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ORIGINAL ARTICLE

Safety of resection margins in CAD/CAM-guided primarily reconstructed oral squamous cell carcinoma—a retrospective case series

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Abstract

Objectives After resection of malignancies of the jaws, CAD/CAM procedures have become standard for primary bony reconstruction. Even so, these techniques may limit surgical resection safety. Therefore, the aim of the study was to examine osseous as well as soft tissue resection margins after CAD/CAM-guided tumor resections and reconstructions.

Methods A retrospective analysis of patients treated with oral squamous cell carcinoma (OSCC) from 2014 to 2019 was performed. Inclusion criteria were CAD/CAM-guided osseous resection and primary reconstruction. Evaluation was performed for histological confirmed resection margins (hard and soft tissue) as well as recurrence of the disease related to the resection status.

Results In 46 patients, bony resection margins were classified: tumor free (R0 41/46), microscopical invasion (R1 1/46), and close margin (R0 < 4 mm 4/46) respectively for soft tissue 29/46 tumor free (R0), 7/46 close margin (R0 < 4 mm), 5/46 R1, and 4/46 could not be further determined (Rx). Fourteen patients (14/46) showed recurrent disease (2/46 locoregional) without association with the bony resection margin status. Recurrence occurred predominantly (13/46) in high-staged tumor patients. R1/close margin/Rx resection of the soft tissue resulted in a significant earlier recurrence when compared with R0 resection.

Conclusion CAD/CAM procedure allows safe tumor resection with the profit of a guided and accurate reconstruction. In contrast to positive soft tissue margins, positive bony resection margins did not increase recurrence parameters.

Keywords Microvascular reconstruction · Primary reconstruction · CAD/CAM guided · Resection margins · Cutting guides

Introduction

In treatment of neoplasms of the jaws, the reconstruction of the defect is a major issue. Loss of supporting jaw bone results in reduction of masticatory function, suspension of swallow, speech and breathing structures, and disfigurement of the patients. The loss of quality of life following those aspects is well documented [1]. Thus, primary or secondary reconstruction is state of the art and several microvascular flaps such as fibula, iliac crest, or scapula are commonly used for this purpose [2–4]. For autologous bony reconstruction, CAD/CAM workflows—outsourced via commercial solutions or conducted via in-house logarithms—became the therapeutic standard in oromaxillofacial surgery [5–7]. Such workflows require trimming of the bone fragments at the recipient site for best fit. Therefore, usage of resection guides for coordination of the cutting plane at both recipient and graft donor site is mandatory [6].

Resection margins should not only be in tumor-free tissue but grant a safe distance to the tumor resection [8] such as stated in several national guidelines [9, 10]. When aiming for primary reconstruction straight after tumor resection, this results in a preoperative definition of the tumor resection. There is an ongoing discussion that this procedure limits the flexibility of the surgeon to adapt to the safety margin required for tumor resection [11]. This implies that tumor resection margins can either not be adapted or reconstruction via CAD/CAM procedure has to be aborted in case of altered resection.

The importance of tumor-free resection margins is highlighted by the fact that 5-year survival of oral squamous

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cell carcinoma (OSCC) drops from 69% for patients with free margins to 38% with positive margins [12]. To control tumor-free margins, secondary resection can be recommended [13]. For CAD/CAM procedures with primary reconstruction, this would undermine the result of the former reconstruction. Case series in orthopedic surgery suggests that CAD/CAM-guided tumor resections do not result in an increase of tumor-positive margins [14, 15]. Nevertheless, the complex shape and anatomy of the head and neck region implies that those results (pelvis and tibia) may differ to those obtained in surgery of the jaws and studies regarding the resection status in combination with CAD/CAM-guided surgery in the orofacial region have not been published yet. Even so, certain methods are described to cope with the risk of restricted resection by CAD/CAM procedures [16].

