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Strategy for preventing skin paddle necrosis in mandibular reconstruction with free fibula osteocutaneous flap

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Abstract

Background: Non-thrombotic skin paddle necrosis occasionally occurs during mandibular reconstructions with free fibula osteocutaneous flaps. The number of perforators, size of the skin paddle, and ischemia time of the flap are considered as causes of skin paddle necrosis. The importance of donor side selection has also been highlighted. This study aimed to investigate the leading cause of skin paddle necrosis and the optimal reconstructive procedure.

Methods: A total of 66 patients who underwent mandibular reconstruction using a free fibula osteocutaneous flap were retrospectively analyzed. Skin paddle necrosis, number of cutaneous perforators, size of the skin paddle, and ischemia time of the flap were investigated. An incorrect "laterality" was defined as a skin paddle (septum) covering the reconstruction plate. Donor-site morbidity was recorded.

Results: Skin paddle necrosis occurred in 15.2% of patients. An incorrect laterality was associated with a higher incidence of skin paddle necrosis (odds ratio, 22.0; 95% confidence interval, 2.5–195; $p = 0.005$). Donor-site morbidity was noted in 18.8% of the patients, without any significant difference in terms of the donor side with and without skin graft ($p =$

0.592). The postoperative activities of daily living were not affected.

Conclusions: To prevent skin paddle necrosis, donor side selection is an important safety strategy during mandibular reconstruction with free fibula osteocutaneous flap. The postoperative activities of daily living were found to be little affected by differences in the donor side.

Keywords: Donor side selection; donor-site morbidity; free fibula osteocutaneous flap; mandibular reconstruction; skin paddle necrosis.

1 INTRODUCTION

Options for mandibular reconstruction include metallic plates, non-vascular bone grafts, and vascularized bone flaps[1, 2]. Recently, the use of free vascularized bone flaps, such as the free fibula osteocutaneous flap (FFOF), has been gaining wide acceptance. It is considered the first-line approach for mandibular reconstructions. Despite its advantages in reconstructing composite bone and soft tissue defects[1, 3], the FFOF occasionally undergoes skin paddle necrosis, which may result in surgical site and/or instrument infection. In turn, the infection may induce vascular pedicle thrombosis. Moreover, in cases of reconstruction with FFOF after ablation of malignant tumors, such complications possibly delay the initiation of adjuvant therapy for malignant tumors[4].

With respect to the pathogenesis of skin paddle necrosis, unstable local blood flow has been proposed as a potential mechanism. Previous reports have described the skin paddle design using a reliable perforator[4, 5], number and diameter of perforators used[6], size of the skin paddle[7], and ischemia time of the flap[8]. Unfortunately, skin paddle necrosis can still occur when all of these conditions are optimal. Yagi et al.[9] proposed an algorithm for donor side selection in which the skin paddle naturally reaches the defect at the shortest distance during mandibular reconstruction with the FFOF; they also reported that reliable reconstruction of the mandible could be performed using their algorithm.

This study aimed to investigate the main causes of skin paddle necrosis and identify predictors of a good outcome of mandibular reconstruction with an FFOF. To this purpose, the relationship between the reconstruction side and the donor side in terms of flap arrangement and flap characteristics, such as the number of septal cutaneous perforators, size of the skin paddle, and ischemia time of the flap, was investigated.

2 PATIENTS AND METHODS

In this retrospective study, the authors reviewed the data of patients who underwent reconstructive surgery with an FFOF after segmental mandibulectomy or hemimandibulectomy from January 2013 to September 2020 at the Department of Oral and Maxillofacial Surgery and Plastic Surgery of Kobe University Hospital. Subjects who developed anastomotic thrombosis were excluded from the analysis. This study was conducted in accordance with the principles embodied in the Declaration of Helsinki and was independently reviewed and approved by the Ethics Committee of Kobe University Hospital (certificate no. B200135). All subjects provided written informed consent for their participation in this study.

