RELATIVE SURVIVAL OF LARYNGEAL CANCER: THE INFLUENCE OF AGE AND INSURANCE STATUS
Runhua Shi, PhD, Matthew Clavenna, MD, Cherie-Ann Nathan, MD, FACS, Vikas Mehta, MD, FACS; LSU Health Shreveport

Objectives/Hypothesis: To describe the relative survival (RS) for patients diagnosed with laryngeal squamous cell carcinoma based on tumor stage and examine predictors significant for mortality.

Study Design: Retrospective cohort study.

Methods: 59,633 patients diagnosed with laryngeal cancer between 1998 and 2006 were obtained from the National Cancer Database (NCDB). Patients were 18-90 years old with stage I to stage IV disease and had at least 5 years of follow up. The year, age, sex and race specific matched life expectancies from the National Center for Health Statistics were used to estimate expected survival for these individuals. Stage-stratified RS rates were calculated for the entire cohort. Factors included in the survival analysis were age, sex, year of diagnosis, facility type, race, income, education level and insurance status. RS of laryngeal cancer was then evaluated for each stage and insurance status. Excess hazard ratios (eHR) were estimated in multivariate analysis utilizing Poisson regression to assess significance of these factors.

Results: In univariate analysis, RS (observed - expected) was worse during the first 2 years after diagnosis for all stages. However, for years 3 to 5, survival for all laryngeal cancer patients was better than their matched counterparts in the general population. When looking at the various predictors for RS in the multivariate analysis, age, race and insurance status were noted to be statistically significant predictors of RS. Specifically, patients older than 50 demonstrated greatly reduced eHR than patients <50 for all stages of laryngeal cancer. Those who were 50-59 years old had an eHR of 0.54, 0.72, 0.63, and 0.74 for stage I to stage IV, respectively, when compared to patients <50 (p<0.001). Patients with private, Medicaid, and uninsured status experienced 8%, 13% and 20% decrease in survival, respectively, at 5 years after diagnosis. However, Medicare patients had a 22% improvement in RS. Uninsured patients had a significantly higher eHR when compared to all insurance types (e.g. eHR = 1.8, 95% CI 1.37 - 2.36, p<0.001 for stage III uninsured vs private insurance). Compared to white patients, other races had a 65% higher eHR in stage I and III patients.

Conclusion: Despite the expected outcome that those diagnosed with cancer would have a worse relative survival, these data suggest that many patients with laryngeal cancer actually demonstrate improved long-term survival. The improved RS seen in older patients and those patients with Medicare and/or private insurance can explain much of these results. Our results also highlight disparities in survival for uninsured patients and non-white individuals with those patients exhibiting worse RS than their matched general population cohort. The reasons for these disparate outcomes remain unclear and warrant further investigation.
Background: The decreased survival recorded for patients with laryngeal cancer in the last decades may be related to changes in patterns of management; in literature a debate has been dedicated to the management of clinical stage T3 due to the disseminated use of organ preservation strategies. In clinical practice the choice of a determined strategy may be influenced by medical experience, hospital infrastructure and patients' wishes but clinical, pathological and therapeutic prognostic factors have to be considered in treatment choice.

Objective: To evaluate clinical, therapeutic and pathological prognostic factors in patients with cT3 laryngeal carcinoma treated in a single institution using four different treatment strategies.

Materials and Method: 145 consecutive patients with diagnosis of advanced laryngeal carcinoma (cT3N0-3M0, all sub-sites) treated in a single institution using four different treatment strategies (surgery alone, surgery with adjuvant therapy, exclusive radiotherapy and chemoradiotherapy) were retrospectively analyzed. Data was obtained from the Cancer Registry, Hospital AC Camargo, São Paulo (1990-2007). A set of clinical and pathological variables were assessed by Kaplan-Meier and Cox regression methods. Treatment option was also assessed as prognostic factor. Associations between clinical-pathological features of the tumor, therapeutic option and cancer specific survival and risk of death, were investigated.