In accordance, the aim of this retrospectively analysis was to analyze the frequencies of positive/close margin resection status after CAD/CAM-guided bony OSCC resections together with primary reconstruction. In addition, recurrences of OSCC in association with the resection margins (osseous and soft tissue) were of interest. The null hypothesis was that there are no differences in CAD/CAM-guided resection margins or recurrences when compared with the literature conducting resection without cutting guides.

Methods

Patients from the department of Oral and Maxillofacial Surgery, University Medical Centre, Mainz, Germany, that received primary microvascular reconstruction through microvascular osseocutaneous graft due to oral squamous cell carcinoma (OSCC) from 2014 to 2019 were analyzed retrospectively. Due to the retrospective nature of this analysis, permission of the ethical board of the LÄK Rhineland-Pfalz was not necessary. All patients gave written informed consent to the treatment procedures.

Resection guides were built through an in-house CAD/CAM procedure as previously described [6, 7]. The procedure was based on virtual planning with PlastyCAD®-Software (3iémme, Cantu, Italy). In early cases, guides were planned digitally and manufactured by a technician in the prosthetic laboratories. Since June 2015, the respective manufacture was conducted using a 3D printer (EDEN 260 V, Stratasys®, Eden Prairie, Minneapolis, USA). For virtual planning, resection sites were determined by a senior resident based on clinical sites and preoperative CT scan. In brief, a distance of 10 mm from the last radiologic sign of tumor (such as osteolysis, contrast enhancement, and clinical manifestation of the soft tissue invasion) was deemed as safe resection. Based on this, resection borders were virtually planned and used as base for resection guides and reconstruction planning (Fig. 1). Planning and surgery were conducted by the same team.

Postoperative final pathologic assessment including follow-up resection was analyzed for tumor occurrence in respect of the osseous and the soft tissue resection margin. In tumor negative resection margin, tumor cells closer than 4 mm to the resection margin were defined as “close margin.” The sample was analyzed for correlation of resection margin and recurrence.

Statistical analyses

Data was analyzed with SAS 9.4 (SAS®, Heidelberg, Germany). Analysis was conducted descriptively, using Spearman correlation for recurrence and the parameters of resection margins as well as chi-square test regarding association between margin and recurrence.

Results

Seventy-five patients treated with microvascular osseocutaneous graft for jaw reconstruction in course of tumor therapy were evaluated from 2014 to 2019. Forty-six patients met the criteria of osseocutaneous graft for primary reconstruction for OSCC simultaneous to tumor resection. Mean age was 57 years (± 11) with a nearly balanced gender distribution of 21 females and 25 males. Mean observation time was 23 months (range from 3 to 68 month). Twelve patients (12/46) were treated for recurrent OSCC disease in terms of salvage surgery. Reconstruction was performed in 36 cases with fibula flap (36/46), 9/46 with scapula flap, and 1/46 with pelvic bone graft. Tumor resection was performed in the mandible in 44 cases and in 2 cases in the maxilla.

Bony resection margins

Resection margins were tumor free for osseous resection in 41 patients (R0 41/46), 1 patient showed microscopical invasion of the bone borders (R1 1/46), and 4 patients had osseous close margin state (4/46) (Fig. 2). No data were missing.

Soft tissue resection margins

Soft tissue resection margins were tumor free in 29 patients (R0 29/46), 7 patients were “close margin” (R0 < 4 mm 7/46), 5 patients were classified as R1 (5/46), and 4 patients could not be determined, for instance due to fragmented resection specimen (Rx 4/46) (Fig. 3). No data were missing.

