

Intraoral and Oropharyngeal Minor Salivary Gland Malignant Neoplasms: Review of 315 Patients Treated in a Single Institution

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INTRODUCTION

Minor salivary gland cancer (MSGTs) accounts for 2-4% of head and neck cancer, 10% of all cavity cancers and 15-23% of all salivary gland cancers. The mainstay of treatment has been surgery with radiotherapy used as an adjuvant modality in advanced cases. There are few large case series which specifically address the prognostic factors of minor salivary gland malignancies. Most large series are typically confined to a specific site of the head and neck, such as the oral cavity, or a specific histological subtype. The rarity and heterogeneous nature of these tumors make the identification of prognostic factors difficult to determine.

OBJECTIVES

This study reviews a large series of malignant intraoral and oropharyngeal MSGTs, and determines the incidence and correlation of the histopathologic features with the clinical characteristics. It also searches for independent prognostic factors for locoregional control, distant metastases, and survival.

PATIENTS AND METHODS

A retrospective chart review was performed at a referral center. Between 1997 and 2007, 315 patients were evaluated for minor salivary gland tumors of the oropharynx and oral cavity at the BNCI. Patients who were included in the study had biopsy proven of the following sites: oropharynx and oral cavity. Computed tomography scans and/or magnetic resonance studies were used to determine the anatomic site of tumors, as well to evaluate tumor extension. Histopathological slides were reviewed by a senior pathologist at BNCI; histological typing was according to the World Health Organization classification of salivary tumours, histological specimens were analyzed for margins, patterns of spread, histological type and tumor grade.

Demographics and clinical presentation, TNM classification, treatment, and outcomes were evaluated. Survival rates and disease recurrence data were used to determine the significance of independent prognostic indicators against survival and recurrence. Outcome measures included recurrences as well as overall survival, disease-specific survival (DSS), and disease free survival (DFS). Recurrence and survival rates were calculated from the date of diagnosis to the event of interest. Recurrences were classified as local, regional, or distant. Survival analysis was performed using Kaplan-Meier estimate and statistical significance determined by log-rank test. Factors with possible prognostic impact were evaluated through univariate analysis.

RESULTS

Most patients (60.3%) were females, with a median age of 69.5 years (range, 1882 years) (Table 1). The mean follow-up was 71.6 months. The hard palate (44.4%) was the most commonly affected site, followed by buccal mucosa (14.6%) and tongue base (8.9%) (Table 2). Adenoid cystic carcinoma (34.3%) and mucoepidermoid carcinoma (32.1%) were the most common histopathological type (table 3). Most patients presented with tumors that were classified as T2 (39.4%), followed by T1 (23.2%), T3 (18.8%), and T4 (18.8%). Sixty-one percent of patients had stage I-II disease and 38.1% of patients had stage III-IV disease. Lymph node and distant metastases were identified in 11% and 4% of cases at presentation, respectively (Table 4). Other characteristics were also evaluated on the surgical specimens including bone invasion (19.5%), perineural invasion (19.9%), angioinvasion (6.2%), as well as the analysis of surgical margins, we found free margins in (94.7%) and close margins (15.5%). Two hundred forty-eight patients underwent surgery (78.7%), the most common surgical intervention was maxillectomy (42.5%). Postoperative radiotherapy was also given to control locoregional disease in 37.8% of cases. Forty-six (14.6%) patients underwent exclusively radiotherapy with curative intent, twenty-one patients received palliative treatment. The overall recurrence rate was 22.3%. Of these recurrences, 33.3% (n=22) were local, 27.1% (n=17) were regional, 20.4% (n=13) were loco-regional and 19.2% (n=12) were distant, with the most common site being the lungs. Twenty-six patients underwent a salvage surgery (5 patients underwent radical neck dissection, 12 maxillectomy and 9 mandibulectomy).

