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'Doing as little as possible and as much as necessary' – Oncological efficacy of marginal mandibulectomy in resection of oral cavity cancers

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ABSTRACT

Background: In carefully selected oral cavity cancers, marginal mandibulectomy is an adequate procedure which achieves good disease control adhering to the principle of "doing as little as possible and as much as necessary".
Methodology: This was a retrospective study done by reviewing the medical records of all patients who underwent marginal mandibulectomy for resection of oral cavity cancers in our institution during a period of 5 years. Data was collected from medical case records and analyzed.
Results: 125 cases underwent marginal mandibulectomy for resection of oral cavity cancers. 88.5% of advanced oral cavity cancers that underwent neoadjuvant chemotherapy followed by marginal mandibulectomy are still disease free. The local recurrence rate was 10.4%. Among cases which recurred, 61.5% were in T2 stage of the disease and 30.8% recurred in buccal mucosa. For lesions on the mandible (26/125), the final histopathology showed bone infiltration in only 12% cases and among them only one recurred. Among 88/125 cases where the lesion was abutting mandible even after stretching mucosa, recurrence was noted only in 11.4% with 3-year overall survival of 79.3%.
Conclusions: The low recurrence rate following marginal mandibulectomy in our study shows good locoregional control when performed for a lesion close to or abutting alveolar periosteum. In management of advanced oral cavity cancers, neoadjuvant chemotherapy followed by marginal mandibulectomy was effective in achieving significant locoregional control. For superficial lesions on the mandible, marginal mandibulectomy gives adequate margin clearance resulting in long term survival.

Introduction

Primary cancers of the oral cavity extend along the mucosa towards gingiva, where periosteum acts as a protective barrier preventing infiltration of the cortical bone. Here the tumour advances from the gingival surface towards the alveolus. In dentulous patients, the tumour spread occurs through dental sockets into the cancellous part of mandible. Hence in cases with early infiltration of alveolar process, marginal mandibulectomy is the preferred option since the cortical bone inferior to the roots of the teeth remains uninvolved and this part of mandible can be preserved. This concept popularized marginal mandibulectomy with resection of alveolar ridge [1,2]. Marginal mandibulectomy helps to maintain the bony architecture preserving the muscle attachments to the mandible, hence resulting in less functional and cosmetic deformity.

Segmental mandibulectomy should be considered only when there is obvious erosion of the cortex of the mandible clinically or intraoperatively (even if the preoperative imaging does not show invasion of the cancellous portion) to avoid a positive bone margins on permanent sectioning. In a small subset of patients, performing a marginal mandibulectomy can limit the dependence on free fibula flaps especially in centres where such flaps are done preferentially. In carefully selected oral cavity cancers without bone involvement, marginal mandibulectomy achieves good disease control as opposed to segmental mandibulectomy adhering to the principle of "doing as little as possible and as much as necessary".

Methodology

This was a retrospective study done by reviewing the medical records of all patients who underwent marginal mandibulectomy for resection of oral cavity cancers from 2011 to 2015 at the Department of

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Head & Neck Surgery, Regional Cancer Centre, Thiruvananthapuram, India. Institutional review board approval was obtained for this study. Oral cavity cancers involving the tongue, floor of mouth, lower alveolus, buccal mucosa and lower lip which were close to or abutting the mandible that underwent marginal mandibulectomy were considered in the study.

All 125 patients in the study underwent wide excision of tumour along with marginal mandibulectomy and neck dissection with or without reconstruction procedures. As an institutional practice marginal mandibulectomy has been performed by removing the entire occlusal surface and the lingual cortex to below the myelohyoid line using microsaw or drill. Intra-operative frozen sectioning was done to attain a pathological soft tissue margin clearance of atleast 5 mm. Frozen section report showing involved margins (less than 2 mm) or close margins (3–5 mm) were revised.

Based on final histopathology report, the patients were subjected to adjuvant treatment if indicated. Such patients received 50–60 Gy over a 5–6 week period by conventional fractionation to the primary site and neck. Concurrent chemoradiation was considered as the adjuvant treatment modality wherever indicated.