Data regarding clinicodemographic characteristics (age, sex, body mass index, primary disease, preoperative albumin levels, smoking status, presence of immunocompromise, and preoperative radiation therapy ≥ 60 Gy) and surgical characteristics (type of mandibular defect according to the "CAT" classification[10], operative time, volume of blood loss, need for blood transfusions, and tourniquet time) were retrieved. Additionally, flap-related factors, such as flap arrangement, number and type of septal cutaneous perforators (septocutaneous or septomusculocutaneous) branched peroneal artery in the skin paddle, size of the skin paddle, and ischemia time of the flap, were investigated. The skin paddle area was measured based on an intraoperative photograph using ImageJ (National Institutes of Health).

2.1 Donor side selection

In the Department of Oral and Maxillofacial Surgery and Plastic Surgery of Kobe University Hospital, the non-dominant side has traditionally been selected as the donor side (the dominant side being that used for kicking a ball) due to patients' preference. All patients underwent preoperative magnetic resonance angiography of the non-dominant lower leg to assess the anatomy of the three main vessels (anterior tibial, posterior tibial, and peroneal arteries) and cutaneous perforators[11]. If abnormal findings were observed on the non-dominant side, the dominant side was chosen as the donor side instead.

2.2 Classification of the flap arrangement and definition of "laterality"

According to the algorithm proposed by Yagi et al.[9], fibula osteocutaneous flaps are classified into four groups based on the relationship between the direction of the vascular pedicle, the position of the skin paddle, and the ideal donor side to the mandibular defect side, as follows:

Group A: The vascular pedicle was directed posteriorly, and the skin paddle was fixed to the oral mucosa; Group B: The vascular pedicle was directed posteriorly, and the skin paddle was fixed to the cervicofacial skin; Group C: The vascular pedicle was directed anteriorly, and the skin paddle was fixed to the oral mucosa; Group D: The vascular pedicle was directed anteriorly, and the skin paddle was fixed to the cervicofacial skin.

In this algorithm, the donor side is contralateral to the reconstruction side in Groups A and D and ipsilateral to the reconstruction side in Groups B and C. In this study, “laterality” was considered as “correct” when the flap arrangement and the donor side fitted within this algorithm (Figure 1).

2.3 Endpoints

The primary endpoint was the occurrence of skin paddle necrosis (including partial necrosis) without vascular anastomotic thrombosis. The absence of anastomotic thrombosis or vascular pedicle thrombosis was assessed using enhanced computed tomography and/or ultrasonography (Figure 2). In cases with little soft tissue defect after resection, even when thought to be partial necrosis, the reefing cases following removing the entire skin paddle to minimize damage were also included in total necrosis. The secondary endpoint was the incidence of late-onset complications on the donor-site (i.e., pain and numbness, toe deformity, edema, difficulty with stair climbing, and anxiety during gait). Donor-site morbidity was evaluated at ≥ 3 months postoperatively[12]. All patients underwent rehabilitation under a physical therapist's guidance during 2 weeks of hospital stay.

2.4 Statistical analyses

For comparisons between the groups of skin paddle necrosis and engraftment survival, Fisher's exact test and Mann–Whitney U test were used for nominal and continuous variables, respectively. The relationship among Groups A–D, laterality, and skin paddle necrosis was evaluated using the Mantel–Haenszel test. Variables associated with skin paddle necrosis in previous reports (number of septal cutaneous perforators, size of the skin paddle, and ischemia time of the flap) and laterality were included in a multivariate logistic regression model[7, 8]. The relationship among complications, donor side, and use of skin graft was evaluated using the Mantel–Haenszel test. Regarding the skin paddle size, the relationship between the skin paddle size and the number of cutaneous perforators was evaluated using Pearson's product-moment correlation coefficient. The cutoff value of skin paddle size for preventing skin paddle necrosis was determined using the receiver operating characteristic analysis with Youden's index. The relationship between the area of (length × width) and the one calculated using ImageJ was evaluated using simple regression analysis. The significance level was set at $p = 0.05$. Statistical analyses were performed using R software version 3.4.1 (R Development Core Team, 2017; R Foundation for Statistical Computing, Austria).

