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Predictors of free flap loss in the head and neck region: A four-year retrospective study with 451 microvascular transplants at a single centre

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ABSTRACT

Introduction: Microvascular free flaps have become an essential part of reconstructive surgery following head and neck tumour ablation. The authors' aim was to investigate the influence of cardiovascular risk factors, preoperative irradiation, previous operations and metabolically active medication on free flap loss in order to predict patients at risk and to improve their therapy.

Materials and methods: All patients who underwent reconstructive surgery with microvascular free flaps in the head and neck region between 2009 and 2013 were retrospectively analysed. Uni- and multivariate logistic regressions were performed to determine the association between possible predictor variables for free flap loss.

Results: We included 451 patients in our analysis. The overall free flap failure rate was 4.0%. Multivariate regression analysis revealed significantly increased risks of free flap failure depending on prior attempts at microvascular transplants ($p < 0.001$, OR = 14.21) and length of hospitalisation ($p = 0.007$, OR = 1.05).

Conclusions: With consistently low rates of flap failure, microvascular reconstruction of defects in the head and neck region has proven to be highly reliable, even in patients with comorbidities. The expertise of the operating team seems to remain the main factor affecting flap success. The only discerned independent predictor was previously failed attempts at microvascular reconstruction.

1. Introduction

Microvascular reconstructive surgery has become an indispensable part of the treatment of tumours of the head and neck region (Mücke et al., 2009, 2010, 2012; Kesting et al., 2011a; Kansy et al., 2015). Despite the enormous achievements and progress in this field regarding surgical finesse, microvascular techniques and monitoring opportunities, the success of microvascular free flap transplantation is dependent on the patient's physical constitution. Diverse diseases and therapies are known negatively to influence wound healing, to impact vascular architecture and therefore presumably to affect the success of microvascular surgical procedures (Howard et al., 2005; Mücke et al., 2010; Pohlenz et al., 2013).

Previous studies have revealed a significant inverse correlation between the American Society of Anaesthesiologists (ASA) Classification of the patient and free flap survival (Mücke et al., 2012). Even though the ASA status seems to be a simple and powerful predictor for the risk of free flap failure, its simplicity only allows the prognosis of success with a wide range, especially in a dispersing cohort of patients.

Most studies confirm no direct influence of irradiation or cardiovascular risk factors on free flap survival but a significant association can be found on postoperative complications (Bourget

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et al., 2011; le Nobel et al., 2012; Mücke et al., 2012). Furthermore, the different types of free flap transplants are associated with the different needs of postoperative care and are affected by different incidences of wound healing disorders (Kesting et al., 2011a), which are only one group of many imaginable confounders.

Therefore, the aim of the present study has been to investigate the influence of cardiovascular risk factors, preoperative radiotherapy, previous microvascular operations and various types of metabolically active medication prescribed on a daily basis on the survival of microvascular free flaps in order to predict the outcome more reliably and precisely and to identify patients at risk so that strategies in their therapy can be changed if necessary.

2. Materials and methods

2.1. Ethical statement and patient recruitment

All clinical investigations and procedures have been conducted according to the principles expressed in the Declaration of Helsinki. Patient consent was written. An exemption from the requirement of ethics approval was granted by the Ethical Committee of the Technische Universität München because of this informed consent with respect to participation in the studies and the willingness of the patients to undergo the required medical procedures (Approval No. 453/15s).

2.2. Surgery and postoperative care

Any patient with extensively operated head and neck cancer and related affections between June 2009 and May 2013 who received any type of microvascular free flap reconstruction at our department was included in our retrospective study. This involved all malignancies of the oral cavity (including oral squamous cell carcinoma (OSCC) and malignancies of the salivary glands), skin cancer, osteoradionecrosis of the jaw and medication-related osteonecrosis of the jaw (Table 1).

The diagnosis was histologically confirmed in all patients prior to major surgery. In cases of malignancies, all patients received an elective or therapeutically ipsilateral functional neck dissection. Further escalation with neck dissection of the levels IV and V ipsilaterally and I-III contralaterally was dependent on the location of metastases intraoperatively. The malignancy or related affection was resected with respect to free margins or vital tissue according to the current guidelines (Wolff et al., 2012a). The resulting defect was immediately reconstructed with a microvascular free flap by using common microsurgical techniques as previously described (Wolff et al., 2008, 2012b). Postoperatively, all patients were kept supervised for one night on the post anaesthesia care unit (PACU) and afterwards were transferred to the ward or, if necessary, to the intensive care unit (ICU). In this context, time at the PACU was considered equal to time at the ICU.

