Article published online: 2024-09-05

THIEME OPEN ACCESS

Original Article

A Real-World Analysis of Oncological Outcomes in Patients with Oral Squamous Cell Carcinoma Requiring Marginal Mandibulectomy for Achieving Clear Surgical Margins

Hemant Nemade[1] Abhinav Thaduri[1] Jonathan T. Gondi[1] Sravan Kumar Chava[1] Anil Kumar[1] Pratheek Raj[1] Uma Neelap[1] L.M. Chandra Sekara Rao S.[1]

[1] Department of Surgical Oncology, Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad, Telangana, India

South Asian J Cancer

Address for correspondence Abhinav Thaduri, MS, MCh, Division of Head and Neck Oncology, Department of Surgical Oncology, Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad 500034, India (e-mail: abhinavthadurient@gmail.com).

Abhinav Thaduri

Abstract

Introduction Marginal mandibulectomy (MM) offers a conservative alternative to segmental resections for patients with oral squamous cell carcinoma (OSCC) requiring clear margins without evident bone invasion. Despite its potential benefits, real-world outcomes related to surgical margins and oncological outcomes have not been studied sufficiently.

Methods This ambispective cohort study analyzed 183 patients undergoing MM from January 2015 to March 2021 to achieve clear margins without clinical bone involvement. The primary objective is to assess the disease-free survival (DFS) in patients with OSCC requiring MM to achieve clear surgical margins, and the secondary objective is to assess the impact of microscopic bone involvement on these outcomes. Kaplan–Meier estimates facilitated the survival analysis.

Results The cohort primarily comprised males (83.2%) with a median age of 50 years, the predominant subsite being the bucco-alveolar complex (94%). Microscopic bone involvement was found in 8.74% of patients. The distribution of surgical margins was 84.24% negative, 15.22% close, and 0.54% positive. The cohort's 3-year DFS and overall survival (OS) rates are 65 and 70%, respectively. Patients with microscopic bone involvement experienced lower DFS (odds ratio [OR] = 0.251, $p = 0.013$), and perineural invasion was also a significant negative prognostic factor for DFS (OR = 0.4, $p = 0.01$). Statistical analyses revealed significant differences in survival distributions based on bone involvement ($p = 0.049$).

Conclusion While MM can achieve favorable surgical margins in selected OSCC patients, microscopic bone involvement compromises DFS. Given the low incidence of bone involvement and high rate of negative margins, more conservative approaches might be justified in select patients. However, these findings require further validation in a larger cohort.

Keywords

- disease-free survival
- marginal mandibulectomy
- microscopic bone involvement
- oncological outcomes
- oral squamous cell carcinoma

DOI https://doi.org/10.1055/s-0044-1790286 ISSN 2278-330X

How to cite this article: Nemade H, Thaduri A, Gondi JT, et al. A Real-World Analysis of Oncological Outcomes in Patients with Oral Squamous Cell Carcinoma Requiring Marginal Mandibulectomy for Achieving Clear Surgical Margins. South Asian J Cancer 2024;00(00):00–00.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

Oral squamous cell carcinoma (OSCC) is a major health issue, especially in Southeast Asia, and the most common cancer among Indian men.[1] Achieving clear-margin en bloc resection is crucial for preventing recurrence and improving survival, but margin definitions are debated.[2,3] Traditionally, segmental mandibulectomy is preferred for tumors near the mandible, despite functional and aesthetic drawbacks. Marginal mandibulectomy (MM) offers a conservative alternative, preserving function and aesthetics while ensuring oncological safety.[4,5] Preoperative imaging, such as computed tomography (CT) and magnetic resonance imaging (MRI), is essential for assessing mandibular involvement, although determining bone involvement remains challenging. Conflicting evidence exists on the impact of microscopic bone involvement on outcomes.[6–8] This study aims to assess disease-free survival (DFS) and the impact of microscopic bone involvement in patients undergoing MM.

Methodology

The study's primary objective is to investigate DFS among patients with oral cancer undergoing MM to achieve clear surgical margins without clinical or radiological bone involvement. A secondary objective is to explore microscopic bone involvement's influence on DFS and overall survival (OS). The current study is a retrospective analysis of prospectively collected data conducted in a high-volume tertiary care teaching cancer hospital. This study spans from January 2015 through March 2021.

