). A wedge-shaped defect was created by the removal of the middle third of the vocal cord till the thyroid cartilage.

6. *Arytenoidectomy procedures*

A. *Total Arytenoidectomy* (AE). In order to simplify the procedure and for the maximal efficacy, the left arytenoid was completely removed along with the surface mucosa.

B. C*alculated Medial Arytenoidectomy* (cMAE) according to *Crumley*.

The partial resection of arytenoid cartilage is presently considered a popular method. The images gained after total AE provided a simple calculation for their efficacy as well. Considering the anatomical structure of the crico-arytenoideal joint, only the real airway improvement was measured, which could be achieved by the removal of the medial obstructing part of the arytenoid cartilage.

3.1.3. Digital image analysis

3.1.3.1. Measurement of glottic enlargement

In our prior morphometric study the parameters describing the posterior commissure were analysed. A task-orientated modification was used. “Fuji” digital image analyzing software was used to measure the glottic configuration changes. First, the glottic area changed was measured on the lateralized side of the larynx from the midline.

3.1.3.2. Proposed phoniatric effect

According to Isshiki’s and Woodson’s suggestion the most important determining parameters were examined:

(1) *The angle* (A) at the anterior commissure between the lateralized vocal cord and the midline.

(2) *The length of vibrating part of the vocal cord* (L) is determined by the two fixation points, which are normally the anterior commissure and the vocal process. This value is proportional to the passive (e.g. not neuro-muscular) strain of the vocal cord. After SLP the vibration length is reduced to the anterior commissure and the closest lateralizing suture. In the case of AE and TC, the anterior fixation point remains unchanged; but the posterior fixation point changes to the attachment of remaining vocal cord at the thyroid cartilage. Theoretically, in case of cMAE, this latter point stays at the remnant of vocal process.

(3) *The maximal deviation* (D) of the free margin of the vibrating part from the line between the two fixating points.

(4) *Maximal deviation to length ratio* (D/L) provides a more precise comparison. The length and the deviation together determine the possible outcome, so their proportion is the normalization of deviation to the actual vibrating length of the vocal folds (e.g. the same deviation on a shorter vocal fold segment can cause a more chaotic vibrating pattern).

Statistical analysis was performed (pairwise comparisons; repeated measure ANOVA; Sidak adjustment for multiple comparisons) by SPSS 20.0.

3.2. ENDOSCOPIC ABDUCTION ARYTENOID LATEROPEXY – CLINICAL RESULTS

3.2.1. Selection of the patients

In our department since 1989 endoscopic abduction arytenoid lateropexy has been applied as the treatment of bilateral vocal cord immobility, more than 300 patients have been operated succesfully.

In this study ten patients, who underwent bilateral thyroidectomy because of malignant thyroid gland tumour in other surgical departments were chosen (eight women, two men, mean age 57,1 year). Each patient had postoperative bilateral vocal cord palsy without any preoperative hoarseness and/or dyspnoe. Eight patients had moderate or severe postoperative dyspnoe, two patients could not be extubated after thyroid surgery because of suffocation. The sudden onset of the breathing complaints required rapid intervention, the average time between the thyroid surgery and glottis enlarging procedure was 2,1 days (0-8 days). The lateralisation side was determined by the surgical chart describing the intraoperative thyroid surgery conditions, especially the possible injury of the inferior laryngeal nerve.

After EAAL the breathing of all patients improved significantly, none of them required any other airway maintenance.

To quantify the clinical results spirometric, phoniatric tests and postoperative CT examination were performed.

3.2.2. Analysis of the postoperative laryngeal configuration - 3D-CT reconstruction

Thyroid tumor patients, who required postoperative CT for oncologic staging, were selected. So unnecessary CT examinations with their radiation exposure could be avoided. The examination was taken in the postoperative 1^{st}-10^{th} month (mean 3,8 months).

The finest available CT scans were performed (0,4-2,5mm slice thickness). This resolution made a good three dimensional reconstruction of the glottic chink possible.

Slicer 3D open source software was used for the anatomic reconstruction of the glottic airway. The horizontal slices were applied for the segmentation. The optimal range of the Hounsfield Unit (HU) was between -130 to -1200. The range of interest (ROI) was signed by the upper and the lower borders of the glottis. These were 2 to 11 slices depended on the thickness of the slices. The volume of the ROI was defined in cubic millimeters.

The same parameters were analyzed as in the cadaver study: glottic area, angle of the anterior commissure, maximal deviation from the midline.