After completion of the arterial anastomosis, all patients received intraoperatively 5000 IE heparin. Subsequently, starting on the first postoperative day, every patient received Clexane® (weight adapted) once a day for the whole period of hospitalisation. Furthermore, antibiotics were administered 30 min prior to surgery and for a postoperative interval of ten days (Mücke et al., 2015).

Table 1
Demographic and clinical characteristics (I) of 451 evaluated cases.

All patients	Total		Flap success		Flap loss		*p*-value
	n	%	*n*	%	*n*	%	
Gender	451	100	433	96	18	4	0.846[1]
Female	160	35.5	154	96.3	6	3.8	
Male	291	64.5	279	95.9	12	4.1	
Entity							
OSCC	329	72.9	317	96.4	12	3.6	0.581[2]
Osteonecrosis	40	8.9	37	92.5	3	7.5	
Mucoepidermoid carcinoma	9	2	9	100	0	0	
Adenoid carcinoma	12	2.7	12	100	0	0	
Ameloblastoma	6	1.3	6	100	0	0	
Sarcoma	11	2.4	11	100	0	0	
KCOT	9	2	9	100	0	0	
Malign melanoma	8	1.8	7	87.5	1	12.5	
Others	27	6	25	92.6	2	7.4	

Abbreviations: [1] = Chi²-test; [2] = Fisher-Exact-test; OSCC = oral squamous cell carcinoma; KCOT = keratocystic odontogenic tumour.

2.3. Data analysis

Descriptive statistics for clinical characteristics are given as the means ± standard deviation (Table 1) and variables were compared with respect to free flap loss by using Chi² tests and Fisher Exact test for low count sizes for all variables except for metric variables, when the non-parametric Mann-Whitney-*U* test was used.

Univariate logistic regression analyses on free flap loss were performed including the following possible predictors: age at date of operation, gender, diagnosis, type of used microvascular free flap, length of stay on ICU (metric and encoded into length of stay of up to 1 day or longer) and total hospital stay, preoperative irradiation in the operation field, prior performed microvascular flaps, history of smoking and alcohol abuse, Body Mass Index (BMI), ASA status at date of operation, history of cardiovascular diseases and preoperative myocardial infarction, operating time and preoperative medication (subcategorized into inhibitors of platelet aggregation, anticoagulants, antidiabetics, antihypertensive drugs, lipid-lowering agents, thyrotropic drugs and glucocorticoids). In instances of significant statistical findings, a complementary multivariate analysis was conducted. The optimal fitting multivariate model was chosen as that minimising the Bayesian Information Criterion (BIC).

The data were analysed with the "Standard Package for the Social Science" (SPSS for Mac, release 22.0.0, 2013; SPSS Inc.; Chicago, IL, USA) and with the freeware "R Statistical Package" (R for Windows, release 3.2.0, 2015; R Foundation for Statistical Computing; Vienna, Austria). Figures were generated with SPSS and Microsoft® Office Excel (Microsoft® Excel for Mac, release 14.5.3, 2010; Microsoft Corporation; Redmond, WA, USA).

All statistical tests were performed at the 0.05 significance level.

3. Results

3.1. General characteristics (Tables 1–3)

From June 2009 to May 2013, 451 free flaps were performed in our department. These consisted of 230 radial forearm flaps (51.0%), 110 anterolateral thigh flaps (24.4%), 76 fibular flaps (16.9%), 22 perforator flaps (4.9%) and 13 iliac crest flaps (2.9%).

The male/female distribution was 291/160 (64.5%/35.5%) and the mean age at the point of operation was 60.04 ± 12.73 years. The ASA status I included 68 cases (15.1%), status II involved 315 cases (69.8%) and 68 cases of ASA status III were found (15.1%).

The causes for microsurgical reconstructions were OSCC in 329 cases (72.9%), osteonecrosis in 40 cases (8.9%), adenoid carcinoma in 12 cases (2.7%), sarcomas in 11 cases (2.4%), mucoepidermoid carcinoma and keratocystic odontogenic tumours in each of 9 cases