Data regarding tumour characteristics, radiology findings, surgical approach and extent of resection were collected from the medical records and analyzed. Details of bone infiltration in decalcified bone sections was collected from histopathology reports. Details during follow-up visits were procured from the medical records to assess the outcomes based on locoregional control. Overall survival (OS) and disease-free survival (DFS) were calculated using Kaplan-Meier curve. Prognostic factors were assessed using Cox-Regression analysis.

Results

There were 125 cases included in the study that underwent marginal mandibulectomy for resection of oral cavity cancers. The mean age of the study population was 52.6 years (SD 12.5 years) at the time of surgery with males comprising of 78% and females comprising of 22% of the study population. 50% (63/125 cases) cases in the study were in T2 stage of disease and 20% cases were in T1 stage at the time of surgery. Majority of the T2 tumours, i.e…50.4% (37/63 cases) were arising in the tongue followed by floor of mouth (19.2%) and buccal mucosa (15.2%) (Table 1). 70% (88/125) cases had lesions abutting the mandible even after stretching the mucosa and 21% (26/125) cases had lesions on the mandible (Fig. 1).

Computed Tomography scan had picked up mandible erosion in 2 of the 125 cases, however intraoperatively there was no obvious cortical bone erosion in any of the 125 cases, hence all cases underwent marginal mandibulectomy as part of resection of primary tumour. 113 cases (90.4%) underwent elective neck dissection along with resection of the primary cancer. None of the 125 patients needed tracheostomy. Postoperatively 85 cases received adjuvant radiotherapy or concurrent chemoradiation.

26 clinically advanced cases with lesion on the mandible received pre-operative neoadjuvant chemotherapy which led to shrinkage tumour. In all such cases, marginal mandibulectomy was sufficient to provide adequate margins during resection which without neoadjuvant chemotherapy would have invariably ended up in segmental mandibulecomy. None of these cases showed bone infiltration in decalcified sections in final histopathology.

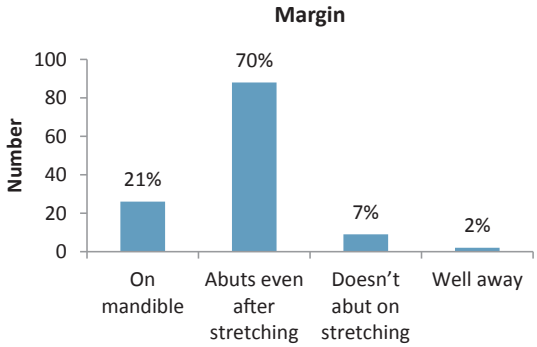

Fig. 1. Margin from the mandible.

Among 125 patients, final histopathology showed close margins (3–5 mm clearance from tumour) in 11 cases and involved margins in 3 cases (less than 2 mm clearance from tumour). All these patients underwent adjuvant radiotherapy. Of the 13 cases (10.4%) which recurred following marginal mandibulectomy, clear soft tissue and mucosal margins were obtained in final histopathology for 11 cases, in 1 margin was close and in 1 margin was involved. Final histopathology showed only 3 cases with bone infiltration, among them only 1 recurred.

Among the 85 cases which received adjuvant treatment, 75 cases underwent radiation therapy alone. Among the cases that received adjuvant treatment for advanced stage of disease, 3 had bone infiltration and 40 had lymph node metastases. Some cases had more than one indication for adjuvant treatment. 10 cases underwent concurrent chemoradiation: 9/10 cases had lymph node metastasis with extracapsular spread whereas 1/10 case had involved margin. Among 13 cases which recurred, 11 had undergone adjuvant treatment. In our study, none of the patients developed mandibular fracture following completion of treatment. 7 cases developed osteoradionecrosis at the completion of treatment.