First, the midline of the larynx was marked, it was the line between the anterior commissure and the inner surface of the crycoid cartilage. The midline divided the unoperated

and the lateralised side of the larynx. The *glottic area* with air density (the glottic air shadow) was defined automatically by the programme. It was settled on each assessed slice. The 'area slices' were summed resulted in *glottic volume* of both unoperated and lateralised halves. Then the mean area was calculated; it was the quotient of the glottic volume and the hight of the glottis. (The glottic hight = slide thickness x number of slides).

Maximal deviation (in millimeters) is the distance between the midline and the most lateral point of the glottis surface.

Angle of the anterior commissure: the lateral arm of the angle was the lateral border of the glottic airway, the medial arm was the midline.

Bilateral analysis was performed, the operated and the untreated half glottis could be evaluated, which is similar to pre- and postoperative status.

Statistical analysis was performed (pairwise comparisons; repeated measure ANOVA; Sidak adjustment for multiple comparisons) by SPSS 20.0.

3.2.3. Evaluation of spirometric results

The spirometric examination is highly dependent on patient cooperation and effort (25, 59), and spirometry can only be used on patients who are able to understand and follow instructions. The maneuver requires maximal effort from the patient and it takes time to perform a quality spirometry. It is essential the procedure carefully and clearly to explaine and to actively coach and motivate the patient to perform maximally.

The performance of spirometry while seated upright in a chair is preferable to standing as this is the most stable position should the patient experience dizziness during the test. The key steps are to urge the patient to breathe in fully (the lungs must be absolutely full, seal the lips around the mouthpiece and immediately blast the air out as fast and as far as possible until the lungs are completely empty. Then breathe in fully again as fast and as far as possible. The test is repeated until three acceptable results are obtained. The best results, the highest values were chosen.

The peak inspiratory flow (PIF) was measured in all patients. The preoperative evaluations – if possible - was made on the day before the operation. The postoperative measures were established on the first and the tenth postoperative weeks. Thor Soft spirometer was used in the study.

Statistical analysis was performed (pairwise comparisons; repeated measure ANOVA; Sidak adjustment for multiple comparisons) by SPSS 20.0.

3.2.4. Evaluation of the phoniatric results

The recording of the patients' voice was analysed by Praat software (Boersma and Weenink, 2009) and the Tascam US 122 MkII PC audio interface (TEAC America, Inc. 1834 Gage Road Montebello, CA 90640). The preoperative voice – if possible - was recorded on the day before the operation. The postoperative recording was in the first month (early postoperative recording) and in the third postoperative month (late postoperative recording).

For the record the patients had to say a sustained vowel [:a]. In our clinic Standard Voice Panel was suggested, containing the following objective and subjective tests (22):

- *MPT*: maximal phonation time, ideal at the range of 15-20 sec.
- *HNR*: harmonic-to-noise ratio, acceptable if more than 12 dB
- *Jitter*: cycle-to-cycle variation of fundamental frequency, i.e. the average absolute difference between consecutive periods contributes to the perception of a rough or harsh voice quality. acceptable at the human voice if less than 1,04%
- *Shimmer*: the variability of the peak-to-peak amplitude in decibels, i.e. the average absolute base-10 logarithm of the difference between the amplitudes of consecutive periods, acceptable if less than 3,81%
- *Pitch* (F_0) : base frequency, in adult male 128Hz, female 225 Hz

Further examinations were the *VHI* and the *VQL questionnaries*.

Statistical analysis was performed (pairwise comparisons; repeated measure ANOVA; Sidak adjustment for multiple comparisons) by SPSS 20.0.

3.3. COMPARISON OF THE RESULTS OF CADAVER AND 'REAL PATIENTS' STUDIES

Finally, the results of the cadaver morphometric study and the CT assessment were compared. First, ten cadaver larynges similar to the ten real patients' organs (gender, age, length of the glottis) were chosen. The cadaver and lateralised positions were compared to the unoperated and the operated glottic halves. The glottic volume, the angle of anterior commissure and maximal deviation were analyzed.