The study included patients diagnosed with oral cancer who underwent surgery as their initial treatment and were candidates for MM to achieve clear surgical margins. Patients with recurrent oral cancer, second primary malignancies, edentulous mandibles, clinical/radiological cortical bone erosion, and significant paramandibular extension were excluded. All the patients underwent contrast-enhanced head and neck CT scans, which confirmed the absence of bone involvement before surgery. In our study, MM was indicated for lesions in the buccal mucosa, tongue, and floor of the mouth near the mandible but without obvious bone involvement. Surgeries utilized a powered saw for mandibular cuts, preserving a minimum of 1 cm of residual mandible height, with reconstruction as needed. Adjuvant therapy was given per institutional protocols based on tumor stage and margin status.

From 3,893 oral cancer patients treated surgically between 2015 and March 2021, 234 patients underwent MM. After excluding 26 patients with missing microscopic bone reports and 25 lost to follow-up, 183 patients were included in the final analysis.

Study Outcomes Defined

DFS: The period from surgery to cancer recurrence, with nonrecurrent cases censored at their last follow-up. OS: The duration from surgical intervention to death from any cause, with those still alive censored at the last follow-up. Microscopic margins are categorized as negative (>5 mm), close (<5 mm), and positive (<1 mm).

Statistics

Mean (standard deviations) and median (interquartile range) were used to present numerical data, while categorical data were shown in percentages. The Kaplan–Meier method calculated the DFS and OS rates, with group differences assessed using the log-rank test. Logistic regression analysis was utilized for assessing factorial significance. Statistical analysis was performed using SPSS 26, with significance set at $p < 0.05$.

Results

Our cohort consisted of 184 patients with oral cancer, predominantly males (83.2%), and almost 60% of patients were younger than 50 years. The bucco-alveolar complex constitutes 94% of cases. In all, 64.7% of the patients were classified as stage T1, T2. Almost two-thirds (73.4%) of patients were suffering from node negative disease with lymphovascular invasion (LVI) present in 19% and perineural invasion (PNI) in 41.2% of the cases. In 84.2% of patients, clear surgical margins (>1 cm) could be achieved. Treatment modalities included surgery alone (53.8%), surgery with radiotherapy (31%), and surgery with chemoradiotherapy (15.2%). Microscopic bone involvement was observed in 8.7% of the patients and all the 16 patients had only cortical involvement. ►Table 1 depicts the clinical and demographic details.

In the study cohort, 38 (20.7%) patients had disease relapse at the mean follow-up of 34 months; out of 16 patients with microscopic bone involvement, only 3 patients had disease relapse, of which only 1 patient had local relapse and other 2 patients had regional and distant relapse.

The mean DFS time was 65.4 months (95% confidence interval [CI]: 57.948–72.905), and the median DFS time was 74 months (95% CI: 61.681–86.319). The mean OS is 81.4 months (95% CI: 74.6–88.2). Patients with bone involvement had a mean OS of 61.7 months (95% CI: 40.5–82.8). Those without bone involvement had a mean OS of 76.2 months (95% CI: 71.0–81.5). The mean DFS was 44.8 months (95% CI: 25.2–64.4) with bone involvement and 63.6 months (95% CI: 57.5–69.7) without bone involvement. The log-rank test showed significant differences based on bone involvement ($\chi^2 = 3.868$, $p = 0.049$) in DFS. ►Figs. 1 and 2 depict the survival curves of the entire cohort and based on bone involvement, respectively.

Logistic regression analysis indicated that bone involvement significantly reduced DFS with an odds ratio (OR) of 0.251 ($p = 0.013$), suggesting patients with bone involvement had a lower likelihood of remaining disease free. Adjuvant radiation therapy was associated with a trend toward improved DFS (OR = 2.3, $p = 0.06$), albeit not reaching statistical significance. Multinomial regression analysis showed that PNI significantly negatively affected DFS (OR = 0.4, $p = 0.01$), and microscopic bone involvement did not significantly affect DFS. ►Supplementary Tables S1–S3

