



Mandible handling in the surgical treatment of oral squamous cell carcinoma: lessons from clinical results after marginal and segmental mandibulectomy

Christoph K. Sproll, MD, DDS,^a Henrik Holtmann, MD, DDS,^b Lara K. Schorn, MD, DDS,^a Theresa M. Jansen, MD,^c Julia Reifenberger, MD,^c Inga Boeck, MD,^d Majeed Rana, MD, DDS, Prof.,^a Norbert R. Kübler, MD, DDS, Prof.,^a and Julian Lommen, MD, DDS^a

Objective. The aim of this retrospective, single-center study was to analyze long-term results after marginal and segmental mandibulectomies in patients with oral squamous cell carcinoma (OSCC).

Study Design. The study included 259 patients treated for OSCC with mandibulectomy between 1996 and 2010. Data acquisition consisted of analysis of operation reports, re-evaluation of histologic bone specimens, and collection of clinical follow-up data.

Results. Of the included patients, 86.5% had received segmental and 13.5% marginal mandibulectomies. Patients who received segmental mandibulectomy generally displayed a higher TNM (tumor–node–metastasis) stage; 47% of patients who received segmental mandibulectomy and 14% of those receiving marginal mandibulectomy showed bone infiltration (pT4 a). Of all patients with bone infiltration, 49% showed an invasive histologic infiltration pattern, and 35% showed an erosive histologic infiltration pattern. We found healthy residual crestal bone height in 43% of all segmental mandibulectomies. Only 8% of all patients were prosthodontically rehabilitated. With regard to prognostic parameters, there was no significant difference between patients receiving marginal mandibulectomy and those receiving segmental mandibulectomy.

Conclusions. Because healthy residual crestal bone height was found in 43% of all patients who had received segmental mandibulectomies, it is conceivable that a significant number of patients would profit from marginal mandibulectomy, at least in cases of absent or erosive bone infiltration pattern, because the residual crestal bone is functionally stable. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;129:556–564)

Malignancies of the oral cavity represent approximately 5% of all cancers.¹ On histopathologic examination, about 95% of these tumors can be classified as oral squamous cell carcinomas (OSCCs).² Incidences of newly diagnosed OSCC worldwide range from 200,000 to 350,000 per year, making OSCC the sixth most common cancer.³ The average age at diagnosis of OSCC is 63 years.⁴ The etiopathogenesis is multifactorial. Alcohol and tobacco abuse, especially in combination, significantly increases the risk of OSCC; in addition, chronic mucosal ulcerations, immunosuppression, and betel nut chewing have been well established as significant risk factors in recent years. The role of human papillomavirus (HPV) in the development of oropharyngeal squamous cell carcinoma is well established; yet its role in the development of OSCC is still unclear.^{5–7} About 30 years ago, OSCC incidence rate was 10 times higher in men compared with women.⁸

Nowadays, with an increase in the number of female smokers, this ratio has dropped to the incidence in men coming down to only twice that in women.⁹ The affected sites are predominantly the tongue and the floor of the mouth.¹⁰ From a clinical point of view, OSCC remains asymptomatic for a long time and can only be detected by the patient and the examiner with the presence of an induration and change in the color of the oral mucosa.¹¹ At later tumor stages, a destructive exophytic or endophytic tumor may cause spontaneous bleeding, tooth loosening, and osteolysis and fractures of the surrounding bony tissue of the maxilla and the mandible.¹² About 30% to 40% of patients initially present in an advanced stage of disease because of persistent pain.¹³ Despite tremendous medical and technologic progress in recent decades, improvement in the 5-year survival rate has been insignificant and currently stands at around 65.3%.¹⁴ Diagnosis is based on clinical examination; imaging modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), orthopantomography (OPG), and ultrasonography, as well as histopathology on fresh-frozen, paraffin-embedded samples of the tumor.¹⁵ For the pri-

^aDepartment of Oral and Maxillofacial Surgery, Heinrich-Heine-University, Düsseldorf, Germany.

^bDepartment of Oral and Maxillofacial Surgery, Malteser Clinic St. Johannes, Duisburg, Germany.

^cDepartment of Dermatology, Heinrich-Heine-University, Düsseldorf, Germany.