3 RESULTS

Of 76 patients who underwent reconstructive surgery with an FFOF during the study period, 10 (13.2%) presented with thrombosis on the anastomosis site and were thus excluded; overall, 66 patients were eligible for analysis. Skin paddle necrosis was noted in 10 cases (15.2%) [total necrosis, 7 cases (2 reefing cases); partial necrosis, 3 cases]. Laterality was correct in 43 cases (65.2%) and incorrect in 23 cases (34.8%). Skin paddle necrosis was noted in 4 cases (10.8%, incorrect = 3) in Group A (n = 37, incorrect = 11), 2 cases (40%, incorrect = 2) in Group B (n = 5, incorrect = 4), 3 cases (20%, incorrect = 3) in Group C (n = 15, incorrect = 4), and 1 case (11.1%, incorrect = 1) in Group D (n = 9, incorrect = 4); between-group differences in this regard were not significant (Mantel–Haenszel test, p = 0.585). Similarly, demographic, clinical, and surgical characteristics were not significantly different between patients with or without necrosis (Tables 1 and 2).

Regarding flap-related factors, the median ischemia time of the flap was comparable between the necrosis and engraftment groups (p = 0.458). Furthermore, there was no significant difference in the number of cutaneous perforators (p = 0.319). Conversely, the size of the skin paddle was significantly smaller in the necrosis group (median, 18.6 cm^2; range of length × width, 5 × 3 cm to 15 × 4 cm) than in the engraftment group (median, 26.4 cm^2; range of length × width, 6 × 3 cm to 9 × 8 cm) (p = 0.036). The size of the skin paddle did not correlate with the number of cutaneous perforators (Pearson's conduct correlation coefficient $r = 0.09$, $p = 0.484$).

Of note, incorrect laterality was present in 90% of patients in the necrosis group, compared with 25% of patients in the engraftment group ($p < 0.001$) (Table 2). Additionally, multivariate logistic regression analysis revealed that incorrect laterality was associated with a significantly higher risk of skin paddle necrosis (adjusted odds ratio, 22.0; 95% confidence interval, 2.5–195; $p = 0.005$) (Table 3). In cases of incorrect laterality, cutoff value of the size of the skin paddle to prevent necrosis was 18.0 cm^2 (n = 23, sensitivity = 55.6%, specificity = 92.9%, area under the curve = 0.651). The relationship between the area of (length × width) and the one calculated by ImageJ was expressed using the following formula: $y = 4.19090 + 1.29871\,x$ (n = 66, $R^2 = 0.90$, $p < 0.001$). The outcomes of patients with skin paddle necrosis were as follows: six cases of bone flap survival, two cases of bone flap removal, and two cases in whom bone flap preservation was possible with residual infection.

Donor-site complications were noted in 18.8%. The most common complications were pain and numbness and toe deformity (6.3% each), followed by edema (4.7%). None of these complications affected the activities of daily living. No significant association among the use of the skin graft, donor side, and donor-site complications was observed (Mantel–Haenszel test, $p = 0.592$) (Table 4).

4 DISCUSSION

In this study, incorrect laterality was found to be closely associated with the development of skin paddle necrosis. Other flap-related factors, such as ischemia time of the flap, number of cutaneous perforators, and size of the skin paddle, were not significantly associated with this complication. However, a tendency toward better outcomes with larger skin paddles was noticed. Therefore, the direction of the vascular pedicle (orientation of the cranial side of the harvested fibula), location of the skin paddle (characteristics of the soft tissue defect), and region of mandibular defect should be considered at the time of donor side selection.

In previous studies, the incidence of non-thrombotic skin paddle necrosis in FFOF was reported to be approximately 14.1% (3.6–30.4%)[4, 5, 8, 13-19]. The present study's result is in line with previous results. Regarding the cause of non-thrombotic skin paddle necrosis, the authors speculate that transferring the skin paddle through the outer side of the reconstruction plate (i.e., covering the reconstruction plate with the septum, including the perforator) to the intraoral or cutaneous side (i.e., incorrect laterality) renders the blood flow unstable due to compression of the cutaneous perforator and/or overstress of the skin paddle, even when a reliable cutaneous perforator is present.

In practice, the ischemia time of the flap is relatively short (approximately 1 h) because the fibular bone is modeled after performing vessel anastomosis. Skin paddle necrosis is very unlikely when the ischemia time of the flap is < 5 h[8]; hence, the current approach is appropriate in this regard.

