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Risk factors for free flap failure: a retrospective analysis of 881 free flaps for head and neck defect reconstruction

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Abstract. The aim of this study was to identify the risk factors for free flap failure after head and neck reconstructive surgery. The data of 881 consecutive patients who underwent free flap surgery at the Department of Oral and Maxillofacial Surgery, Peking University School and Hospital of Stomatology, between January 2013 and November 2016, were reviewed retrospectively. All surgeries were performed by a single head and neck surgical team. Patient demographic and surgical data that may have an influence on free flap outcomes were recorded. The χ^2 test and multivariate logistic regression analysis were used to identify relevant risk factors. In total, 881 free tissue transfer surgeries were included in this study. Free flap failure occurred in 26 of 881 flaps (2.9%). A history of irradiation (odds ratio 0.205, 95% confidence interval 0.07–0.56; $P = 0.002$) was a statistically significant risk factor for free flap failure. Age, diabetes mellitus, history of previous neck surgery to the anastomosis side, donor site, choice of recipient vein, use of a coupler device, and postoperative anticoagulation were not associated with free flap outcomes. Thus, it is concluded that when performing head and neck reconstructive surgery, special attention should be paid to patients who have previously undergone irradiation.

Key words: risk factors; free flap failure; head and neck.

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With improvements in microsurgical techniques and instruments, free tissue transfer has become the most reliable method of treating head and neck defects. Although free flap transfers have high success rates (ranging from 90% to 99%), flap loss, which can be devastating for both the patient and surgeon, remains a possibility[1–4]. A better understanding of the causes of flap loss is necessary to avoid this disastrous outcome.

Numerous possible risk factors have been reported for flap loss, including age, sex, hypertension, diabetes mellitus, tobacco and alcohol use, preoperative irradiation and chemotherapy, previous neck surgery to the anastomosis side, type of recipient vessel and donor site, use of a coupler device, timing of the operation, and use of postoperative anticoagulants[5–24]. Some of these factors have been shown

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to have no association with free flap failure. However, there is as yet no international consensus concerning whether factors such as diabetes mellitus, previous irradiation, previous neck surgery to the anastomosis side, choice of recipient vessel and donor site, use of a coupler device, and use of postoperative anticoagulants influence free flap outcomes.

Most studies investigating these factors have had their own limitations, such as a small sample size, differences in surgeon preferences and experience, and the inclusion of cases of breast or extremity reconstruction. This retrospective analysis of the data of 881 patients who underwent head and neck free flap reconstructions performed by a single surgical team (XP and YW) over a 4-year period was performed to overcome these limitations. The aim was to identify the risk factors for free flap failure after head and neck reconstruction.

Patients and methods

Patients

This study constituted a retrospective review of 881 consecutive free flaps in head and neck surgeries performed by a single surgical team between January 2013 and November 2016 at Peking University School and Hospital of Stomatology. The study was approved by the ethics committee for human experiments at the Peking University School and Hospital of Stomatology. The patient characteristics and surgical data, including patient age, diabetes mellitus, previous irradiation, history of previous neck surgery to the anastomosis side, donor sites, type of recipient vein, use of a coupler device, and use of postoperative anticoagulants, were recorded.

Data analysis

Each possible risk factor was examined by univariate analysis using the χ^2 test. Factors with *P*-values of <0.10 were included in multivariate logistic regression models to identify significant independent risk factors for free flap failure. All measured data were analyzed using SPSS version 17.0 software (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

This retrospective study consisted of 881 microvascular free flap transfer surgeries. The surgeries were performed on 534 male subjects and 347 female subjects; their mean age was 48.87 years (range 6–83 years; median 51 years). The free flaps used for reconstruction included 548 fibula flaps, 165 anterolateral thigh flaps (ALTF), 134 radial forearm free flaps (RFFF), 20 iliac crest free flaps, 11 submental free flaps, and three rectus abdominis flaps (Table 1).

In all, 26 flaps were lost; the total free flap success rate was 97.0%. Venous thrombosis was the main cause of free flap failure (16/26), followed by arterial crisis (seven flaps: six arterial thrombosis, one vasospasm), haematoma (two flaps), and infection (one flap) (Table 2). Thrombosis developed in 19 flaps (63.3%) in the first 48 h postoperatively and 11 flaps in the next 72 h (Tables 2 and 3).

