

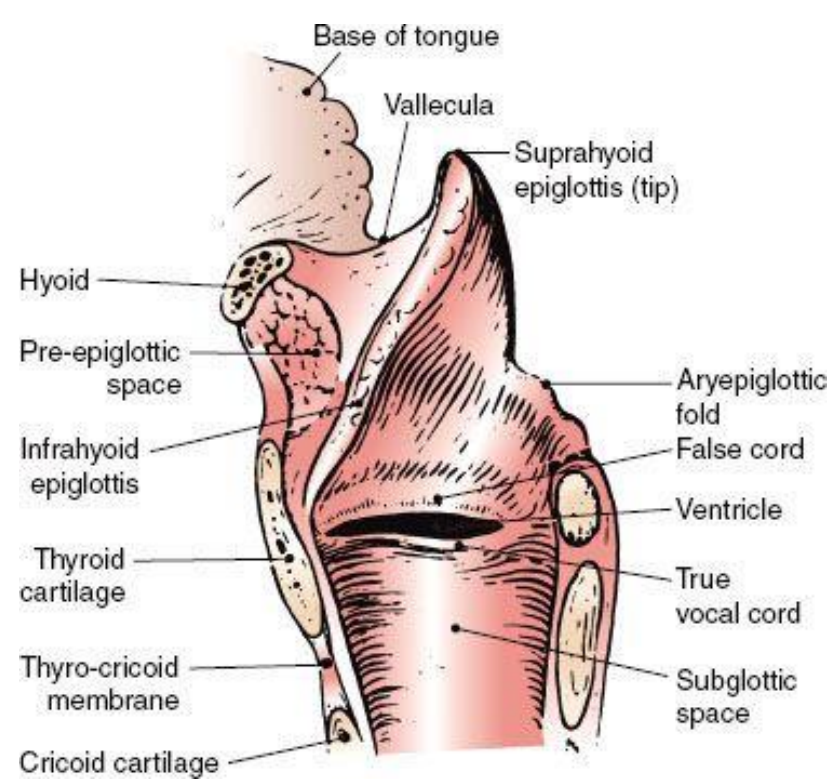
Impact of Mucosal Versus Soft Tissue Positive Final Margin Status on Survival Outcomes in Total Laryngectomy Patients

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INTRODUCTION

- Positive surgical margin status on final pathology is a known prognostic factor for local recurrence and survival outcomes in patients with laryngeal cancer.¹
- The relationship between type of final positive margin—mucosal versus soft tissue—remains underexplored.
- Achieving margins > 5 mm is challenging in the larynx because resections are constrained by complex anatomy.
- Aim:** To determine if positive margin type following total laryngectomy is predictive of recurrence and survival.



METHODS

- Multi-institutional large retrospective analysis
- Inclusion criteria:** patients who received total laryngectomy (TL) for oncologic resection and had positive margins on final pathology between 1999-2024
- Positive margin defined as invasive carcinoma, carcinoma in situ, or severe dysplasia present at the ink
- Covariates:** age, pathology T and N stage, lymphovascular invasion (LVI), perineural invasion (PNI), extranodal extension (ENE), prior radiation, adjuvant radiation, adjuvant chemotherapy
- Analysis:** Chi-square test and independent t-tests for categorical and continuous variables. Kaplan-Meier (log-rank) and Cox Proportional Hazards for univariate and multivariate survival analysis

