

TUMOR VOLUME AS A PREDICTOR OF SURVIVAL IN ADVANCED LARYNGEAL CANCER TREATED WITH TOTAL LARYNGECTOMY

Marna A. List, MD^{1,2}; Spencer Nichols, BS¹; Danny DeJesus, MD; Tara C Massini, MD³; William Mendenhall, MD⁴; Deepa Danan, MD, MBA²; Robert Amdur, MD⁴; Kathryn Hitchcock, MD, PhD⁴; Brian Hughley, MD²; Jing Zhao, MS, PhD⁵; Ji-Hyun Lee, PhD⁵; Peter T Dziegielewski, MD, FRCS C 2

1. College of Medicine, University of Florida, Gainesville, Florida 2. Department of Otolaryngology, University of Florida, Gainesville, Florida 3. Department of Radiology, University of Florida, Gainesville, Florida. 4. Department of Radiation Oncology, University of Florida, Gainesville, Florida . 5. Department of Biostatistics, University of Florida, Gainesville, Florida.

Contact Information: marna.list@gmail.com

Background

More than 12,000 new cases of laryngeal cancer (LC) will be diagnosed this year in the United States, and of those, about 3,750 patients will succumb to the disease¹. While 5-year survival for cancer of all sites has consistently increased since the mid 1970s, LC represents one of the rare sites in which survival has decreased in the past 30 years². Many studies have been conducted to determine predictive factors in survival of LC^{3,4}. It has recently been shown that tumor size is an independent factor influencing survival outcomes in LC^{3,4}. One study found that tumor area >1.8 cm² significantly decreased overall survival and disease-free survival in patients with LC treated with primary surgery³. Another found that patients with tumors >2.5cc are less likely to have long-term disease-free status and more likely to need a salvage laryngectomy following RT⁴. These studies suggest that tumor volume should be considered for estimating survival outcomes and planning treatment. Thus, at the University of Florida, it has been the strategy of the multidisciplinary head and neck tumor board to include tumor volume during treatment making decisions.

Methods

Institutional review board research ethics approval was granted at the University of Florida in accordance with the Health Insurance Portability and Accountability Act Data were collected from inpatient and outpatient records of the Head and Neck Oncology Team at the University of Florida Health/ Shands Hospital system. The design was a retrospective cohort study with data collected from the years 2013-2020.

Results

117 patients were included in this study. Of these, 93 (79.5%) patients had primary TL and 24 (20.5%) had salvage TL after radiation therapy (RT). 95 (81.2%) of patients were male and 22 patients were female (18.8%). 3 patients had pathologic tumor stage of T2 (2.6%), 113 had pathologic tumor stage of T3-T4a/b (96.6%), and 1 patient had missing pathologic T stage. 71 (60.7%) patients had pathologic nodal stage of N0-N1 and 46 (39.3%) had pathologic nodal stage of N2-N3. 8 patients had clinical stage I-II LC and 109 patients had clinical stage III-IV LC. 5 patients had pathologic stage II laryngeal cancer, 106 patients had pathologic stage III/IV laryngeal cancer, and 6 patients did not have information for pathologic stage. 106 patients were found to have p16 negative tumors, 10 patients had p16 positive tumors, and 1 patient did not have p16 data. 68 patients had perineural invasion (PNI), 65 patients had lymphovascular invasion (LVI), and 34 patients had extracapsular extension (ECE) at the time of treatment. 62 patients had greater than or equal to 5 mm margins for the tumor resection and 21 patients had less than 1 mm margins on the resected tumor. At the end of the study, 13 patients had local recurrence and 21 patients developed distant metastasis. 34 patients died by the end of this study, of those 19 patients died from LC and 15 died from other causes. BMI, CCI, PNI, and volume were found to have significance ($p < 0.05$) on OS. MFS was found to be impacted by advanced pathologic N stage (N2-N3) and BMI ($p < 0.05$). DSS was found to be significantly impacted by age, BMI, CCI, advanced pathologic N stage, as well as whether the treatment was primary TL or salvage TL. The impact of volume on DSS was found to be insignificant at $p=0.55$.

