



Assessing the Prognostic Value of Up-front Neck Disease in Olfactory Neuroblastoma: A Multicenter, Matched Cohort Study

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Introduction

- Olfactory neuroblastoma (ONB) is a rare sinonasal/skull base malignancy known for its predilection for delayed metastasis ¹
- Nodal disease at presentation (N+) is uncommon (5-11.5%) and is associated with increased modified Kadish staging and worse overall survival ^{1,2}
- Most centers generally advocate for aggressive treatment of the neck via neck dissection and adjuvant RT ^{2,3}
- However, there is no standardized approach to the treatment of N+ disease in ONB
- Given the rarity of N+ ONB, its impact on survival/recurrence outcomes and patterns of disease recurrence are not well-studied

Methods and Materials

- Retrospective review of 257 patients with histologic confirmed ONB from February 2005 until April 2021 from nine tertiary care, academic medical centers within North America
- Epidemiologic parameters and tumor characteristics were recorded for each patient including: age and gender, margin status, Hyams grade, Kadish staging, dural invasion, and survival follow up data.
- 1:4 cohort match was performed due to rarity of upfront neck disease on presentation (N+)
 - Co-variables used for matching: age, sex, Kadish staging and Hyams grade (low vs. high)
 - After 1:4 cohort matching, the final cohort matched 94 N0 patients with 27 N+ patients (121 total)
- Survival analysis was performed using Kaplan-Meier and conditional logistic regressions
- Recurrence-free survival (RFS) and overall survival (OS) were the primary and secondary endpoints respectively

Table 1. Cohort demographic and pathologic characteristics by up-front neck disease status. Students t-test performed for continuous variables and Fisher Exact Test performed for categorical variables. SD – standard deviation

Variable	With Up-front Neck Disease (n = 27) n (%)	Without Up-front Neck Disease (n = 94) n (%)	p-Value
Age (years)			
Mean (SD)	48 (14.2)	49.9 (15.1)	0.547
Follow-up (months)			
Mean (SD)	54.0 (37.7)	60.9 (42.8)	0.416
Sex			1.0
Female	10 (37%)	36 (38.3%)	
Male	17 (63%)	58 (61.7%)	
Hyams Grade			0.662
Low (I or II)	15 (55.6%)	57 (60.6%)	
High (III or IV)	12 (44.4%)	37 (39.4%)	
Margin Status (n = 108)			0.154
Negative	13 (52.0%)	57 (68.7%)	
Positive	12 (48.0%)	26 (31.3%)	
Kadish Staging			0.116
A	0 (0%)	2 (2.1%)	
B	2 (7.4%)	17 (18.1%)	
C	25 (92.6%)	75 (79.8%)	
Primary Neck Dissection			< 0.001
None	16 (59.3%)	93 (98.9%)	
Unilateral	8 (29.6%)	1 (1.1%)	
Bilateral	3 (11.1%)	0 (0%)	
Primary Neck Irradiation (n = 101)			< 0.001
None	6 (25.0%)	60 (77.9%)	
Unilateral	7 (29.2%)	3 (3.9%)	
Bilateral	11 (45.8%)	14 (18.2%)	
Site of Recurrence			
Nasal Cavity/Paranasal Sinuses	4 (14.8%)	17 (18.1%)	0.781
Neck	4 (14.8%)	19 (20.2%)	0.781
Intracranial	2 (7.4%)	2 (2.1%)	0.215
Distant	2 (7.4%)	3 (3.2%)	0.310

Results

- Overall rate of N+ on presentation was 10.7%
- Patients with N+ disease were more likely to undergo a unilateral (29.6% vs. 1.1%, p < 0.001) or bilateral neck dissection (11.1% vs 0%, p < 0.001), compared to N0 patients
- Patients with N+ disease were more likely to undergo neck radiation (75.0% vs. 22.1%, p < 0.001)
- There were no differences among the patterns of recurrence between the N+ and N0 groups (Table 1):
 - Nasal cavity/paranasal sinuses (14.8% vs. 18.1%)
 - Neck (14.8% vs. 20.2%)
 - Intracranial (7.4% vs. 2.1%)
 - Distant metastasis (7.4% vs. 3.2%)
- There were no statistically significant difference in 10-year OS (37.8% vs. 63.7%, p = 0.11) or 10-year RFS (30.4% vs. 32.6%, p = 0.44) between N+ and N0 patients, respectively
- N+ disease was not an independent, statistically significant predictor for RFS (OR: 1.1, 95% CI: 0.47 - 2.60, p = 0.828) and OS (OR 1.98, 95% CI 0.77 - 5.10, p = 0.156)

