The Current Practice of Open Neck Mass Biopsy in the Diagnosis of Head and Neck Cancer: A Retrospective Cohort Study

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Objective: To characterize current use of open neck mass biopsy for diagnosis of squamous cell carcinoma in patients presenting with a neck mass.

Methods: Using the University of Michigan Specialized Program of Research Excellence in Head and Neck Cancer patient database (2008–2014), we reviewed patients' referral documentation to identify those who received open neck mass biopsies as part of their squamous cell carcinoma diagnosis. We compared subsequent treatment between patients who did and did not receive an open neck mass biopsy.

Results: Of 940 patients, 50 patients had received open neck mass biopsy leading to squamous cell carcinoma diagnosis. Only 19 of 50 patients (38%) had undergone fine-needle aspiration prior to open neck mass biopsy. There were no statistically significant differences in treatment or outcomes between patients who did and those who did not receive open neck mass biopsy.

Conclusion: Optimal care for patients who present with a neck mass is fine-needle aspiration. Unfortunately, these data show that many patients undergo open neck mass biopsy for diagnosis, often without prior fine-needle aspirate. Compared to fine-needle aspiration, open biopsy incurs additional risks of general anesthesia and greater surgical risks. While our data did not find statistically significant differences between treatment offered and outcomes, this small study was not expected to demonstrate a difference in outcomes. Further work is needed to promote the utility of fine-needle aspiration for diagnosis of neck mass and to discourage use of open neck mass biopsy as a primary diagnostic intervention.

Key Words: Head and neck squamous cell cancer, metastatic lymph node, open neck mass biopsy.

Level of Evidence: 2c (Outcomes Research)

INTRODUCTION

In patients who present with a neck mass, potential cervical metastasis of carcinoma and particularly head and neck squamous cell carcinoma (HNSCC) should always be a

consideration. For this reason, the diagnostic modality utilized in these patients must be chosen carefully to maximize accuracy while minimizing the risk. In the past, open neck mass biopsy was utilized as a primary method for obtaining definitive diagnosis of a suspicious node, especially for neck masses concerning for melanoma, salivary, and thyroid malignancies.[1–3] However, with the increased availability of fine-needle aspiration (FNA) testing, this minimally invasive technique has become the test of choice. The National Comprehensive Cancer Network (NCCN) Guidelines indicate comprehensive clinical examination should be accompanied by FNA as the primary diagnostic test. According to NCCN Guidelines, open neck mass biopsy should only be performed if an FNA is non-diagnostic.[4] Furthermore, at the time of open biopsy, if the open biopsy reveals HNSCC then the patient and surgeon must be prepared for definitive surgical management including neck dissection.[4]

A surgeon who performs open neck mass biopsy in the setting of HNSCC risks local wound complications, distortion of anatomy, and possibly oncologic seeding.[5–7] The traditional teaching in head and neck surgery is that open biopsies may lead to an increased risk of metastases and decreased survival.[5] For these reasons, violating the neck with an open biopsy may have implications on treatment recommendations, with most of the current literature recommending adjuvant radiotherapy to these patients.[8–11] Despite the recommendations against performing open biopsy, it is still frequently performed. We

sought to characterize the current practice of open biopsy for patients presenting with a neck mass. Given the controversial effect of open neck mass biopsy on HNSCC treatment options, we also sought to evaluate treatment received by the group of patients whose HNSCC was diagnosed with an open neck biopsy, in comparison to those who did not receive an open neck mass biopsy.[7]

MATERIALS AND METHODS

Data Sources and Subjects

A retrospective chart review was conducted on 940 patients identified from the University of Michigan Head and Neck Cancer Specialized Program of Research Excellence (SPORE) II Project 3 database. Patients in the database had been prospectively enrolled between November 10, 2008 and April 4, 2014. All patients had a new diagnosis of HNSCC and all patients provided informed consent. Medical record documentation was examined to identify patients who received an open neck mass biopsy prior to diagnosis of HNSCC and referral to our institution. Documented indications for open neck biopsy were recorded, along with additional testing patients underwent as part of their diagnosis prior to open biopsy. Our comparison cohort was patients who presented with a neck mass but did not undergo open neck mass biopsy prior to diagnosis of HNSCC. Definitive treatment received by patients in both cohorts was recorded. Demographic information, details about tumor location, definitive therapy undergone, and disease outcomes along with mortality data up to 2014 were compiled for all patients from existing data in the SPORE database, which was obtained through yearly epidemiologic survey. Patients with a primary tumor site identified as the oral cavity were excluded.