4. RESULTS

4.1. SURGICAL ANATOMICAL MORPHOMETRIC STUDIES – COMPARISON OF ENDOSCOPIC GLOTTIS ENLARGING TECHNIQUES ON CADAVER LARYNGES

4.1.1. Glottis enlargement

All SLP provided larger glottic area compared to cadaveric position. However, a significant enlargement (P<0,05) was found with EAAL, SELP and AE. At the glottic level, AE provided the largest gap; but considering the anatomy of the cricoarytenoid joint, the large part of the improvement is located on the cricoid plate on the lower facet of the joint. Therefore, the real improvement was effectively the same as achieved by cMAE. There was no significant difference comparing CP, VCLs, TC, and cMAE. The arytenoid abduction methods produced the largest area increases ($p<0.05$). EAAL was found to be a bit more effective than SELP. This was thought to be due to the more effective rotation of the arytenoid but the difference was not statistically significant.

4.1.2. Phoniatric parameters

All suture lateralizing procedures significantly increased the anterior glottic commissure's angle; however, TC and AE did not significantly change it ($p<0,05$).

The largest angle, the worst configuration from a voicing perspective, was found after VCL-Suture2. SELP provided a smaller angle change than EAAL due to the slightly more medial vocal process ($p<0,05$).

The length of the vibrating cord: The VCL-Suture2 and TC significantly shortened the vocal cord length. VCL-Suture1 and AE caused insignificant changes. The vocal cord length was significantly greater, higher in tension, after SELP and EAAL.

Unfavorable curving of the altered cord resulted from the VCLs, TC, and AE. This curving was negligible after EAAL and SELP. AE caused the maximal deviation (from straightness) in this series. Considering D/L, SELP and EAAL were the most advantageous ($p<0.05$).

4.2. ENDOSCOPIC ABDUCTION ARYTENOID LATEROPEXY – CLINICAL RESULTS

4.2.1. Analysis of the postoperative laryngeal configuration - 3D-CT reconstruction

All examined parameters of the operated ’lateralized half’ glottis was found significantly larger.

4.2.2. Evaluation of spirometric results

Because of severe dyspnoe or intubated status of the patients the preoperative spirometric examination could be performed in six out of ten patients. All the ten persons participated in the postoperative spirometric tests.

Significant PIF improvement was found in all cases after EAAL, and the late values were even better.

4.2.3. Evaluation of the phoniatric results

Similar to spirometry the phoniatric evaluation could be done only on six patients preoperatively.

After the intervention Jitter and HNR values were wrecked in all cases in the early postoperative period. But the late postoperative values were even better than the preoperative ones. Shimmer and MPT values improved immediately. The pitch frequency (F_0) increased HNR and F_0 were in the normal range.

Subjective questionnaires also presented better voice quality and the satisfaction of patients. According to their opinion their voice changed from ’severe impairment’ to acceptable, almost normal condition.

4.3. COMPARISON OF THE RESULTS OF CADAVER AND ‘REAL PATIENTS’ STUDIES

All of the compared parameters were similar, no significant difference was found between the two groups.

5. DISCUSSION

5.1. SURGICAL ANATOMICAL MORPHOMETRIC STUDIES – COMPARISON OF ENDOSCOPIC GLOTTIS ENLARGING TECHNIQUES ON CADAVER LARYNGES

The measurement of the efficacy of glottis enlarging procedures is a challenging task because several factors influence any evaluation. These include the patients' satisfaction, their occupation, and activity level, etc. The most important factor to the clinician is doubtlessly the patient's breathing and phonation following the interventions.

The ability to surmise the effect of these surgical options on breathing is easier, because it can be described by the change of glottic cross-section area. A difficult, complex morphometric study on shock frozen cadaver larynges compared the resection of the vocal cord and the removal of arytenoid cartilage in this regard. Our study is based on the assessment of the airway effect of these operations determined by a digital image analyzing method, which is more reliable, in our opinion to compare large series of different methods. This has proved that methods using physiologic arytenoid abduction (EAAL; SELP) are likely more effective in improving the airway. Considering the laryngeal anatomy, the cricoid arch is located in a more distal position than the posterior surface of the cricoid lamina, which holds the arytenoid cartilages. This means that at the level of the glottis, resection of the vocal cord markedly increases the glottic airway area. However, in the case of arytenoidectomy, only a part of the arytenoid cartilage is located over the cricoid lumen, so only the removal of the protruding part (similar to medial arytenoidectomy) is really effective in airway widening.