RESULTS

Table 1. Patient Demographics

	Total (n = 142)	Mucosal (n = 71, %)	Soft Tissue (n = 71, %)	p-value
Age (years)				
Mean (std)	62.5 (8.4)	62 (8.2)	63 (8.5)	0.48
Median (range)	63 (55-69)	63 (55-67)	63 (58-69)	
Sex				0.68
Male	115 (81)	56 (79)	59 (82)	
Female	28 (19)	15 (21)	13 (18)	
Prior Radiation				p < 0.001
No	53 (37)	37 (52)	16 (22)	
Yes	90 (63)	34 (48)	56 (78)	
Pathologic T Stage				p = 0.015
T2	18 (13)	6 (9)	12 (14)	
T3	28 (20)	9 (13)	19 (26)	
T4	97 (68)	56 (79)	41 (57)	
Pathologic N Stage				0.33
Nx	12 (8)	6 (8)	6 (9)	
N0	52 (37)	25 (35)	27 (38)	
N1	16 (11)	11 (15)	5 (7)	
N2	29 (20)	16 (22)	13 (18)	
N3	34 (24)	13 (18)	21 (29)	
LVI				0.79
N/A	15 (11)	8 (11)	7 (10)	
No	60 (42)	31 (44)	29 (40)	
Yes	68 (48)	32 (45)	36 (50)	
PNI				0.29
N/A	14 (10)	5 (7)	9 (13)	
No	38 (27)	22 (31)	16 (22)	
Yes	91 (64)	44 (62)	47 (65)	
ENE				0.20
N/A	32 (23)	17 (24)	15 (21)	
No	63 (44)	35 (49)	28 (39)	
Yes	48 (34)	19 (27)	29 (40)	
Adjuvant Radiation				0.74
No	85 (60)	41 (58)	44 (61)	
Yes	58 (40)	30 (42)	28 (39)	
Adjuvant Chemotherapy				0.29
No	91 (64)	48 (68)	43 (60)	
Yes	52 (37)	23 (32)	29 (40)	