Table 1 Demographic and clinical details of the cohort

Sl. no.	Detail		Frequency ($n = 184$)	Percentage
1	Gender	Male	153	83.2
		Female	31	16.8
2	Age	< 50 y	110	59.7
		> 50 y	74	40.3
6	Subsite	Bucco-alveolar complex	173	94
		Tongue and FOM	11	11
7	pT category	T1	38	20.7
		T2	81	44
		T3	29	15.8
		T4a	36	19.6
8	pN category	N0	135	73.4
		N1	21	11.4
		N2a	7	3.8
		N2b	8	4.3
		N3	13	7.1
9	LVI	Yes	35	19
		No	149	81
10	PNI	Yes	74	41.2
		No	110	59.8
11	Margins	Negative	155	84.2
		Close	28	15.2
		Positive	1	0.5
12	Trismus	Yes	50	27.2
		No	134	72.8
13	Skin involvement	Yes	25	13.6
		No	159	86.4
14	Reconstruction surgery	Nasolabial	21	11.4
		ALT	38	20.6
		PMMC	70	38.04
		C-FAM	12	6.5
		Submental	19	10.5
		RAFF	7	3.8
		Tongue	15	8.2
		Buccal pad	2	1.1
15	Tracheostomy	No	178	96.7
		Elective	6	3.3
16	Complete treatment	Surgery only	99	53.8
		Surgery + radiotherapy	57	31
		Surgery + chemoradiotherapy	28	15.2
17	Bone involvement	Present	16	8.7
		Absent	168	91.3

Abbreviations: ALT, anterior lateral thigh flap; C-FAM, cervicofacial-facial artery myocutaneous flap; FOM, floor of the mouth; LVI, lymphovascular invasion; PMMC, pectoralis major myocutaneous; PNI, perineural invasion; RAFF, radial artery forearm free flap.

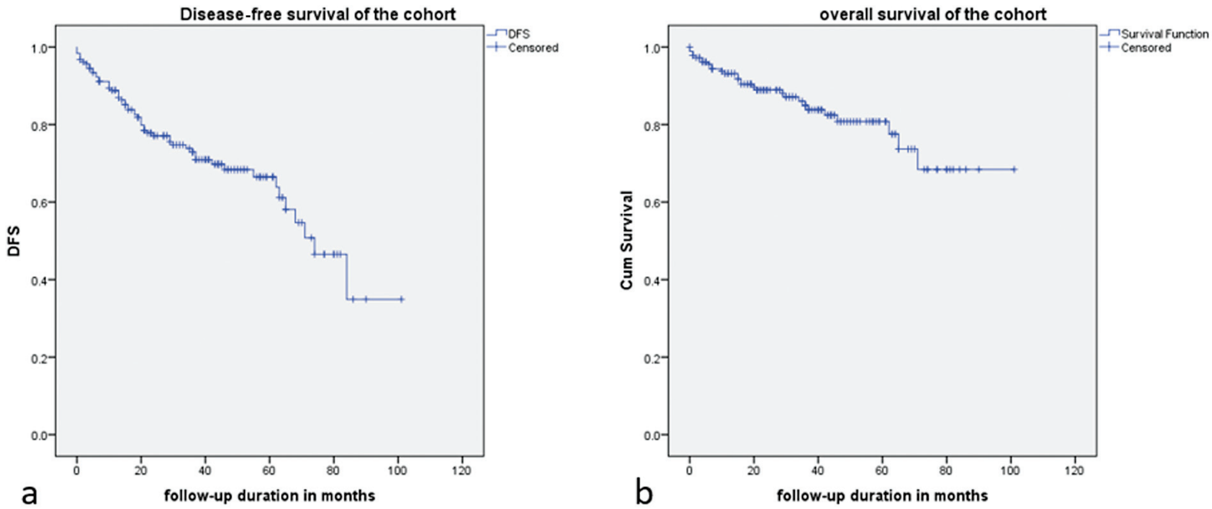

Fig. 1 (**a**, **b**) Survival curves of the entire cohort.