The University of Michigan Institutional Review Board reviewed and approved this study.

Statistical Analysis

Descriptive statistics were calculated regarding demographic and clinical characteristics of all patients. Total percentage of patients who underwent each diagnostic test utilized prior to open neck mass biopsy was calculated, as well as total percentage of patients for each indication for open neck mass biopsy that was documented. Of note, HPV status was not available for over half of subjects in this cohort and is therefore not reported. The total percentage of patients in both cohorts who received surgery, chemotherapy, and/or radiation as treatment for HNSCC was calculated. Two sample test of proportion was then used to determine whether the difference in the proportion of patients receiving each type of treatment in each cohort was statistically significant. Statistical analyses were performed using STATA SE 12 (StataCorp, College Station, TX) statistical software.

RESULTS

Examination of referral documents from 940 patients representing a 6-year recruitment window identified 50 patients presenting with neck mass who underwent open neck mass biopsy prior to diagnosis with HNSCC, and 77 patients presenting with neck mass that did not. The majority of patient in these cohorts were male (40/50 or 80% and 69/77 or 90%), European American/White (48/50 or 96% and 73/77 or 95%), and had an average age of 58 years (Table I). Community referral practices

consisted mainly of otolaryngology practices (44/50 or 88%), including one DO provider office, with the remainder of referral practices as community cancer centers with medical oncology provider referrals. Tumor site and stage distribution after patient review and diagnosis at the tertiary care center revealed that most cancers in both cohorts were eventually found to originate in the oropharynx (Table I). We excluded primary tumors identified as oral cavity cancers, given that current NCCN guidelines state that surgery is the primary treatment for oral cavity tumors regardless of prior diagnostic testing,[4]

TABLE I.
Patient Demographics.

Patient Characteristics	Open Biopsy Patients % (count) N = 50	Non-Open Biopsy Patients % (count) N = 77
Sex		
Male	80 (40)	90 (69)
Female	20 (10)	10 (8)
Age (Years)	58 (50)	58 (77)
Race		
European American/White	96 (48)	95 (73)
Asian	2 (1)	4 (3)
Other	2 (1)	1 (1)
Tumor Site		
Larynx	0	9 (7)
Oropharynx	70 (35)	55 (42)
Hypopharynx	2 (1)	8 (6)
Nasopharynx	6 (3)	1 (1)
Salivary gland	2 (1)	0 (0)
Unknown primary	20 (10)	27 (21)

TABLE II.
Diagnostic Testing Prior to Open Neck Mass Biopsy.

Test or procedure	Open Biopsy Patients % (count)* N = 50
Neck mass FNA[a]	38 (19)
Neck mass ultrasound	26 (13)
CT[b] of the head and neck	88 (44)
CT of the chest	30 (15)
PET[c]	58 (29)
MRI[d] of the neck	6 (3)
CXR[e]	8 (4)
Flexible laryngoscopy	36 (18)
Direct laryngoscopy	42 (21)
Neck dissection at time of open neck mass biopsy	0

*Many patients had more than one test or procedure.
[a]FNA, Fine Needle Aspirate.
[b]Computerized Tomography.
[c]Positron Emission Tomography.
[d]Magnetic Resonance Imaging
[e]Chest x-ray

TABLE III.
Documented Indication for Open Neck Mass Biopsy.*

	Patients % (count)
Indication documented	N = 50
FNA nondiagnostic	14 (7)
FNA suspicious for lymphoma	2 (1)
Clinical suspicion for lymphoma	20 (10)
FNA negative for malignancy	4 (2)
Suspected branchial cleft cyst	6 (3)
Unclear	52 (26)

*Only one indication was listed per patient chart reviewed.

and one of our primary objectives of this study was to analyze whether treatment options may be changed once a patient has undergone open neck mass biopsy.