Vocal cord lateralization techniques are effective in widening the airway. The insertion of a second lateralizing suture does not add significant benefit, though it may decrease the vocal cord's medialization tendency over time. This is a surgical concept rather than a direct result of this study. Having two sutures pulling the vocal cord over makes it less likely that either will cut into the tissue, the so-called "cheese wire" effect. The main limitation is that the arytenoids effectively remain in the medial position and therefore partially block the airway lumen above the cricoid. The vector of pulling that the sutures generate differs significantly from natural arytenoid abduction. Therefore, the arytenoid rotation that results is negligible. This also offers an explanation as to why the sutures intraoperatively tended to slip onto the membranous vocal cord even if placed directly onto the vocal process**.** Surprisingly the above mentioned methods do not result in significant

airway area improvement compared to the cadaver position (CP), but it must be accepted that CP is generally more lateral compared to the paramedian position observed after recurrent laryngeal nerve palsy (RLNP). However, in both cases the airway improvement values vary widely and surgery for RLNP is often indicated to improve the airway when it is a bilateral palsy, a life threatening situation.

Arytenoid abduction procedures open and fix the larynx simulating the physiological arytenoid abduction, as described by *Wang*. The vocal cord unit including the arytenoid, the vocal process *and* the vocal cord are not only lateralized but elevated approximately 1-2 mm cranially above the Rima Glottidis (the axial plane of the vocal cord rim). The vocal cord is pulled not only laterally but upward toward the Sinus of Morgagni, while the thyroarytenoid muscle gets passively longer and thinner, parallel with the inner surface of the thyroid cartilage. Thus, by this simple maneuver the whole arytenoid and practically the whole vocal cord are removed from the airway lumen above the cricoid. Therefore, these methods provide not only the largest improvement in the horizontal plane, as could be measured in this study, but this vertical vocal cord repositioning gives an additional enlargement of the airway compared to the other procedures. This result is consistent with the excellent spirometry results in multiple clinical studies.

The estimation of the voice impact of this surgery is more challenging because it is influenced by many passive and active factors. Isshiki described the length, the elasticity, and the mass of the vocal cord as the outcome-determining factors during phonosurgery, which can be justified by physical principles as well. A paralyzed vocal cord subjected to surgery-related scarring, such as in cordotomy and cordectomy operations, can produce an even more chaotic vibratory pattern which deteriorates the already abnormal voice. Therefore, it is proposed that the preservation of the vocal cord’s structural integrity is beneficial for postoperative voice production. These observations are well-known in the phonosurgery literature. AE, TC, and VCLs are evidently disadvantageous from this perspective. Based on this concept, the vocal cord length and angle change is found to be the smallest after the resection procedures because the anterior vocal cord segment is left in its original position. As the vocal fold heals, the scar might pull it laterally and posteriorly, increasing the angle. This may indicate that these procedures would impact the voice less. However, this is not the case because they more adversely affect the voice secondary to the loss of cord straightness and vibratory substance in contrast to cMAE, SELP, and EAAL. These three techniques produce a significantly larger anterior commissure angle and retain a natural vocal cord tension and straightness and therefore may support the voice quality better than the rest even in the case of

a completely paralyzed larynx. The VCLs produced the poorest parameters in regard to voice potential. The resulting cord is most curved (of the cord procedures not involving tissue resection) and the vibratory surface is neutralized by the effect of the sutures themselves (particularly VCL-2).

The standard endoscopic procedures designed for static vocal cord paralysis treatment are directed only towards the above-mentioned "passive" factors. The voice is inversely diminished in proportion with the airway improvement. The "active" components, however, which may occur after the recurrent nerve is injured, may effect the postoperative voice positively by maintaining tone or adversely by synkinesis. Anatomic studies prove that the ratio of adduction and abduction fibers in the recurrent nerve is approximately 4:1. This might explain Woodson's observation about a preferential adduction reinnervation after the cut of recurrent nerve in an animal study. Publications bring up a possible accessory parallel adduction innervation via the interior branch of superior laryngeal nerve to the inter-arytenoid muscles. The 'communicating nerve' (between the superior and inferior laryngeal nerves), which can be identified in 50% of the population, may also provide a direct innervation to the TA muscle.

In clinical practice, adduction reinnervation recovery can also be observed. This entity can be detected generally after some months following arytenoid adduction procedures where the above-mentioned neural framework and muscular structures remain largely intact. The abducted position of the lateralized arytenoid cartilage provides not only the best airway improvement but also room for adduction beyond the midline for the contralateral side during phonation. Sine there is a straight and passively tensed vocal cord on the operated side, *active* adduction with improved closure and phonation can occur this way. The other tested procedures (the TC and the AE) leave the arytenoids in their original paralyzed position and intrinsically injure the true cords, and thus cannot benefit from these phenomena.