^dInstitute for Pathology, Cytology and Molecular Pathology GbR, Wet- zlar, Germany.

Received for publication Dec 23, 2018; returned for revision Nov 14, 2019; accepted for publication Nov 21, 2019.

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2212-4403/\$-see front matter

<https://doi.org/10.1016/j.oooo.2019.11.011>

Statement of Clinical Relevance

Reducing the extent of bone resection in patients with oral squamous cell carcinoma seems to offer equivalent clinical outcomes and improves postoperative health-related quality of life.

mary tumor, surgery in combination with neck dissection and reconstruction is still one of the pillars of therapy with curative intention. To maintain sufficient surgical safety margins, bone resection is necessary for the treatment of OSCC with close proximity or infiltration to the maxilla or the mandible. For the mandible, there are 2 types of resection: marginal mandibulectomy and segmental mandibulectomy.¹⁶ Marginal mandibulectomy allows for preservation of basal or lateral mandibular bone continuity, which is lost in segmental mandibulectomy, causing detrimental effects on phonation, mastication, and facial aesthetics.¹⁷⁻¹⁹ According to the TNM classification, a crucial factor for deciding between marginal and segmental mandibulectomy is possible tumor cell infiltration into underlying bone. Here, erosive and invasive bone infiltration can be distinguished through histopathologic examination.^{20,21}

Historically, carcinomas of the perimandibular region have routinely been treated with segmental resection because the procedure was considered oncologically necessary to obtain adequate safety margins²² because of the ease of surgical handling²³ and because it was thought tumors would grow continuously through the lymphatics in the lingual periosteum into bone.²⁴ We have taken advantage of the longstanding practice of extensive jaw resections in our department and are now able to report on one of the largest cohort of patients who underwent mandibular segmental resection as part of surgical therapy for their OSCC. The present study retrospectively compared the rates of tumor recurrence, postoperative survival, complications, and prosthodontic rehabilitation in patients after marginal and segmental mandibulectomies. Additionally, in a novel approach, we re-evaluated all of the bone specimens with respect to tumor involvement, infiltration pattern, and residual crestal bone height. We hope that these results will contribute to refining the existing treatment options for OSCC, by enabling the surgeon to sacrifice only as much bone as oncologically necessary.

MATERIALS AND METHODS

Ethics

Ethical approval for this retrospective study was given by the Ethics commission of Heinrich-Heine-University Düsseldorf, Germany (case No. 5020).

Patients

This study included all patients who were diagnosed with OSCC and treated surgically by either marginal or segmental mandibulectomy between 1996 and 2010 at the Department of Oral and Maxillofacial Surgery at Düsseldorf University Hospital (Düsseldorf, Germany).

Also, we included patients who had been treated for OSCC and now had secondary OSCC.

Operation data

Operation reports for the years 1996 to 2010 were retrospectively reviewed for all OSCC resection procedures, including marginal or segmental mandibulectomy. On the basis of these operation reports, a standardized questionnaire for all reports was developed. Here, personal patient data, such as date of birth and death, tobacco and alcohol consumption, comorbidities, and pre- and postoperative therapies, were recorded. Adjuvant radiochemotherapy, including medications applied, was documented. The operational procedures were evaluated for type of mandible sectioning (marginal or segmental), type of performed neck dissection, and primary reconstruction (osteosynthesis, reconstruction plates, soft tissue or bone). Histologic characteristics analyzed were TNM classification, OSCC localization, and bone involvement. Follow-on operations were divided into secondary and complication-associated operations. Documented secondary operations included mandible reconstruction with use of the iliac crest, scapula, or fibula transplants, as well as insertion of dental implants with subsequent prosthodontic treatment. Complication-associated operations under general anesthesia were necessary in cases of bleeding, hematoma, seroma, abscess, infection of osteosynthesis, exposed osteosynthesis, fracture of osteosynthesis, fistula, need for skin or split-skin grafts, necrosectomy of skin or bone, and application of vacuum bandages. Also, cases of OSCC recurrence were documented. Patients' general practitioners as well as dentists were contacted to gain detailed information about follow-up appointments and the death rate.

To allow for conclusive follow-up data, the minimum interval between operation and data acquisition was 3 years.