Figure 1

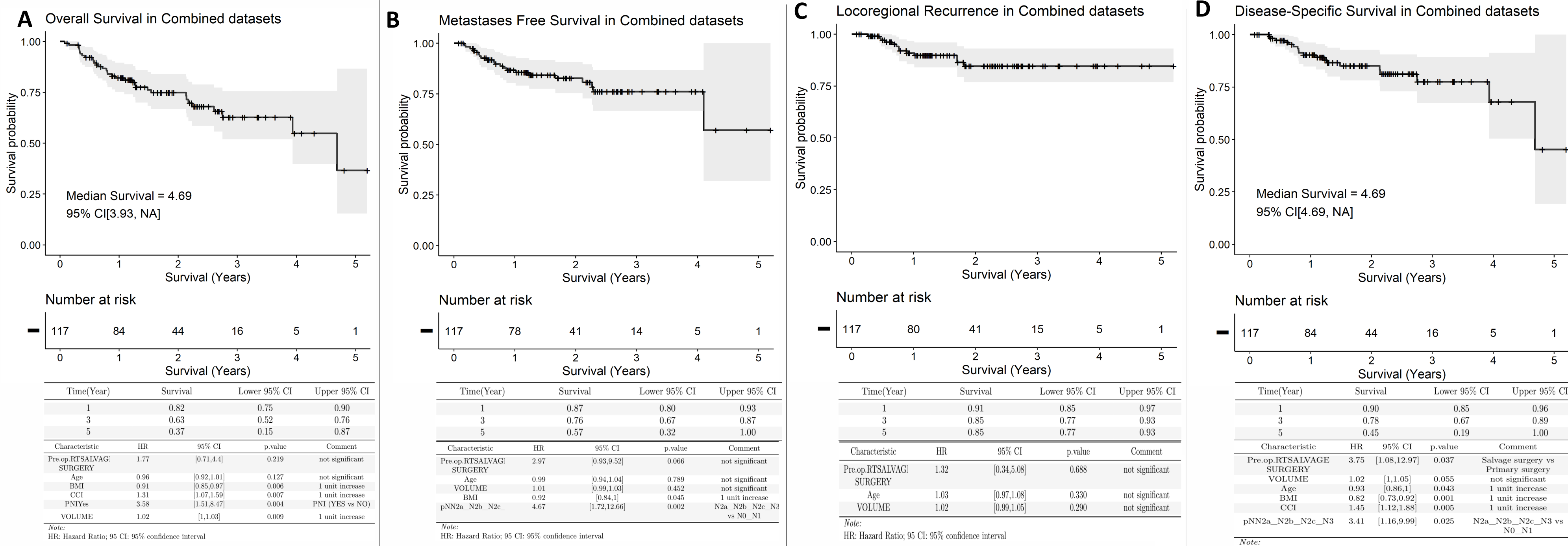


Figure 1:
A. KM curve for overall survival (OS) in combined dataset with tables showing OS at 1 year, 3 year and 5 year and survival analysis.
B. KM curve for metastasis free survival (MFS) in combined dataset with tables showing OS at 1 year, 3 year and 5 year and survival analysis.
C. KM curve for locoregional recurrence (LRC) in combined dataset with tables showing OS at 1 year, 3 year and 5 year and survival analysis.
D. KM curve for disease specific survival (DSS) in combined dataset with tables showing OS at 1 year, 3 year and 5 year and survival analysis.

