SURGICAL FUNCTION SPARING PROTOCOLS IN THE MANAGEMENT OF INTERMEDIATED-ADVANCED LARYNGEAL CANCER

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For the intermediate-advanced stages, demolitive surgery provides a better control of disease if compared with chemoradiotherapy, but it not preserves larynx function. Supracricoid partial laryngectomies (SCPLs) have been described as a function-sparing surgery for intermediate/advanced laryngeal cancer without large sub-glottic extension while supratracheal partial laryngectomies (STPLs) are aimed at functional management of this latter category of patients. The study focuses on the oncologic results in pT3 (442, 79.6%) and selected pT4a (113, 20.3%) glottic (506, 91.2%) and supraglottic (49, 8.8%) cancers, undergoing open partial laryngectomies (SCPLs and STPLs). All patients, not requiring an upfront total laryngectomy, were also studied to assess laryngeal function preservation and to report the complications and late sequelae after surgery.

Methods Case series with medical record review, analyzing the outcomes of a large patient cohort [n=555 patients with laryngeal squamous cell carcinoma, 510 males and 45 females, aged between 16 and 83 yrs, average 59.9 yrs (sd 9.4); 459 (82.7%) previously untreated and 96 (17.3%) treated pts, 32.5% aged 65 yrs or over]. All patients underwent SCPL (454, 81.8 %) or STPL (101, 18.1%).

Results at 3 and 5 years, the disease-free survival rates were 87.7%, and 84.2%; overall survival rates were 89.8%, and 86.4%; locoregional control rates were 88.5%, and 86.3% respectively. Aspiration pneumonia (52, 9.3 %) and laryngeal soft tissue stenosis (43, 7.7 %) were the most common complication and late sequelae observed. The 3 and 5 years laryngeal function preservation rates (no tracheostomy, no naso-gastric tube, no gastrostomy, no total laryngectomy, intelligible voice) were 93.1% and 90.9%. In the present series, the proportion of patients subjected to total laryngectomy for either functional or oncological purposes, was significantly low (35, 6.3 %). Furthermore clinical, radiological, surgical and pathological data were reviewed and the glottic tumors were accordingly divided in 5 pT3 subtypes and 2 pT4a subtypes: statistically significant differences were found only for glottic pT3 vs pT4a in terms of 3 years disease free survival, loco-regional control and laryngeal function preservation (91.2%, 91.8%, 97.0% vs 74.2%, 75.0%,88.3%-- p<0.001). No statistically significant differences were found between pT3 subtypes.

Conclusions Surgical function sparing protocols for selected glottic and supraglottic intermediate (pT3) and also advanced (pT4a) laryngeal cancer allows excellent oncologic and functional results. Taking into account the need of a good selection of patients, the choice of surgical function sparing protocols vs chemo-radiation protocols can be considered competitive not only in prognostic terms, but also in terms of functional results such as reduction in the number of total laryngectomies.
OBJECTIVE EVALUATION CRITERIA FOR CHROMOSOME INSTABILITY DETECTION BY FISH TO PREDICT MALIGNANT PROGRESSION IN PREMALIGNANT LARYNGEAL LESIONS

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Objective: A dilemma in the diagnosis of lesions of the head and neck mucosa is to decide which precursor lesions will progress into squamous cell carcinoma (HNSCC). Several studies have shown that chromosome instability (CI), defined as the presence of chromosomal imbalances and/or polyploidization for chromosomes 1 and 7, might help to predict the patient’s risk for progression. In these studies different evaluation criteria for the assessment of chromosome copy number alterations were used to discriminate between progressive and non-progressive lesions. The aim of this study was to develop objective evaluation criteria for this purpose.