Histologic data

All histologic bone specimens that showed invasion by tumor were re-evaluated by both a specialist in pathology and a specialist in oral and maxillofacial surgery. Of each resected part of the mandible, 3 specimens were stored in the institute of pathology: 1 adjacent to the center of the tumor and 1 each of the resection margins. Criteria evaluated were resection margins, type of infiltration (erosive or invasive), tumor size, localization (cranial, centered, caudal), stage of mandibular atrophy, and residual crestal bone height. The correct stage of mandibular atrophy was determined by using the *Atlas of Craniomaxillofacial Osteosynthesis: Microplates, Miniplates, and Screws*, by Haerle et al.²⁵

Statistics

Statistical analysis was performed by using Microsoft Excel 2016 (Microsoft Corp., Redmond, WA) and the statistic software R version 3.1.3.

The χ^2 test was used to test for the dependency of the 2 variables and whether the 2 groups showed homogeneity with regard to a certain value. Distribution of an ordinal value in the 2 groups was analyzed by means of the Wilcoxon rank-sum test. Significance level was set at $P \leq .05$. Kaplan-Meier survival curves were calculated, and a log rank test was used to test for the equality of the various survival curves.

RESULTS

Demographic analysis

Between the years 1996 and 2010, a total of 259 patients underwent mandibulectomy for OSCC. On average, 17 mandibulectomies were performed per year. The highest number of mandibulectomies occurred in 2002, with 26 operations, whereas the lowest number was found in 2010, with 6 operations.

Out of 259 patients, 224 (86%) received segmental mandibulectomy, with an average of 15 operations per year. Here, the highest number of segmental mandibulectomies occurred in 1996, with 21 operations, and the lowest number in 2010, with 6 operations. Overall 35 (14%) marginal mandibulectomies were performed, with a mean of 2.3 operations per year. In 1999 and 2010, no marginal mandibulectomies were performed. Here, with 7 operations, the highest number was also documented for the year 2002.

Gender distribution

The male/female ratio in this study was approximately 2:1. In total, 178 patients were males (68%), and 83 were females (32%). Over the 15-year follow-up period, the gender ratio shifted slightly toward females. Impressive differences were found between the years 1996, with a ratio of 6:1, and the year 2010, with a ratio of 1:2. For segmental mandibulectomies, the male/female ratio was 2.3:1 and for marginal mandibulectomies 1.3:1.

Age distribution

The mean age of all patients ($n = 259$) was 62.3 years (range 32–91 years). Most patients were 51 to 80 years of age, with the greatest number seen in the 51- to 60-year age group. The mean age of female patients was 66.2 years, whereas that of males was 60.4 years, showing that, on average, women were 5.8 years older at the time of surgery. Most patients who received segmental mandibulectomy were 51 to 60 years of age, whereas patients who received marginal mandibulectomy were 61 to 70 years of age. Over the 15-year timespan, the average age at the time of surgery increased from 57.7 years in 1996 to 69.2 years in 2015.

Tobacco and alcohol consumption

Retrospectively, daily smoking was reported by 169 (65%) of 259 patients; 43 (17%) denied smoking, and 47 (18%) did not provide any details. Daily alcohol consumption was reported by 135 patients; 70 denied alcohol consumption, and 54 (21%) did not provide further information on the matter. According to patient report, 127 (49%) consumed both tobacco and alcohol on a daily basis; 78% of male patients consumed either tobacco or alcohol daily, and 68% consumed both tobacco and alcohol daily. Among females, 48% reported daily tobacco or alcohol consumption, and 24% consumed both tobacco and alcohol daily.

Neck dissection

Of the 259 patients, 167 (64%) received bilateral neck dissection. Ipsilateral neck dissection was performed on the right side in 31 cases (12%) and on the left side in 30 (12%) cases. At time of mandibulectomy, 25 patients (10%) had already undergone neck dissection during previous OSCC resection. In only 6 cases (2%), no indication for neck dissection was seen. When segmental mandibulectomy was performed, simultaneous bilateral neck dissection was conducted in 67% of cases, whereas only 52% of cases with marginal mandibulectomy received bilateral neck dissection. Performed neck dissection type (functional, selective, or radical) did not differ between segmental and marginal mandibulectomies.