Results: Treatment impacted on cancer specific survival at 5 years, it decreases at 51.6% if adjuvant treatment (positive pathological findings on operative specimen), up to 41.5% in exclusive radiotherapy group (p = 0.039); surgery alone and chemoradiotherapy influenced survival similarly (74.0%; 77.5%). Three clinical variables [filling of pre-epiglottic space (45.5%, p = 0.003), positive clinical neck (37.6%, p = 0.031), invasion of retrocricoid area (0.0%, p = 0.009)] and five pathological variables [lymphatic invasion (44.1%, p = 0.015), extra-capsular nodal spread (43.1%, p = 0.003), positive pathological neck (42.9%, p = 0.001), positive IV-VI levels cervical nodes (33.3%, P = 0.008), positive surgical margins (22.2%, P = 0.001)] were statistically significant in estimating cancer specific survival at 5 years. Among clinical and therapeutic variables, invasion of paraglottic space (HR adjusted 1.92; IC 1.02-3.61), positive clinical neck nodes (cN) (HR adjusted 2.24; IC 1.11-4.50), invasion of pre-epiglottic space (HR adjusted 2.65; IC 1.46-4.81) and exclusive radiotherapy (RR adjusted 2.88; IC 1.31-6.30) were independent prognostic factors. After inclusion of pathological variables, extracapsular node invasion (HR adjusted 3.09; IC 1.56-6.12) and positive resection margins (HR adjusted 3.45; IC 1.11-10.75) were independent prognostic factors.

Conclusion: Exclusive radiotherapy was associated with the highest risk of death (RR adjusted 2.88) but with inclusion of pathological findings, the need of adjuvant post-surgical treatments increased the risk of death to almost 3.5 fold.
A POPULATION BASED PERSPECTIVE ON TREATMENT AND OUTCOME OF GLOTTIC LARYNGEAL CARCINOMA STAGE T3 AND T4 - DOES ORGAN PRESERVATION JEOPARDIZE SURVIVAL?

Johan Wennerberg, MD, PhD, Johan Reizenstein, MD, Erik Holmberg, PhD, Martin Beran, MD, PhD, Gunnar Adell, MD, PhD, Eva Brun, MD, PhD, Lena Cederblad, MD, Lena Damber, PhD, Tomas Ekberg, MD, Mats Engström, MD, PhD, Lovisa Farnebo, MD, PhD, Eva Hammerlid, MD, PhD, Hedda Haugen, MD, PhD, Anders Högmo, MD, PhD, Göran Laurell, MD, PhD, Freddie Lewin, MD, PhD, Magnus Niklasson, MD, PhD, Jan Nyman, MD, PhD, Anders Westerborn, MD, Helena Sjödin, MD, Björn Zackrisson, MD, PhD, Karin Söderström, MD, Magnus Wahlgren, MD; Depts. of ORL/H&N Surgery, Oncology and Oncologic Centers at the University Hospitals in Lund, Gothenburg, Örebro, Stockholm, Uppsala, Umeå, Linköping and the Swedish Quality register for H&N Cancer (SweHNCR), Sweden

BACKGROUND: In recent years there has been a debate concerning organ preservation therapy and the possible risk of a less favourable outcome in the long run for patients with advanced laryngeal carcinoma. In Sweden virtually all new H&N Cancer cases are referred to and treated at one of seven University ENT - H&N Surgery and Oncology departments. The Swedish Quality Register for Head and Neck Cancer (SweHNCR) started in 2008 and has coverage of > 98% of all incident new cases. According to national guidelines in Sweden the primary treatment intention for glottic T3 tumours is organ preservation and primary treatment is radiotherapy +/- concomitant chemotherapy with salvage laryngectomy for residual or recurrent cancer. For glottic T4 tumours primary treatment is laryngectomy with postoperative radiotherapy.