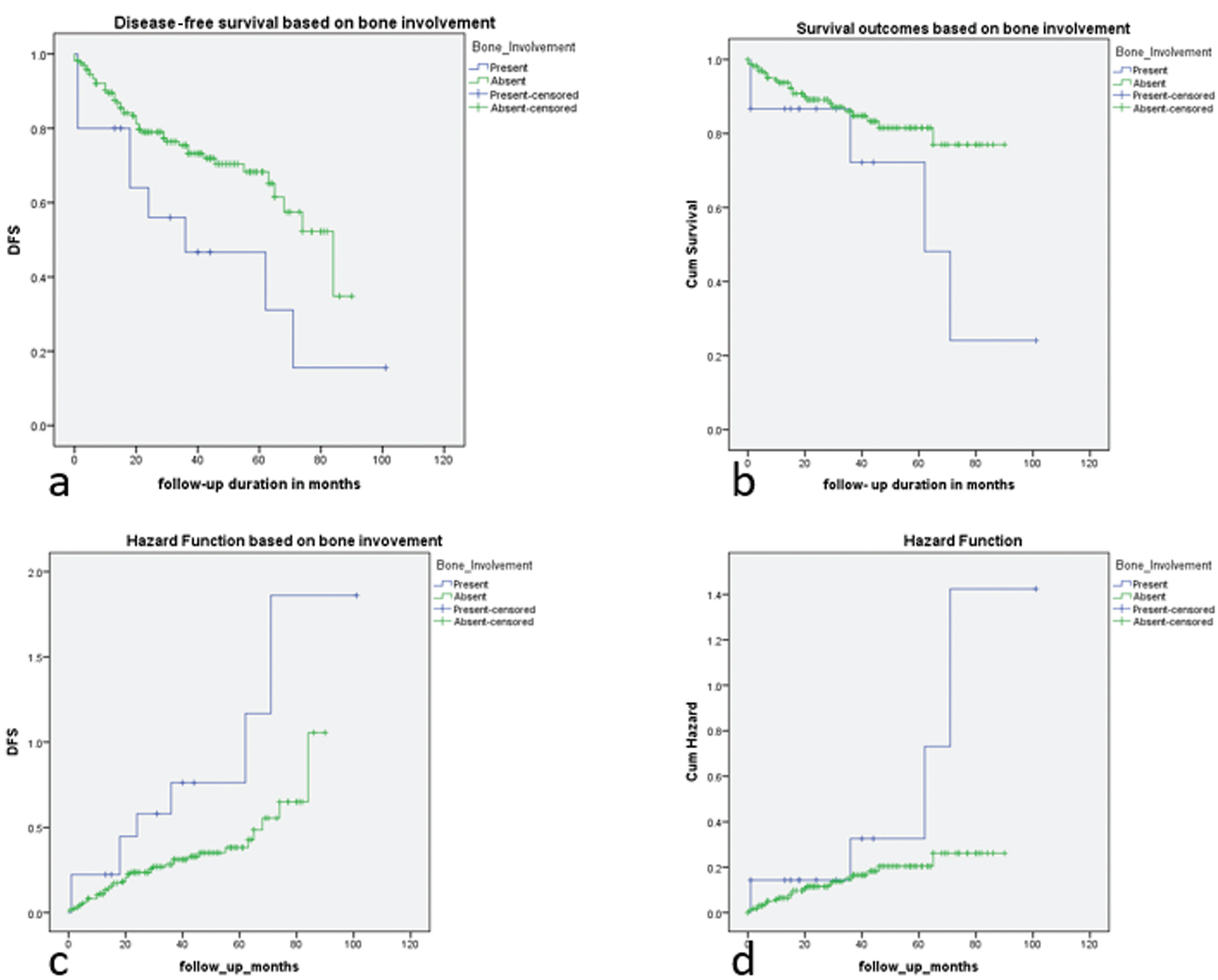

Fig. 2 (**a–d**) Survival curves based on bone involvement.

(available in the online version only) depict the logistic regression analysis for DFS and OS.

Discussion

The current principle for resecting oral cancers is achieving three-dimensional (3D) clear surgical margins with en bloc resection. For tumors abutting the mandible or within 1 cm of it, conservative resections like MM are performed even if the mandible is not involved, while segmental resections are used for paramandibular spread. MM offers a conservative approach for OSCC, aiming to ensure oncological safety while preserving mandibular function and aesthetics. The primary objective of this study is to investigate DFS in OSCC patients undergoing MM to achieve clear surgical margins, with a secondary objective to explore the impact of microscopic bone involvement on DFS and OS.

No single investigation is superior for assessing mandibular involvement. CT and MRI have almost similar sensitivities and specificities for detecting bone involvement; however, CT is more sensitive in detecting superficial cortical erosion.[9–11] Following our institutional protocol, patients underwent preoperative imaging with contrast-enhanced CT scans to evaluate the primary tumor and nodal burden. There are no strict criteria for performing MM, but it is best suited for cancers near the nonradiated mandible or superficially eroding it, where adequate 3D margins and at least 1 cm of mandibular height can be preserved to withstand mastication.[12] In our series of 3,893 patients from 2015 to 2021, only 234 (16.3%) underwent MM, mainly due to the prevalence of advanced oral cancers, trismus, and edentulous patients.

