Modeling the Risk of Occult Metastatic Disease in Head and Neck Cancer

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Introduction

- Oral cavity and oropharyngeal cancers make up over 60% of head and neck malignancies.
- Lymph node metastasis is a critical prognostic indicator in head and neck cancer. Even with appropriate clinical workup, occult lymph node metastasis is found in ~30% of clinically node-negative patients.
- Occult nodal metastasis is associated with worse survival, compared to pathologically node-negative patients or patients with all positive nodes identified pre-operatively. Occult nodal metastasis also increases the rate of regional recurrence by 10-fold.

This study aimed to model the risk of occult nodal metastasis in patients with oral cavity and oropharyngeal cancers as a function of lymph node yield.

Methods

- Using the **National Cancer Database** (NCDB, 2004 – 2017), patients with cancer of the oropharynx (OPC) or oral tongue and floor of mouth (OTFOM) were identified who had:
  - One primary tumor
  - Surgical procedure of the primary site
  - Clinical absence of regional lymph node metastasis
  - At least 2 regional nodes removed during surgery
- A **β-binomial distribution model** was used to estimate the probability of occult nodal disease with the following steps:
  1. Calculation of probability of false negative lymphadenectomy
  2. Estimation of the prevalence of false negative lymphadenectomy in the study population, correcting for probability in step 1.
  3. Estimation of the risk of occult nodal metastasis by combining the calculations of steps 1 and 2.
- **Overall survival** was estimated using the Kaplan-Meier method for each cancer group by the quartiles of probability of occult nodal disease. Log-rank tests were used to compare overall survival between quartiles.

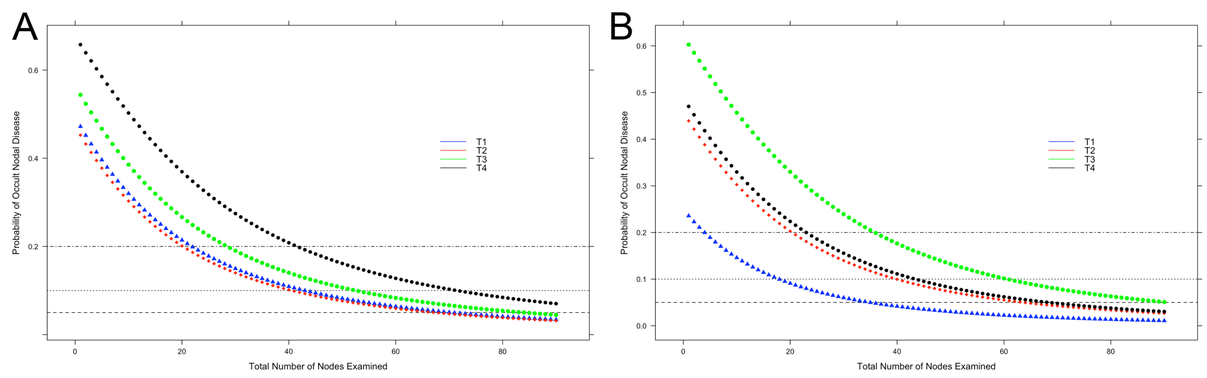
Patient Characteristics

	Overall (n = 13,657)	Node-Negative (n = 9,804)	Node-Positive (n = 3,853)	P-value
Age at Diagnosis (years) Mean (SD)	59 (12)	59 (12)	59 (12)	0.42
Female n (%)	4,883 (36%)	3,592 (37%)	1,291 (34%)	<0.001
Race n (%)				0.31
White	12,168 (90%)	8,708 (90%)	3,460 (91%)	
Black	739 (5.5%)	530 (5.5%)	209 (5.5%)	
Other	588 (4.4%)	438 (4.5%)	150 (3.9%)	
Unknown	162	128	34	
T Stage n (%)				<0.001
T1	5,707 (45%)	4,554 (51%)	1,153 (32%)	
T2	4,531 (36%)	3,051 (34%)	1,480 (41%)	
T3	984 (7.8%)	545 (6.1%)	439 (12%)	
T4	1,360 (11%)	812 (9.1%)	548 (15%)	
Unknown	1,075	842	233	

Results

Step 1: Estimated Risk of False Negative Lymphadenectomy

- Probability of false negative lymphadenectomy decreased as the number of nodes examined increased and was **reduced to <10% when 47 nodes** were dissected in either group.