Although the size of skin paddle was reported as length × width in previous reports, the actual size was calculated more accurately in this study. Considering that one or two septocutaneous perforators of the peroneal artery provide perfusion to a skin paddle of approximately 22–25 cm in length and 10–14 cm in width[20], it is not surprising that the size of the skin paddle was not associated with paddle necrosis. However, univariate analysis revealed that the size of the skin paddle was significantly smaller in the necrosis group than in the engraftment group, which was contrary to what was reported in a previous study[7]. This inconsistency may be explained if the size of the skin paddle is considered as a confounding factor; that is, many subjects with a small skin paddle also had incorrect laterality coincidentally. In these cases, a small flap would further compromise the blood supply, thereby increasing the stress to both the skin paddle and the cutaneous perforator. Therefore, it is likely that necrosis may be prevented by increasing the size of the skin paddle. Based on these results, it may be desirable that the size of the skin paddle be at least 18.0 cm^2 (27.6 cm^2 when calculated as length × width) in cases of incorrect laterality, although this depends on the characteristics of the soft tissue defect.

Donor-site morbidity rates and the type of complications in this study were comparable to those reported in previous studies[21-26]. No significant difference was noted between the donor sides in this regard; this is in accordance with the findings of a previous report[27]. It is worth emphasizing that activities of daily living were not affected by these complications, regardless of the donor side. In previous studies, the limb functions were comparable between the sides in which the fibular flap was harvested and the non-harvested side[28]. Further, the limb functions were comparable between the side of the harvested fibular flap and the limbs of healthy controls[29]. As a result, in the present study, it was suggested that daily life was almost unaffected, even when the flap was harvested from the dominant leg.

A simple method for selecting the donor side was devised. In the present study, the most common location of the defect was the mandibular body (between points A and T of the CAT classification), and flaps were most commonly arranged with a posterior direction of the vascular pedicle and intraoral location of the skin paddle. This situation (i.e., Group A), in which the donor side was contralateral to the reconstruction side, was considered the basic pattern (Figure 3a). When either the direction of the vascular pedicle or the position of the skin paddle was different from the basic pattern, the donor side was ipsilateral to the defect side (Figure 3b, c). When both these characteristics differed from the basic pattern, the donor side was contralateral to the defect side (Figure 3d).

Based on the present study’s results, the selection of a donor side with correct laterality may promote improved outcomes, regardless of whether the flap is harvested from the dominant or non-dominant leg. There was scarcity of studies that described donor side selection; the few studies identified were reviewed based on the "laterality" concept (Table

5)[9, 14, 30-33].

Incorrect laterality may be inevitable in cases of vascular anomalies of the lower extremity and the absence of reliable cutaneous perforators. In this situation, two major alternative approaches can be taken. One is altering the direction of the vascular pedicle. However, even if a long recipient vasculature is secured and changing the direction of the vessel from posterior to anterior seems feasible, kinking of the vascular pedicle may still occur. The other alternative to overcome incorrect laterality would be to relieve the overstress of the cutaneous perforator and skin paddle by enlarging the latter. In a cadaveric study[34], it was reported that when the skin paddle was passed through the outside of the reconstruction plate, approximately 3–4 cm of the skin paddle's width was required to be larger than when it was not passed through the outside of the plate. Considering this, it would be necessary to use a skin paddle that is at least 3 cm wider than the area of the defect when the laterality is incorrect. However, if the skin paddle is large, it may be difficult to obtain a good match between the harvested skin paddle and the defect area.

In the case of the composite defect (i.e., both oral and cutaneous defect), which is not too large, if one of the defects is significantly smaller than the other, it is considered reasonable to apply the concept of laterality to the side with the larger defect. However, if both defects are large, it may be difficult to apply the concept of laterality. In such cases, it may be advisable to use two skin paddles, a double flap (with such as a radial forearm free flap), or change the type of flap, such as a rectus abdominis myocutaneous flap.

This study has several limitations. First, due to the retrospective design, observer and recorder biases might have been introduced during data collection. Second, the size and blood flow of cutaneous perforators could not be evaluated. Third, late-onset complications were evaluated subjectively. Therefore, a future prospective study on this topic, including objective assessments of both cutaneous perforators and complications, is warranted.