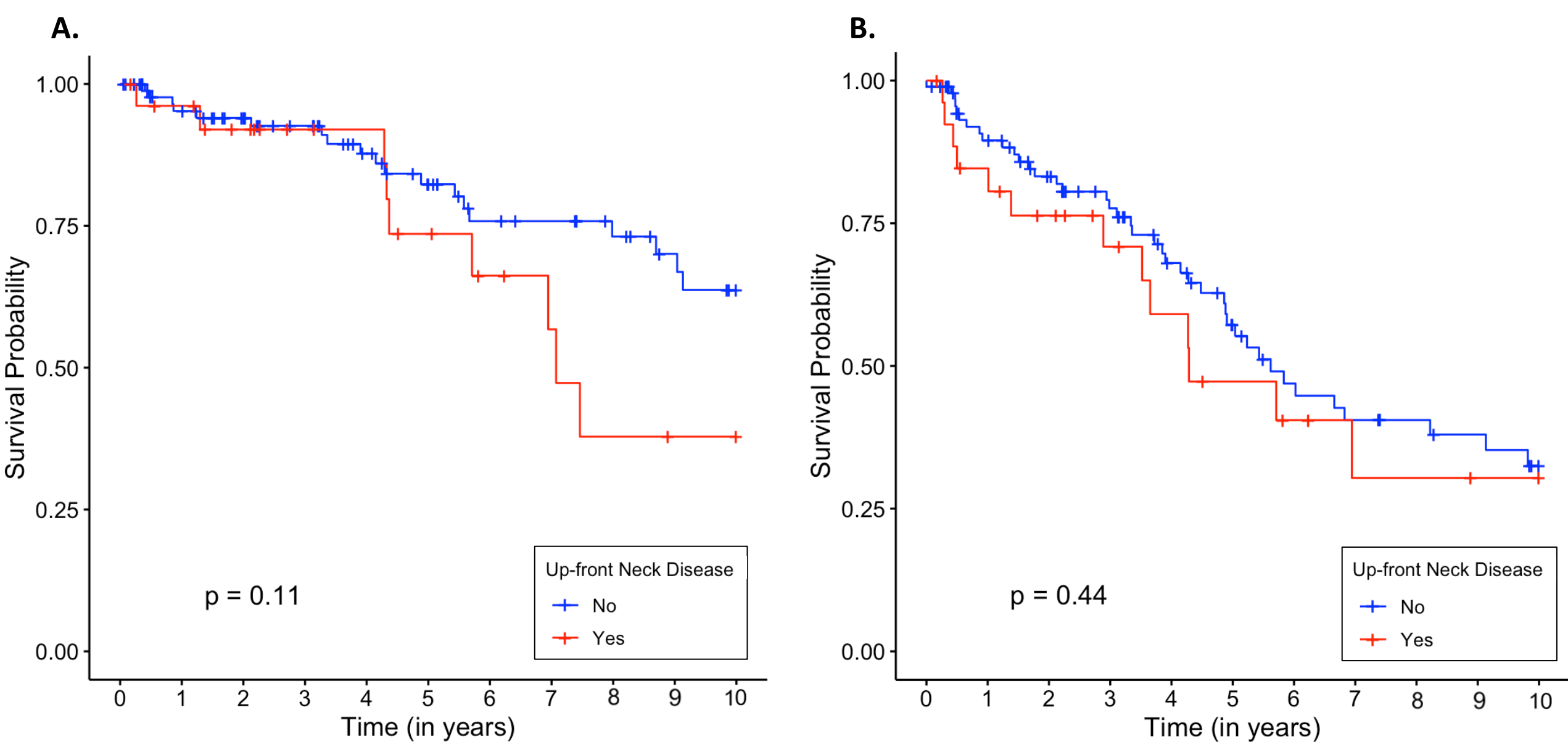


Figure 1. A. Overall survival (OS) by up-front neck disease status **B.** Recurrence free survival (RFS) by up-front neck disease status. P-value generated via log-rank testing.

Discussion

- One of the largest reported cohorts of ENB in the literature
- Rate of N+ disease on presentation is similar to previously reported studies (5-11.5%) ^{1,2}
- When N+ patients were treated with neck dissection, unilateral neck dissection were most commonly performed
- When N+ patients were treated with neck irradiation, bilateral neck irradiation was most commonly performed
- Similar to several other studies, the most common pattern of recurrence occurred within locoregional cervical nodal stations (14.8 – 20.2%) ²
- In contrast to other studies, when controlling for Kadish staging and Hyams grade, nodal disease on presentation did not independently predict worse OS or RFS, especially at the 5-year timepoint used by other literature ^{2,3,4}

Limitations

- Retrospective chart review across several institutions in North America limit our study's generalizability to other patient populations
- Treatment approaches varied from institution to institution
- Limited study scope to compare the efficacy of definitive treatment regimens for N+ disease on presentation

Conclusions

- In this matched cohort study, no survival differences were demonstrated in ONB patients who presented with N+ vs N0 disease
- Despite receiving definitive treatment of the neck more frequently, N+ patients did not significantly differ in their rates of local and locoregional recurrences

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