Univariate analysis showed that T4-Stage (p=0.001), high grade tumors (p<0.001), non-surgical treatment (p<0.001), positive margins (p<0.001) were significant prognostic factors for death. Stage III-IV (p=0.05), exclusive radiotherapy (p<0.001) and perineural invasion (p=0.028) were significant adverse factors recurrence. The 5- and 10-year DSS rates were 84.4% and 79.1% (Figure 1), whereas the 5- and 10-year DFS rates were 81.1% and 78.2% (Figure 2), respectively. When the DSS was compared according to tumor grade, patients with high grade tumors had the worst survival and DFS rates (p<0.001 and p=0.018, respectively) (Fig. 3 and 4). Advanced T stage (T4) was identified as a significant factor for DSS and DFS compared early stage tumors (T1-3) (p<0.001 and p<0.001, respectively) (Fig. 4). Patients with stage III-IV disease had worse DSS and DFS than patients with stage I-II disease (p<0.001 and p<0.001, respectively)(Fig. 5). Surgery plus postoperative radiation therapy provided the best DSS and DFS rates compared to other treatment modalities (p<0.001 and p<0.001, respectively) (Fig. 6). The analysis of factors associated with DSS and DFS is presented in table 5.

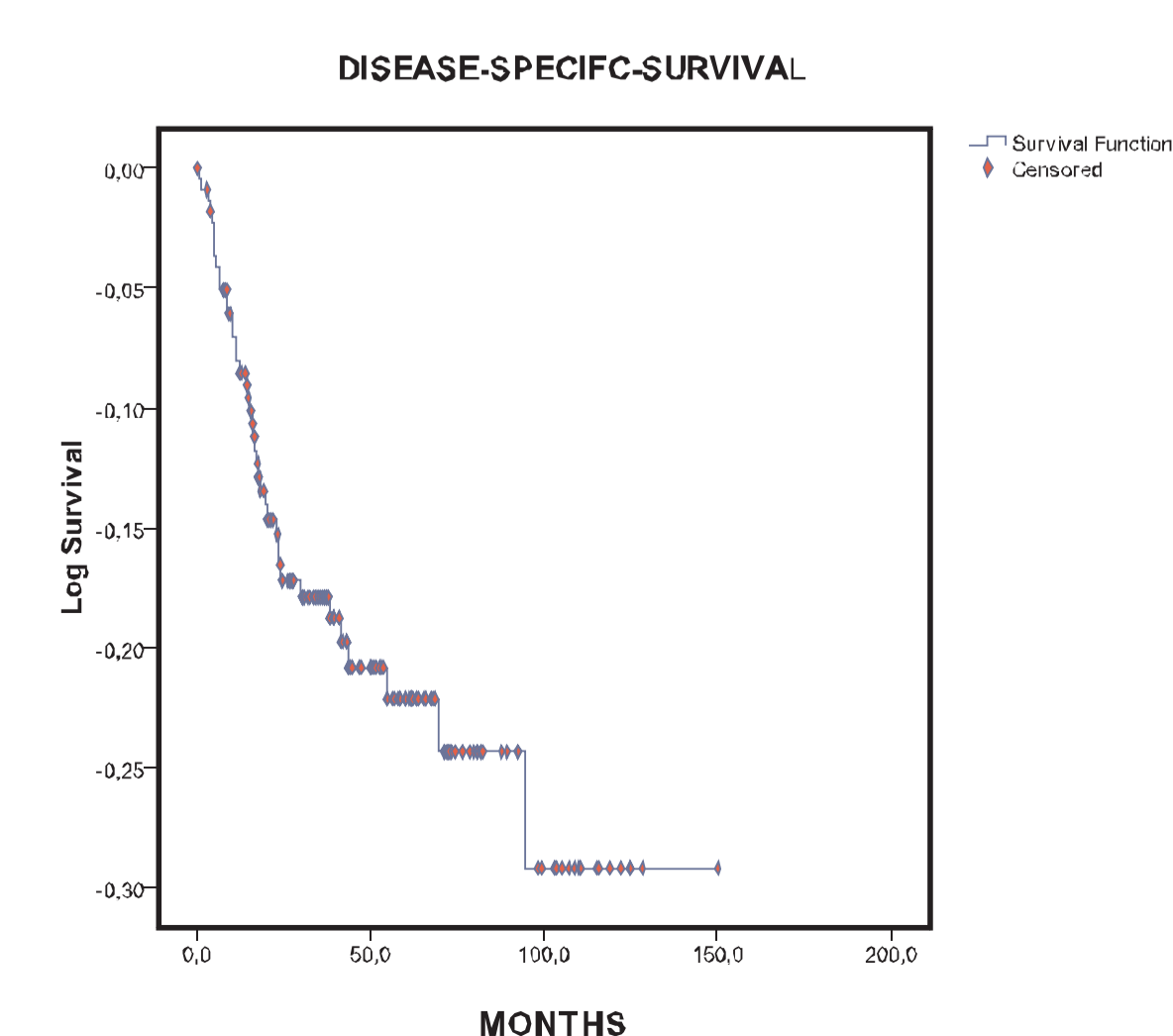


Figure 1 - Disease Specific Survival

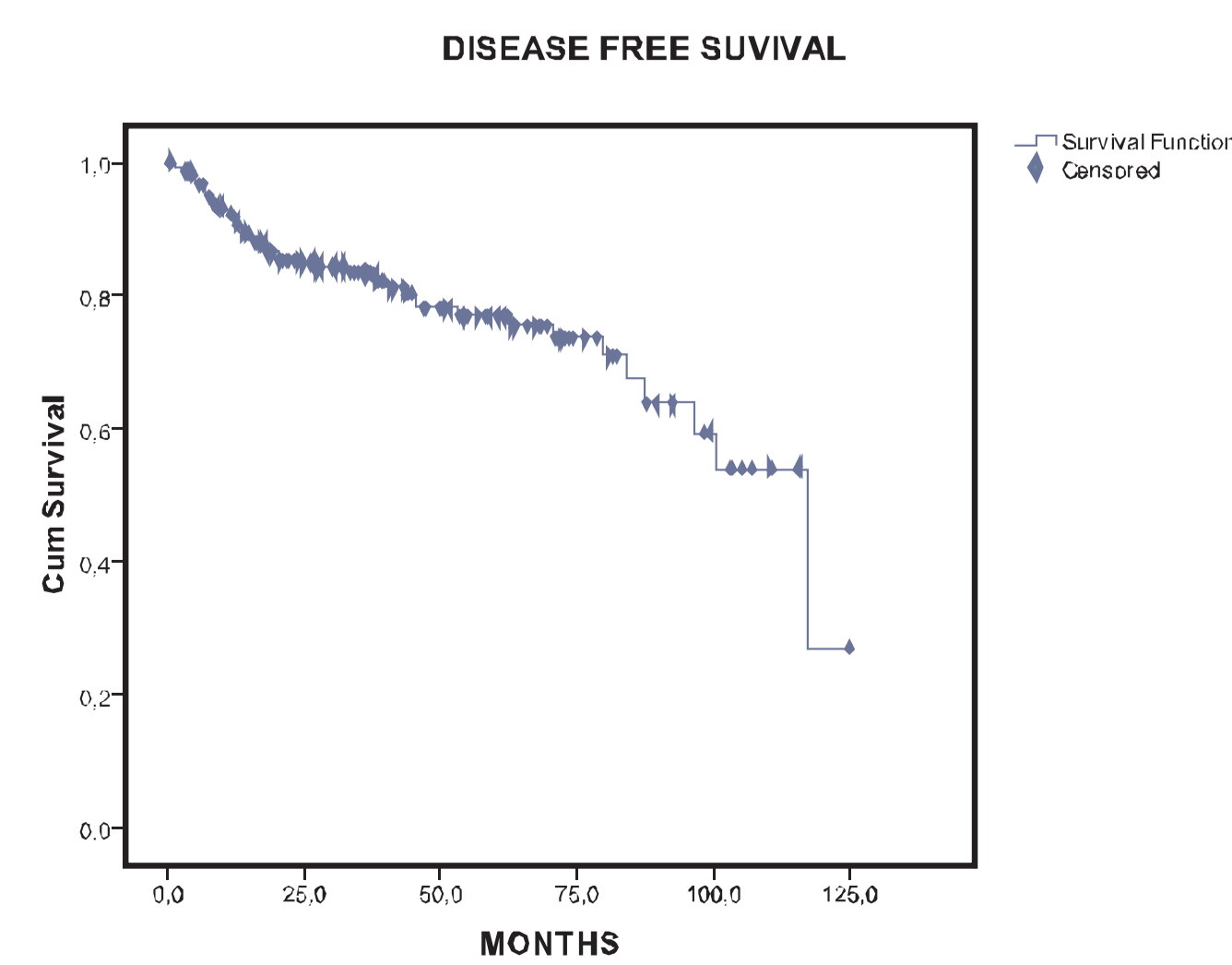


Figure 2 - Disease Free Survival

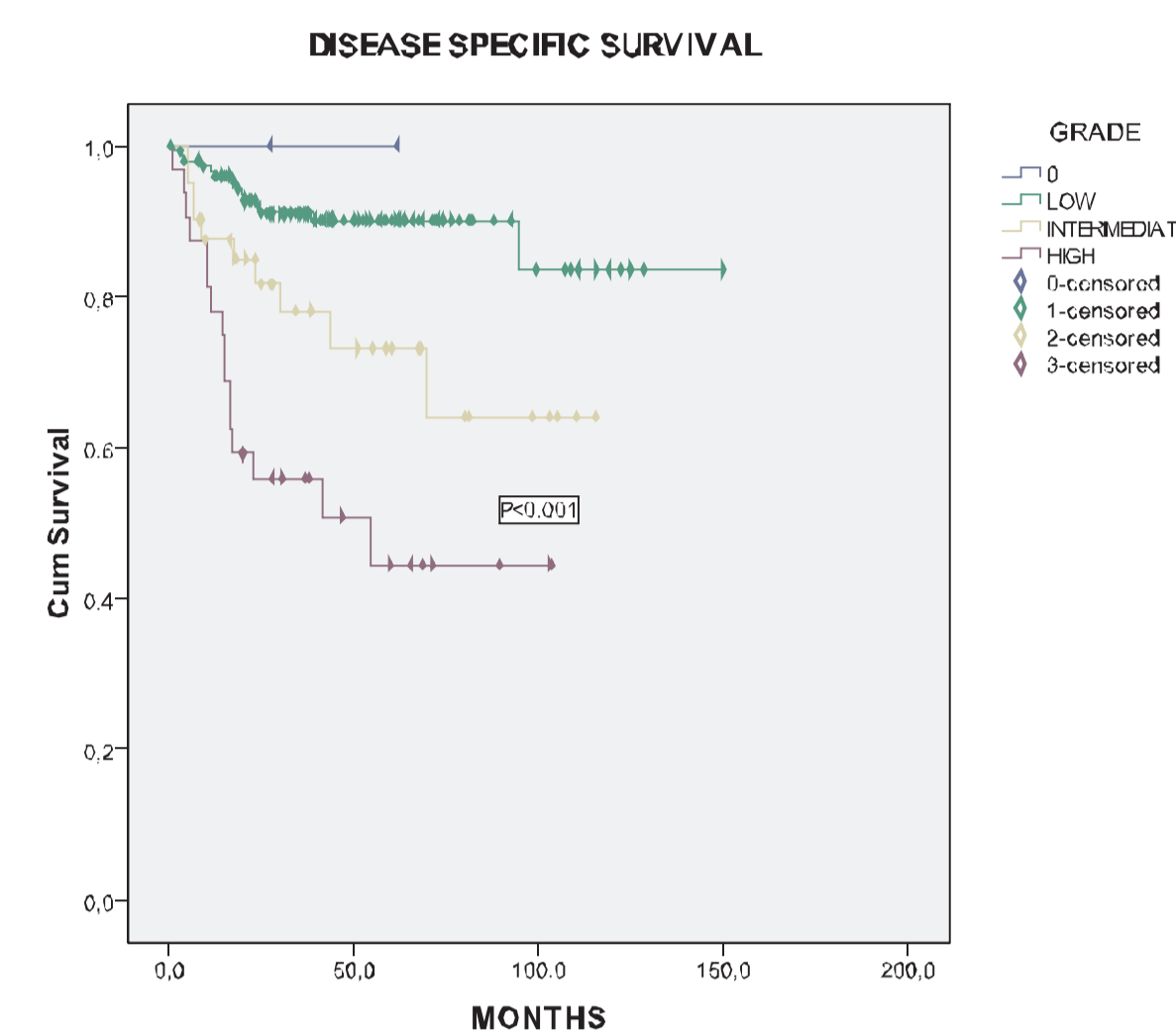


Figure 3 - Disease Specific Survival by Tumor Grade

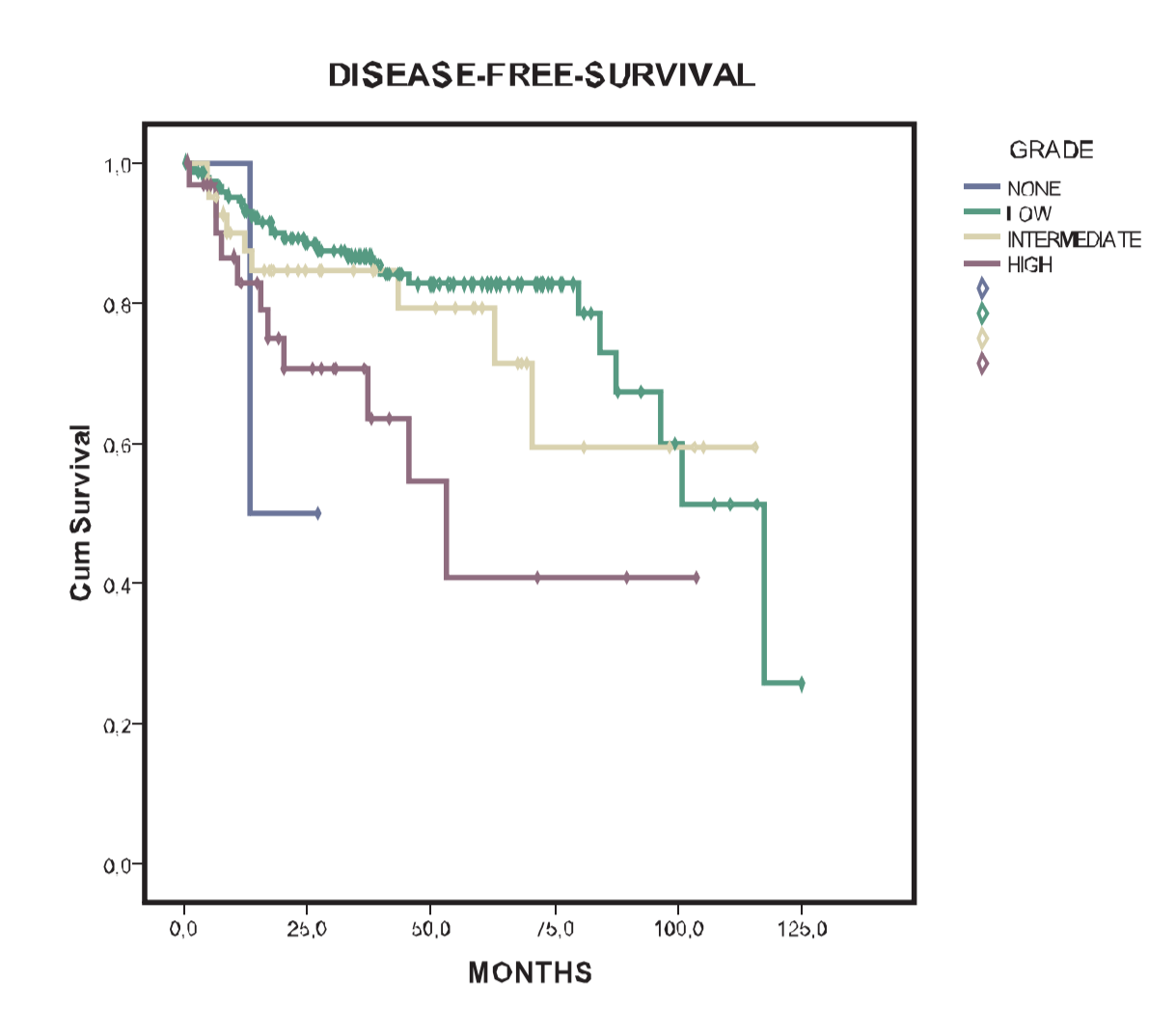