5 CONCLUSIONS

The present study showed that in patients undergoing mandibular reconstruction with an FFOF, skin paddle necrosis was closely related to incorrect laterality. Additionally, donor-site complications did not affect the activities of daily living, regardless of whether these occurred on the dominant or the non-dominant leg. Therefore, it is considered that the concept of laterality, rather than considering the dominant/non-dominant limb, should guide the choice of an appropriate FFOF for mandibular reconstruction. Based on the present study’s results, it is believed that more reliable and safer mandibular reconstructive surgeries, using FFOF, could be performed.

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AUTHOR CONTRIBUTIONS

J.K. and K.H. designed the study. J.K., A.S., and N.M. performed data collection. J.K. performed most of the statistical analyses and wrote the initial draft of the manuscript. K.H., A.S., N.M., and M.A. critically reviewed the manuscript. All authors read and approved the final manuscript.

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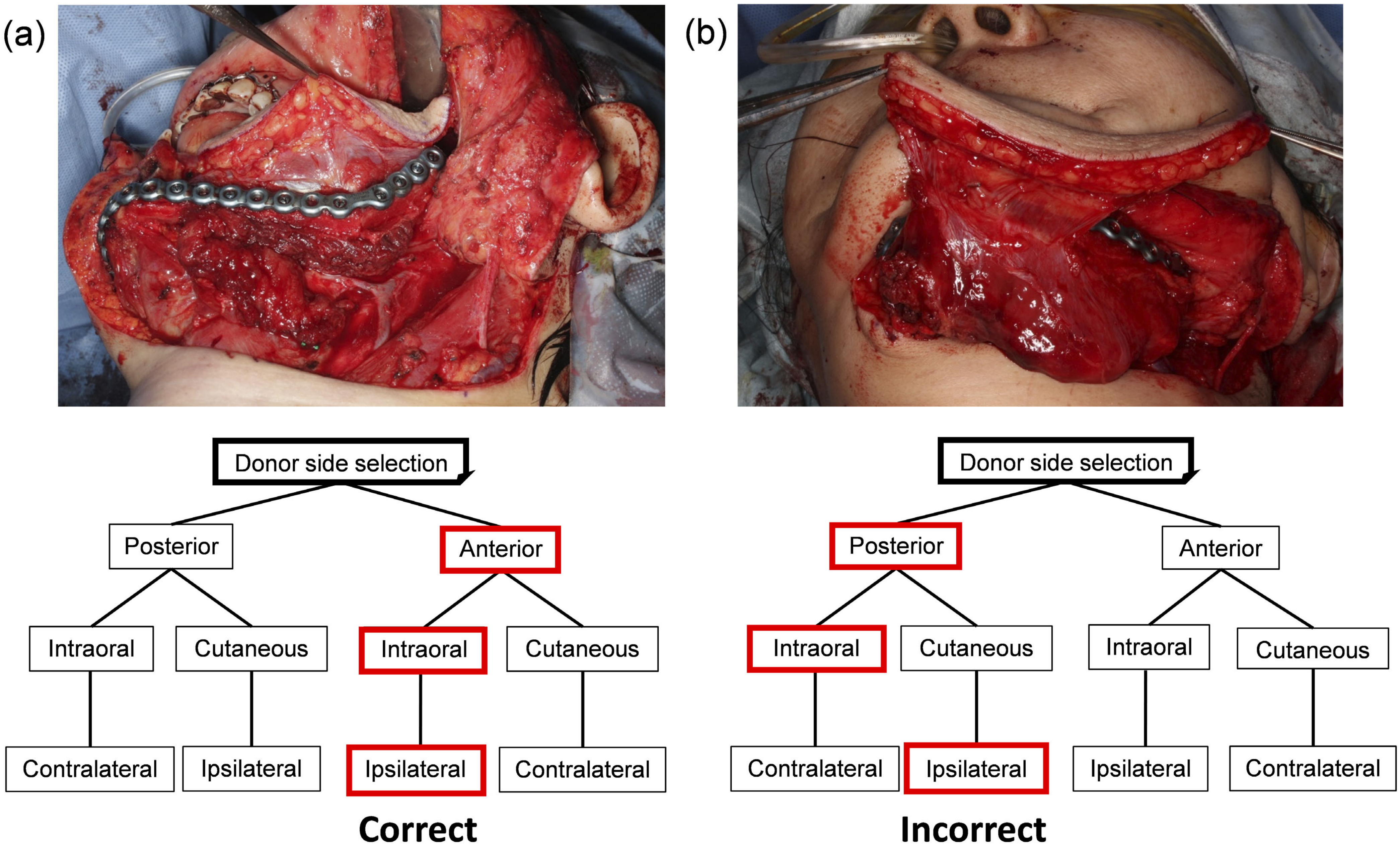
FIGURES LEGENDS