Soft tissue reconstruction

Of the included patients, 71 (27%) had received intraoperative primary wound closure; local flaps in 88 (34%) cases and free or pedicle flaps in 80 cases (31%), were performed. In 17 cases (7%), information on soft tissue reconstruction could not be obtained retrospectively. Tongue or cheek rotation flaps were the most common local flaps used. The free or pedicle flaps used were radial forearm flaps, pectoralis major flaps, acromion pectoral flaps, and deltopectoral flaps. Primary wound closure or local flaps were sufficient for reconstruction in 136 patients (60%) who had received segmental mandibulectomy and in 23 patients (65%) who had received marginal mandibulectomy. Radial forearm flaps were performed in 20% of cases in both groups. A combination of pedicle distant flaps was necessary in 8 patients who had received segmental mandibulectomy.

Primary bone reconstruction

In 217 (84%) of all mandibulectomy cases, the insertion of a titanium reconstruction plate was necessary; 40 patients (15%) did not receive a reconstruction plate, and in 2 cases (0.8%), the method of primary bone reconstruction could not be determined.

retrospectively. In the 217 cases with insertion of a reconstruction plate, segmental mandibulectomy was performed. Insertion of a reconstruction plate was not necessary in any of the 35 cases (100%) with marginal mandibulectomy. Primary bone reconstruction was achieved with a fibula transplant in 3 patients, with a scapula transplant in 2 patients, and temporarily with bone cement (Palacos) in 10 patients.

Radiochemotherapy

Of all 259 patients, 77 (30%) received adjuvant radiotherapy, and 2 patients (1%) received neoadjuvant radiotherapy. In 124 cases (48%), no radiotherapy was performed. Neoadjuvant radiochemotherapy was performed in 9 cases (3%), and adjuvant radiochemotherapy was performed in 47 cases (18%). The most commonly used chemotherapeutics were cisplatin, cisplatin + 5-fluorouracil, and carboplatin. Two patients received mitomycin and 3 patients a combination of cisplatin + 5-fluorouracil and cetuximab. In 1 case, adjuvant chemotherapy was provided along with cisplatin and vinorelbin. In 24 cases (69%) with marginal mandibulectomy, no neoadjuvant or adjuvant radiochemotherapy was necessary, whereas radiochemotherapy could be waived in 100 patients who had received segmental mandibulectomy (45%).

OSCC localization

In most cases, OSCC was located at the floor of the mouth (36%), followed by the alveolar process (31%), the tongue (11%), and the cheek (10%); 19% of OSCCs showed multilocular infiltration of the floor of the mouth, alveolar process, or cheek.

pTNM classification

Overall, the OSCC stage Tx was diagnosed in 1 patient (< 1%), T1 in 48 (18.5%), T2 in 82 (31.7%), T3 in 18 (6.9%), and T4 in 110 (42.5%). T1 was found in 12.5% of those who had received segmental mandibulectomies and 57.1 % of those who had received marginal mandibulectomies. T2 was diagnosed in 32.6% of those who had received segmental mandibulectomies and in 25.7% of those who had received marginal mandibulectomies. T3 occurred in 7.6% of those who had received segmental mandibulectomies and in 2.9 % of those who had received marginal mandibulectomies. In 46.9 % of those who had received segmental mandibulectomies, OSCC was staged as T4, but only in 14.3% of those who had received marginal mandibulectomies. The only case of Tx (0.4%) was found in the segmental mandibulectomy group. Preoperative indication for segmental mandibulectomies was set when cT4 stage could not be excluded by head and neck CT imaging with a contrast agent (because of questionable bone infiltration or poor image quality resulting from restorative dental artefact buildup) or the required clinical

safety margin of 1 cm or greater was surgically not achievable, hence the disparity between 86.5% cT4 and 46.9% pT4.