In all, 65 patients (7.4%) had a history of diabetes and 55 patients (6.2%) had undergone radiotherapy before surgery. Fourteen patients (1.6%) had a history of neck surgery to the anastomosis side. Branches of the internal jugular system (59.4%) and the external jugular vein (40.6%) were used as the recipient veins for anastomosis. Coupler devices were used to anastomose the blood vessels in 328 patients (37.2%). No anticoagulants were prescribed postoperatively in 158 patients (17.9%).

Univariate analysis in the 26 cases of unsuccessful free flap transfer indicated that a history of irradiation ($P < 0.001$) and a history of the previous neck surgery to the anastomosis side ($P = 0.007$) were two potential risk factors for free flap failure. Patient age ($P = 0.056$), diabetes mellitus ($P = 0.750$), choice of recipient vein ($P = 0.298$), use of a coupler device ($P = 0.130$), and anticoagulant use ($P = 0.141$) were not associated with free flap outcomes (Table 4). Logistic regression analysis identified a history of irradiation as a statistically significant risk factor for free flap failure ($P < 0.002$; Table 5).

Table 1. Patient characteristics and the donor sites used.

	Flap success	Flap failure	Total
Sample size	855	26	881
Sex, male	522	12	534 (60.6%)
Age (years), mean ± SD	50.88 ± 16.09	48.81 ± 16.08	48.87 ± 16.08
Donor site			
Fibula flap	536	12	548 (62.2%)
ALTF	157	8	165 (18.7%)
RFFF	130	4	134 (15.2%)
Iliac crest flap	18	2	20 (2.3%)
Submental free flap	11	0	11 (1.2%)
Rectus abdominis flap	3	0	3 (0.3%)

SD, standard deviation; ALTF, anterolateral thigh flap; RFFF, radial forearm free flap.

Table 2. Causes and outcomes of 49 take-back free flaps.

Cause	Number of flaps	Flap survival	Flap loss
Venous thrombosis	24	8	16
Arterial thrombosis	6	0	6
Arterial vasospasm	1	0	1
Haematoma	13	11	2
Misplacement	4	4	0
Infection	1	0	1
Total	49	23	26

Table 3. Impact of timing of take-back surgery on flap survival.

Characteristic	Number of flaps	Salvage
Venous thrombosis		
0–48 h	15	6
>48 h	9	2
Arterial thrombosis		
0–48 h	4	0
>48 h	2	0
Arterial vasospasm	1	0
Haematoma		
0–48 h	10	10
>48 h	3	1
Vessel misplacement	4	4
Infection	1	0

Table 4. Univariate analysis of potential risk factors for free flap failure.

Characteristic	Flap success ($n = 855$)	Flap failure ($n = 26$)	*P*-value
Age (years)			
≤50	426	8	0.056[a,*]
>50	429	18	
Diabetes			
Yes	64	1	0.750[b]
No	791	25	
Previous neck surgery to the anastomosis side			
Yes	11	3	0.007[c,*]
No	844	23	
Previous irradiation			
Yes	48	7	<0.001[b,*]
No	807	19	
Donor site			
Fibula flap	536	12	0.558[a]
ALTF	157	8	
RFFF	130	4	
Recipient vein			
IJS	505	18	0.298[a]
EJV	350	8	
Coupler device			
Yes	322	6	0.130[a]
No	533	20	
Anticoagulants			
Yes	705	18	0.141[b]
No	150	8	

ALTF, anterolateral thigh flap; RFFF, radial forearm free flap; IJS, internal jugular system; EJV, external jugular vein.
[a] Pearson's χ^2 test.
[b] continuity correction.
[c] Fisher's exact test.
[*] $P < 0.1$.

Table 5. Logistic regression analysis of risk factors for free flap failure.

	OR	95% CI	*P*-value
Age	0.455	0.19–1.07	0.072
Previous neck surgery to the anastomosis side	0.244	0.05–1.11	0.069
Irradiation	0.205	0.07–0.56	0.002[*]

OR, odds ratio; CI, confidence interval.
[*] $P < 0.05$.