13 of 125 cases recurred locally with a recurrence rate of 10.4%. Among them 10 cases underwent surgery for recurrence. Overall, 10/13 cases died due to disease whereas 3 died due to other causes. 2 among the 13 locally recurred cases had nodal recurrence as well. 3 cases which recurred in advanced T4 stage of disease had distant metastases as well. The median time interval of recurrence was 34 months (Minimum time interval of recurrence was 9 months and maximum time interval being 52 months). Maximum number of recurrences were noted in tumours presenting in T2 stage, i.e…10/13 cases (76.9%). Among the subsites, buccal mucosa had the highest recurrence rate of 15.8% followed by tongue 8.6% (Table 2). For lesions abutting mandible even after stretching mucosa, recurrence was noted in only 10/88 cases (11.4%) whereas for lesions on the mandible, recurrence was noted only in 3/26 cases (11.5%) (Table 3). Among the clinically advanced tumours who received neoadjuvant chemotherapy, recurrence

Table 1
Site of origin and T stage of tumour.

Subsite	T1	T2	T3	T4	Total
Buccal mucosa	4	9	4	2	19
FOM	4	11	3	6	24
GBS	1	0	0	0	1
Lip	0	1	0	0	1
Lower alveolus	4	5	0	1	10
RMT	3	0	1	3	7
Tongue	9	37	10	7	63
Total	25	63	18	19	125

Table 2
Disease free survival based on subsites.

	Alive	Recurrence	3 year DFS (%)	Std error	P-value
Buccal mucosa	16	3	88.8	7.5	0.005
FOM	22	2	90.3	6.5	
GBS	1	0	100	–	
Lip	0	1	0.0	0.0	
Lower alveolus	7	2	87.5	11.7	
Lower GBS	1	0	100	–	
RMT	7	0	100	–	
Tongue	58	5	96.4	2.5	

Table 3
Disease-free survival based on margin from mandible.

Margin	No Recurrence	Recurred	3 year DFS (%)
On mandible	23	3	95.8
Abuts even after stretching	78	10	91.0
Doesn't abut on stretching	9	0	100
Well away	2	0	100

Table 4
Overall survival and disease-free survival based on T stage.

T stage	3 year OS (%)	3 year DFS (%)
1	88.0	91.8
2	82.2	92.9
3	83.3	100
4	72.9	87.7

was noted only in 3 cases (11.5%).

The 3-year OS for patients who underwent marginal mandibulectomy as part of resection of oral cavity cancers was 82.1% and DFS was 92.9%. Considering the T2 oral cavity lesions (63 cases, 48%) that underwent marginal mandibulectomy, the OS was 82.2% and DFS was 92.9% (Table 4). For lesions abutting mandible even after stretching mucosa, DFS was 91% and OS was 79.3% as compared to DFS of 95.8% and OS of 83.9% for superficial lesions on the mandible (Table 5, Fig. 2).

Discussion

Usually mandible erosion is initiated by osteoclasts eroding the bone followed by direct tumour cell invasion. There are two histological patterns of tumour invasion into mandible by squamous cell carcinoma of the oral cavity. The first pattern is infiltrative type with finger-like extension of tumour into the cancellous spaces without intervening connective tissue layer and osteoclastic activity. The second pattern is erosive type, where tumour progresses on a wider front with an intervening connective tissue layer and increased osteoclastic activity forming a clear distinction between bone and tumour [3]. Marchetta et al. [4,5] studied post-operative mandible specimen and concluded that the spread of tumour occurs directly through the periosteum and not through periosteal lymphatics.

In dentate individuals, tumour cells migrate into the mandible through dental sockets whereas in edentulous patients tumour cells migrate onto the occlusive surface of alveolus, entering mandible through the cortical bone defects in the mandible due to tooth loss. Histological examination of decalcified bone sections show that tumour cell migration in non-irradiated mandible occurs through a single focus, whereas in irradiated mandible, due to breach of periosteum, tumour cells enter through multiple points. Hence marginal mandibulectomy becomes an oncologically inadequate procedure for irradiated patients [3]. There were no cases in our series which underwent marginal mandibulectomy following radiotherapy.