FIGURE 1 Concept of “laterality”. Cases matching those in the algorithm were defined as having correct “laterality”, and the unmatched cases were considered to have incorrect “laterality”. (a) In this case, the mandibular defect was on the left side, the direction of the vascular pedicle was anterior, and the location of the skin paddle was intraoral. As the donor side was on the left, and thus, ipsilateral to the mandibular defect, the “laterality” was correct. (b) In this case, the mandibular defect was on the left side, the direction of the vascular pedicle was posterior, and the location of the skin paddle was intraoral. As the donor side was on the left (leg), and thus, ipsilateral to the mandibular defect, the “laterality” was incorrect.

FIGURE 2 Skin paddle necrosis. A case of skin paddle necrosis with no underlying thrombosis of vascular anastomoses. (a) Congestive change in skin paddle. Subsequently, the skin paddle progressed to necrosis. (b, c) Enhanced computed tomography showing the vascular pedicle until caudal ligation (white arrow).

FIGURE 3 The proposed method for donor side selection in relation to the reconstruction side, direction of the vascular pedicle, and position of the skin paddle. (a) The basic pattern was the combination of “the mandibular defect was in the body,” “the direction of the vascular pedicle was anterior,” and “the location of skin paddle was intraoral.” When the reconstruction side was on the right, the donor side was on the left (i.e., opposite of the reconstruction side), and vice versa. (b) In this case, the direction of the vascular pedicle was anterior. When there was only one difference with respect to the basic pattern, the donor side was opposite to the basic pattern. (c) In this case, there was also only one difference with respect to the basic pattern, but it referred to the cutaneous position of the skin paddle. (d) Here, both the direction of the vascular pedicle (anterior) and the position of the skin paddle (cutaneous) were different from those of the basic pattern. When there were two differences with respect to the basic pattern, the donor side was opposite to the "opposite to basic pattern"; that is, the donor side was on the left (contralateral to the reconstruction side).