Achieving clear surgical margins in OSCC surgery is essential for reducing local recurrence and improving survival. In our study, 84.24% of patients had negative margins, 15.22% had close margins, and 0.54% had positive margins, aligning with Anderson et al's meta-analysis and Singh et al's findings. Anderson et al's study indicated that margins over 5 mm reduced local recurrence risk by 21%, while Singh et al found better survival with each millimeter increase, optimal at 7.6 mm.[13,14] However, in our study, margin status did not significantly affect locoregional control (LRC) or OS, possibly due to an inadequate sample size.

In our series of marginal mandibulectomies, the 3-year DFS and OS rates were 65 and 70%, respectively. Pathak and Shah reported 2- and 5-year cause-specific survival rates of 85.6 and 72.2%, respectively, in 137 patients.[15] The memorial sloan kettering cancer center (MSKCC) group's study of 326 patients found 5-year local recurrence-free survival (LRFS) and regional recurrence-free survival (RRFS) rates of 74.6 and 85.2%, respectively.[7] Du et al reported 5-year LRC and disease-specific survival (DSS) rates of 85 and 88%, respectively,[16] while Chen et al's study found local control rates between 77.8 and 87.5%.[17] Variations in survival outcomes across studies can be attributed to differences in patient selection and tumor characteristics, including PNI, LVI, and nodal positivity. In our study, PNI was the only significant negative prognostic factor for DFS (OR $= 0.4$, $p = 0.01$), consistent with literature reporting PNI as a significant predictor of poor outcomes.[18,19]

In our cohort, microscopic bone involvement was observed in 8.74% of patients, significantly impacting DFS (OR $= 0.251$, $p = 0.013$). Patients with bone involvement had lower DFS (mean: 44.8 months) and OS compared to those without bone involvement (mean: 63.6 months). However, multivariate analysis showed microscopic bone involvement was not a significant DFS factor; only PNI was significant. The MSKCC study found 15% of patients had microscopic bone involvement, with lower DSS (66 vs. 79.7%) but not statistically significant.[7] The Tata Memorial Hospital study reported 8.1% bone involvement with no survival difference,[15] while Muscatello et al found it in 1.8% of 56 patients, with 5-year survival rates of 60.7 and 77.3%.[20] In our study, bone involvement was confined to cortical bone, and all cases received adjuvant therapy. While microscopic bone involvement may indicate poor prognosis, this study cannot conclude its sole impact on outcomes.

While MM achieves negative surgical margins, it has potential complications such as remanent mandibular fractures and Osteo radionecrosis (ORN). Muscatello et al reported 1 fracture in 56 cases, and Sukegawa et al reported 5 fractures in 37 cases, with an average fracture time of 305 days.[20,21] In our series, no fractures occurred. Given our findings of negative margins in nearly all patients and the low incidence of microscopic bone disease, personalized, less aggressive approaches like periosteal stripping may be feasible without compromising oncological safety.

Strengths and Limitations

A key strength of this study is the prospectively collected data on 3,893 patients over 7 years at a high-volume tertiary care teaching hospital, providing comprehensive analysis. Including 183 patients, it is one of the largest series from Southeast Asia. The study was conducted at a teaching hospital, and surgeries performed by different cadres of surgeons reflected the real-world scenario of surgical outcomes.

Despite its strengths, the study has limitations. The ambispective nature of the study, mainly the exclusion of 26 patients due to missing microscopic bone reports and 25 patients lost to follow-up, may introduce selection bias. The study failed to report the incidence of ORN and tumor involvement in the periosteum. Additionally, the study could have comprehensively assessed MM's functional and aesthetic outcomes, which are critical factors in evaluating the overall outcomes of the treatment. The study's findings regarding the impact of microscopic bone involvement on DFS were not statistically significant in multivariate analysis, suggesting that the sample size may have needed to be more significant to detect these differences conclusively. Future studies with larger cohorts, center collaborative studies, and extended follow-up periods are needed to understand the outcomes better.

Conclusion

This study demonstrates that MM is an effective conservative surgical approach for achieving clear margins in OSCC patients without clinical or radiological bone invasion. The 3-year DFS and OS rates were 65 and 70%, respectively. While MM achieved high rates of negative margins (84.24%), microscopic bone involvement and PNI were significant adverse prognostic factors for DFS. Despite the low incidence of complications such as mandibular fractures, potential complications should be considered.