Figure 4 - Disease Free Survival by Tumor Grade

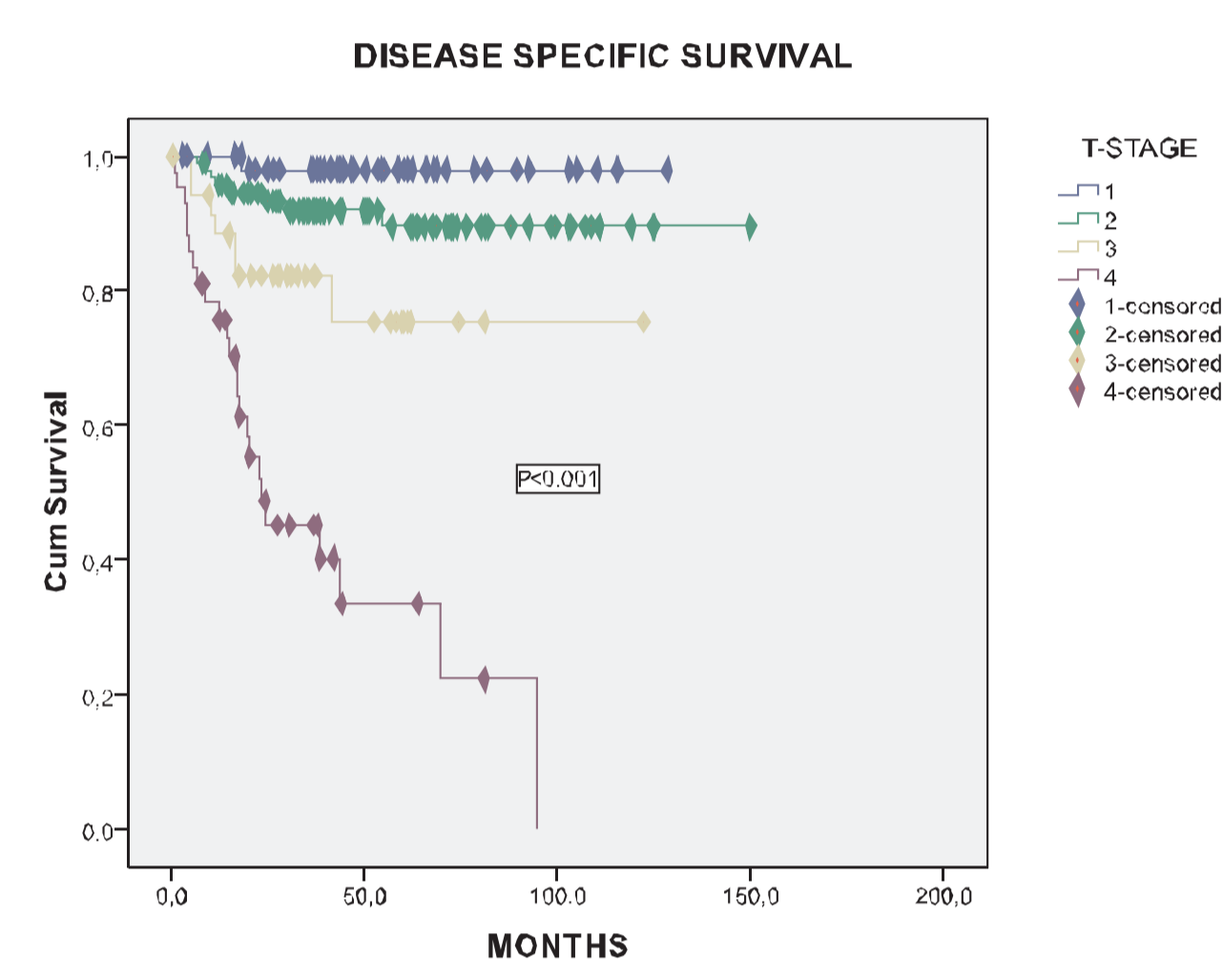


Figure 5 - Disease Specific Survival by TNM

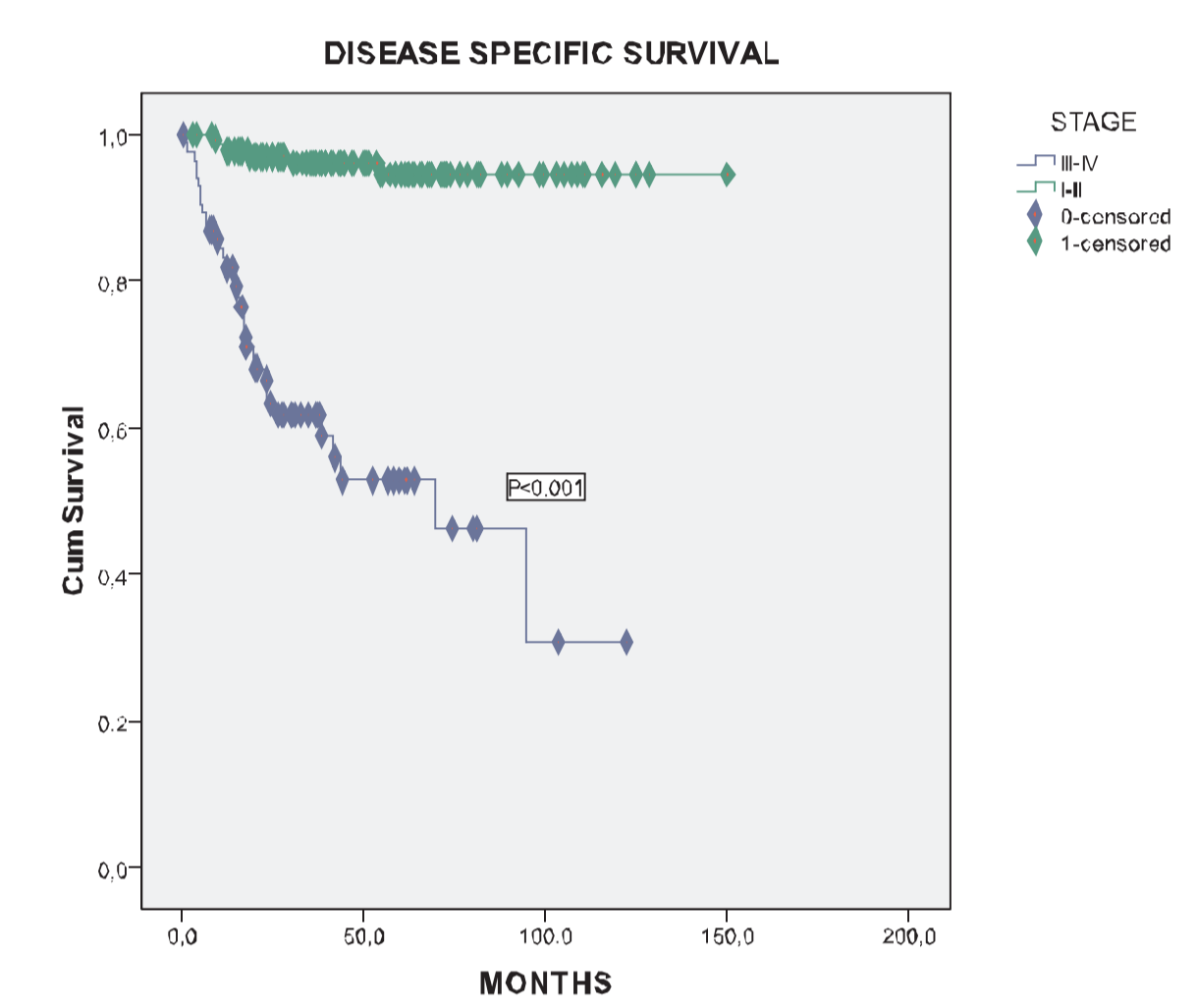


Figure 6 - Disease Specific Survival by Tumor Stage

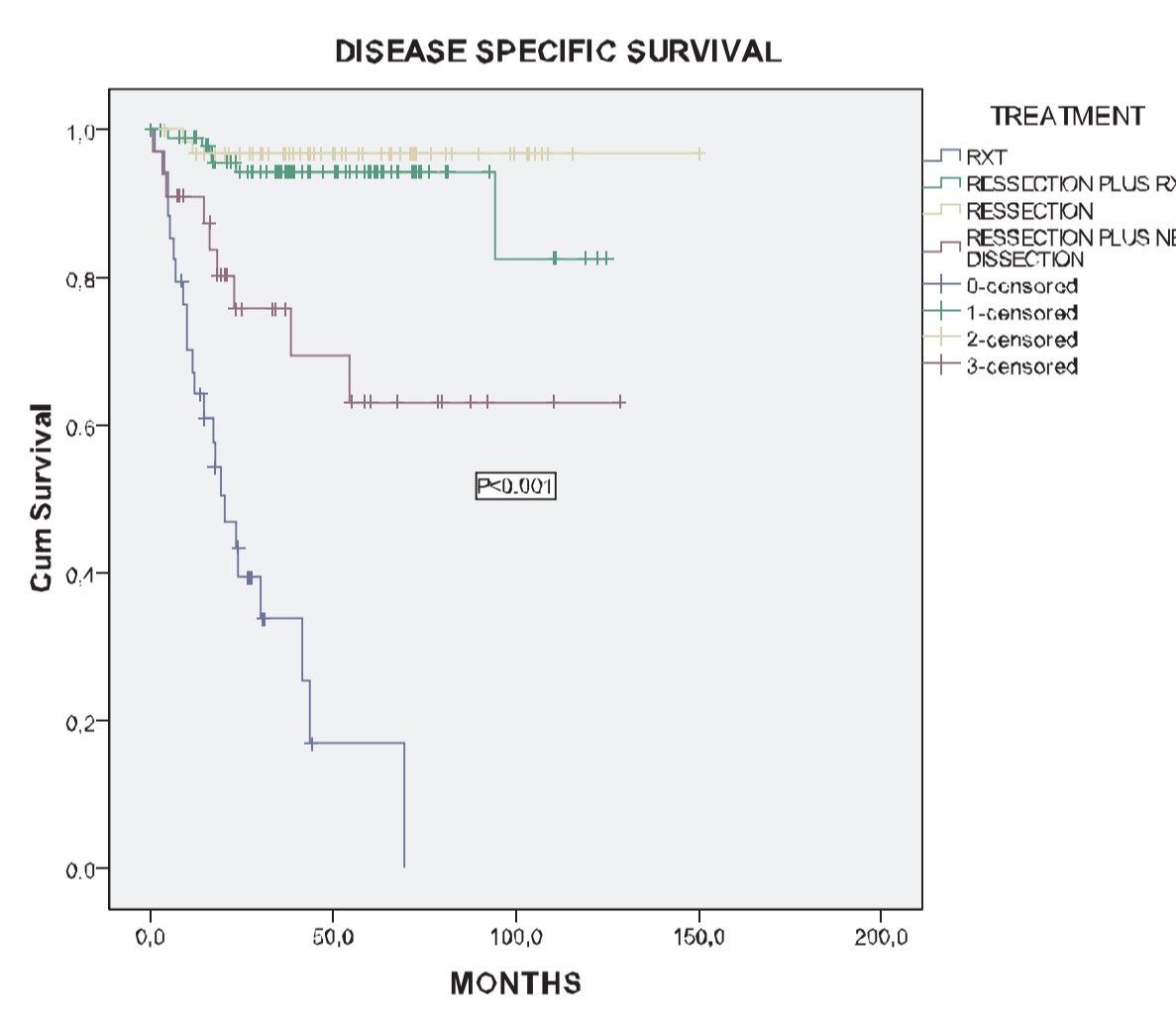


Figure 7 - Disease Specific Survival by Treatment Modality

Table 1 - Demographic Data

Parameter	No. of patients (%)
All Patients	315 (100)
Sex	
Women	190 (60.3)
Men	125 (39.7)
Age, y	
Mean	69.5