Among the open neck mass biopsy cohort, total percentage of patients undergoing a variety of diagnostic procedures prior to open neck mass biopsy revealed that only 38% (19/50) of patients had received an FNA prior to open neck mass biopsy. None of these patients underwent concurrent neck dissection at time of open neck mass biopsy (Table II). Indications for performing an open neck mass biopsy varied, with the majority of indications unclear from the documentation reviewed from the outside institution (26/50 or 52%) (Table III). Clinical suspicion for lymphoma represented the most common reported indication (10/50 or 20%), although an inconclusive FNA was also relatively common (7/50 or 14%). When definitive treatment of patients in the cohort undergoing open neck mass biopsy was compared to treatment of the cohort who did not undergo open neck mass biopsy, there were no statistically significant differences (Table IV). However, of note, the number of open neck mass biopsy patients who required both surgery and radiation as primary therapy was 4 of 50 or 8% compared to 1 of 77 or 1.4% of non-open biopsy

TABLE IV.
Treatment for Stage 3 or 4 HNSCC by Open Neck Mass Biopsy Status.

Treatment	Open Biopsy Patients % (count) N = 50	Non-Open Biopsy Patients % (count) N = 77	P value*
Surgery as primary therapy	14.0 (7)	10.4 (8)	.49
Surgery alone	2.0 (1)	2.6 (2)	.83
Surgery with adjuvant radiation	8.0 (4)	1.3 (1)	.06
Surgery with adjuvant chemoradiation	4.0 (2)	6.5 (5)	.55
Chemotherapy or radiation as primary therapy	68.0 (34)	69.2 (81)	.68
Radiation alone	6.0 (3)	7.8 (6)	.70
Chemoradiation	62.0 (31)	61.0 (47)	.91
No documented treatment received	18.0 (9)	16.3 (19)	.60
No curative treatment provided	6.0 (3)	6.5 (5)	.91
Treatment unknown	12.0 (6)	11.7 (9)	.96

*P value determined from two-sample test of proportion

TABLE V.
Outcomes of Stage 3 or 4 HNSCC Patients by Open Neck Mass Biopsy Status.

Outcome	Open Biopsy Patients % (count) N = 50	Non-Open Biopsy Patients % (count) N = 77	P value*
Death due to malignancy	12 (6)	13.0 (10)	.87
Death due to other cause	4 (2)	3.9 (3)	.98
Recurrence of disease	14 (7)	16.9 (13)	.66
Persistence	10 (5)	10.4 (8)	.94

*P value determined from two sample test of proportion.

patients, approaching statistical significance with a $P = .06$ (Table IV). When comparing outcomes of both cohorts, there were no statistically significant differences between death due to disease, death due to other cause, tumor recurrence, and tumor persistence (Table V).

DISCUSSION

Our study is the first to characterize how often the NCCN guideline regarding diagnosis of neck mass is followed, and is the first study to characterize the proportion of patients who received open neck biopsy without prior FNA. In our regional cohort, we found that 31 of 50 or 62% of patients fall in this category. Despite patient care guidelines that advise against open neck mass biopsy,[12] this procedure is still being used as a primary diagnostic test for some patients. In assessing clinical documentation stating why surgeons conducted an open biopsy, the majority (26/50 or 52%) use vague terms and cite non-evidence–based findings, such as cystic neck mass, as indications. Therefore, data that sheds light on this clinical practice and evidence that augments efficacy and approaches to neck mass would allow improved diagnosis and ultimately treatment for patients with a neck mass.