MATERIALS & METHODS: During the period 2008-12 a total of 896 new cases of laryngeal carcinoma were entered into the register. Of these 67 % were glottic, 25% supraglottic, 2,5 % subglottic and 5,5% classified "Overlapping lesion or unspecified (NOS)". 95% of tumours stage T3-4 was treated with curative intention.

RESULTS: Only patients with glottic tumours treated with curative intention were included in the analysis (n: 582). Of these 116 had stage T3-4 tumours. At the time of diagnosis 12% with T3 glottic tumours were node positive and out of patients with T4 tumours 17% were node positive. Primary treatment for patients with T3 tumours was radiotherapy (+/- chemotherapy) in 81% and in 19% surgery (+/- radiotherapy, +/- chemotherapy). Corresponding figures for patients with T4 tumours were 13% and 87% respectively. Relative 4-year survival for patients with T3 tumours (n: 63) was 58% (42-72, 95% CI) and for glottic T4 (n: 53) it was 66% (48-80, 95% CI). Corresponding figures for clinical stage was 57% for stage III and 62% for stage IV.

CONCLUSION: The TNM-classification is designed to stratify stage as a major determinant of prognosis. Thus patients with a glottic T3 cancer should have a more favorable outcome than T4. Our findings in a population based cohort, where the majority of patients with T3 tumours, in contrast to patients with T4 tumours, were treated with an organ sparing intention, do not support the expected outcome. This raise concerns on the principles of management of advanced glottic laryngeal cancer.
RACIAL DISPARITIES IN LARYNGEAL CANCER OUTCOME IN THE UNITED STATES: A POPULATION-BASED SEER ANALYSIS OF 24,069 PATIENTS

Jacob Y Shin, MA, Minh Tam Truong, MD; Boston University School of Medicine

Background: To determine the impact of race on overall survival (OS) in patients with squamous cell carcinoma (SCC) of the larynx who received primary treatment.

Methods: Data were extracted from the NCI SEER database that included eighteen population-based registries from 1988-2010. Chi-square test, Kaplan-Meier method, and Cox regression models were employed in SPSS 20.0 for data analyses.

Results: 24,069 patients with laryngeal SCC received primary treatment. The median age was 64 years. 18,166 (75.5%) patients were White, 3,475 (14.4%) Black, 1,608 (6.7%) Hispanic, and 820 (3.4%) patients were Asian. Compared to other races, Black patients were more likely to be diagnosed at younger age (p<0.001), present with supraglottic disease (p<0.001), undergo lymph node dissection (p<0.001), have nodal metastasis (p<0.001), have advanced stage disease (p<0.001), and less likely to be married (p<0.001).

The 5-year OS for the cohort was 59.6%. The 5-year OS for White, Black, Hispanic, and Asian races, respectively, was 60.6%, 52.7%, 59.5% and 65.7% (p<0.001). This 5-year OS difference by race persisted regardless of age, gender, year of diagnosis, primary treatment, disease stage, nodal status, or tumor grade.

On multivariate analysis, Black race, older age at diagnosis, subglottic site of disease, non-surgical therapy, nodal metastasis, advanced stage disease, higher tumor grade, and not being married were significant for inferior OS.

Conclusion: Race is an independent prognostic factor for OS in patients with laryngeal SCC. Black patients are more likely to present at a younger age, with locally advanced disease presentation, and be unmarried, which may contribute to underlying racial disparities in outcome.
S041 TREATMENT TRENDS AND SURVIVAL IN T3-T4 LARYNGEAL CANCER TREATED IN THREE CANCER CENTERS
Genival B Carvalho, MD, João G Filho, PhD, Samuel P Lima, Laura Mannarini, PhD, André L Carvalho, PhD, Ansarin Mohssen, PhD, Fausto Chiesa, PhD, Luiz P Kowalski, PhD; A.C. Camargo Cancer Center, São Paulo, Brazil; Cancer Hospital of Barretos, Barretos, Brazil; Instituto Europeo di Oncologia, Milan, Italy

Introduction: Until the early 90s, most T3 and T4 laryngeal tumors were treated with total laryngectomy followed by radiotherapy. Starting from the VA and RTOG 91-11 laryngeal preservation trials, chemoradiotherapy became the standard of care for selected patients. Recently some studies have demonstrated decreased survival in patients with laryngeal cancer.