Figure 1a. Overall Survival

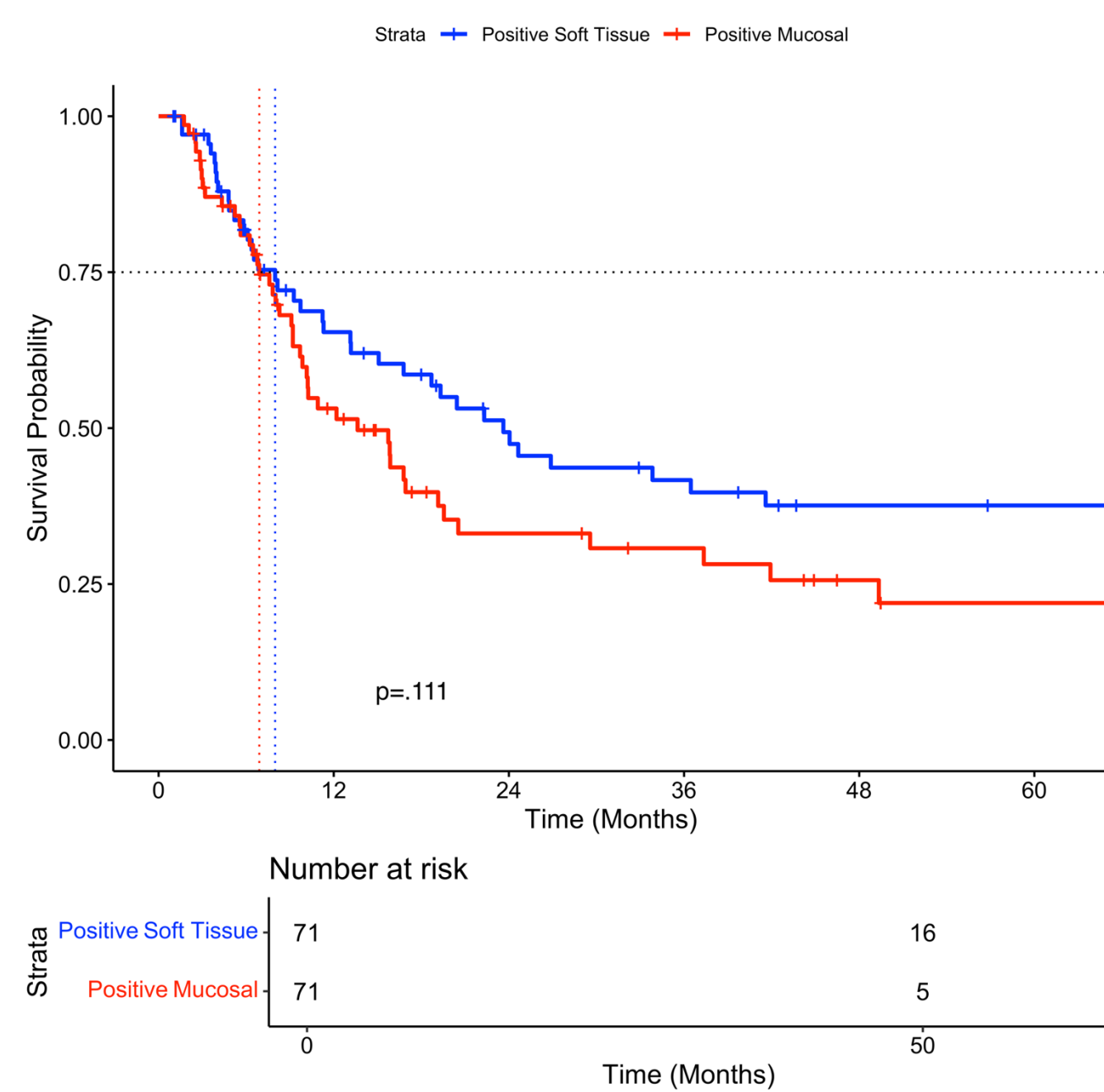


Figure 1b. Disease-Free Survival