Discussion

Flap failure in head and neck reconstruction is usually caused by vascular thrombosis[24,25]. In this study, thrombosis accounted for 22 of the 26 unsuccessful free flaps (84.6%), which is consistent with the published literature[26,27]. A poor condition of the recipient vessels and endothelial damage to the anastomosed blood vessels both contribute to the occurrence of thrombosis and vasospasm. The condition of the recipient vessel typically depends on preoperative factors, such as patient age, history of diabetes, history of irradiation, and history of previous neck surgery to the anastomosis side. Endothelial damage of the anastomosed blood vessels is associated with intraoperative factors, such as the microsurgical technique, choice of recipient vessels and donor sites, and use of a coupler device. In addition, postoperative factors such as the monitoring protocol, anticoagulant administration, and surgical intervention may also influence free flap outcomes.

In the aspect of preoperative factors, several studies have reported that advanced age is not a risk factor for free flap failure in head and neck reconstruction[5–8]. In the literature, no exact age seems to be associated with the word 'elderly'. As the mean age of the study population was 48.87 years and the median age was 51 years, the subjects were divided into an older group (>50 years) and a younger group (≤50 years). Consistent with previous studies, the present study found no statistically significant correlation between age and free flap failure ($P = 0.056$). Nevertheless, the possibility cannot be ignored that a worse condition of the peripheral vessels and poor tolerance of surgical manipulation in older patients make advanced age a confounding factor in analyses of the risk factors for free flap failure.

Several studies have associated diabetes mellitus with complications in head and neck free flap reconstructions[9–13]. However, few of these studies have assessed the role of diabetes mellitus in microsurgical failure. Rosado et al. reviewed 7890 patients who had undergone microsurgical reconstruction of the head and neck region in a retrospective study; they found that the incidence of diabetes mellitus was 2.3 times higher in patients with free flap failure than in patients with successful free flap transfer[14]. Similarly, Valentini et al. reviewed 122 free flaps used for head and neck reconstructions and concluded that diabetes mellitus was significantly associated with adverse postoperative outcomes ($P < 0.01$)[12]. The current practice is to use local flaps as much as possible rather than free flaps for the reconstruction of head and neck defects in diabetic patients. In the present study, the total incidence of diabetes mellitus was 7.4%, and the free flap failure rate did not differ between patients with and without diabetes mellitus ($P = 0.750$).

With the increased use of radiotherapy to treat tumour recurrences and the occurrence of radiotherapy-induced complications, reconstruction in an irradiated area has become common in recent years. Numerous studies have examined the relationship between previous irradiation and free flap failure. Although flap complications have been reported to be more common after irradiation, most studies have confirmed that previous irradiation does not adversely affect flap survival[11,15]. However, a few studies have reported the opposite results. Benatar et al. reviewed 429 patients who underwent free flap transfers in the head and neck region, including 136 patients who had undergone previous irradiation[16]. They concluded that previous neck irradiation at doses ≥60 Gy was associated with an increased risk of free flap failure ($P = 0.04$). In the present study, the irradiation dose was more than 60 Gy in all patients because 60 Gy is the baseline radiotherapy dose in China. Of the 881 patients in this study, 55 (6.2%) had undergone radiotherapy before surgery. The free flap failure rate was significantly higher ($P < 0.001$) in patients who had undergone previous irradiation (12.7%) than in those who had not (2.3%). Thus, a history of irradiation should be taken into consideration during the preoperative risk assessment of patients requiring free flap reconstruction.

For patients with a history of previous neck surgery, in order to decrease the

influence of the formation of scar tissue and the status of the blood vessels, microsurgeons often prefer to use the contralateral blood vessels for anastomosis, or use a pedicle flap for reconstruction. Due to limitations of sample size, few previous studies have reported the relationship between a history of previous neck surgery to the anastomosis side and free flap outcomes. In total, 39 patients with a history of previous neck surgery required reconstructive surgery for a head and neck defect between January 2013 and November 2016 in the study department. Among these, 13 patients underwent reconstruction with a pedicle flap and were not included in the study. Twelve patients underwent anastomosis with the contralateral blood vessels and 14 patients underwent anastomosis on the same side as the previous neck surgery. The free flap failure rate was significantly higher ($P = 0.007$) in patients who had undergone previous neck surgery (21.4%) than in those who had not (2.7%).