Objective: The aim of this multiinstitutional study was to evaluate therapeutic trends and survival results in T3 or T4 laryngeal cancer and report survival according to the period in which the treatment was performed.

Material and Methods: This was a multicenter retrospective study with laryngeal cancer patients who underwent treatment in three cancer centers from 1995 to 2007.

Results: Three hundred twenty-four patients were evaluated, 277 (85.5%) were male, 217 (67%) patients had tumors staged as T3 and 107 (33%) as T4. Of these, 176 (54.3%) underwent surgery, 129 (39.8%) chemoradiotherapy and 19 (5.9%) radiotherapy. Patients were grouped according to the period in which they were treated: 93 (28.7%) patients were treated between 1995 and 2000, 94 (29%) were treated between 2001 and 2003, 137 (42.3%) were treated between 2004 and 2007. Of patients undergoing surgical treatment, total laryngectomy was the most frequently performed (110 patients). In relation to the treatment according to the time period, between 1995 and 2000, 76 (81.7%) patients underwent surgery. In the period 2001-2003, 54 of the 94 treated patients (57.4%) underwent chemoradiotherapy and between 2004 and 2007, of the 137 treated patients, 66 (48%) underwent surgery (p<0.001). No significant differences in overall survival were observed according to the period that the treatment was performed (p=0.10). However, from 2001 to 2003, with the predominant use of chemoradiotherapy, cancer-specific survival was lower (p=0.011).

Conclusion: T3 or T4 staged laryngeal tumors have been preferentially treated with surgery and overall survival did not differ between study periods, while on the other hand, between 2001 and 2003, cancer-specific survival was worse. Possibly, a careful selection of patients, including surgery for the more advanced T4 tumors, improved prognosis of patients treated during the last years of the study.
S042  T3 LARYNGEAL CANCER SURVIVAL RATES: CONCOMITANT CHEMORADIATION VERSUS TOTAL LARYNGECTOMY.
Diana E Khalil, MD, Mohammed Alessa, MD, FRCSC, Paul D Kerr, MD, FRCSC; Department of Otolaryngology - Head and Neck Surgery, University of Manitoba

Objectives: Organ preservation chemoradiation protocols are standard treatment for the majority of patients with stage 3 and 4 laryngeal cancer. However, there are concerns that treatment of locally advanced tumors with chemoradiation may not result in acceptable organ preservation rates and may ultimately compromise survival. Our goal is to assess the oncologic outcome of concomitant chemoradiation versus total laryngectomy for T3 laryngeal carcinoma.

Methods: A retrospective population based consecutive cohort of T3 laryngeal cancer patients treated with concomitant chemoradiation were compared to a matched cohort of patients treated with total laryngectomy.

Settings: Academic tertiary care referral center.

Results: A total of 79 patients met inclusion criteria. 24 patients were treated with concomitant chemoradiation, and compared to a matched cohort of 55 patients that underwent total laryngectomy. Kaplan-Meier analysis showed that chemoradiation resulted in a similar two year disease specific survival rate (86.5 ± 0.1 vs 86.3 ± 0.05 p =0.74). The laryngeal preservation rate at two years was 76%, with a laryngectomy free survival rate of 47%.