Material and method: We performed Fluorescence In Situ Hybridization (FISH) for chromosome 1 and 7 centromeres on 35 formalin fixed, 4 µm-thick, paraffin embedded normal head and neck mucosa tissue samples and on a test-population consisting of 36 patients who had undergone laryngeal biopsies which revealed a hyperplastic or dysplastic lesion. Patients with lesions containing severe dysplasia or carcinoma in situ (CIS) were excluded. Follow-up data were collected from patient’s records and progression was documented. Copy numbers of chromosomes 1 and 7 were counted in 100 nuclei to determine 7/1 ratios in both normal cases and patients (with and without progression) in order to define a reliable, objective cut-off value for high-risk lesions, which will progress to HNSCC.

Results: The normal control group had a mean ratio of 0.97 (s.d. 0.05, range 0.84-1.07). Based on this range \( + 3 \times \text{s.d.} \) a chromosome 7/1 ratio of <0.82 or >1.12 could be considered as chromosome instable. In the patient group the mean ratio was 1.0 (s.d. 0.2, range 0.6-1.6). A sensitivity/specificity analysis was performed with as predictor the distance of the 7/1 ratio to 1. A ROC curve which represents the relation between sensitivity and specificity of the model was obtained. The ROC curve showed an area under the curve (AUC) of 0.89 (s.e. 0.047) with the ideal sensitivity/specificity trade-off at 0.8 for both, corresponding with a cut-off value of 0.16 for the distance to 1 (ratio <0.84 or >1.16). However, this ideal cut-off value may differ from the expected values based on the data from the normal control population, which may be explained by patient-related factors and others such as thickness of the tissue samples. Validation of these results on an independent patient-set remains required.

Conclusion: CI detection by ratio assessment of chromosomes 7/1 copy numbers provides an additional objective diagnostic tool for application in the prediction of malignant progression of premalignant laryngeal lesions.

References:


Diagonal segments are produced by ties.
Objective Supracricoid laryngectomy with Cricohyoidoepiglotto-pexy (SCL-CHEP) is a reliable procedure for laryngeal preservation. Due to the limited anatomy of the larynx, close surgical margins are often inevitable. We perform intraoperative margin studies in all procedures but local recurrences do occur. In this study, we conducted a thorough clinicopathologic analysis of local recurrence in SCL-CHEP patients.

Patients and Methods Between 1997 and 2013, 100 patients with laryngeal cancers received SCL-CHEP at our institute, a tertiary referral center and university teaching hospital. In all procedures, margin study was conducted by histopathologically examining surrounding mucosal strips between the resected specimen and the residual larynx using frozen sections. Margin study influenced the intraoperative decision to convert from SCL-CHEP to total laryngectomy (TL) in two instances, and these patients were not included in the 100 patients. The incidence, pathogenesis, management, and prognosis of the local recurrence were investigated.

Results Among the 100 patients, local recurrence was recognized in six (6%). All recurred patients were initially staged as T3 or T4; only one had received radiation therapy previously. Recurrences were identified at the submucosal region of the remaining ipsilateral arytenoid in five and at the ipsilateral infraglottis in one patient. Interval between SCL-CHEP and recurrences ranged from four to 60 months (average 23 months). Five patients were salvaged by completion TL except one, who refused to receive further treatment.

Conclusions Local recurrence was identified in six (6%) of 100 laryngeal cancer patients operated with SCL-CHEP over the past 16 years. All except one was successfully salvaged by completion TL. Ipsilateral arytenoid and infraglottis were the recurrence sites; the clinical symptoms for recurrence were often subtle and insignificant. Close and underestimated margins were the most common pathogenesis. Extra precaution must be paid when applying SCL-CHEP to the patients with advanced stage lesions.
RETROSPECTIVE ANALYSIS OF FACTORS INFLUENCING ONCOLOGICAL OUTCOME IN 595 PATIENTS WITH EARLY-INTERMEDIATE GLOTTIC CANCER TREATED BY TRANSORAL LASER MICROSEGURGERY (TLM)

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Objective: To assess the oncological results in terms of disease free survival, overall survival, and organ preservation in early-intermediate glottic cancer treated by transoral laser microsurgery (TLM).

Design: Retrospective mono institutional study.

