Outcome in patients with partial and full-thickness cheek defects following free flap reconstruction – A multicentric analysis of 47 cases

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Abstract

Objectives: To evaluate whether the extent of tumor resection and free flap reconstruction influences functional outcome and complications in patients with solid malignancies of the cheek. **Design and Participants:** We retrospectively assessed recipient site complications and functional outcomes in 47 patients with solid malignancies of the cheek who underwent either partial (n=30; 63.8%) or full-thickness (n=17; 36.2%) cheek resection with free flap reconstruction. **Setting:** Retrospective, multicentric analysis **Results:** Full thickness resections with creation of through-and-through defects were not associated with significantly higher complication rates (70.6% vs. 46.7%; p=0.138) compared to partial defects. Recipient site complications occurred in 55.3% of patients and were noticed most likely after reconstruction of suborbital defects (69.2%; p=0.268) of which occurrence of salivary fistulae was the most common (46.2%; p=0.035). Similarly, functional outcomes including oral incompetence, ectropion, and trismus were not affected by the extent of resection (p=0.766). However, oral incompetence was higher in patients with tumors originating from oral cavity (p=0.020) and after the performance of mandibulectomy (p=0.003). **Conclusions:** There was no difference in functional outcome or recipient site morbidity between tumor resections resulting in full-thickness and partial defects.

Study Cohort

We conducted a retrospective, multicenter chart review of patients with solid malignancies originating of the cheek who underwent tumor resection and free flap reconstruction between 2012 and 2017. Patients were treated at the Department of Otorhinolaryngology, Head and Neck Surgery, Medical University of Vienna, Austria (Center 1), the Institute of Head and Neck Diseases, Evangelical Hospital Vienna (Center 2), the Department of Otolaryngology, Head and Neck Surgery, Icahn School of Medicine at Mount Sinai, New York, USA (Center 3), and the Department of Head and Neck Surgery, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan (Center 4).

Data of potential patients were provided by attending centers that were further evaluated regarding appropriateness by two authors individually (S.J., B.E.). Patients had to fulfill following inclusion criteria: carcinomas with infiltration of the cheek, including oral carcinomas, carcinomas of the nasal cavity, skin and parotid gland (I), solid carcinomas (II), radical tumor resection with free flap reconstruction (III), primary or recurrent carcinomas (IV). In case of any disagreement, cases were reevaluated until consensus could be achieved. Finally, 47 patients were eligible for inclusion and analysis.

Classification of cheek carcinomas

From the aesthetic point of view, the cheek region can be divided into three overlapping aesthetic zones including the suborbital (I), the preauricular (II), and the bucco-mandibular (III) zone.[9] Anatomically, the cheek consists (from inside to outside) of buccal mucosa, submucosa, loose connective tissue, muscles, the parotid gland in zone II and III, and the skin. Depending on the extent of resection and consequently the depth of defect, patients were dichotomized into patients with partial or through-and-through (full) defects.

Free Flap Reconstruction

Depending on the size and depth of the defect, cutaneous, myocutaneous or osteocutaneous flaps were used. In cases with partial defects, harvested skin paddles were used for the inner lining of the oral cavity or for reconstruction of the skin if required. Conversely, in patients with through-and-through defects, split or full thickness skin grafts were used for the inner lining, while harvested skin paddles were used for the outer lining (Figure I).

Complications and Functional Outcome

We assessed recipient site complications and functional outcomes as main endpoints of the study. Recipient site complications were further classified either as minor complications including wound dehiscence and local infection or major complications including salivary fistula and free flap failure. Presence of ectropion, oral incompetence and trismus were used as functional endpoints. All outcomes were rated by treating head and neck surgeons.