5.2. ENDOSCOPIC ABDUCTION ARYTENOID LATEROPEXY – CLINICAL RESULTS

5.2.1. Analysis of the postoperative laryngeal condfiguration - 3D-CT reconstruction

According to the cadaver morphometric studies endoscopic arytenoid abduction lateropexy proved to be the most effective suture lateralizing procedure. Are these good results reproducible in real patients?

The development of the modern imaging technology provides a great opportunity for non-invasive morphometric measurements. During conventional computer tomography the detector and X-ray tube unit are rotated round the fixed examination table. The modern helical CT enables quicker image processing, because the examination table is moved through the continuous radiation source, thus large number of slices can be made during one breathhold. It is advantageous especially in the diagnosis of the airways, because the artefacts resulting from respiratory movements can be ruled out. The total length of the trachea can be scanned within 30-50 sec. The advanced multislice CT system is aquipped with multiple parallel detectors to obtain even thinner slices. The high resolution and the less than 1 mm thickness of slices make precise analysis of even small organs possible. For the correct marking out the maximal deviation of the vocal procces the labelling of the arytenoid cartilage is required. The density of the arytenoid cartilages and neighboring soft tissues are almost the same or equal. According to *Bakhshaee* et al the acceptable arytenoid recontruction needs plenty of postcorrections and very high definition CT scans, 0.6-1 mm slice thickness.

The evaluation of the airways in early childhood is a great challenge. *Yunus* applied helical computed tomography 2-D and 3-D images, and virtual endoscopy in the evaluation of airway disease in neonates, infants and children. The accuracy of virtual endoscopy and 3D reconstruction was 98%, the classic 2D helical CT imaging provided 86%. He concluded that these methods could replace conventional endoscopy in the assessment of airway disease without any additional risk. *Burke* found that this method was suitable for analyzing fixed airway lesions, but it seemed to be less useful in case of dynamic, functional stenoses.

Unfortunatelly, according to our experiences feasible high resolution CT imaging is not generally available in our country. It was really hard to find even ten appropriate quality CT scans for optimal three-dimensional processing.

For the assessment postoperative CT scans were applied. The images were feasible for the reconstruction of the glottic airway because of the high difference in density of laryngeal tissues and air; glottic air shadow could be easily labelled in Hounsfield Unit. By choosing the appropriate range of density the three-dimensional model of the airway could be visualized. The airway could be figured in real size from every different views, so precise morphometric measurements were possible. All the parameters we applied in surgical anatomical cadaver study could be analysed also in real patients.

5.2.2. Evaluation of spirometric results

The lung function tests have become an indispensable tool for the clinical evaluation of respiratory health and disease since the 1970s. It plays an essential role in the diagnosis and management of respiratory diseases, especially asthma and chronic obstructive pulmonary disease (COPD).

Spirometry may be applied also in cases of glottic and subglotto-tracheal stenoses, in which the cross-section diameter of the larynx and/or trachea is decreased leading to inspiratory dyspnea. *Kashima* and *Cantarella* proved that inspiratory flows were significantly reduced, whereas with the exception of PEF, the expiratory flows were in the normal range. *Dursun* found FEV1, FEV1/FVC and PEF values significantly reduced. According to *Vössing* Peak expiratory flow was the most sensitive parameter, it reacted earlier than did peak inspiratory flow and seemed to be the most reliable parameter for detecting an extrathoracic stenosis.

In our previous work the changes of the spirometric indices were analyzed in different grades of artificial stenoses. They did not change too much if 25% or 50% airway stenosis was applied. But the 75% stenosis significantly decreased the values. PIF and PEF were found to be the most sensitive their values decreased about 50%. Peak inspiratory flow (PIF) was found to be the most reliable.

This simple spirometric test can be easily performed before and after the operation, it is useful for monitoring the resistance of the upper airways. In our patients an immediate significant PIF value improvement was detected after the procedure and the late results were often even better. This could be explained by the diminishing of the postoperative laryngeal edema and the advanced overall physical condition of patients.

5.2.3. Evaluation of the phoniatric results

The pathophysiology of the vocal cord paralysis is not completely understood despite the numerous meticulous animal and human studies. According to the literature the intraoperative stretching, thermal damage are the main causes of laryngeal function degeneration during thyroid surgery. Later some kind of reinnervation can often be observed, which generally ranges from the complete or almost complete recovery of the vocal cords to

poorer outcomes with different types of synkinesises or total complete permanent paralyses at worst.