Management of R1/close margin/Rx status

Four patients with soft tissue R1 state (this includes 1 patient with osseous R1 state) underwent adjuvant radiochemotherapy (4/14). These patients also represented with high-stage disease (UICC III/IV) and needed irradiation due to tumor size or

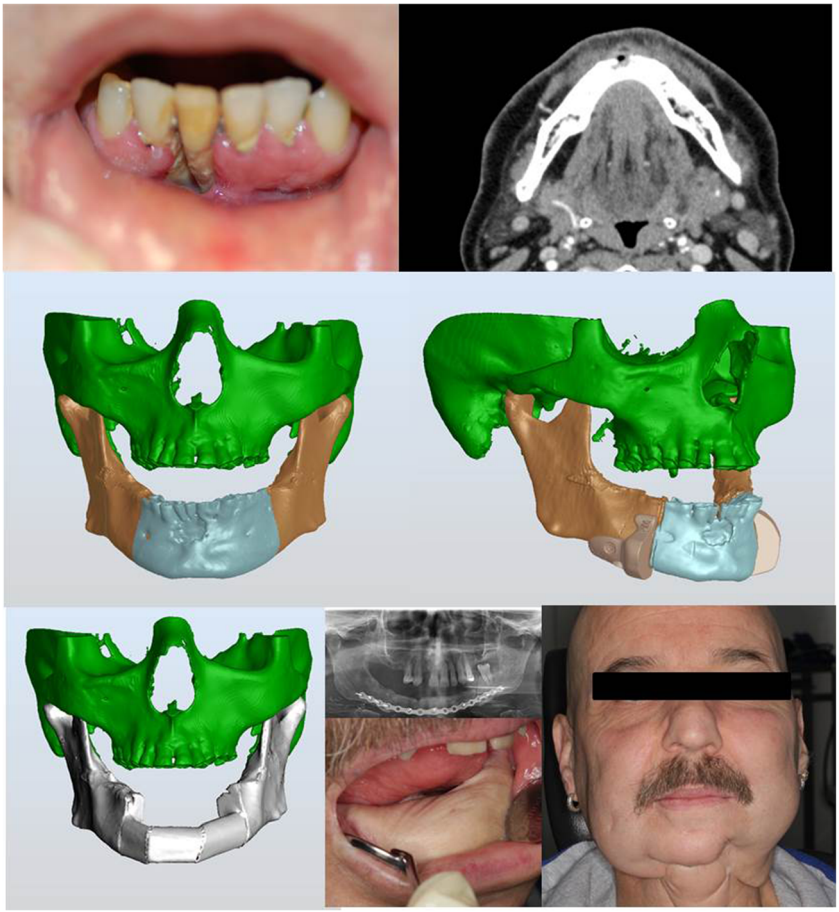

Fig. 1 Full CAD/CAM workflow in the case of OSCC of the lower jaw. Clinical presentation, radiologic findings, conversion into resection guides and reconstruction, outcome after 1.5 years, and adjuvant radiochemotherapy (note: patient with recurrence 6 months after initial reconstruction, recurrence site: lymphatic nodes)

positive lymphatic nodes as well. One patient with soft tissue R1 state underwent follow-up resection with tumor-free resections margin. Five out of 7 patients with close margin soft tissue resection underwent adjuvant irradiation (this included 2 of the bony close margin patients). Two patients with osseous and soft tissue close margin resection went into short-term follow-up; these patients had undergone radiation in a previous tumor treatment.