One of the concerns in performing FNA that clinicians often voice is the lack of diagnostic accuracy. However, FNA has high utility and relative safety: in comparison to open biopsy, this test is comparatively inexpensive, well tolerated by patients with few complications, and avoids the need for general anesthesia. FNA has additionally been shown to have high diagnostic accuracy with sensitivities ranging from 83% to 97% and specificities ranging from 91% to 100%.[9,13,14] When combined with ultrasound guidance and on-site cytopathologic analysis, diagnosis can be made in 93% of cases.[15] Historically the diagnostic accuracy of FNA for lymphoma was unclear, which has been a source of many clinician's lack of reliance on FNA. In this retrospective cohort, the indication documented for an open neck biopsy prior to diagnostic FNA was clinical suspicion for lymphoma in 20% of cases. While further reasons for that clinical suspicion were not typically outlined in the documentation, we can infer that appearance on imaging may have contributed to this reasoning. Typical imaging characteristics of lymphomatous lymph nodes can include a pseudocystic

appearance, however, metastatic HNSCC can also be commonly associated with cystic appearance and particularly cystic necrosis.[16,17] Studies have attempted to delineate lymph node characteristics most defining between lymphoma and metastatic etiologies, but note that no imaging findings can be considered pathognomonic for either tumor type.[16,17] For this reason, diagnostic FNA is still recommended as the first diagnostic test before proceeding to open neck biopsy.[12] Fortunately, recent research confirms that FNA can accurately diagnose lymphoma when there is close coordination between the head and neck surgeon and an experienced cytopathologist and when cytomorphology is supplemented by modern flow cytometry.[18,19] While additional tissue collection in the form of core needle biopsy or open biopsy is often recommended after FNA results suggest lymphoma,[20] other pathologies must first be ruled out by the FNA, hence the emphasis on FNA as the first-line diagnostic measure.

In addition, evidence exists to suggest open neck mass biopsy may cause harm. Historically, open neck mass biopsy has been shown to have an adverse effect on survival and the rate of recurrence in the neck and can also make subsequent examination of the neck more difficult.[21,22] In a series of 190 patients with cervical HNSCC, excisional and incisional biopsy of the cervical nodes increased the incidence of regional failure two to three times when compared with FNA.[8] Our data does not reveal any statistically significant associations between having had an open neck biopsy and subsequent treatment options, disease persistent, recurrence, or survival. However, these calculations are limited by sample size, and there were trends that suggested open neck biopsy patients required both surgery and adjuvant radiotherapy. While a recent study comparing patients diagnosed with HPV-related HNSCC who underwent open neck mass biopsy with matched controls showed no significant difference in disease-specific survival,[23] there is still no question that in comparing overall utility of diagnostic tests, FNA compared to open neck mass biopsy is still far less invasive and complication prone. If a test with proven clinical utility and minimal morbidity is available, it should be used to the fullest capacity prior to more invasive tests requiring general anesthesia.

Open biopsy also affects future treatment options for the patient. For stage 3 and 4 HNSCC, management option is either surgery with radiation, or chemotherapy with radiation, with disease-free survival currently accepted as relatively equal between these two strategies. However, it is currently recommended that patients who have had open biopsy should receive radiotherapy either as the only form of treatment or in addition to surgery due to concerns of re-entering the neck space and causing further oncologic seeding.[10,11] This would introduce additional physical and financial burden to the patient, who could have avoided radiation. Future studies would be required to study the differences in final treatment offered to each patient and their survival outcomes comparing patients with and without open neck mass biopsy.

Finally, in assessing which tests were performed on open neck biopsy patients in their work-up as a whole,

less than half of patients underwent a flexible laryngoscopy (18/50 or 36%), direct laryngoscopy (21/50 or 42%), or were evaluated for HPV status (21/50 or 42%). Although it is possible that evaluation of HPV status was intentionally deferred to the tertiary care center after diagnosis of HNSCC, flexible or direct laryngoscopy is standard of care prior to open neck mass biopsy.[12] This indicates a lack of knowledge about the standardized work up of a neck mass and is an opportunity for education.

CONCLUSIONS

Our study demonstrates that despite NCCN guidelines recommending against open neck mass biopsy as the first line diagnostic test for adults presenting with a neck mass, it is still commonly conducted in lieu of recommended tests like FNA. There is a lack of evidence-based justification for open neck biopsy as a first-line diagnostic management, and compared to FNA it remains more invasive and complication-prone. It may also have important implications for future treatment options. Further studies investigating the treatment trends, outcomes, as well as the recurrence rate in a high powered, perhaps multi-institutional study are needed to further explore the impact that open neck biopsy has on patients.

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