Statistical Methods

Statistical analyses were performed using SPSS software (version 22; IBM SPSS Inc., Chicago, IL, USA). Unless otherwise specified, data in the results section are shown as median $\pm$ standard deviation. Chi-square test was used to assess associations between nominal variables. In cases with expected cell counts below 5, p-values of the Fisher's exact value was reported. Moreover, the unpaired student's t-test was used to compare means of normally distributed variables of two independent groups. GraphPad Prism 7 (GraphPad Software Inc., California, USA) was used for graphical display of all figures in this manuscript.

RESULTS

Study Cohort

Forty-seven patients, including 29 men (61.7%) and 18 women (38.3%), with a median age of 64 $\pm$ 15.2 years (range: 30y - 93y), were included in this retrospective, multicentric analysis. All of whom underwent tumor resection and free flap reconstruction of the cheek. SCC was the predominant tumor histology (n=38; 80.9%) followed by adenoid cystic carcinoma (ACC; n=3; 6.4%), sarcoma (n=2; 4.3%), melanoma (n=2; 4.3%), merkel cell carcinoma (MCC; n=1; 2.1%), and malignant adnexal skin tumor (n=1; 2.1%). Malignancies originated from buccal mucosa, oral cavity, parotid gland, nasal cavity and skin in 22 (46.8%), 10 (21.3%), 4 (8.5%), 3 (6.4%) and 2 (4.3%) cases, respectively. With respect to aesthetic zones, tumors were located predominantly at zone I, II, and III in 13 (27.7%), 11 (23.4%), and 23 (48.9%) cases, respectively (Table I).

Tumor Characteristics

Patients had 3 T1 (6.4%), 11 T2 (23.4%), 12 T3 (25.5%), and 21 T4 (44.7%) tumors, respectively, with a median tumor size of 3.9 $\pm$ 1.9 cm (range: 1.0 - 8.8 cm). At initial presentation, 30 (63.8%), 6 (12.8%), and 7 (14.9%) patients had N0, N1 and N2 disease, while cervical lymph node classification (Nx) was unknown

in 4 patients (8.5%). Altogether we had 3 stage I (6.4%), 8 stage II (17.0%), 11 stage III (23.4%), and 25 stage IV (53.2%) malignancies (Table I).

Surgical Resection

Radical tumor resection created partial and through-and-through defects in 30 (63.8%) and 17 (36.2%) patients, respectively. Socio-demographic characteristics, including male to female ratio (21:9 vs. 8:9), age (65.1 $\pm$ 15.8y vs. 60.7 $\pm$ 14.0y) , and body-mass-index ($25.1 \pm 4.4 kg/m^2$ vs. $24.5 \pm 4.6 kg/m^2$) did not significantly differ in patients with partial and through-and-through defects, respectively (p=0.211; p=0.388; p=0.677). Moreover, T-classification (p=0.901), N-classification (p=0.372), and AJCC tumor stage (p=0.492), did also not significantly differ between both groups (Table I).

ND was performed in 80.9% of patients. Level I-III, I-IV, II-IV, and II-III ND was done in 13 (27.7%), 9 (19.1%), 8 (17.0%), and 4 (8.5%) cases, respectively. In two patients (4.2%) the extent of ND was not indicated. Maxillectomy was necessary to perform in 19 out of 47 patients (40.4%), including partial-, hemi-, and total maxillectomy in 5 (10.6%), 9 (19.1%), and 5 (10.6%) cases, respectively. Otherwise, partial and total mandibulectomy was done in 11 (23.4%) and 1 patient (2.1%). Primary tumor resection was further accompanied by partial glossectomy and orbital exenteration in 4 (8.5%) and 3 patients (6.4%).