Figure 2

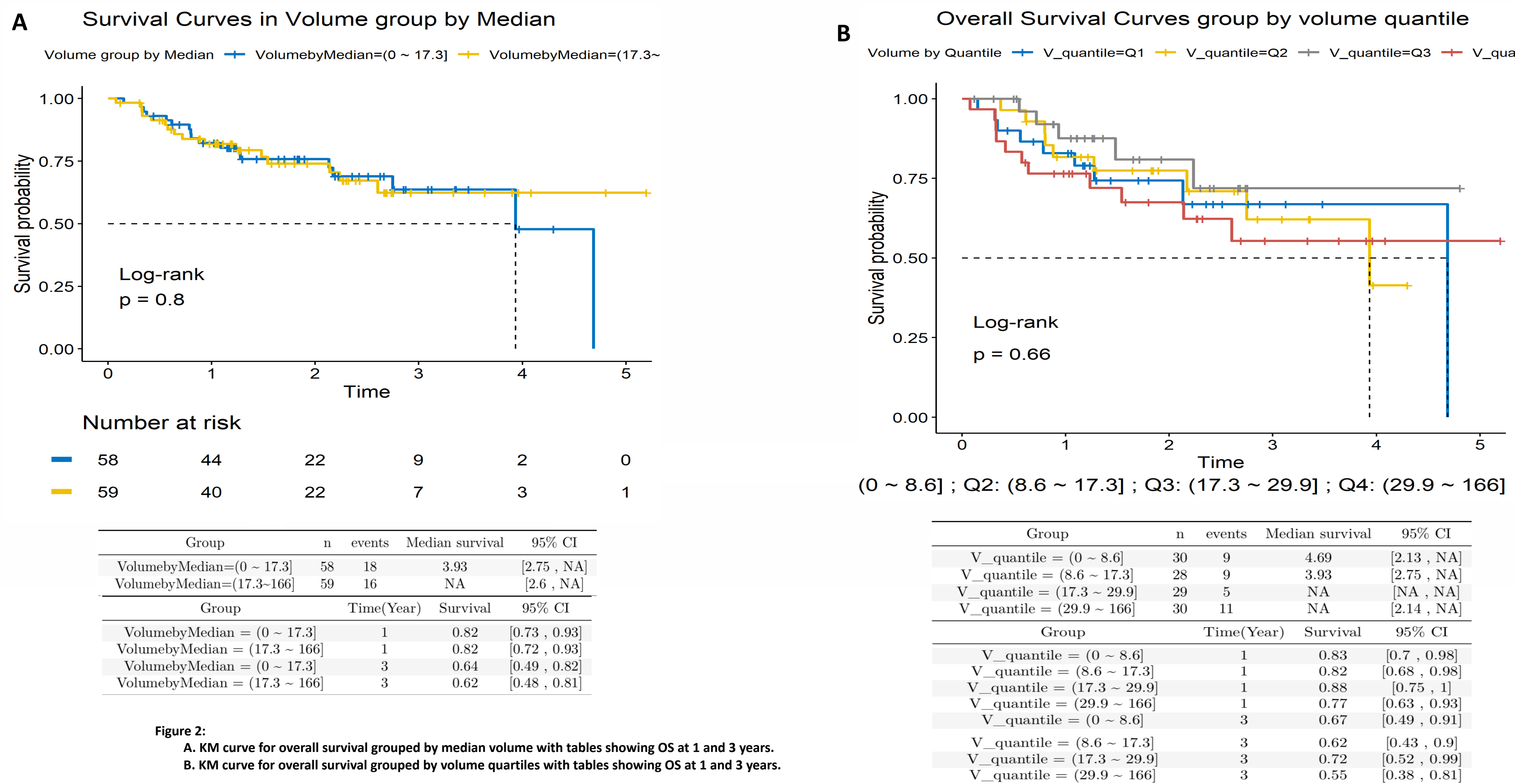


Figure 2:
A. KM curve for overall survival grouped by median volume with tables showing OS at 1 and 3 years.
B. KM curve for overall survival grouped by volume quartiles with tables showing OS at 1 and 3 years.

Discussion

This study analyzed the clinical tumor volume of 117 patients diagnosed with LC who underwent primary or salvage TL. We found that tumor volume was a prognostic factor in overall survival but not in metastasis free survival, disease specific survival, or locoregional control over a 5 year follow up period. We also found that older patients, patients with more comorbidities, patients with a lower BMI, and patients with PNI had worse OS. Advanced N stage and low BMI were found to decrease MFS and DSS. We did not find a cut off for tumor volume that led to worse survival outcomes. Our study found that host factors such as age, BMI, and CCI all have prognostic value for patients with LC. The current data on survival outcomes as a function of age remains controversial with some studies citing that lower age confers a higher 5 year survival^{5,6} and others attributing higher rates of recurrence in patients under 70⁷. We found that higher age negatively impacted DSS ($p < 0.05$). This study further confirms the influence of various host and tumor factors on survival. Based on these results it is important to factor in the patients age, BMI, CCI, tumor volume, presence of PNI, and N stage into treatment planning.

Conclusion

Increasing tumor volume in laryngeal cancer decreases OS in patients treated with primary or salvage total laryngectomy. Other factors that influence survival outcomes include age, BMI, CCI, PNI, and nodal stage. These factors should be considered during treatment planning and patients with larger tumor volumes should be considered for surgical management.

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