In his thesis *Smehák* analyzed the postoperative voice of groups of patients with different degree of regeneration. In cases of complete or almost complete regeneration the voice became normal, but, in case of total permanent paralysis it was much worse.

Although in the literature the transverse cordotomy is considered to be one of the most voice preserving intervention, a significant postoperative voice deterioration can be expected compared to the normal voicing. According to *Harnisch et al* and *Dursun et al* the early postoperative phoniatric outcomes are deteriorated, but they become later better, but the parameters do not reach the normal range. Our EAAL results were almost similar, the 'aperiodicity' values (Jitter, Shimmer) were a bit better. According to our opinion this proved that EAAL provided tensed and straightened vocal cords and despite their more lateral position a more favorable situation for phonation can be ensured than the preoperative medial, but flaccid condition.

In our study Standard Voice Panel suggested by *Smehák* was a useful tool for the evaluation of our patients' overall voice quality. However the examined patients could have been divided into the non-regeneration group, their postoperative voice became better, socially acceptable.

5.3. COMPARISON OF THE RESULTS OF CADAVER AND 'REAL PATIENTS' STUDIES

The cadaver morphometric studies unambiguously proved that the most beneficial glottic configuration could be created by EAAL.

The 'real patients' study showed that in most cases the same results could be achieved as well. In some cases the postoperative endoscopy or imaging revealed that the suture loop was not placed perfectly round the vocal process, it slipped into a less favorable position, to the free edge of the the vocal cord (2/10 patients).

According to our opinion there are two 'key factors' which could improve the efficacy. First, it is really important for the surgeon during his 'learning curve' to perform this procedure on several cadaver larynges to understand the main concept of the method. Second, the precise suture positioning is really important. In further studies the size and shape of ETGI device has been optimalized to different anatomical conditions; special infant, male and

female thread guide instruments have been designed. The more precise intralaryngeal maneuverability of the device may make more precise suture insertion possible, which might improve the postoperative results.

6. CONCLUSIONS AND NEW RESULTS

6.1. SURGICAL ANATOMICAL MORPHOMETRIC STUDIES – COMPARISON OF ENDOSCOPIC GLOTTIS ENLARGING TECHNIQUES ON CADAVER LARYNGES

This study demonstrates that the factors that impact the quality of life, such as voice potential and breathing comfort; fundamentally depend on the chosen method to treat the airway deficit. The outcome also depends on the post-surgical healing from the paralytic process, the multiple surgical modifications; something a cadaver study cannot address. While the TC and MAE may be technically easier and might provide acceptable voice results, it only produces a moderate airway improvement compared to those procedures, which utilize the physiological abduction of the arytenoid cartilage. The voice after SELP and EAAL would be worse in a complete BVCP; but if adduction recovery occurs, the voice might improve. Consistent with this the absence of the destructive basis to these procedures their application is considerable in potentially reversible BVCI-s as well.

6.2. ENDOSCOPIC ABDUCTION ARYTENOID LATEROPEXY – CLINICAL RESULTS

Analysis of postoperative high resolution CT scans proved the efficacy of EAAL, significant glottic area impovement was found.

Spirometry, objective and subjective phoniatric tests showed an improved postoperative condition as well. The postoperative voice became acceptable, the physical endurance improved, which meant that both main functions of the larynx, breathing and phonation could be preserved. The patients became satisfied with their condition.

6.3. COMPARISON OF THE RESULTS OF CADAVER AND ‘REAL PATIENTS’ STUDIES

Although the number of participants were too low for a precise statistical evaluation, all examined parameters of the cadaver and the ’real patients’ studies were similar, showed high level of parity.

EAAL provided as favorable results in ’real patients’ as on cadaver larynges. With the newly designed ETGI device the same precise suture positioning can be achieved in vivo, in real patients as on cadaver larynges.

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PUBLICATIONS related to the PhD Thesis

I. ***Szakács L***, Sztanó B, Matievics V, Bere Z, Bach A, Castellanos PF, Rovó L.
A comparison between transoral glottis-widening techniques for bilateral vocal fold immobility.
Laryngoscope. 2015 Jun 8. [Epub ahead of print]

II. Sztanó B, ***Szakács L***, Madani S, Tóth F, Bere Z, Castellanos PF, Rovó L
Comparison of endoscopic techniques designed for posterior glottic stenosis--a cadaver morphometric study.
Laryngoscope. 2014 Mar;124(3):705-10