Setting: Tertiary referral center.

Patients: A total of 595 patients with untreated cTis, cT1a/b, cT2, and selected T3 cN0 glottic cancer; no contraindications to general anesthesia; and the ability to give informed consent.

Interventions: European Laryngological Society laser cordectomy patients with negative margins (1 mm) were followed, patients with close margins (1 mm) or 1 positive margin (tumor on margin) had second-look TLM, and patients with more than 1 positive margin, not suitable for further TLM had postoperative radiotherapy. Type I-III cordectomies were performed in 72.5% of cases (432/595 pts), while in 163/595 patients (27.5%) type IV, V or VI cordectomy was performed. Postoperative radiotherapy or radiochemotherapy was administered to 52 patients (8.7%).

Main Outcome Measures: Five-year disease-free survival, 5-year overall survival, and organ preservation rate.

Results: A single (TLM) procedure was performed in 82% of cases. A second-look TLM was performed in (103/595 patients (17%). The pathological staging revealed pTis in 60, pT1 in 317, pT2 in 90, pT3 in 34 and PT0 in 91 cases. Median follow-up was 62 months. Sixty one (10%) patients experienced local recurrence and 4 patients regional recurrence. A second laryngeal tumor was discovered in 11 (1.8%) patients. Five year relapse-free survival, overall survival were, respectively, 80.1% and 90.9%. The larynx was preserved in 96,6% of cases.

Conclusions: Our experience shows the TLM to be a mature approach for early-intermediate glottis cancer. Positive margin and paraglottic space involvement negatively influence DFS and organ preservation rate.
PROGNOSTIC FACTOR OF VOCAL CORD MOBILITY IN 148 STAGE II SQUAMOUS CELL CARCINOMAS OF THE GLOTTIS

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Background: A recent meta-analysis pooling 7600 patients (Higgins, J Otolaryngol Head Neck Surg, 38:6, 603-12, 2009) found no difference in local control and larynx preservation between exclusive radiotherapy and transoral laser surgery in early-stage squamous cell carcinoma of glottis. However stages II (T2N0) include neoplasms selected by 2 different criteria: (1) supraglottic and/or subglottic extension and (2) impairment of the vocal cord mobility. We retrospectively analyzed 148 patients treated for a T2N0 carcinoma of the glottis, and we described different local behaviors, survival prognostic and suggested treatment strategies.

Material and Methods: Between 2001 and 2012 we treated 107 patients with glottis carcinoma with supraglottic and/or subglottic extension, and 41 patients with glottis carcinoma with impaired vocal cord mobility. First line treatment was surgery (n=72), exclusive radiotherapy (n=42), and laryngeal preservation protocol (n=34) by chemoradiotherapy (n=24), or by induction chemotherapy first (n=10) followed by radiotherapy (n=6), chemoradiotherapy (n=2) or surgery (n=2). The statistical analyses were performed using univariate Kaplan-Meier model with log-rank tests for curves comparisons.

Results: At 5 years the global OS rate was 82.3% and the global DFS rate was 68.3%. The only local extension factors associated with modification of both OS and DFS were epiglottis and posterior commissure. However, the vocal cord mobility at diagnosis appeared to be a major prognostic factor for both OS and DFS. When looking at the treatments, the survivals were better when first treatment was surgery. When distinguishing T2 lesions with normal vocal cord mobility, DFS was better for surgery but OS were not significantly different between different treatments. For T2 lesions with impaired vocal cord mobility, OS and DFS were similar for surgery and induction chemotherapy groups, significantly better than radiotherapy.

Discussion: UICC and AJCC classification of T2 glottis have not changed since their first editions in 1972 and 1977. However since Mendenhall in 1988 numerous authors plead for distinction between T2a (normal vocal cord mobility) and T2b (impaired vocal cord mobility) because of the differences in local control and survivals, and in failure rates of transoral laser surgery or exclusive radiotherapy. Our results are consistent with this distinction between the T2a and T2b lesions and argue for strongly considering the vocal cord mobility in treatment decision tree.