Lymph node metastases were found in 112 (43%) of all patients. Of these, 38 (15%) were N1, 70 (27%) were N2, and 4 (1%) were N3. These numbers were almost identical to those found in those who received segmental mandibulectomy. In patients who had received marginal mandibulectomy, the amount of N0 stage was higher, with 63% of cases. M1 was found in 3 patients (1%) in the lung, liver, or skin, and they all had received segmental mandibulectomy. In 145 (56 %) of all cases, R0 could be achieved, with 5 cases having close margins. In 76 (29 %) of cases, R status was not mentioned in the histopathologic report. Histopathologically, 37 resections (14%) showed R1, and 1 (1%) showed R2. R0 was achieved in 55% of patients who had received segmental mandibulectomy and in 60% of those who received marginal mandibulectomy. R1 was 15% higher in patients who had received segmental mandibulectomy compared with 11 % in marginal mandibulectomy.

Grading

Gx was found in 1 patient (1%), G1 in 11 (4%), G2 in 194 (75%), G3 in 51 (20%), and G4 in 2 (1%). These numbers were almost identical to the ones found in patients who had received segmental mandibulectomy. Among patients who had received marginal mandibulectomy, G1 was found in 14% and G3 in 9% of cases.

Mandibular infiltration

Overall, bone infiltration was found in 110 (42 %) of all patients; 149 (58%) of all mandibulectomies did not show bone infiltration. Bone infiltration was found in 105 (47%) of patients who had received segmental mandibulectomies ; 5 (14%) of the specimens after marginal mandibulectomies showed bone infiltration, whereas 30 (86%) did not (Table 1). These findings were significantly different between the 2 resection types ($P < .0003$).

Table 1. Fourfold table showing segmental and marginal mandibulectomies in patients with or without cancerous bone infiltration

	Without cancerous bone infiltration	With cancerous bone infiltration	Total
Segmental mandibulectomy	119	105	224
Marginal mandibulectomy	30	5	35
Total	149	110	259

χ^2 test = 13.158.
 $P < .0003$.

Patterns of bone infiltration upon histopathology and infiltration depth

Upon re-evaluation of all fresh-frozen, paraffin-embedded bone specimens, invasive bone infiltration was found in 54 cases (49%), whereas erosive infiltration was observed in 38 cases (35%). In 18 cases (16%), the type of cancerous bone infiltration could not be differentiated. Both erosive and invasive tumorous bone infiltration reached bone marrow and qualified for the pT4a stage. The described differences merely describe the histologic growth pattern of the tumor. Of segmental mandibulectomies 51 (49%) showed invasive and 37 (35%) erosive cancerous bone infiltration; 17 (16%) of cases could not be differentiated. In patients who had received marginal mandibulectomies, invasive cancerous bone infiltration was found in 3 (60%) and the erosive type in 1 (20%). In 1 case, differentiation could not be made.

Localization of cancerous bone infiltration

For segmental mandibulectomy, cranial cancerous bone infiltration was found in 73 cases (66%), buccal or lingual infiltration in 15 cases (14%), and caudal infiltration in 1 case (1%). A combination of the above-mentioned localizations was found in 4 cases (4%). In 17 resections (15%), localization of cancerous bone infiltration could not be determined. Three of 5 marginal mandibulectomy cases with cancerous bone infiltration showed infiltration from cranial. The other 2 cases could not be differentiated.

Stages of mandibular atrophy

Of the included patients who received segmental mandibulectomies and had bone infiltration, 62 (59%) showed atrophy stages between I and III. In 31 (30%) cases, advanced atrophy stages between IV and VI were found. In 12 cases, determination of mandibular atrophy was not possible.

Size of cancerous bone infiltration and residual crestal bone height

In all 110 cases of cancerous bone infiltration, the size of the tumor mass was evaluated, with special emphasis on residual crestal bone height in erosive cancerous bone infiltration because generally only superficial bone infiltration is expected. Residual crestal bone height was only measured in patients who had received segmental mandibulectomies. In 45 (43%) of these cases, residual crestal bone height of unaffected bone of at least 11 mm was found. In 12 patients who had received segmental mandibulectomies, residual crestal bone height was between 16 and 20 mm and in 6 cases greater than 2 cm. In 13 cases, residual crestal bone height could not be determined.

Table II. Fourfold table showing differences in the amount of residual crestal bone height between erosive and invasive cancerous bone infiltration

	<i>Residual crestal bone height < 11 mm</i>	<i>Residual crestal bone height ≥ 11 mm</i>	<i>Total</i>
Erosive bone infiltration	10	26	36
Invasive bone infiltration	30	15	45
Total	40	41	81

χ^2 test = 12.101.
P < .0005.