Ethical Statement

The study was conducted in accordance with the Declaration of Helsinki. Confidentiality and anonymity of the participants were strictly maintained throughout the research process.

Conflict of Interest

None declared.

References

1 Cancer Today [Internet]. 2024. Accessed August 23, 2024 at: https://gco.iarc.who.int/today/
2 Misra S, Chaturvedi A, Misra NC. Management of gingivobuccal complex cancer. Ann R Coll Surg Engl 2008;90(07):546–553
3 Park H. Surgical margins for the extirpation of oral cancer. J Korean Assoc Oral Maxillofac Surg 2016;42(06):325–326
4 Rao LP, Shukla M, Sharma V, Pandey M. Mandibular conservation in oral cancer. Surg Oncol 2012;21(02):109–118
5 Marchetta FC, Sako K, Murphy JB. The periosteum of the mandible and intraoral carcinoma. Am J Surg 1971;122(06):711–713
6 O'Brien CJ, Adams JR, McNeil EB, et al. Influence of bone invasion and extent of mandibular resection on local control of cancers of the oral cavity and oropharynx. Int J Oral Maxillofac Surg 2003;32(05):492–497
7 Petrovic I, Montero PH, Migliacci JC, et al. Influence of bone invasion on outcomes after marginal mandibulectomy in squamous cell carcinoma of the oral cavity. J Craniomaxillofac Surg 2017;45(02):252–257
8 Shah JP. The role of marginal mandibulectomy in the surgical management of oral cancer. Arch Otolaryngol Head Neck Surg 2002;128(05):604–605
9 Qiao X, Liu W, Cao Y, et al. Performance of different imaging techniques in the diagnosis of head and neck cancer mandibular invasion: a systematic review and meta-analysis. Oral Oncol 2018;86:150–164
10 Li C, Yang W, Men Y, Wu F, Pan J, Li L. Magnetic resonance imaging for diagnosis of mandibular involvement from head and neck cancers: a systematic review and meta-analysis. PLoS One 2014;9(11):e112267
11 Acton CH, Layt C, Gwynne R, Cooke R, Seaton D. Investigative modalities of mandibular invasion by squamous cell carcinoma. Laryngoscope 2000;110(12):2050–2055
12 Randall CJ, Eyre J, Davies D, Walsh-Waring GP. Marginal mandibulectomy for malignant disease: indications, rationale, and results. J Laryngol Otol 1987;101(07):676–684
13 Anderson CR, Sisson K, Moncrieff M. A meta-analysis of margin size and local recurrence in oral squamous cell carcinoma. Oral Oncol 2015;51(05):464–469
14 Singh A, Mishra A, Singhvi H, et al. Optimum surgical margins in squamous cell carcinoma of the oral tongue: is the current definition adequate? Oral Oncol 2020;111:104938
15 Pathak KA, Shah BC. Marginal mandibulectomy: 11 years of institutional experience. J Oral Maxillofac Surg 2009;67(05):962–967
16 Du W, Fang Q, Wu Y, Wu J, Zhang X. Oncologic outcome of marginal mandibulectomy in squamous cell carcinoma of the lower gingiva. BMC Cancer 2019;19(01):775
17 Chen YL, Kuo SW, Fang KH, Hao SP. Prognostic impact of marginal mandibulectomy in the presence of superficial bone invasion and the nononcologic outcome. Head Neck 2011;33(05):708–713
18 Quintana DMVO, Dedivitis RA, Kowalski LP. Prognostic impact of perineural invasion in oral cancer: a systematic review. Acta Otorhinolaryngol Ital 2022;42(01):17–25
19 Binmadi N, Alsharif M, Almazrooa S, et al. Perineural invasion is a significant prognostic factor in oral squamous cell carcinoma: a systematic review and meta-analysis. Diagnostics (Basel) 2023;13(21):3339
20 Muscatello L, Lenzi R, Pellini R, Giudice M, Spriano G. Marginal mandibulectomy in oral cancer surgery: a 13-year experience. Eur Arch Otorhinolaryngol 2010;267(05):759–764
21 Sukegawa S, Saika M, Tamamura R, et al. Risk factors for mandibular fracture after marginal mandibular resection. J Craniofac Surg 2020;31(05):1430–1433