Conclusion: T2 glottis carcinoma with impaired vocal cord mobility are intermediate-stage lesions with poorer survival rates than early-stage T2 lesions with normal vocal cord mobility. The TNM classifications should take into consideration this distinction between T2a and T2b. Glottis lesions with impairment of vocal cord mobility should probably be considered for laryngeal-preservation surgery in first line treatment. If the local extension does not allow this preservation, lesions should be evaluated for laryngeal preservation protocols of which treatments and methods have to be evaluated in further studies.
TRANSORAL CO2 LASER CORDECTOMY FOR GLOTTIC CANCER INVOLVING THE ANTERIOR COMMISSURE

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Introduction: Recommended treatment for glottic squamous cell carcinoma (SCCA) involving the anterior commissure has pendulated between surgical resection and external beam radiotherapy. We aim to describe the outcomes following transoral CO2 laser cordectomy for SCCA of the anterior commissure.

Methods: Patients who received CO2 laser cordectomy as their primary treatment for glottic cancer between March 2008 and March 2013 were included in this academic medical center retrospective study. Surgical resections were described according to the European Laryngological Society cordectomy classification. Patients receiving only cordectomy type Va or type VI were included. Phonation quotient is computed by dividing the vital capacity (cc) by the maximum phonation time.

Results: 30 patients received CO2 laser cordectomy for anterior commissure SCCA. 27/30 (90.0%) underwent type VI and 3/30 (10.0%) underwent type Va. Average clinical follow up time was 47.6 (Range= 11-95; SD=19.3) months. Local recurrence was found in 5/30 (16.7%) of patients. Local recurrence was not associated with age, gender, Tumor stage, or Type of cordectomy (p>0.05). 2/5 recurrences were successfully salvaged by repeat CO2 laser resection, while 2/5 underwent salvage total laryngectomy resulting in an overall laryngeal preservation rate of 27/29 (93.1%), as one patient with local recurrence also developed a second cancer which prevented further curative treatment. 16 of the patients underwent post-surgical voice evaluation. Objective voice measures included mean postoperative maximum phonation time: 7.3 (SD=5.8) seconds, and mean postoperative phonation quotient: 515.5 (SD=268.4) cc/second. Voice handicap index-120 (VHI) was used for patient-based outcomes. Mean post-cordectomy VHI scores was 36.9 (SD=21.4). No association was seen between VHI scores and Gender, Tumor stage, or Type of cordectomy. Perceptual voice measures were evaluated with the GRBAS-scale. Mean scores: G=2.07 (SD=0.92), R=1.28 (SD=1.07), B=1.57 (SD=1.22), A=0, S=1.36 (SD=1.08). 5/26 (19.2%) patients required voice augmentation procedure (injection laryngoplasty or medialization thyroplasty) at an average of 17.8 months following initial cordectomy.

Conclusion: Though glottic SCCA of the anterior commissure remains a challenging anatomic subsite, transoral CO2 laser cordectomy results in encouraging oncologic and voice outcomes without the need for external beam radiation therapy. Additional confirmatory study is required.
S202 CLINICAL STAGING IN LARYNGEAL CANCER: ACCURACY OF THE 0 AND 30 DEGREE HOPKINS ROD IN MEASURING TUMOR EXTENT
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**Background:**
Accurate clinical staging in head and neck cancer is of the utmost importance, particularly given recent trends towards organ preserving strategies, which require careful patient selection.

The use of endoscopic mapping of tumor extent remains a key facet of clinical staging. The Hopkins rod-lens (HR) endoscope can be used during rigid endoscopy to measure tumor length. However, the accuracy of this method has not previously been shown. We aimed therefore to determine the accuracy of the 0- and 30-degree HR in measurement of laryngeal tumor length.

