



American Head and Neck Society - Journal Club

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AHNS Skull Base Surgery Section Edition

This Issue of the AHNS Journal Club has been compiled and reviewed by members of the AHNS Skull Base Surgery Section (Ian Witterick, MD, Chair and Shirley Su, MBBS Vice-Chair)

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The AHNS Skull Base Surgery Section is created to elucidate and address issues important to improving the care of skull base cancer patients and to advance the field of skull base oncology and patient care through research, education, and advocacy by facilitating multidisciplinary.

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[The effectiveness of radiotherapy in the treatment of head and neck mucosal melanoma: Systematic review and meta-analysis](#)

Marc C Grant-Freemantle, Billy Lane O'Neill, Anthony James P Clover

From the *Head and Neck*. January 2021

Introduction: Mucosal melanoma (MM) is a rare condition with a poor prognosis. Surgery is the corner stone of treatment; however, radiotherapy has been commonly employed as a treatment strategy and recent studies suggesting that survival outcomes may be improving are emerging.

Methods: A systematic 'review and meta-analysis comparing risk ratios of radiotherapy and surgery and radiotherapy (SRT) with surgery for 5-year overall survival, local recurrence and distant metastasis in head and neck mucosal melanoma (HNMM).

Results: SRT has a lower risk of death compared to surgery [RR 0.93 [95% CI = 0.87, 0.98] (P = .01)] and a reduced risk of local recurrence [RR 0.63 [95% CI = 0.48, 0.82] (P = .005)]. SRT has no effect on distant metastasis. Radiotherapy has worse survival when compared to surgery [RR 1.2 [95% CI = 1.03, 1.33] (P = .0006)].

Conclusions: SRT confers a moderate survival advantage in HNMM compared to surgery. This is most likely secondary to reduced local recurrence.

Summary statements:

This is a systematic review of the literature published on outcomes for HNMM treated with surgery, surgery and adjuvant radiotherapy, or radiotherapy alone and includes studies beginning and concluding in 2015. The pooled risk of local and distant recurrence was 0.63 and 0.95 in 5 years, respectively. Distant metastatic disease, therefore, is the current driver of mortality.

Strengths:

- Analyzes a large group of patients with HNMM, 2489 patients, to compare outcomes when treated with surgery alone (1039 patients), surgery with adjuvant radiotherapy (1276) and radiotherapy alone (174) are used to treat head and neck mucosal melanoma.
- This is the first and only study to demonstrate survival benefit from the addition of radiotherapy, which may be due to lower relative risk of local recurrence. RR 0.63 [95% CI = 0.48, 0.82] (P = .005)].
- Identifies distant metastasis as the driver of mortality in HNMM.

Weaknesses:

- Pools retrospective data, which has inherent bias and does not represent high level data and reflects the limitations of the literature in studying rare diseases.
- Pools outcomes for all HNMM treated by multiple surgical procedures (including open and endoscopic) which may impact outcomes differently.



- Cannot provide meaningful subgroup analysis of sinonasal mucosal melanoma due to small numbers, which presents later and has a worse overall prognosis than other subsites.

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[Contemporary Multidisciplinary Management of Sinonasal Mucosal Melanoma](#)

Shorook Na'ara, Abhishek Mukherjee, Salem Billan, Ziv Gil

*From the **Onco Targets Ther.** March 2020*

Introduction: The advent of immunotherapy has impacted both the management and, to a lesser extent, the outcomes for patients with head and neck mucosal melanoma. As a consequence, one might expect that the role of the surgeon would be limited to the diagnostic work-up and that systemic therapies would be the mainstay of treatment.

Methods and Results: Here, we present the surgical aspects of the recently published United Kingdom Head and Neck Mucosal Melanoma Guideline to highlight the continued role of surgeons in the management of this disease. We highlight key areas where surgeons remain the lead clinician and reinforce the multidisciplinary requirement for exemplary patient care.

Conclusions: Despite the advent of immunotherapy, surgeons continue to have a key role to play in this disease. When indicated, it is essential that appropriate surgery is offered by a suitably experienced team.

Summary statements

This is a helpful contemporary review that discusses the role of the surgeon in a disease whose outcomes are dictated by distant recurrence. It provides useful information in the treatment plan and counseling of patients who will continue to require a head and neck surgeon to lead the disease treatment team.

Strengths

- Is a comprehensive, thoughtful, and useful review of the recent literature for all aspects of care from presentation to surveillance with discussion of the most likely presentation, recommended work-up (radiologic, pathologic, and molecular markers), treatment of the primary, treatment of the neck, adjuvant treatment, and palliation.
- Identifies mutations that are helpful to identify within tumors as potential molecular targets, including BRAF and C-KIT which should be performed at the time of first diagnosis to offer treatment options in both the adjuvant and metastatic settings.

Weaknesses

- This is an expert review of the most recent literature which reflects current practice guideline/treatment paradigm in the United Kingdom (a developed Western nation with resources that are not necessarily readily accessible in developing nations or underserved areas of developed nations).
- The article does not discuss current trials ongoing but does identify the various immunotherapy or targeted therapies available and situations in which they ought be considered.