Among patients who received segmental mandibulectomies and had erosive cancerous bone infiltration, 26 (68%) demonstrated residual crestal bone height of at least 11 mm. In general, in cases with invasive cancerous bone infiltration, the amount of uninfiltred residual crestal bone height was significantly smaller (*P* < .0005) (Table II).

Secondary and complication-associated operations

Patients who received segmental mandibulectomy, on average, underwent 2.71 secondary or complication-associated operations (median = 2). Of these patients, 50 (22.3%) did not undergo secondary operations. One patient underwent 16 further operations. Patients who received marginal mandibulectomy, on average, underwent 1.51 secondary or complication-associated operations (median = 1). Of these patients, 16 (45%) did not undergo secondary operations. One patient underwent 8 further operations. Differences between the 2 surgical methods were significantly different (*P* = .0315) (Table III).

Because of the very small number of patients who had cancerous bone infiltration and had received marginal mandibulectomy, we only compared patients who had received marginal or segmental

Table III. 2 × 4 table with differences in the amount of secondary or complication-associated operations between segmental and marginal mandibulectomy

	<i>Number of secondary or complication-associated operations</i>				<i>Total</i>
	<i>None</i>	<i>1</i>	<i>2</i>	<i>≥ 3</i>	
Segmental mandibulectomy	50	52	32	90	224
Marginal mandibulectomy	16	6	4	9	35
Total	66	58	36	99	259

χ^2 test = 8.833.
P < .0315.

Table IV. 2 × 6 table with differences in the amount of secondary or complication-associated operations between segmental and marginal mandibulectomy without cancerous bone infiltration

	Number of secondary or complication-associated operations						Total
	None	1	2	3	4	≥ 5	
Segmental mandibulectomy without cancerous bone infiltration	24	18	21	12	7	37	119
Marginal mandibulectomy without cancerous bone infiltration	13	5	4	3	3	2	30
Total	37	23	25	15	10	39	149

χ^2 test = 11.5471.
P < .04155.

mandibulectomies but did not have cancerous bone infiltration (Table IV). A detailed analysis of the probabilities for secondary and complication-associated operations showed significant differences between the marginal and segmental mandibulectomy groups (*P* = .002).

Prosthetic treatment

In total, only 22 (8%) of all 259 patients received subsequent prosthetic treatment. Of all patients who received segmental mandibulectomies, 19 (8%) were treated prosthetically, whereas only 3 patients (9%) who received marginal mandibulectomy received such treatment. No difference was found between the 2 groups (*P* = .98) (Table V).

OSCC recurrence

Of the 259 included patients, 65 (25%) had OSCC recurrence after the initial operation. No significant differences for OSCC recurrence were found between the marginal and segmental mandibulectomy groups (*P* = .75) as well as between those with cancerous bone infiltration and those without (*P* = .91) (Tables VI and VII).

Overall survival rate

In 166 (64%) of 259 cases, day of death or actual survival could be determined. In 93 cases, last follow-up day was determined. No differences in overall survival were found between the marginal and segmental

Table V. Fourfold table with differences in prosthetic treatment between segmental and marginal mandibulectomies

	With prosthetic treatment	Without prosthetic treatment	Total
Segmental mandibulectomy	19	205	224
Marginal submandibulectomy	3	32	35
Total	22	237	259

χ^2 test = 0.0003.
P = .98.

Table VI. Fourfold table with differences in oral squamous cell carcinoma (OSCC) recurrence between segmental and marginal mandibulectomies

	With OSCC recurrence	Without OSCC recurrence	Total
Segmental mandibulectomy	57	167	224
Marginal submandibulectomy	8	27	35
Total	65	194	259

χ^2 test = 0.108.
P = .75.

