

Review Article

Controversies in Management of Head and Neck Cancers: A Review

Prasoon S Babu¹, Harihara Jothi V², Abin Ann Abraham³, Vikesh Kumar R Shah⁴, Nirav R Shah⁵, Koustabh Kumar⁶

1. Consultant Oral and Maxillofacial Surgeon, Smile craft Dental Studio, Yelahanka New Town, Bangalore, Karnataka;
2. Resident, Dept of General Surgery, Jubilee Mission Medical College Hospital and Research Institute, Thrissur, Kerala, India;
3. Senior Resident, Dept of Oral and Maxillofacial surgery, GDC Kottayam, Kerala;
4. Consultant Immunooncotherapist, Stat Care Clinic, Ahmedabad, Gujarat;
5. Consultant Periodontist and Implantologist, Stat Care clinic, Ahmedabad, Gujarat;
6. MDS, Oral and maxillofacial surgery, Clinical Observer, HCG Cancer Hospital, Bangalore, Karnataka.

ABSTRACT:

In treating head and neck cancer (HNC), the objectives are provided for best functional results and minimal risk of serious complications. The choice of appropriate management depends primarily on specific site and stage of primary tumor at diagnosis. Although surgical resection remains the primary treatment modality, several areas of controversy exist about work-up, management of the primary and neck tumors, and adjuvant therapy. As surgical techniques evolve, so has the delivery of radiotherapy and systemic treatment, which have helped to improve the outcomes for patients with advanced disease. Future study of the molecular biology and pathogenesis of OCC should offer additional insight into screening, treatment selection, and novel therapeutic approaches.

Keywords Depth of invasion, carcinoma, perineural spread, chemoradiotherapy.

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Corresponding Author: Dr Prasoon S Babu, Consultant oral and maxillofacial surgeon, Smilecraft Dental Studio, Yelahanka New Town, Bangalore, Karnataka.

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INTRODUCTION

The cause of heterogeneity in the practice of diagnosis and treatment of head and neck squamous cell carcinoma (HNSCC) can be associated with multiple factors: differences in health care policies, financial and logistic factors, variations in tradition and medical culture between geographical areas, institutions, or even among physicians working in the same hospital. The incidence of synchronous HNSCC around 5–6% is considered high enough to require a diagnostic pan-endoscopy. Usually, the second primary is of small size and thus curable. Hence, the diagnosis of synchronous lesions usually alters the therapeutic approach.¹

Most patients are diagnosed with locally advanced disease at the time of presentation, and treatment

options have traditionally included surgery, radiation therapy (RT) and chemotherapy (C), or combinations of these therapeutic modalities, depending on primary location. In fact, HNC is a heterogeneous group of malignancies, consisting of various anatomic sites, including nasopharynx, paranasal sinuses, oral cavity, oropharynx, hypopharynx and larynx. Worldwide, more than 650,000 new cases of HNC are reported annually and more than 350,000 deaths from HNC occurred yearly. Due to its rarity, as well as its complexity in optimal strategy plan and patients support care through treatment, high-volume centers including the presence of multidisciplinary tumor board should be prioritize in HNC management.²

POSITRON EMISSION TOMOGRAPHY SCAN (PET)

Since 18F-fluorodeoxyglucose positron emission tomography combined with computerized tomography (18FDG-PET/CT) is often performed during the evaluation or treatment planning, some have suggested that a 18FDG-PET/CT scan could replace endoscopy. However, 18FDG-PET/CT will not detect small superficial lesions which are focus of endoscopy. However, this practice can be questioned in non-smoker patients who are diagnosed with a Human Papillomavirus (HPV)-associated oropharyngeal squamous cell carcinoma (OPSCC) due to the decreased rates of secondary malignancies. There is no high-level evidence for or against the value of the 18FDG-PET/CT for an accurate estimation of the extent of the disease, especially for the primary site. Since the gold standard is the assessment of the surgical specimen, a correlation between parameters such as dimensions, volume, depth, or involvement of critical structures obtained radiologically and pathologically is sought. Because of the distortions and shrinkage of surgical specimen, few studies have been undertaken especially for 18FDGPET/ CT. The available data for 18FDG-PET/CT is restricted to laryngo-hypopharyngeal primaries and is based on a total of 19 patients: tumor volume estimation seems accurate but the superficial extension was inaccurate.³

SENTINEL NODE BIOPSY (SLNB)

The arguments against a SLNB approach when comparing it to the traditional elective neck dissection include: oncologic inferiority, unavailability or unreliability of frozen sections in SLNB, need of a second procedure in case of SLNB positivity, technical challenges and learning curve of the procedure, lack of conviction in the difference in morbidity between the two approaches. The arguments for a SLNB include- less invasive approach, second stage completion neck dissection only necessary in the minority of patients (25–30%), selective detection of the lymph nodes of highest risk to harbour metastatic disease, the pathologic workup of sentinel lymph nodes allows for the detection of small metastatic disease such as isolated tumor cells and micro-metastases rather than macro-metastases only leading to a more accurate staging of the neck. Because of the pathology processing, most pathologists are reluctant to recommend frozen sections in a sentinel lymph node approach. Since frozen section of a sentinel lymph node usually consists in the examination of a single section, several studies have found this technique is suboptimal or unreliable.⁴