In the aspect of intraoperative factors, it has been reported that the surgical technique is the most important component of free flap success[17]. In the study department, the two surgeons who performed the microvascular anastomoses (XP and YW) both have more than 5 years of experience in microvascular anastomosis. In every case, the standard protocol for vessel anastomosis was followed: (1) selection of a recipient vessel of the same diameter as the donor vessel; (2) removal of the attached soft tissue from the anastomosis site; (3) widening of the diameters of both the donor and recipient vessels by pressing microforceps against the inner membrane of the vessels; (4) irrigation with heparin before anastomosis; (5) gentle suturing of the vessels without tension; (6) checking the patency after vessel anastomosis; (7) adjusting the position of vessels to ensure no blind bend; (8) use of papaverine to prevent vasospasm. The success rate has increased gradually every year at the study institution. The present authors also believe that the surgical technique is the most important factor associated with free flap success.

Several studies have assessed donor flaps for head and neck reconstructions. Reiter et al. reviewed 437 flaps, with no flap loss in all cases[28]. They concluded that there was no increased risk of flap loss for buried flaps in their study. In the present study, the most popular free flaps used for reconstruction were the fibula flap, ALTF, and RFFF. The success rates in these three groups were 97.8%, 95.2%, and 97.0%, respectively. No statistically significant difference was found between these three groups ($p = 0.558$).

Few studies have compared the rates of flap failure between anastomoses to the internal jugular system and the external jugular vein. Generally speaking, the larger the diameter of the vessels, the lower the rate of flap failure. Chalian et al. concluded that compared to the internal jugular system, the external jugular vein shows a relatively low flow rate and small calibre[18]. They found better results with the internal jugular vein system than with the external jugular vein. However, another study reported no difference between these two vessels[19]. In the present study, no statistically significant difference was found between the types of recipient vessel ($P = 0.298$). It is considered that the choice of the vessel to be anastomosed is not fixed, but rather depends on the degree of match with the donor vessel.

The coupler device is a relatively new instrument for anastomosis and was introduced in the study institution in 2013. The advantages of coupler devices are that they provide physical support at the anastomosis site, may reduce the incidence of vasospasm to some degree, and reduce the anastomosis time as well as damage to the vascular epithelium. However, the use of coupler devices is limited by their high cost and complicated vessel conditions. As arterial walls are too thick to overturn, coupler devices are mainly used for venous anastomoses. Yap et al. reported no statistically significant difference between anastomoses established using coupler devices and hand-sewn anastomoses[20]. In the present study, coupler devices did not significantly improve free flap outcomes ($P = 0.130$).

In the aspect of postoperative aspect, to reduce the possibility of thrombotic occlusion after free flap transfer, antithrombotic agents are administered routinely after reconstructive procedures. Although several studies have examined different methods of preventing thrombosis and flap failure, clear evidence for the clinical benefit of antithrombotic agents has not yet been established[21–25]. In the study institution, the protocols written in the textbook are followed, namely the administration of a combination of low-dose aspirin and low molecular weight dextran for the prevention of thrombosis after free tissue transfer surgery[26]. In the current study, anticoagulants were not administered postoperatively in 158 patients for various reasons. The flap failure rate did not differ significantly between patients who did not receive anticoagulants (5.1%) and those who did receive anticoagulants (2.5%) ($P = 0.141$). Although anticoagulants were previously prescribed routinely at the study institution, it is now no longer considered necessary to administer anticoagulants to all patients.

All patients were monitored immediately after the reconstruction surgery. Trained nurses examined the patients for flap colour and temperature, and by pin prick test every hour for the first 72 h and every 2 h for the next 48 h. The risk of thrombosis is highest (80%) during the first two postoperative days and decreases to 10% after postoperative day 3[29,30]. Arterial crisis typically manifests with a pale flap, low flap temperature, capillary refill time >1 s, and no bleeding after the pin prick test. Being less common than venous crisis, arterial crisis is difficult to identify in the early stage, and is characterized by a lack of bleeding after the pin prick test. For the reasons given above, free flaps with arterial crisis suffered worse outcomes than flaps with venous thrombosis.

In conclusion, it is recommended that greater attention should be paid to patients who have a history of irradiation when performing head and neck reconstructive surgery. A meticulous surgical technique, adequate postoperative surveillance, and immediate management of complications can improve the outcomes of free flaps in head and neck reconstruction.

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Competing interests

The authors declare no conflict of interest.

Ethical approval

Ethical approval was obtained from the Biomedical Institutional Review Board of Peking University School and Hospital of Stomatology (PKUSSIRB-201731114).

Patient consent

Not required.

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