(a)
(b)
Donor side selection
Posterior
Anterior
Intraoral
Cutaneous
Intraoral
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Contralateral
Ipsilateral
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Contralateral
Correct
Donor side selection
Posterior
Anterior
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Intraoral
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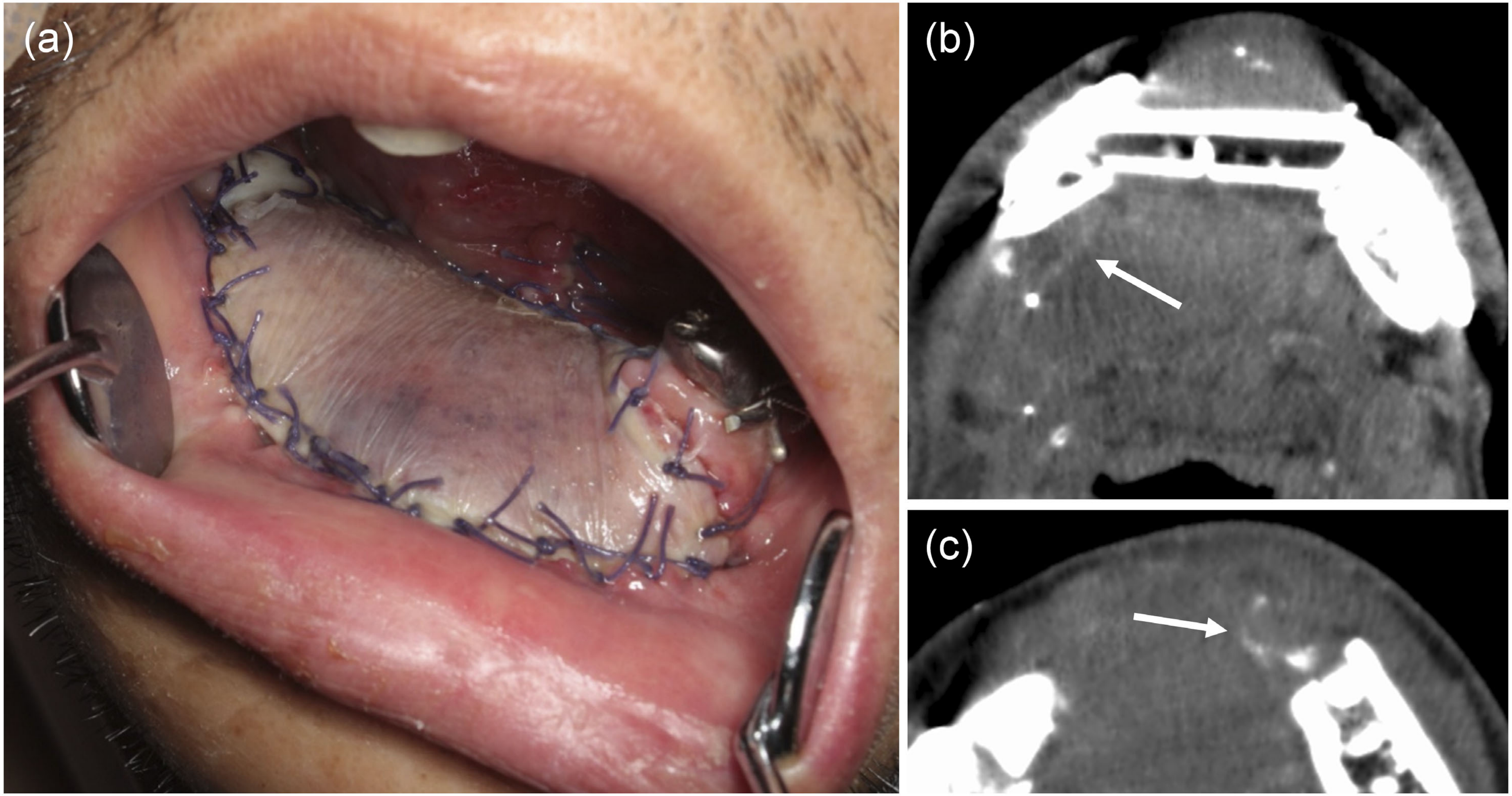
(a)
(b)
(c)