Conclusions: Chemoradiation for T3 laryngeal cancer allows for laryngeal preservation in the majority of patients with similar disease specific survival compared to total laryngectomy.
Background: The optimal management of Stage III laryngeal carcinoma remains controversial. There are pertinent concerns that the paradigm shift favouring larynx preservation strategies including chemoradiotherapy (CRT) over the gold standard of primary laryngectomy±adjuvant therapy is compromising patient survival. Within our centre, we noted a reduction in survival associated with period with favouring non-operative management. Subsequently our threshold for surgery lowered and our cause-specific survival (CSS) seemed to improve, however it was unclear whether this represented cause and effect. Our objective was to identify factors associated with survival and laryngeal function in a contemporary, population based study of stage III laryngeal carcinoma.

Methods: Patients presenting with Stage III Laryngeal Carcinoma to the Edinburgh Cancer Centre between 1999 and 2010 were included. Multiple variables were evaluated including the Adult Co-morbidity 27 score. Primary outcomes were 5YCSS and recurrence; secondary outcomes included laryngeal function. Kaplan-Meier and Cox-proportional hazards analyses were performed.

Results: Of the 137 patients included, 24.1% received Surgery+/Adjuvant Therapy (SURG±Adj) (n=33), 32.8% Chemo-radiotherapy (CRT) (n=45), 36.5% Radiotherapy alone (XRT) (n=50) and 6.6% None/Palliative (n=9). Over time our clinical practice shifted, with increasing adoption of CRT and reduced use of XRT. SURG±Adj declined from 28.6% in 1999-2002 to 11.1% from 2003-2006 before returning to 24.1% in 2007-2010, after audit revealed a decline in CSS between 2003 and 2006. T3N0M0 tumours accounted for 72.3% (n=99) of cases. For radically treated patients 5YCSS was 81.0%, 2 year local relapse rate was 27.5% and 5 year overall survival (5YOS) was 50.6%. XRT was associated with the highest rate of local recurrence (6.1% vs. 11.2% vs. 46.6%/ SURG±Adj vs. CRT vs. XRT; p<0.01), lowest 5YCSS (90.8% vs. 87.8% vs. 68.9%/ SURG±Adj vs. CRT vs. XRT/p=0.0026) and lowest 5YOS (p=0.001). XRT patients had the greatest prevalence of ‘severe’ co-morbidities (p<0.001) and after correcting to for this, differences in CSS by treatment modality were non-significant. SURG±Adj and CRT had similar co-morbidity scores, recurrence, 5YOS and 5YCSS even after accounting for treatment related deaths.

At 6 months following treatment, those post-laryngectomy had the lowest requirements for supplementary enteral feeding (3.2% vs. 16.7% vs. 11.2% / SURG±Adj vs. CRT vs. XRT), however 16% had ‘markedly disordered’ communication following laryngectomy compared to 0% in patients with larynx preservation.

Of the 39 patients who had local recurrence following XRT/CRT only 16 (41%) actually received salvage laryngectomy, of which only one had a baseline of severe co-morbidity. Overall 87 patients have died, 36.1% with tumour present, 11.5% from complications of treatment and 51% died from causes unrelated to tumour or treatment. Nineteen patients (21.8%) died from synchronous or secondary tumours.

Conclusions: CRT and SURG±Adj had similar survival outcomes, but with trade-offs in early functional outcomes. Severe co-morbidity is associated with selection bias to XRT and has a significant impact upon 5YCSS. The optimal management of severely co-morbid patients merits attention, particularly as few of these patients are unlikely to be offered salvage laryngectomy.
ONCOLOGIC OUTCOMES OF TOTAL LARYNGECTOMY: IMPACT OF MARGINS AND PREOPERATIVE TRACHEOSTOMY

Naveed Basheeth, Dr., Gerard O'Leary, Patrick Sheahan, Mr; Dept. of Otolaryngology - Head & Neck Surgery, South Infirmary Victoria University Hospital, Cork, Ireland

Background

In the past, tracheostomy performed before total laryngectomy was considered to be a risk factor for stomal recurrence, however this view has been challenged. In recent years, there have been massive shifts in treatment paradigms for larynx cancer, but despite this, concerns have been raised regarding possibly increasing mortality rates. The purpose of the present study was to investigate risk factors for local recurrence and death among patients undergoing total laryngectomy at our institution, with particular emphasis on pattern of local recurrence (stomal versus pharyngeal / base of tongue (BOT), and impact of preceding tracheostomy.