Table VII. Fourfold table with differences in oral squamous cell carcinoma (OSCC) recurrence between cancerous and no cancerous bone infiltration

	With OSCC recurrence	Without OSCC recurrence	Total
With cancerous bone infiltration	28	82	110
Without cancerous bone infiltration	37	112	149
Total	65	194	259

χ^2 test = 0.013.
P = .91.

mandibulectomy groups (*P* = .344). Because of the small number of marginal mandibulectomy cases, the calculation remains uncertain. Significant differences in overall survival were found between those with cancerous bone infiltration and those without cancerous bone infiltration (*P* < .00003). Furthermore, significant differences were found in overall survival between those who received segmental mandibulectomies and had or did not have cancerous bone infiltration (*P* < .00005), as well as between those who received marginal mandibulectomies and did not have cancerous bone infiltration and those who received segmental mandibulectomies and had cancerous bone infiltration (*P* = .031). No differences in overall survival were found between patients

who received marginal or segmental mandibulectomies, with and without OSCC recurrence ($P = .418$). The 5-year survival rate was 59% in all patients, 68% in those who received marginal mandibulectomies, 57% in those who received segmental mandibulectomies, 69% in those without cancerous bone infiltration, 43% in those with cancerous bone infiltration, 53% in those with OSCC recurrence, and 60% in those without OSCC recurrence.

DISCUSSION

We retrospectively analyzed 259 patients who had received marginal and segmental mandibulectomies, resulting in one of the largest collectives of such patients reported so far. Therefore, the acquired data can be compared with at least 2 other large studies that also evaluated clinical long-term differences between marginal and segmental mandibulectomies in 136 and 334 patients, respectively.^{26,27} The OSCC male/female ratio was found to be 2.1:1 in this study, in agreement with data released by the German Robert-Koch-Institute from 2006 and 2010 with male/female ratios of 2.7:1 in both years. Recently conducted studies have shown that this ratio currently almost equals 1.1:1.^{28,29} The mean patient age of 62.3 years in this study reflects common scientific data reported by other studies.³⁰ With tobacco and alcohol consumption being the highest risk factors for OSCC, we found that 65% of all patients had a smoking habit and 52% of all patients had a drinking habit. Other studies have shown an even higher correlation.³¹ We have to point out that our study evaluated an unequal distribution, with 224 segmental mandibulectomies and only 35 marginal mandibulectomies. However, regional studies from Spain and Australia, where marginal mandibulectomies were conducted on a broader basis, showed higher numbers of marginal mandibulectomies than segmental mandibulectomies.^{32,33} In our study and others, the floor of the mouth was the most frequent location of OSCC.³⁰ With regard to TNM classification, 112 (43%) patients in the present study were diagnosed at the pT4 stage. This relatively high number can be explained by the fact that we only included patients who had received marginal or segmental mandibulectomy and not all patients with OSCC seen at our clinic. Accordingly, studies that included a higher number of patients who had not received mandibulectomies presented a lower number of patients at the pT4 stage.³⁰ In the present study, in 55% of patients who received segmental mandibulectomies and 60% of those who received marginal mandibulectomies, R0 status could be achieved. Other studies have described even higher rates with R0 status with 94% of segmental mandibulectomies and 97% of marginal mandibulectomies.³⁴ The discrepancy between these results can be explained by the high