Free Flap Reconstruction

The radial forearm free flap (RFFF) was most commonly used for cheek reconstruction (n=15; 31.9%) followed by anterolateral thigh (ALT) flap (n=13; 27.7%), scapular / parascapular free flap (n=10; 21.3%), FFF (fibula free flap; n=6; 12.8%), supraclavicular free flap (n=2; 4.3%), and serratus anterior free flap (SAFF; n=1; 2.1%), respectively. Altogether, cutanoues, myocutcaneous and osteocuteanous free flaps were harvested in 19 (40.4%), 12 (25.5%) and 16 (34.0%) cases, respectively (Table II). As indicated in Table II, RFFF was most commonly used for reconstruction of one-layer skin or mucosal defects (14 out of 19; 73.7%), while the ALT flap was mostly used as myocutaneous flap (10 out of 12; 83.3%), and the scapular / parascapular free flap for bone reconstruction (10 out of 16; 62.5%) (Table II). In 8 patients (17.0%) free flaps were oversized and too bulky. Bulkiness of the free flap occurred particularly in zone I defects (30.8% vs. 11.8%), more likely in through-and-through defects (29.4% vs. 10.0%), and after harvest of free scapular / parascapular free flaps (40.0% vs. 10.8%). However, differences failed to reach statistical significance (p=0.288; p=0.118; p=0.331) and revision surgery with thinning of the free flap was performed in 6 out of 8 patients in order to optimize final cosmetic results.

We had two losses of free flaps resulting in a free flap success rate of 95.7%, while flap revision due to venous congestion was necessary in 3 (6.4%) cases. In those two cases with flap loss an ALT and a latissimus dorsi flap were used for revision surgery.

Complications

Recipient site complications occurred in 26 (55.3%) patients, which was not statistically significant different between patients with partial compared to those with through-and-through defects (46.7% vs. 70.6%; p=0.138). Wound dehiscence, formation of salivary fistula, local infections and free flap failure occurred in 14 (29.8%), 10 (21.3%), 9 (19.1%), and 2 (4.3%) cases, respectively, but did not significantly differ between both groups (Table III).

However, with regards to affected aesthetic zones, we observed formation of salivary fistula particularly in 46.2% of zone I defects, which was significantly higher compared to 9.1% and 13.0% in zone II and III defects, respectively (p=0.035). It is noteworthy to mention that extent of resection (p=0.136), performance of maxillectomy (p=0.496) or mandibulectomy (p=1.000), T-classification (p=0.751) or size of defect (p=0.145) had no significant impact on the development of salivary fistulae.

Functional Outcome

Oral incompetence, ectropion, and trismus occurred in 9 (19.1%), 8 (17.0%), and 6 patients (12.8%), respectively. Again, the extent of resection had no significant impact on the development of any functional

impairment (Table III). Nonetheless, solely patients with malignancies originating of the buccal mucosa and oral cavity suffered from oral incompetence (22.7% and 66.7%; p=0.020). Performance of mandibulectomy (p=0.003), but not maxillectomy (p=0.064), affected significantly oral competence, which was otherwise significantly associated with the occurrence of trismus (p=0.009). In addition, size of used free flaps was 14.7 ± 5.1 cm in patients with oral incompetence, which was significantly larger compared to 7.4 ± 2.7 cm in patients with oral competence (p=0.008), while primary tumor size did not significantly differ (4.4 ± 1.4 cm vs. 3.5 ± 1.9; p=0.206) (Table III).

DISCUSSION

We have analyzed clinical outcome of 47 patients with solid malignancies of the cheek that underwent radical tumor resection with creation of partial or through-and-through defects and free flap reconstruction. Within our study, SCCs were the predominant histologic subtype (80.9%) and malignancies mainly originated from the oral cavity (80.8%). This is consistent with literature, reporting mostly on oral carcinomas and rarely on skin carcinomas, requiring cheek reconstruction with free flaps following oncological resections. [3,4]Nonetheless, our data further display the great diversity of tumors affecting the cheek region that may hamper analysis of more homogenous subgroups with large patient numbers.