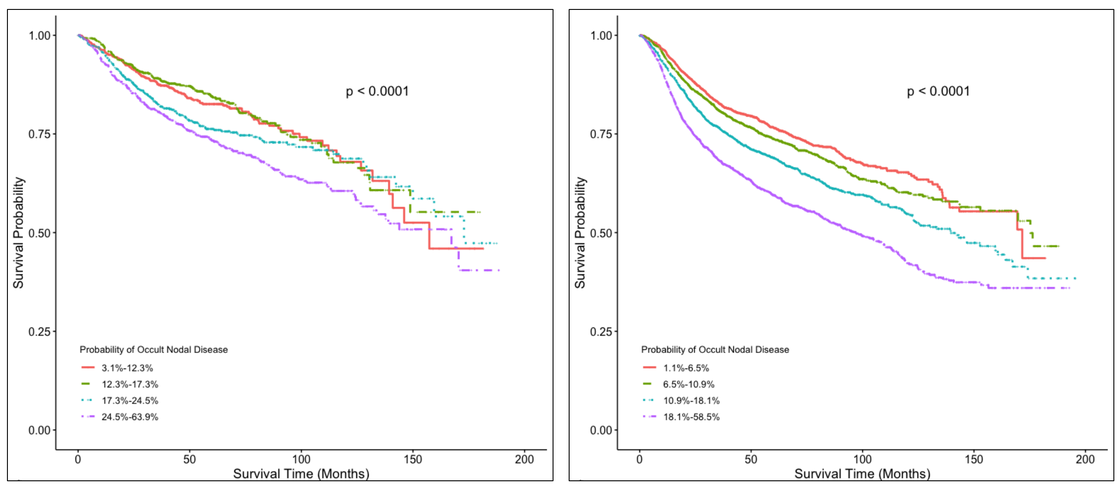
- A – oropharyngeal cancer; B – oral tongue and floor of mouth cancer

Step 2: Estimated True Prevalence of Lymph Node Metastasis

Prevalence	T1 (%)	T2 (%)	T3 (%)	T4 (%)	All (%)
Oropharyngeal Cancer					
Observed Prevalence	33.22	34.05	42.06	51.78	35.34
Corrected (True) Prevalence	49.31	47.34	56.48	67.65	49.10
Oral Tongue and Floor of Mouth Cancer					
Observed Prevalence	16.87	31.99	46.21	37.67	25.69
Corrected (True) Prevalence	24.92	45.75	62.03	48.87	36.45

Step 3: Estimated Probability of Occult Nodal Disease as a Function of Lymph Node Yield and Tumor Stage

- To limit the **risk of occult lymph node metastasis to 10%** for stages T1, T2, T3, and T4 respectively, the model estimated that:
  - **42, 40, 52, and 71 nodes** should be examined for OPC
  - **17, 39, 60, and 43 nodes** should be examined for OTFOM
- Overall survival varied significantly by quartile of occult nodal disease risk ($p < 0.0001$), with patients at the highest quartile having the worst survival.



- Left – oropharyngeal cancer; Right – oral tongue and floor of mouth cancer

Conclusions

- Our model demonstrated that the risk of false negative lymphadenectomy in patients with oral cavity or oropharyngeal cancers increases with fewer lymph nodes dissected and with increasing tumor stage.
- Patients with an elevated risk for occult nodal disease also have worse long-term survival compared to those with lower risk.
- These results showed be considered when evaluating the need for adjuvant radiation to the neck.

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