In the study by Brown et al. [6], there was no evidence of spread of tumour through along the inferior alveolar nerve, hence they concluded that there was no need to include neurovascular bundle during marginal mandibulectomy. Erosion beyond the cortical bone into the medullary bone of mandible warrants segmental mandibulectomy over

Table 5
Overall survival & disease-free survival based on margin from mandible.

Gross	Alive	Dead	3 year OS (%)	3 year DFS (%)
On mandible	17	9	83.9	95.8
Abuts even after stretching	64	24	79.3	91.0

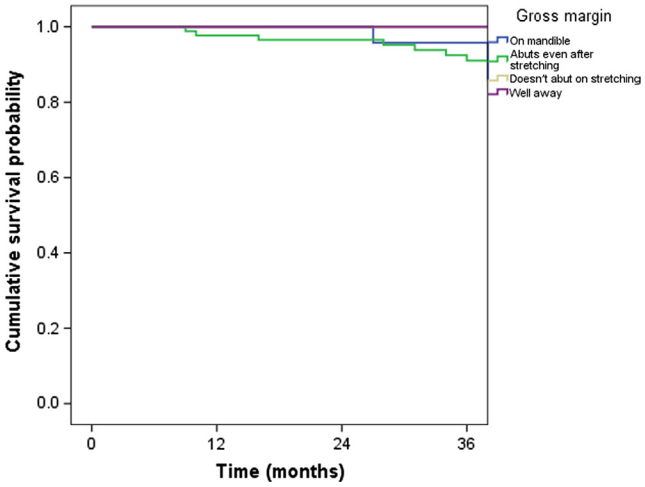

Fig. 2. Disease-free survival based on margin from mandible.

marginal mandibulectomy. However for tumours of the oral cavity with limited involvement of alveolar periosteum, marginal mandibulectomy would suffice [2].

There are mainly three different types of marginal mandibulectomy: vertical, horizontal and oblique. The choice of type of marginal mandibulectomy depends on the site and size of the lesion, depth of invasion of the tumour and absence of radiological evidence of invasion. Oblique marginal mandibulectomy removes the inner cortex of mandible including myelohoid muscle and areas involved by the tumour while retaining the outer cortex, whereas horizontal marginal mandibulectomy retains lower part of the inner cortex of the mandible. Shaha [7] preferred oblique marginal mandibulectomy over other types in resection of floor of mouth cancers since oncological safety and mandible stability were both ensured through the procedure.

Specificity of MRI is higher than CT (93 vs 87%, respectively) in identifying early mandible involvement [8]. Though MRI is a more sensitive investigation, the cost is MRI was not affordable for most of our patients; hence MRI was not routinely done in all cases. In our study CT scan was done in all cases and bone involvement was identified in only 2 cases, however there was no evidence of bone erosion during surgery.

Wax et al. [9], suggested intraoperative frozen section of mandible periosteum to decide on the extent of mandible resection. However intraoperative frozen section for bone is not practised in many oncology centres worldwide including ours due to resource constraints. The perioperative findings like closeness of lesion to mandible usually helps the surgeon decide on the extent of mandible resection required.

Muscutello et al. [2] had mentioned mandibular fracture as a complication in 1.8% cases. For elderly, edentulous patients where the alveolar process recede leading to a pipe-stem mandible, feasibility of marginal mandibulectomy depends on vertical height of body of mandible. Some authors recommend preservation of atleast 1 cm of mandibular thickness to avoid stress fractures [10]. For edentulous patients who have been previously irradiated, due to high chance of significant damage to endosteal blood vessels, chances of pathological fracture of mandible is also high following marginal mandibulectomy [1]. However in our study, none of the 125 cases had pathological fracture and 87% of the patients were able to use the remaining dentition to chew food following marginal mandibulectomy.