In solid malignancies, and for patients with SCCs in particular, surgical tumor resection with adjuvant therapy in selected cases represents the most frequent treatment modality.[5,6,10]However, despite radical surgical resection, recurrence rates range from 45.0% to 80.0% in patients with buccal SCCs.[11,12]Several authors assume that the absence of "real" anatomic boundaries limiting tumor growth and spread might contribute to the high rate of recurrences.[11,13] This prompted Ren ZH and coworkers (2017) to perform a more extensive resection of functional anatomic buccal units to achieve better oncologic outcome.[3] In fact, they analyzed data of 127 patients with buccal SCCs reporting on significantly better 2-year overall survival (OS: 83.3% vs. 60.1%) and DFS (76.6% vs. 51.9%) in patients undergoing more extensive unit resection compared to conventional surgery.[3]

Although oncologic principles must supersede reconstructive desires[7], we were particularly interested in knowing how the extent of resection impacts functional outcome. Oral incompetence represented the main functional complication occurring in 9 (19.1%) patients followed by occurrence of ectropion and trismus in 8 (17.0%), and 6 patients (12.8%), respectively. This is in line with the results of other publications, reporting on problems with oral incompetence in 4.8% up to 40% of patients with cheek carcinomas.[8,14,15] It is noteworthy to mention that the extent of resection had no significant impact on functional outcome in our cohort, which is in accordance to the work of Ren ZH et al. (2017). The authors assume that insignificantly changed functional outcomes in patients with conventional surgery compared to more extensive unit resections, have resulted from the loss of function of preserved structures secondary to induction of fibrosis and loss of functional adjacent structures / attachments by tumor resection.[3] However, we found a strong association between oral incompetence and trismus in patients after mandibulectomy. This indicates that functional outcomes more likely depend on the preservation of certain anatomic structures and chosen surgical approach than on the depth of defect.

Recipient site complication rate was 55.3% (n=26), of which wound dehiscence was the most common complication occurring in 29.8% (n=14) of cases. Although the majority of complications were of minor concern, 10 patients developed salivary fistulae (21.3%) that occurred significantly more often in suborbital zone I defects (p=0.035). This is in accordance to former studies reporting on fistula rates of 4.3% to 27.3% of patients.[8,14,16-18] The development of fistulae is characteristic for maxillary reconstruction and occurs typically near to the medial canthus (zone I) due to breakdown of suture lines.[16] In alignment to that, we observed the highest rate of wound dehiscence (38.5%) in patients with zone I defects compared to 18.2% and 30.4% in zone II and III defects, respectively.

Until now, a number of different free flaps have been described for cheek reconstruction including the ALT [19], RFFF[19], FFF [20] and the scapular / parascapular free flap [21]. Recently, the versatility of the SAFF has been demonstrated for general head and neck reconstruction, and in particular for cheek and tongue

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reconstruction.[22,23] In our study, the RFFF was used in 31.9% (n=15) of cases followed by the ALT free flap and the scapular / parascapular free flap in 27.7% (n=13) and 21.3% (n=10) of patients, respectively. Among those, the RFFF was mainly harvested for cutaneous reconstruction (73.7%), the ALT flap for reconstruction of myocutaneous defects (83.3%), and the scapular / parascapular free flap for bone reconstruction (62.5%). Our flap survival rate was 95.7%, which is comparable to 95% to 96% reported in former studies.[17,19]

We believe that the strength of this study lies in its multicentric nature and the analysis of functional outcomes as well as complications. We see three limiting factors: first, the retrospective study design bears an inherent risk of information and selection bias. Second, the heterogeneity of our cohort with solid malignancies originating from different parts of the cheek allows only limited conclusions. Third, the lack of standard measures for functional outcomes in head and neck oncology[24] and the fact that functional and aesthetic outcomes have been rated by treating head and neck surgeons as opposed to patient reported outcomes, represent further limitations.

Conclusion

More extensive resections with creation of through-and-through defects did not automatically correlate with worse functional outcome or higher recipient site complications. However, further prospective studies with homogenous patient cohorts are highly required to define and identify additional factors that may contribute to the functional outcome of patients with carcinomas of the cheek.