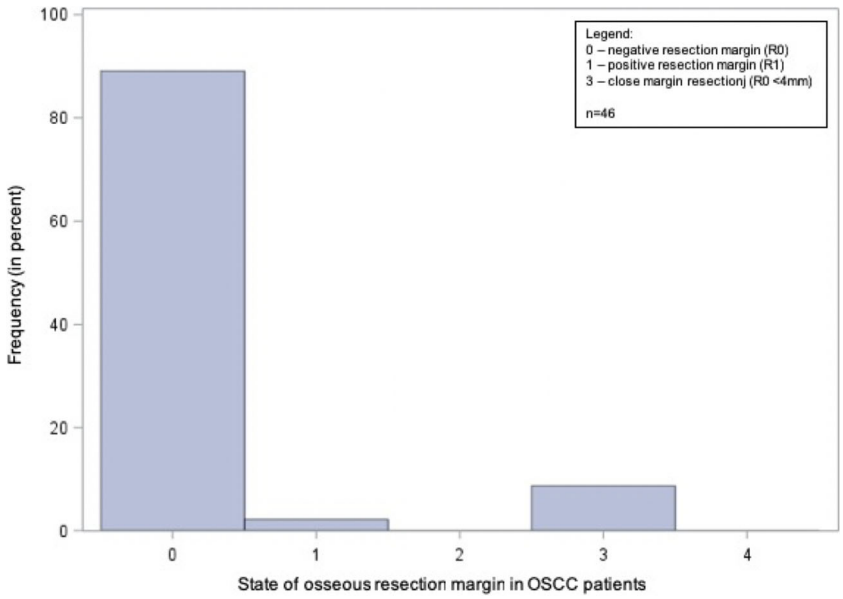

Fig. 2 Distribution of osseous resection margins in OSCC patients with CAD/CAM guides ($n = 46$)

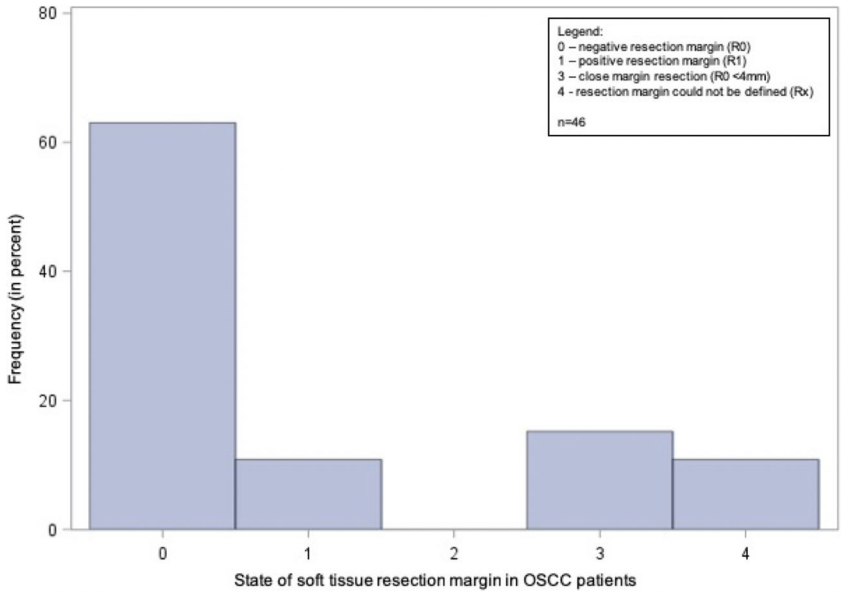

Fig. 3 Distribution of soft tissue resection margin in OSCC patients with CAD/CAM guides ($n = 46$)

Recurrences of the disease after primary reconstruction

Fourteen patients (14/46) presented with recurrent disease. Median time to recurrence was 9 months (range 1–26 month). Location for recurrence were skin of the neck region ($n = 4$), lymphatic nodes ($n = 2$), multiple metastasis (e.g., pulmonary and locoregional or other combinations; $n = 2$), locoregional recurrence (oral mucosa at same location as primary tumor, $n = 3$), or secondary tumor (oral mucosa at other location as primary tumor, $n = 3$) on the contralateral side (Fig. 4).

Initially, 13 patients (13/14) with OSCC presented a high-staged disease (T3/T4 $n = 12$; positive lymphatic nodes $n = 4$). Even so, recurrence showed no correlation to T or N stage ($r = -0.22$ for T, $r = 0.16$ for $n = 46$, Spearman). Six patients (6/14) with OSCC recurrence died, 4/14 due to the recurrence. The recurrence occurred after a median of 6 months after initial surgery. The time interval was shorter for non-R0 resection of the soft tissue (Fig. 5) as there was an interval of 7 months for R0 resection vs. 2–2.5 months for R1/close margin/Rx resection ($p < 0.05$, T test). This was not true for the osseous resection margin as there were no patients with R1/close margin/Rx resection in the recurrence group (Fig. 6).