Range	18 - 82

Table 2 - Anatomic site

Parameter	N	%
Hard palate	140	44.4
Buccal mucosa	46	14.6
Tongue base	28	8.9
Floor of mouth	25	7.9
Soft palate	24	7.6
Superior alveolar ridge	14	4.4
Retromolar trigone	11	3.9
Tonsil	9	2.9
Lower alveolar ridge	8	2.5
Oral Tongue	6	1.9
Lip	3	1.3
Total	315	100

Table 3 - Histological types

Parameter	N	%
Adenoid Cystic Carcinoma	108	34.3
Mucoepidermoid Carcinoma	101	32.1
Adenocarcinoma, NOS	88	27.9
Acinic Cell Carcinoma	5	1.6
Others	13	4.2
Total	315	100

Table 4 - Disease Characteristics

Parameter	No. of patients (%)
TNM classification	
T1	73 (23.2)
T2	124 (39.4)
T3	59 (18.8)
T4	59 (18.8)
N0	28 (89)
N+	35 (11)
M1	12(4)
Clinical stage	
I-II	195 (61.9)
III-IV	120 (38.1)

Table 5 - Correlation of pathology, stage and treatment with disease-specific (DSS) and disease-free (DFS) survivals

Parameter	5 years DSS(%)	P value	5 years DFS(%)	P value
Tumor Grade				
Low grade	90	<0.001	86.5	0.018
Intermediate grade	64		59.5	
High grade	44.5		40.8	
TNM				
T1	97.9	<0.001	75.7	<0.001
T2	89.6		71.6	
T3	75.4		61.9	
T4	22.3		58.9	
Clinical Stage				
I-II	96.1	<0.001	92.2	<0.001
III-IV	58.9		61.4	
Treatment				
Surgery	82.5	0.001	77.3	<0.001
Surgery plus Radiotherapy	91		86.4	
Surgery plus neck dissection	63.2		32.0	
Radiotherapy	16.9		31.8	

CONCLUSIONS

Several prognostic factors for locoregional and distant control were found. Radical surgery with postoperative radiotherapy was found to improve locoregional control.