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TABLES

Table I. Patient Characteristics.

VARIABLES
Sex

Tumor Site

Histology

T - Classification

N - Classification

AJCC Tumor Stage

Aesthetic Zone

Abbreviation: ACC, adenoid cystic carcinoma; AJCC, American Joint Committee on Cancer; MCC, merkel cell carcinom

Table II. Free flap Reconstruction.

		Total	Total		USED FREE FLAPS	USED FREE FLAPS	USED FREE FLAPS	USED FREE FLAPS	USED FREE FLAPS	USED FREE FLAPS	U F F
VARIABLES VS	VARIABLES	Total	Total		RFFF	RFFF	ALT	Scapular / Parascapular	FFF	Supraclav Free Flap	V
Depth of Defect	Depth of Defect										
	Partial	30 (63.8)	30 (63.8)		8 (26.7)	8 (26.7)	11 (36.7)	5 (16.7)	4 (13.3)	2 (6.7)	0
	Full	17 (36.2)	17 (36.2)		7 (41.2)	7 (41.2)	2 (11.8)	5 (29.4)	2 (11.8)	0 (0)	1 (
Type of Reconstruction	Type of Reconstruction										
	Cutaneous	19 (40.4)	19 (40.4)		14 (73.7)	14 (73.7)	3 (15.8)	0 (0)	0 (0)	2 (10.5)	0
	Myocutaneous	12 (25.5)	12 (25.5)		1 (8.3)	1 (8.3)	10 (83.3)	0 (0)	0 (0)	0 (0)	1 (
	Osteocutaneous	16 (34.0)	16 (34.0)		0 (0)	0 (0)	0 (0)	10 (62.5)	6 (37.5)	0 (0)	0
Aesthetic Zone	Aesthetic Zone										
	Zone I	13 (27.7)	13 (27.7)		4 (30.4)	4 (30.4)	4 (30.4)	4 (30.4)	0 (0)	0 (0)	1 (

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					USED FREE FLAPS	USED FREE FLAPS	USED FREE FLAPS	USED FREE FLAPS	USED FREE FLAPS	USED FREE FLAPS	U F F
	Zone II	11 (23.4)	11 (23.4)		1 (9.1)	1 (9.1)	4 (36.4)	3 (27.3)	3 (27.3)	0 (0)	0
	Zone III	23 (48.9)	23 (48.9)		10 (43.5)	10 (43.5)	5 (21.7)	3 (13.0)	3 (13.0)	2 (8.7)	0
Total	**Total**	47 (100)	47 (100)		15 (31.9)	15 (31.9)	13 (27.7)	10 (21.3)	6 (12.8)	2 (4.3)	1 (

Abbreviations: ALT, anterolateral thigh flap; FFF, fibula free flap; RFFF, radial forearm free flap; SAFF, serratus anterior free flap

Table III. Complications and functional outcome according to depth of defect and aesthetic zone

COMPLICATIONS
Recipient Site
No
Yes

COMPLICATION
Recipient Site
No
Yes
Infection
Dehiscence
Fistula
Flap Failure

FUNCTIONAL OUTCOME

FUNCTIONAL O

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Functional Impairment		Functional Imp
No		No
Yes		Yes
		Ectropion
		Oral Incompeten
		Trismus

Abbreviation: Full, Through-and-Through defects; n, number of patients; p, p-value; [a] chi-square test   **Abbreviation:**

FIGURE LEGENDS

Figure I. Reconstruction of a Through-and-Through Defect. A 60 years old female patient experienced regional failure of a sinonasal carcinoma. Radical tumor resection was performed resulting in creation of a through-and-through defect with 4.0 x 5.0 cm in size (**A-C**). A free radial forearm free flap (RFFF) was used for reconstruction. The harvested skin paddle was used for the outer lining (**D,F**), while full thickness skin graft of the neck was used for inner lining (**E**). Postoperative (**G**) and 2-year follow up results are shown (**H**).