number of patients with Rx status in our study because determination of R status was not generally performed 10 to 20 years ago. Likely, many of the Rx statuses may, indeed, represent R0 status. It was shown that the metastatic potential of OSCC increases with the stage of grading.³⁵ Our study supports this finding because all our patients with lung metastases had G3 tumors and none of the patients with lymph node metastases had G1 tumors. Unique to this study was the high number of re-evaluated histologic mandibular resection specimens with bone infiltration ($n = 110$). In the current literature, the numbers of patients with OSCC with cancerous bone infiltration vary from 12% to 56%.^{21,23,36} Nomura et al. analyzed 176 mandible bone resections from patients with OSCC and found 65% with cancerous bone infiltration and 35% without cancerous bone infiltration.³⁷ Brown et al. found cancerous bone infiltration in 33% of patients who had received marginal mandibulectomies and 83% of those who had received segmental mandibulectomies, with a total of 100 analyzed patients.³⁸ In another study, Brown et al. demonstrated cancerous bone infiltration in 91% of patients who had received segmental mandibulectomies and 44% of those who had received marginal mandibulectomies.³⁹ Patel et al. found cancerous bone infiltration in 94% of patients who had received segmental mandibulectomies and 46% of those who had received marginal mandibulectomies.⁴⁰ These studies and the results of our study indicate that a pre-operative cancerous bone involvement is overestimated rather than underestimated. However, the present study and many other studies found invasive cancerous bone infiltration to be more frequent compared with erosive cancerous bone infiltration.^{41,42} Wong et al. reported significantly worse prognoses for patients with invasive cancerous bone infiltration compared with those with erosive cancerous bone infiltration.⁴³ Brown et al. and Ord et al. regarded marginal mandibulectomy as especially suitable for the treatment of erosive cancerous bone infiltration.^{44,45} Brown et al. and Bartelbort et al. stated that the Cawood and Howell classification for mandibular atrophy is important to determine whether segmental or marginal mandibulectomy should be performed.^{39,46} Generally, marginal mandibulectomy is achievable with a residual crestal bone height of ≥ 10 mm or greater. The results of our study indicated that in 45 patients, marginal mandibulectomy, rather than segmental mandibulectomy, could be performed without taking the risk of an R1-status or instability of the mandible. A study by Wolff et al. demonstrated that the need for further operations was higher in segmental mandibulectomies (73%) than marginal mandibulectomies (52%).²⁶ Our data support this finding. The analysis of prosthodontic rehabilitation showed that only 8% of all of our 259 patients with

mandibulectomy received postoperative prosthodontic treatment. A study by Rogers et al. showed similar results, with only 5% of 130 patients receiving postoperative prosthodontic treatment.⁴⁷ Reasons for this could be high rates of OSCC recurrence, insufficient osseointegration of bone grafts, poor patient compliance, or short overall survival rates. Our data show that marginal mandibulectomy is not associated with a higher risk of OSCC recurrence. This was also shown by other studies.⁴⁸ In the present study, 5-year overall survival was not significantly different between patients who received marginal mandibulectomies and those who received segmental mandibulectomies, but it was significant between patients who had cancerous bone infiltration and those who did not. This is in agreement with data from other studies.³²

Taken together, what can be learned from the presented data? For various reasons, extensive jaw resections were performed in earlier years. We and other authors were able to show that the prognosis of the patients is independent of the type of jaw resection and bone involvement.⁴⁹ Nevertheless, oncologic safety is paramount. To plan the resection accurately, knowledge of the routes of invasion into the mandible is indispensable.⁵⁰ To our knowledge, so far, no other study has tried to clinically determine bone invasion pattern preoperatively. However, because considerable efforts are being made in animal models to better depict tumors with nanoparticles, specific imaging, and augmented reality, a better understanding of bone invasion should be possible preoperatively in the near future.⁵¹

Similarly, the routine clinical investigation must be complemented by the best available imaging modalities. Extensive work has been done in this area in recent years; meanwhile, meta-analyses on each of these topics are available in the literature.⁵² Currently, the combination of cone beam computed tomography (CBCT) with another modality (magnetic resonance imaging [MRI] or computed tomography [CT]) seems to have emerged as the best method.²³

The modern concept of immediate reconstruction could reduce the rate of follow-up surgeries and increase the rate of patients who can be successfully rehabilitated.

CONCLUSIONS

In this study, we found bone infiltration in 47% of patients who had received segmental mandibulectomies and in 14% of those who had received marginal mandibulectomies. Furthermore, a healthy and stable residual crestal bone height of at least 11 mm was detected in 43% of patients treated with segmental mandibulectomy. Of these, 28% showed an invasive histologic growth pattern, and 68% showed an erosive histologic growth

pattern. It is possible that at least the patients treated with segmental mandibulectomy would profit from marginal mandibulectomy instead because the residual height of the crestal bone is found to be tumor-free and functionally unaffected. If frank infiltrative bone invasion does take place, then the appropriate treatment would be segmental mandibulectomy. Understandably, the need for further operations and the rate of complications were significantly lower in marginal mandibulectomy. Nevertheless, preoperative cancerous bone infiltration should be assessed thoroughly before choosing the appropriate treatment modality.

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Reprint requests:

Henrik Holtmann
Department of Oral and Maxillofacial Surgery
Malteser Clinic St. Johannes
Johannisstraße 21
47198 Duisburg
Germany
Henrik-holtmann@malteser.org