In total, no correlation between recurrence and resection margin was shown (osseous resection margin $r = -0.19$; soft tissue resection margin $r = 0.11$). Statistical dependence between osseous or soft tissue resection margins and recurrence could not be proven (chi-square test osseous resections margins vs. recurrence, $p = 0.29$–chi-square test soft tissue resections margins vs. recurrence, $p = 0.48$).

Discussion

Patients with oral squamous cell carcinoma (OSCC) affecting the jaws can be safely treated via primary reconstruction with the help of CAD/CAM-guided techniques as the present study shows no loss of resection margin safety using this approach when planned by an experienced team. The safety of osseous resection is hereby based on careful preoperative evaluation and translates into tumor-free resection. This does not apply to the soft tissue aspect as the resection guides will only code the

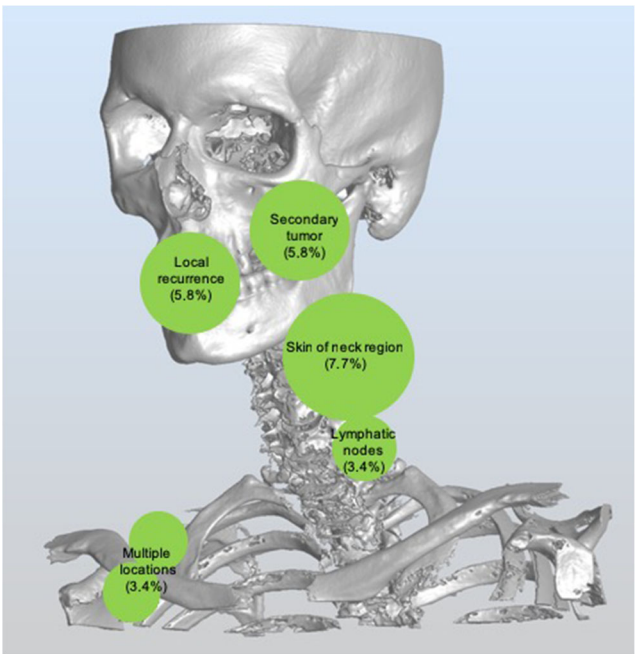

Fig. 4 Location and frequencies of recurrences in OSCC patients after resection using CAD/CAM guides ($n = 14$)

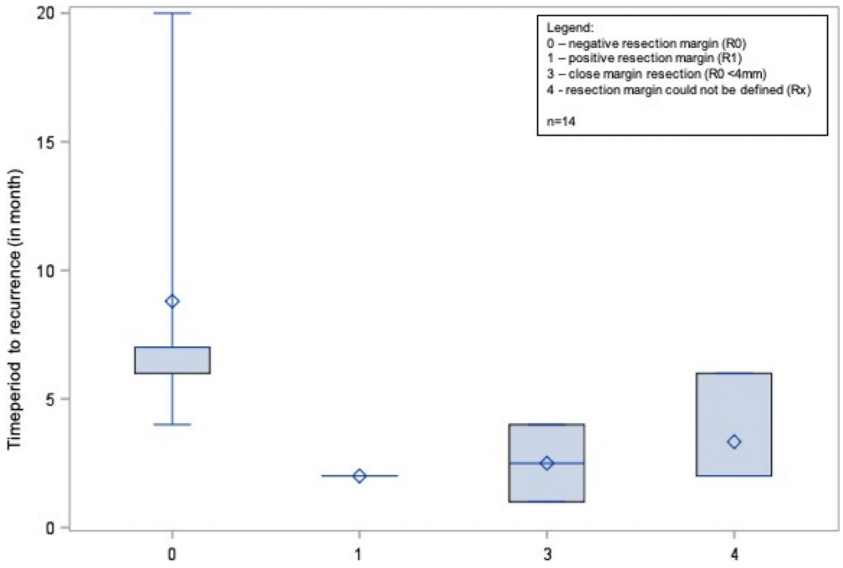

Fig. 5 Time period to recurrence in respect of soft tissue resection margins in OSCC patients ($n = 14$)

osseous margins. On the other hand, some authors state that bony tumor invasion of the resection margin may not be responsible for a worse outcome if OSCC is resected with free soft tissue margins [17]. Though, as highlighted by the earlier recurrences in the case of positive soft tissue resection margins in the study population, the presence of less than 5 mm tumor-free resection in histological specimens is an important risk factor and needs close follow-up controls [18].