**Methods:**
A basic experimental study was performed over a 2-month period at a London teaching hospital.

Two anatomically accurate laryngeal models were constructed, one containing a 0.5cm and one a 1.5cm simulated tumor, just below the vocal folds. 23 volunteer surgeons were asked to measure the length of these tumors using a 0- and 30-degree HR and suspension laryngoscope (figure 1). This was performed by making a mark on the HR relative to a specific point on the laryngoscope, at the distal and then proximal extent of the tumor, with the help of an assistant.

Participants ranged in seniority from SHO to consultant (resident and attending respectively).

![Image](74x189 to 385x353)

Figure 1: Experimental setup.

**Results:**
For the 1.5cm tumor, the 30-degree endoscope was more accurate in 87.0%, equivalent in 4.3% and less accurate than the 0-degree endoscope in 8.7% of cases. On average the 30-degree endoscope was 0.22cm more accurate (95% CI 0.14-0.29) p<0.0001.
For the smaller, 0.5cm tumor, the 30 degree endoscope was more accurate in 78.3%, equivalent in 17.4% and less accurate than the 0-degree endoscope in 4.3% of cases. On average the 30-degree endoscope was 0.13cm more accurate than the 0-degree endoscope (95% CI 0.08-0.18), p<0.0001.

Results are summarized in figure 2 below.

![Graph showing mean and standard deviation for 'error' obtained using 0- and 30-degree endoscopes.](image)

Figure 2: Mean and standard deviation for 'error' obtained using 0- and 30-degree endoscopes.

There was no statistically significant difference in accuracy according to seniority. All but one participant preferred using the 30-degree endoscope.

**Discussion:**

To our knowledge, no other studies have addressed the accuracy of 0- and 30-degree HR endoscopes for measuring the length of laryngeal tumors.

We have shown that the 30-degree HR is significantly more accurate than the 0-degree HR in determining the length of a simulated laryngeal lesion found beyond the vocal folds. The increased
average accuracy of 0.22cm and 0.13cm represents 14.7% and 26.0% of total lesion size for the 1.5cm and 0.5cm tumors respectively.

In pivotal areas this difference may determine extension into a different laryngeal subsite, for example from glottis into the subglottis. In turn, this may influence prognosis and treatment decision-making. The level of increased accuracy demonstrated here therefore carries important clinical implications.

We would suggest, where choice is available, the 30-degree HR should be employed.
OUTCOMES, COMPLICATIONS AND CONSIDERATIONS FOR ELECTIVE NECK DISSECTION IN PATIENTS UNDERGOING SALVAGE LARYNGECTOMY
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Background:
Most patients treated with organ-preservation schemas for laryngeal cancer have no nodal disease at the time of recurrence. The oncologic benefit of an elective neck dissection (END) in a patient with clinically/radiologically N0 neck at the time of salvage laryngectomy (SL) is still controversial. Furthermore, there is a paucity of data in the literature regarding the impact of END in surgical complications. We sought to determine the perioperative and oncologic outcomes for END and identify predictors for pN(+) status.

Methods:
Retrospective chart review of 180 patients who underwent laryngectomy between 2004 and 2013. Fifty-eight patients met inclusion criteria defined as: SL following radiation or chemoradiation for oncologic indication, preoperative N0 status confirmed clinically and by imaging, and full documentation available for review. The cohort was divided on 2 groups depending upon the END status. Demographics, pathology, radiation, length of stay, complications and oncologic outcomes were compared. Statistical analysis was performed with Student’s t-test and Fisher’s exact tests on SPSS v22.