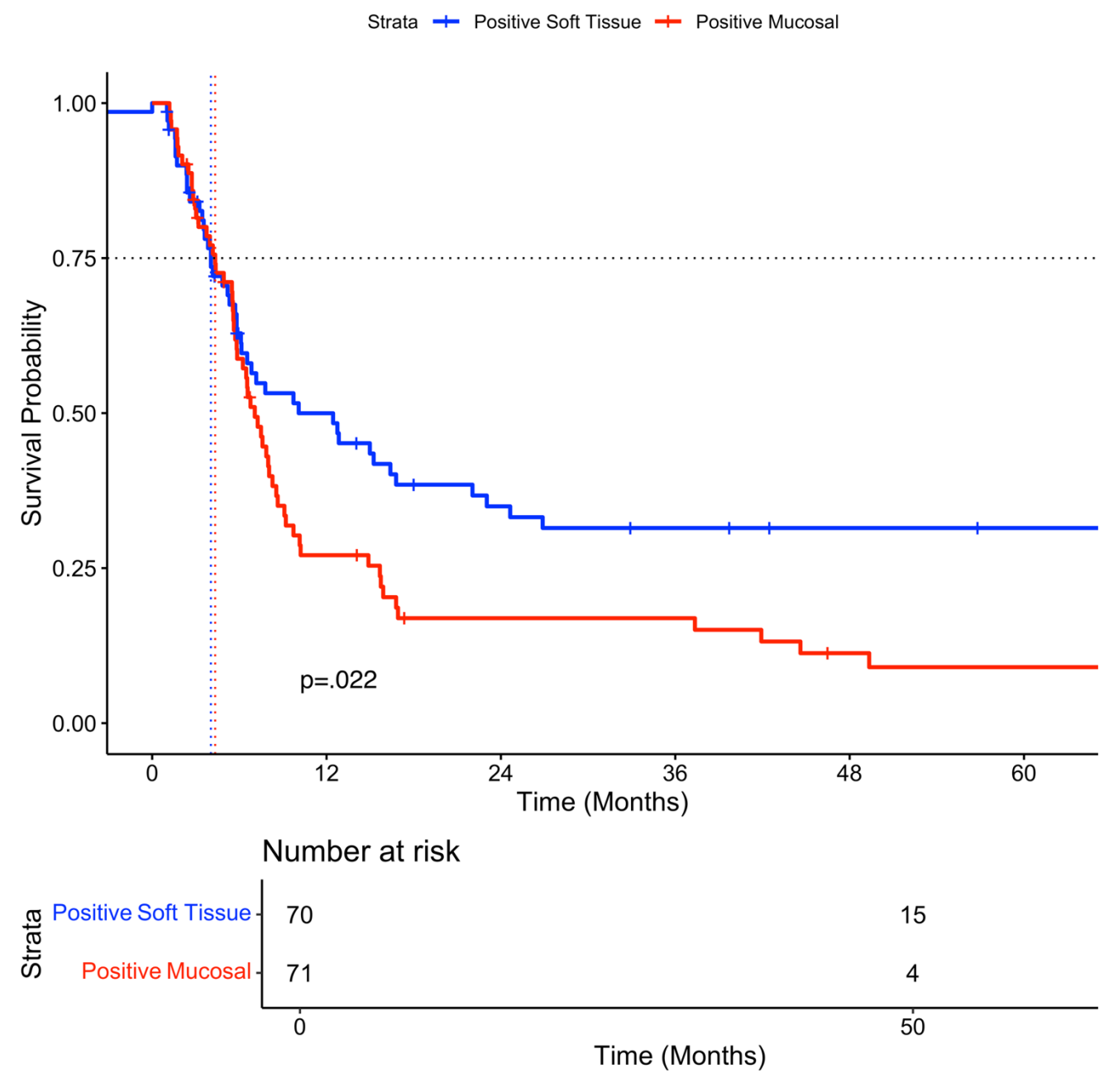
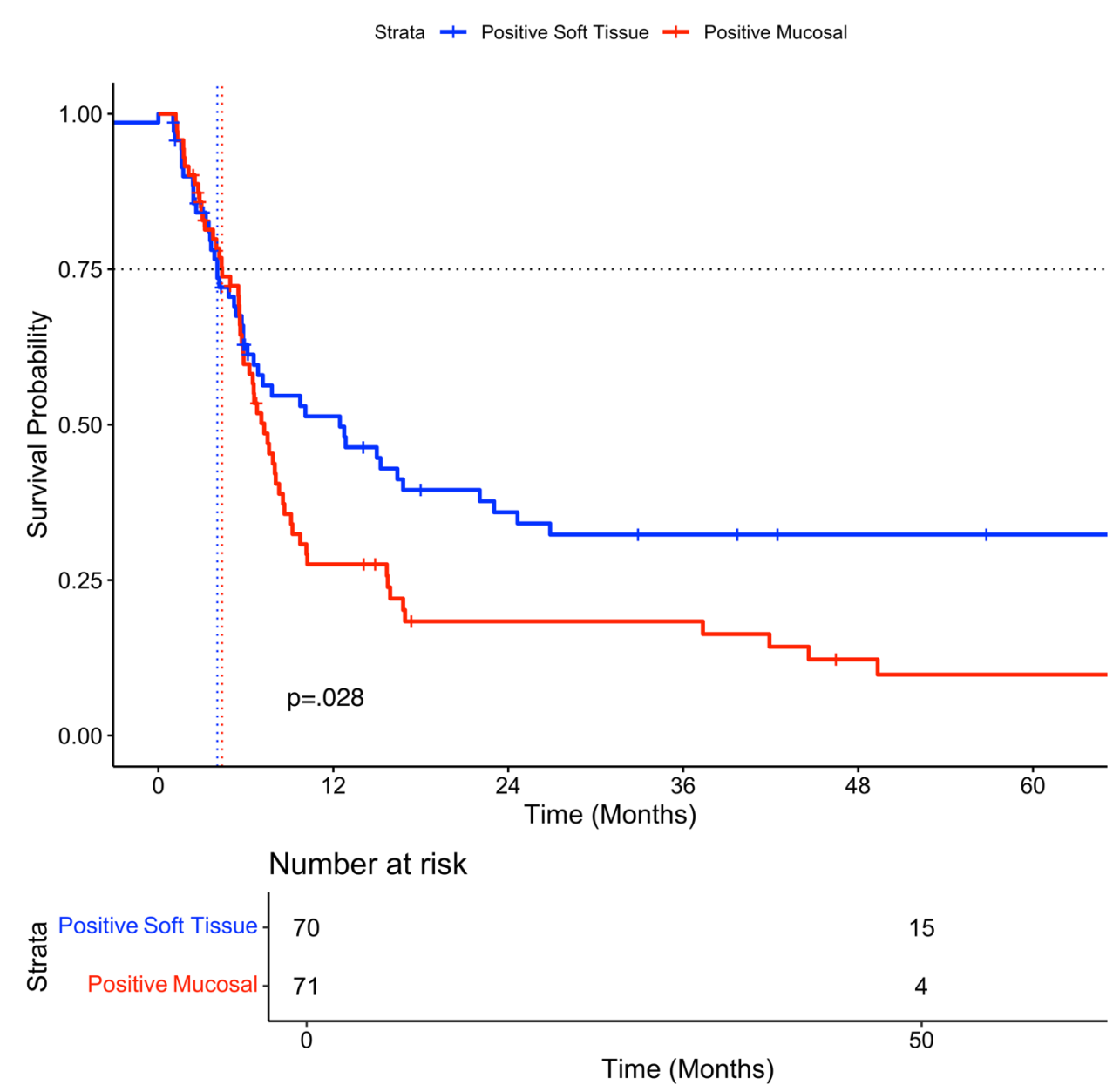