Regarding the resection, a surgeon's flexibility is said to be limited through the use of guided surgery [11, 16], but only regarding the modeling of the bone. Osseous local resection margin control through fresh frozen specimens are impossible yet [19] and the consequence of further resection of the bony part would jeopardize the planned reconstruction. On the other hand, soft tissue resection is completely unrestricted.

Comparison of both techniques—primary and secondary reconstruction—shows similar recurrence rates and outcomes but secondary reconstruction can be more challenging due to scaring or soft tissue deficiencies [20]. Furthermore, primary reconstruction combines both steps—tumor resection and reconstruction—of surgery, sparing the patient multiple procedures. A delayed primary reconstruction may be an alternative if anatomical sites are complex and safe resection cannot be obtained with high certainty [13].

Tumor recurrence is not only associated with positive resection margin but also increases significantly with progredient tumor stage [9]. Camuzard et al. present a survival rate of 71–57% (2- to 5-year survival rate) and a recurrence rate of 50% when conducting primary reconstruction in T4 mandibular cancer. Survival was also positively associated

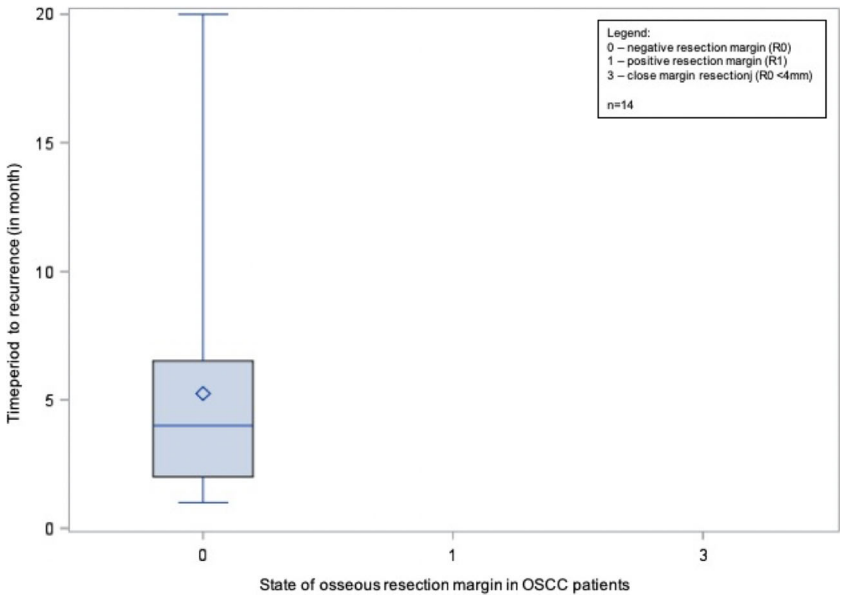

Fig. 6 Time period to recurrence in respect of osseous resection margins in OSCC patients ($n = 14$)

with tumor-free resection margins [21]. Namin et al. showed positive osseous resections margins in 12% (6/51) of OSCC patients in bone marrow evaluation when conducting conventional resection [22]. Camuzard et al. [21] stated positive bony resection margins for around 7% for OSCC patients in final histological examination. In the presented study using the described CAD/CAM technique, considerably fewer positive osseous resection margins (1/46) were detected. This highlights the safety of this procedure even if the findings may not be fully comparable and the sample size is low. In conclusion, a CAD/CAM procedure allows safe tumor resection in the jaws providing the benefits of a guided and accurate reconstruction without augmenting the risk of recurrence because of positive resection margins. This proofs the procedure to be valuable for primary reconstruction.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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