CHEMORADIOTHERAPY (CRT)

CRT has become the preferred strategy for pharyngeal and laryngeal primaries in some centers. Advanced stage disease is often associated with bulky (N3) or

multiple (N2b/c, N3) neck lymph node metastasis and the optimal strategy to treat these metastatic neck diseases remains controversial. Until recently, the debate has been centred on whether a planned neck dissection after CRT is necessary and whether a post-treatment 18FDG-PET/CT scan can be used to select patients needing surgery. This has been settled in a randomized controlled trial showing that a post-treatment 18FDG-PET/CT scan would safely identify patients not requiring neck dissection after CRT.⁵ The mainstay of treatment for oral cavity cancer is surgery followed by adjuvant (C)RT in case of pathological T3-4, N2-3 nodal disease, positive surgical margins, extracapsular nodal spread, perineural invasion and lympho-vascular invasion. Whereas RT is usually considered as definitive treatment in the remainder HNC cancer sites, especially in locally advanced stage disease to propose an organ preservation strategy. The update meta-analysis of 87 randomized trials including 16,485 patients showed that the addition of concomitant C to RT improved OS in HNC treated by surgery and/or RT.²

PERINEURAL INAVSION (PNI)

Slootweg and Muller described two patterns of mandibular invasion: an “erosive pattern” carrying a good prognosis and associated with direct bone infiltration by the carcinoma, on a broad front, without infiltration of the periodontal ligament and of the inferior alveolar nerve. The “infiltrative pattern” carries a worse prognosis. According to the Dutch Guidelines Database, in the erosive pattern a bony margin of 1 cm is sufficient, while the infiltrative pattern requires bony margins of 1.5 cm and invasion within the canal of the mandibular nerve 2 cm.⁶

RESECTION MARGINS

A “sufficient” pathological margin implies a low risk for tumor recurrence and possibly makes adjuvant treatment redundant. However, this issue for oral squamous cell carcinoma is still a subject to debate. Combined analysis of the EORTC 22931 and the RTOG 9501 trials concluded that the adverse prognostic factors requiring adjuvant CRT following surgical resection included extracapsular extension (ECE) of metastatic lymph nodes and positive margins. A review of the literature on the subject seems to confirm that most studies consider 5mm as a negative margin, following the Guideline of the UK Royal College of Pathologists: >5mm clear, 1–5mm close, and <1mm positive margin. This discussion pertains to margins assessed by the pathologist and given about 50% shrinkage of the specimen; resection should start about 10mm from the tumor edge.⁷

DISCUSSION

Treatment decisions in OSCC are mostly dependent on tumor site, TNM classification, pathologic parameters and patient’s clinical status and preferences. Several studies have showed the

significance of pathologic findings, such as the type of invasive edge, inflammatory response, stromal component, tissue eosinophilia, and PNI.⁸ The majority of head and neck carcinomas are tobacco and alcohol-related, occur in older patients, affect tongue and floor of the mouth and has well-established morphological prognostic factors such as pattern of invasion, tumor grade, and PNI. However, in the last three decades, the advent and increasing occurrence of human papillomavirus (HPV) infection resulted in significant changes in the clinical presentation, treatment planning and outcomes.⁹ Cervical metastasis has a tremendous impact on prognosis in patients with head and neck squamous cell carcinomas (HNSCCs). However, to date management of clinically negative neck in HNSCC is still a controversial subject. Tumor thickness (TT) is a strong predictor for lymph node involvement in oral squamous cell carcinomas (SCCs). However, controversy exists about the optimal TT cutoff point for a clinically relevant risk to the neck.¹⁰ The historical practice of a planned neck dissection either before or after a definitive course of radiotherapy has been of considerable controversy in the management of head and neck squamous cell carcinomas and reflects the strong prognostic influence of nodal metastases. Of these planned neck dissections, a prophylactic or elective neck dissection (i.e., one after a complete clinical response to radiotherapy) evolved because of increasing concerns of unsalvageable nodal relapses, especially in the treatment of bulky nodal metastases. The premise was that despite a complete clinical response in the nodal metastases, residual radioresistant microscopic carcinoma could eventually lead to nodal relapse that was often not detected early enough before becoming unresectable and unsalvageable.¹¹

CONCLUSION

A more accurate preoperative diagnosis and strict follow-up are required to provide minimally invasive treatment while ensuring the therapeutic effect. It is also necessary to narrow down the target based on the risk-benefit balance. The depth of invasion should be considered in cases involving head and neck malignancies and it is an important factor for the management of these cancers.

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