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Head and neck mucosal melanoma: The United Kingdom national guidelines

Pablo Nenclares, Derfel Ap Dafydd, Izhar Bagwan, Donna Begg, Cyrus Kerawala, Emma King, Ken Lingley, Vinidh Paleri, Gillian Paterson, Miranda Payne, Priyamal Silva, Neil Steven, Nancy Turnbull, Kent Yip, Kevin J Harrington

From Eur J Cancer. June 2021

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Sinonasal mucosal melanoma: 20-year experience at a tertiary referral center

Bobby A Tajudeen, Nopawan Vorasubin, Yas Sanaiha, Miguel Fernando Palma-Diaz, Jeffrey D Suh, Marilene B Wang

*From **Int Forum Allergy Rhinol.** July 2014*

Background: Sinonasal melanoma (SNM) is a rare cancer with extremely poor prognosis. Detecting melanoma on frozen section has historically been considered to be unreliable. A review of cases of sinonasal melanoma treated at a tertiary referral center was conducted to analyze treatment outcomes and identify prognostic factors for survival. In addition, an investigation was performed correlating sinonasal melanoma on frozen section and permanent analysis.

Methods: An institutional review board-approved search of the pathology database for cases of primary sinonasal melanoma treated between 1991 and 2011 was performed. Fourteen cases were identified, and the medical charts were reviewed.

Results: Eleven patients had tumors arising from the nasal cavity, 2 arose from the maxillary sinus, and 1 from the ethmoid sinuses. Mean duration of follow-up was 20.7 (range, 1.4 to 84.5) months. Overall, 5-year recurrence-free survival and overall survival was 23% and 35%, respectively. All patients had surgical resection with intent for cure and all, but 1 patient had adjuvant therapy. Survival analysis showed that positive margin status (log rank $p = 0.031$) and the presence of perineural/lymphovascular invasion (log rank $p = 0.021$) negatively affected recurrence-free survival and overall survival, respectively. Nine cases had evaluation of intraoperative frozen sections with 32 total sections submitted for analysis. When compared with final pathology, there was a 0% false negative rate.

Conclusions: Based on this series, positive margins, and the presence of perineural/lymphovascular invasion are negative predictors of survival. In addition,

intraoperative frozen section analysis of sinonasal mucosal melanoma correlates well with final pathology.

Summary statements

This is a relatively small, single centre, retrospective review of sinonasal melanomas resected over a 20-year period. It particularly focuses on efficacy of intraoperative frozen section analysis.

Strengths:

Highlights the difficulty of obtaining final surgical margin clearance despite reportedly excellent frozen section analyses intraoperatively

Weaknesses:

- Staging system used is extremely dated and as such affects prognostic utility of results and conclusions. This is also compounded by the small cohort size limiting subgroup analysis
- As surgical margin control is tantamount to treatment success and frozen section has such variable accuracy in the literature, an analysis in to why this group has had such a significant success (100% accuracy) would have been a useful insight to include.

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[Clinical outcomes and patterns of failure of head and neck mucosal melanoma treated with multiple treatment modalities](#)

Qing-Qing Xu, Yan-Zhen Lai, Zi-Lu Huang, Zi-Yi Zeng, Ya-Ni Zhang, Rui-Yao Ou, Wen-Min Wu, Lei Chen, Li-Xia Lu

*From **Radiat Oncol.** July 2021*

Objectives: The study aims to analyze the clinical characteristics of head and neck mucosal melanoma (MMHN) and the effects of multiple treatment modalities on distant metastasis, recurrence, and survival rates to provide a reference for the individualized treatment of MMHN.

Methods: We retrospectively reviewed 262 patients with stage III-IVb MMHN treated from March 1986 to November 2018 at our cancer center.

Results: The median follow-up time was 34.0 months (range 1-262 months). The 5-year overall survival (OS), distant metastasis-free survival (DMFS) and disease-free survival (DFS) probabilities were 37.7%, 30.2%, and 20.3%, respectively. The 5-year OS rates for patients with stage III, stage IVA, and stage IVB MMHN were 67.0%, 24.1% and 8.3%, respectively ($P < 0.001$). A total of 246 (93.9%) patients received surgery, 149 (56.9%) patients received chemotherapy, and 69 (26.3%) patients received immunologic/targeted therapy. A total of 106 (40.5%) patients were treated with radiotherapy: 9 were treated with preoperative radiotherapy, 93 were treated with postoperative radiotherapy, and 4 were treated with radiotherapy alone. In the multivariate Cox regression analysis, primary tumor site, T stage, and immunologic/targeted



therapy were independent factors for OS (all $P < 0.05$). Irradiation technique, T stage, and N stage were independent prognostic factors for DMFS (all $P < 0.05$). T stage, N stage, and surgery were independent prognostic factors for DFS (all $P < 0.05$). Distant metastasis was observed in 107 of 262 patients (40.8%), followed by local [74 (28.2%)] and regional [52 (19.8%)] recurrence.

Conclusions: The main reason for treatment failure in MMHN is distant metastasis. Immunologic/targeted therapy and surgery are recommended to improve the survival of MMHN. The American Joint Committee on Cancer (AJCC) 8th edition staging system for MMHN does stage this disease effectively.

Summary statements

This is a large, single centre retrospective series of patients with good long term follow up assessing merits of multimodal treatments and outcomes.

Strengths

- One of the largest single centre cohorts reported to date.
- Highlights the importance of long-term surveillance and need for better systemic treatment as distant recurrence is primary source of treatment failure

Weaknesses

- Retrospective nature of review clearly susceptible to bias including selection bias responsible for purported lack of effect of adjuvant radiation on local relapse-free survival
- Lack of information regarding surgical details such as types and extent of surgery, margin status, treatment of nodal basins, etc. All of these factors have been proven to correlate to both survival and recurrence rates and would have been worth evaluating in such a large cohort.

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