Table 2. Cox Proportional Hazards for DFS

Variable	Univariate			Multivariate		
	HR	CI	P Value	HR	CI	P Value
Age	0.99	0.97-1.02	0.65	1.00	0.98-1.03	0.91
Sex	1.59	0.97-2.64	0.07	1.44	0.83-2.52	0.19
Pathologic Tumor (T) Stage	1.23	0.66-2.3	0.52	1.31	0.64-2.68	0.45
Pathologic Nodal (N) Stage	1.65	1.07-2.53	0.02	2.62	1.6-4.29	< 0.01
History of radiation	2.01	1.32-3.07	< 0.01	2.50	1.4-4.43	< 0.01
Adjuvant Chemotherapy	0.86	0.57-1.29	0.46	0.78	0.38-1.59	0.49
Adjuvant radiation	0.77	0.52-1.15	0.20	0.97	0.45-2.08	0.94
Positive mucosal margin	1.55	1.05-2.3	0.03	1.29	0.8-2.07	0.30

Figure 1c. Local Disease-Free Survival



DISCUSSION

- The adverse impact of mucosal margin positivity likely reflects both biologic and technical factors.
- Biologically, residual carcinoma at the mucosal edge lies adjacent to highly vascularized and dense submucosal lymphatic networks, facilitating locoregional dissemination.
- By contrast, soft tissue margin involvement is often mitigated by concurrent neck dissection or postoperative radiation fields, limiting its independent prognostic weight.

CONCLUSIONS

- In this multi-institutional cohort, **final positive mucosal margins** following TL was associated with worse DFS compared to positive soft tissue margins on univariable analysis.
- Further studies are necessary to understand whether mucosal margin positivity represents a high-risk subset, potentially warranting closer surveillance and tailored adjuvant treatment.

REFERENCES

- Hinni ML, Ferlito A, Brandwein-Gensler MS, et al. Surgical margins in head and neck cancer: A contemporary review. *Head Neck*. 2013;35(9):1362-1370. doi:10.1002/hed.23110
- Bradford CR, Wolf GT, Fisher SG, McClatchey KD. Prognostic importance of surgical margins in advanced laryngeal squamous carcinoma. *Head Neck*. 1996;18(1):11-16. doi:10.1002/(SICI)1097-0347(199601/02)18:1<11::AID-HED2>3.0.CO;2-1
- Cooper JS, Pajak TF, Forastiere AA, et al. Postoperative Concurrent Radiotherapy and Chemotherapy for High-Risk Squamous-Cell Carcinoma of the Head and Neck. *N Engl J Med*. 2004;350(19):1937-1944. doi:10.1056/NEJMoa032646
- Bernier J, D'Amico C, Ozsahin M, et al. Postoperative Irradiation with or without Concomitant Chemotherapy for Locally Advanced Head and Neck Cancer. *N Engl J Med*. 2004;350(19):1945-1952. doi:10.1056/NEJMoa032641
- Bernard SE, Van Lanschot CGF, Sewnaik A, et al. Clinical Relevance of Resection Margins in Patients with Total Laryngectomy or Laryngopharyngectomy. *Cancers*. 2024;16(11):2038. doi:10.3390/cancers16112038