Results:
The study cohort was comprised of 58 patients, 46 (79.3%) males and 12 (20.7%) females with a mean age of 60.5 years [24-88, SD=10.8]. Average definitive radiation dose was 65.7Gy [51-70.2, SD=4.5]. Nineteen patients (32.8%) were managed conservatively while 39 (67.2%) had END, uni or bilateral. These groups were statistically comparable in age, sex, tumor staging and closure technique. The mean length of hospital stay (LOS) was 8.9 days [3-36, SD=6.5] while the most frequent complications were: pharyngocutaneous fistula (n=17, 29.3%), fluid collection (n=6, 10.3%), severe cardiovascular events - including one death- (n=4, 6.9%), and pneumonia (n=4, 6.9%). Overall, 58.6% of the patients presented with at least one adverse perioperative event. A total of 71 ENDs were studied and only 5 necks in 4 patients were found to have pathologically positive nodal disease. The only statistically significant predictor for pN(+) status was T-stage (p=0.017); contrary to other reports tumor location (glottic vs. supraglottic) was not a factor. Conversely, only 9 of the 1,196 total lymph nodes analyzed (0.75%) were pathologically positive. END did not significantly increase the LOS nor the risk of total or specific complications, except for pharyngocutaneous fistula which trended (p=0.100). The 2- and 5-year disease-free survival (DFS) was 64.1% and 53.8% respectively, and it was significantly lower for patients who underwent an END (5-year DFS: 55.9% vs. 52.8%, p=0.032). The overall 2- and 5-year survival for the cohort was 69.3% and 56%, respectively and was not affected by elective treatment of the neck (p=0.257).

Conclusion:
Elective neck dissection in a salvage laryngectomy setting does not have a significant impact on LOS or overall complications, although it could be associated with a higher fistula rate. We found that only 7%
of the dissected necks had positive disease, and the only predictor for pN(+) status was tumor T-stage. The procedure did not improve locoregional control, disease-free or overall survival when compared to observation. Our findings suggest that END is warranted in patients presenting with locally advanced recurrences, while observation might be preferable in all other instances.
LARYNGECTOMY SUPPORT GROUPS ON FACEBOOK
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Introduction

Laryngectomees and their family members have engaged in online support groups for many years, but have only in recent years started engaging in more interactive platforms such as Facebook. Healthcare professionals routinely recommend and encourage new laryngectomees to join such support groups, but it is not known what benefits or harms they might derive from these online supports.

Aim:

To conduct a survey of Facebook laryngectomy support group users to determine their demographics and perceived benefits or harms associated with group membership.

Methods:

An on-line search was conducted using Facebook’s dedicated search engine to identify existing laryngectomy support groups. A self-administered on-line survey was forwarded to all members of all identified support groups. A combination of open-ended questions and Likert scale questions were included in the survey. Only adult members were invited to respond to our survey.

Results:

Ten English-speaking laryngectomy support groups were identified, of which two agreed to participate. Across all groups, thirty responses were received; of which six respondents did not complete the survey or declined to have their responses included in analysis. Respondents had an average age of 54 years (SD=11.4) and 60% were male. Twelve (50%) of the respondents were from North America; the rest were spread over two major areas, Europe (n=2, 8%) and Australasia (n=3, 13%), or not indicated (n=3, 13%). Nine (38%) lived in an urban setting. Seventeen (71%) declared being members of multiple online support groups for people affected by laryngectomy, with a mean number of ‘joined’ groups being 2.38 per respondent. The top reasons as to why these respondents joined the support groups were: to socialize with people who understand (n=18, 75%), to gain knowledge (n=21, 88%) and to share my knowledge (n=20, 83%). The main two areas of benefit that they reportedly derived from the groups included: obtaining information (n=22, 92%) and meeting people from all over the world (n=21, 88%). All but one of the respondents reported negative experiences, although most of these experienced them rarely. Respondents indicated the following harms were experienced as a result of joining these groups: induced worry (n=13, 54%), confusing advice from fellow patients (n=8, 33%), and feeling annoyed when visiting the group (n=10, 42%). Four (17%) respondents mentioned that they received incorrect advice on more than five occasions each. Four (17%) reported feeling actual distress as a result of their use of the site.

Conclusions

Our findings suggest a high rate of negative experiences and drawbacks to joining online laryngectomy support groups. A finding that has not been previously identified in the literature. This timely survey provides clinicians and researchers with urgently needed information about the benefits and risks to
participating with online disease based support groups that they can then use to provide information
and advice to their patients.