

## Systematic Review and Meta-Analysis Head and Neck Oncology

# Marginal or segmental mandibulectomy: treatment modality selection for oral cancer: a systematic review and meta-analysis

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**Abstract.** Surgery is the most well established mode of initial definitive treatment for the majority of oral cancers. The most important decision in terms of tumour ablation in oral cancers when the jaws are potentially involved is the management of the mandible. The aim of this study was to explore the differences in survival rate and disease control between patients undergoing marginal mandibulectomy and patients undergoing segmental mandibulectomy using a systematic review and meta-analysis approach. A total of 15 cohort studies, including 1672 participants, were identified. Meta-analysis provided weak evidence in favour of segmental mandibulectomy for local control. Segmental mandibulectomy gave 73% better disease-free survival than marginal mandibulectomy when the marrow was invaded ( $P = 0.04$ ). The overall survival rate was evaluated, and no statistically significant difference was found between the two different mandibulectomy approaches, although the results showed a trend in favour of segmental mandibulectomy which could increase the overall survival by 23%. Based on these findings regarding the survival rate and efficacy of disease control, this study indicates that a marginal mandibulectomy may be recommended for cases with no invasion or superficial invasion of the mandibular cortex, and a segmental mandibulectomy may be a more reasonable choice for patients with extensive mandibular cortex invasion or medullary invasion.

**Key words:** oral squamous cell carcinoma; mandibulectomy; systematic review; local control; disease-free survival; overall survival; meta-analysis.

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Head and neck squamous cell carcinoma is the sixth most common malignant tumour worldwide, with a high prevalence in south-central Asia<sup>1</sup>. Estimates indicate

more than 650,000 new cases annually<sup>2</sup>, and an estimated 300,400 new cases and 145,000 deaths from oral cavity cancer occurred in 2012 worldwide<sup>3</sup>. Oral cancer

includes the group of neoplasms arising from any region of the oral cavity and the minor salivary glands. This term tends to be used interchangeably with oral

squamous cell carcinoma (OSCC), which is the most frequent of all oral neoplasms. It has been reported that squamous cell carcinoma encompasses at least 90% of all oral cancers<sup>4,5</sup>.

A variety of methods are currently available for the treatment of oral cancer. Among these, surgery is the most well established mode of initial definitive treatment for the majority of oral cancers<sup>6</sup>. For instance, surgery is the single modality treatment for patients affected by OSCC at an early stage (I/II). However, this approach often results in significant functional and/or cosmetic defects in the oral and maxillofacial region, especially in patients with advanced disease invading the jaws.

It is generally agreed that patients with mandibular invasion should be treated surgically, but the extent of mandibular resection required is not always clear. Historically, it was assumed that tumours of the oral cavity had the potential to spread via the lymphatics within the mandibular periosteum. As a result, tumours abutting the mandible were commonly treated with a bloc/segmental mandibulectomy that left the patient with significant functional and aesthetic deficits. Subsequently, Marchetta et al.<sup>7</sup> and Carter et al.<sup>8</sup> demonstrated that such cancer spreads to the mandible by direct invasion rather than lymphatic spread, and preservation or partial resection of the mandible became oncologically feasible. Since then, the question has become how to select appropriate patients with oral cancer for segmental or partial thickness (marginal) mandibulectomy.

Most oncological surgeons agree that the marginal mandibulectomy represents the best choice to preserve mandibular form and function in patients with disease approaching but not directly invading the mandibular cortex. This procedure is performed in such a way that safety margins around the primary tumour are obtained. However, for cases in which the mandibular bone is involved by the disease, the decision is more problematic. For some clinicians, a marginal resection would be reasonable for cancers encroaching on, adherent to, or superficially invading the mandibular cortex unless the medullary cavity is extensively invaded<sup>9,10</sup>. However, another opinion is that not only should the advanced tumours classified as T4 by the American Joint Committee on Cancer (AJCC) staging system be subjected to segmental resection (which is the current standard of treatment), but tumours referred previously should all be subjected to a segmental resection procedure, since a

marginal mandibulectomy might compromise tumour control.

Therefore, the aim of this study was to explore the survival rate and disease control in patients with histological evidence of bone invasion and to compare the differences in survival rate and disease control between patients undergoing marginal mandibular resection and patients undergoing segmental mandibulectomy, using a systematic review and meta-analysis approach.

## Materials and methods

As this was a systematic review, it was exempt from institutional review board approval. All investigators followed the guidelines of the Declaration of Helsinki during the entire research process. Two reviewers performed the study inclusion, data extraction, and risk of bias protocols in duplicate. Any disagreement was resolved by discussion.

## Inclusion criteria

The following inclusion criteria were applied to select the studies: (1) Study design: randomized, controlled clinical trials and cohort studies investigating the effectiveness of different mandibulectomy modalities (marginal mandibulectomy vs. segmental mandibulectomy) were included. Studies focusing on the invasion of other bones (mandible not specified) were also considered if the percentage of invasion in the other bones besides the mandible did not exceed 10%. (2) Participants: all participants who underwent surgery for the treatment of OSCC or other malignant tumours of the oral cavity with different mandibulectomy modalities and with pathological results available for the resected mandible were included. (3) Intervention group: participants included those who underwent marginal mandibulectomies for the preservation of the mandible. Studies with neck dissection and/or reconstructive surgery performed if necessary were also considered. (4) Control group: participants included those who underwent a segmental, hemi, subtotal, or total mandibulectomy. Studies with neck dissection and/or reconstructive surgery performed if needed were also considered. (5) Outcome: the two primary outcomes were disease-free survival (DFS; defined as the length of time after primary treatment for a cancer until the time at which the patient was confirmed to have local, regional, or distant recurrence of the cancer) and overall survival (OS; defined as the length of time that the

patient diagnosed with the disease was still alive, starting from either the date of diagnosis or the start of treatment for the disease), expressed as the hazard ratio (HR) or with a Kaplan–Meier survival curve. The secondary outcomes were the 2-year/5-year survival rate and local control; for the 2-year/5-year survival rate, studies adopting the risk ratio (RR) were considered, and for local control, studies adopting either the RR or HR were considered.

## Search strategy

Bibliographic databases were searched, including the Cochrane Oral Health Group Trials Register, the Cochrane Central Register of Controlled Trials, MEDLINE (via OVID), Embase, Cumulative Index for Nursing and Allied Health Literature (CINAHL), Latin American and Caribbean Health Sciences Information (LILACS), Chinese BioMedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), VIP Database, Wanfang Database, Sciencepaper Online, System for Information on Grey Literature in Europe (SIGLE), and the World Health Organization (WHO) International Clinical Trials Registry Platform. The search was performed from database inception to May 3, 2016.

A combination of medical subject heading (MeSH) terms and free text words were used in the search strategy. The MeSH terms used were “Mouth Neoplasms”, “Mandibular Osteotomy”, “Neoplasms invasiveness”, and “Mandible”. The free text words used were “marginal mandibulectomy”, “segmental mandibulectomy”, “bone invasion”, “squamous carcinoma”, and “gingival cancer”. A hand-search of 14 Chinese dental journals was also performed. The references of all studies included were also hand-searched to find additional potentially eligible studies.

## Study inclusion

Two reviewers scanned the titles and abstracts of all studies identified, and any study that met the eligibility criteria was recorded. The full texts of these papers were retrieved and carefully read to allow a final decision to be made on inclusion.

## Risk of bias assessment

The risk of bias was assessed using the method of Saltaji et al.<sup>11</sup> (Table 1). For each single question, an answer of ‘yes’

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