Methods

Retrospective review of 88 consecutive total laryngectomies performed for squamous cell carcinoma of the larynx or hypopharynx. Multivariate analysis of risk factors for recurrence and survival was performed.

Results

32 patients underwent primary laryngectomy, and 56 underwent salvage surgery. 20 underwent preoperative tracheostomy. Preoperative tracheostomy was a significant predictor of local recurrence (p=0.03), disease-specific survival (p=0.006), and overall survival (p=0.01). With regard to pattern of local recurrence, preoperative tracheostomy (p=0.05) and pathological nodal status (pN+) (p=0.03) were significant for stomal recurrence, but not pharyngeal / BOT recurrence; whereas positive surgical margins was significant for pharyngeal / BOT recurrence (p=0.01) but not stomal recurrence. Other significant factors for disease specific survival were pN+ (p=0.005) and poor differentiation (p=0.01), and for overall survival, pN+ (p=0.007), poor differentiation (p=0.01), and positive margins (p=0.04).

Conclusions

Preoperative tracheostomy and pathological nodal status appear to be significant risk factors for stomal recurrence after total laryngectomy, whereas positive surgical margins is significant for pharyngeal or BOT recurrence. These findings provide evidence for distinct causative factors for these two patterns of local recurrence.
Purpose: To validate a published population-based nomogram for prediction of overall survival and local control in laryngeal carcinoma patients, in the RTOG-9111 clinical trial dataset.

Methods: The published nomogram (available in www.predictcancer.org) is population-based and developed using a dataset of 466 (T2-T4) laryngeal carcinoma patients, treated with radiotherapy (RT) alone [Figure 1A], and was validated using data from the RTOG-9111 trial of 172 patients (T2-T4) treated with RT. The variables in the model are age of the patient at start of treatment (years), hemoglobin level (mmol/L), clinical T-stage, clinical N-stage, patient’s gender and equivalent RT dose (Gray). The model performance was evaluated using the C-index. The log rank test was used to compare survival curves between the nomogram estimated risks groups on the validation set.

Results: All variables in the model showed statistically significant differences between the nomogram-based dataset and the validation dataset (p < 0.001). The nomogram validation resulted in a C-index for overall survival of 0.66 (95% CI, 0.56-0.73) and a C-index for local control of 0.62, (CI, 0.50-0.74). Stratification of model’s estimated probabilities using the cut-off values derived on development dataset resulted on significantly different risk groups on the RTOG-9111 validation dataset (p <0.0001; Figure 1B).

Conclusion: A prognostic model based on patient data from routine clinical care was able to assign patients from a clinical trial cohort (RTOG-9111) into distinct risk groups. This is important for rapid learning, which aims to derive knowledge from routine care databases. The lower validation C-indexes are due to the large differences between the two populations.
Figure 1. A: A published nomogram for overall survival and local control in patients with cancer of the larynx treated with radiotherapy. Clinical and treatment variables are associated with outcome status at follow-up durations of 2 and 5 years. The predictors are age of the patient (in years), haemoglobin level (in mmol/l), clinical tumour stage (T-stage), clinical nodal stage (N-stage), patient’s sex and equivalent dose (in Gy). A probability for local control can be calculated by drawing a vertical line from each predictor value to the score scale at the top—‘points’. After manually summing up the scores, the ‘total points’ correspond to the probability of local control, which are estimated by drawing a vertical line from this value to the bottom scales to estimate local control (Lambin et al. Nat. Rev. Clin. Oncol. 2012). B: Kaplan-Meier curves of risk group stratification for overall survival. All survival curves are statistically different (log rank test, p < 0.0001).