Dubner et al. [11] in his study had a local recurrence rate of 19% following marginal mandibulectomy and in the study by Muscutello et al. [1], recurrence was noted in 14.3% cases. According to Guerra et al. [12], the local recurrence rate following marginal mandibulectomy was higher (20%). In our study the local recurrence rate was 10.4% (13 cases among the 125 cases) which shows a better local disease control as compared to previous studies. Pradhan [13] in his

study had achieved a locoregional control of 79% following marginal mandibulectomy for buccal mucosa cancers lying close to the lower alveolus. In our study, the local recurrence rate following marginal mandibulectomy was independent of the size of the primary tumour (p value = 0.726).

There were 189 cases which underwent segmental mandibulectomy for resection of oral cavity cancers during the same period in our institution. Among them 38 cases (20.1%) recurred locally probably due to the advanced stage of disease at initial presentation. In our study, local recurrence rates of 10.4% and 20.1% for cases which underwent marginal and segmental mandibulectomy respectively are better than the local recurrence rates (20% and 33% for marginal and segmental mandibulectomy respectively) mentioned in the study by Guerra et al. [12].

According to Lecitra et al. [14], pre-operative chemotherapy had a significant role in reducing the number of patients who underwent segmental mandibulectomy. Among the 26 advanced oral cavity cancers that underwent neoadjuvant chemotherapy prior to surgery, only 3 cases (11.5%) recurred locally and had to undergo salvage surgery, remaining 88.5% cases were disease free following marginal mandibulectomy.

In the study by Muscutello et al. [2], following marginal mandibulectomy the 5-year OS and DFS were 60.7 and 77.3% respectively, whereas in our study, the 3-year OS and DFS were 82.15 and 92.9% respectively. In the same study, the maximum number of cases that underwent marginal mandibulecomy presented in T2 stage of disease similar to our study. In the above mentioned study, OS and DFS for T2 tumours were 64.7% and 84.6% which was comparable to the results of our study: OS and DFS for T2 tumours being 82.2% and 92.9% respectively.

Chen et al. [15] identified bone invasion in final histology in 16.3% cases that underwent marginal mandibulectomy. In our study, 26 patients were clinically observed to have lesion on the mandible without imageological evidence of bone destruction. Final histopathology showed 3 out of these 26 patients (12%) with bone infiltration, of whom only one recurred. This proves the efficacy of marginal mandibulectomy in the treatment of superficial alveolar lesions, which can be further affirmed with larger studies.

Among oral cavity cancers that underwent marginal mandibulectomy, considering the 3 subsites with maximum number of cases, buccal mucosa had maximum recurrences (15.8%) followed by tongue (8.6%) and floor of mouth (8.3%). Hence among the 3 common subsites, buccal mucosa cancers had a worse prognosis in our study. Tumour biology and pattern of spread is probably the reason for high propensity to buccal mucosa, however this will require further studies to draw conclusions. Contrary to results of our study, the study published by Pathak et al. [16] showed a superior 5-year survival for patients with buccal mucosa cancers over floor of mouth cancers among those who underwent marginal mandibulectomy.

Conclusions

Marginal mandibulectomy is an oncologically safe procedure providing safe margins of resection margins in the treatment of oral cavity cancers where the lesion abuts mandible or lie on the alveolar aspect when no imageological evidence of bone infiltration is present. In management of advanced oral cavity cancers, neoadjuvant chemotherapy followed by marginal mandibulectomy was effective in achieving significant locoregional control. For superficial lesions on the mandible, marginal mandibulectomy gives adequate margin clearance and resulting in long term survival. Recurrence rate following marginal mandibulectomy in our study is lesser than that of many previous studies. Pattern of local recurrence was independent of size of tumour.

Ethical statement

i. **Compliance with Ethical Standards:** There was adherence to ethical standards in this study
ii. **Funding:** There was no funding for this research work.
iii. **Conflict of Interest:** There is no conflict of interest pertaining to this study.
iv. **Ethical approval:** All procedures performed in studies were in accordance with the ethical standards of Regional Cancer Centre, Thiruvananthapuram approved by the Institutional Ethics Committee.

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