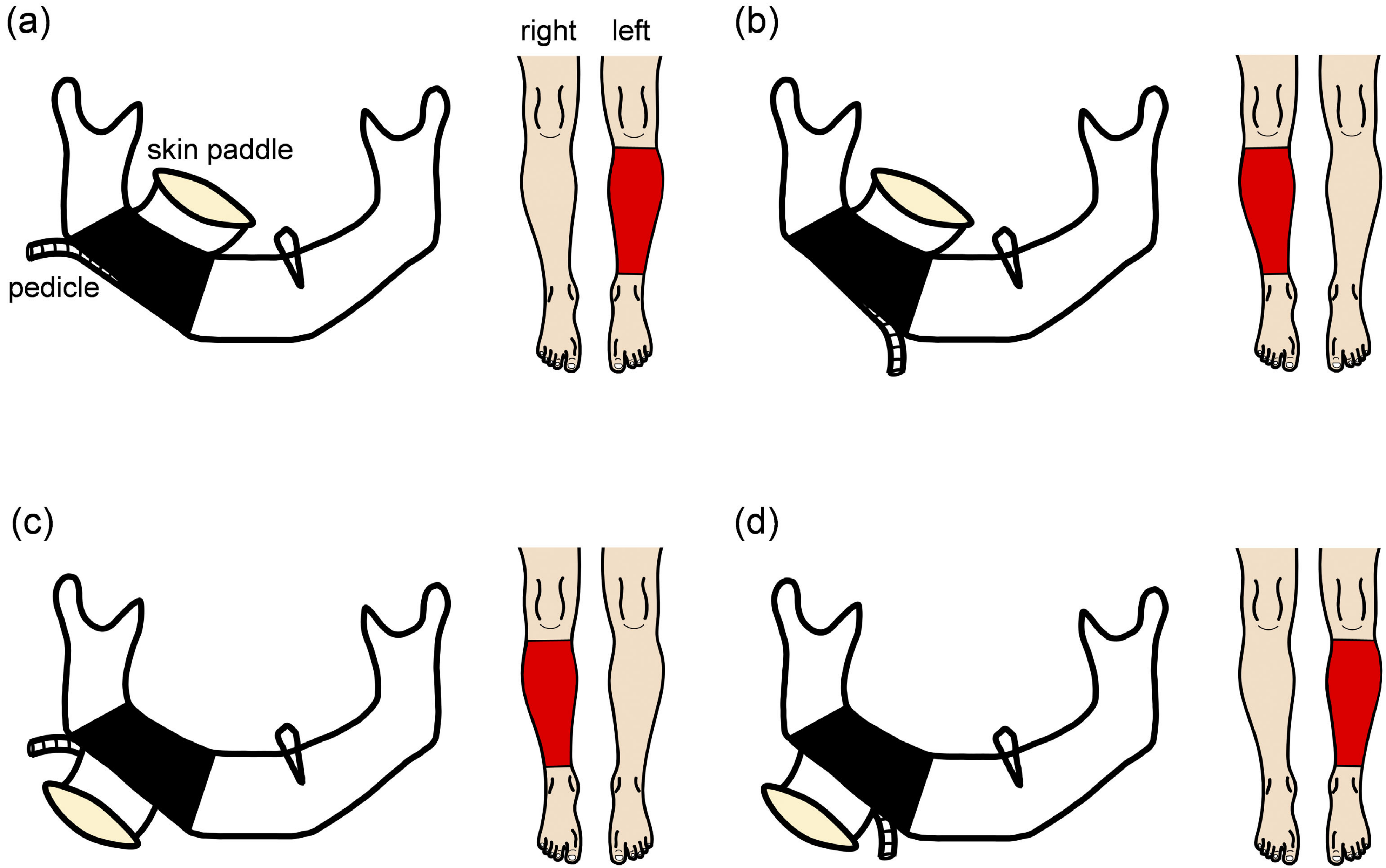
(a)
right
left
skin paddle
pedicle
(b)
(c)
(d)

Table 1. Comparison of baseline characteristics between patients with and without skin paddle necrosis: univariate analysis

Variables	Necrosis group (n = 10)	Engraftment group (n = 56)	p-value
Age	69 (62.0, 78.3)	68 (60.3, 73.0)	0.415
Male sex	6 (60%)	33 (58.9%)	1.000
Body mass index (kg/m^2)	22.4 (20.1, 25.7)	21.8 (20.0, 24.1)	0.426
Albumin (g/dl)	3.9 (3.8, 4.4)	4.1 (3.7, 4.3)	0.993
Smoking	6 (60%)	26 (46.4%)	0.505
Radiotherapy (≥ 60 Gy)	4 (40%)	18 (32.1%)	0.720
Immunocompromise	7 (70%)	26 (46.4%)	0.303
Primary disease			0.332
Malignant tumor[a]	3 (30%)	28 (50.0%)	
Osteomyelitis[b]	4 (40%)	18 (32.1%)	
Reconstruction plate problem[c]	3 (30%)	5 (8.9%)	
Benign tumor, cyst[d]	0	3 (5.4%)	
Other	0	2 (3.6%)	

Data are shown as median (first quartile, third quartile) or n (%).

[a] Squamous cell carcinoma; adenoid cystic carcinoma; ameloblastic carcinoma

[b] Osteoradionecrosis; medication-related osteonecrosis of the jaw; idiopathic osteomyelitis

[c] Exposure; fracture; infection

[d] Ameloblastoma; odontogenic keratocyst

Table 2. Surgical and flap factors affecting skin paddle necrosis risk: univariate analysis

Variables	Necrosis group (n = 10)	Engraftment group (n = 56)	*p*-value
Operation time (min)	653 (528, 699)	658 (582, 721)	0.617
Tourniquet time (min)	46 (43, 50)	48 (42, 54)	0.579
Bleeding (ml)	275 (223, 505)	430 (288, 645)	0.406
Blood transfusion	2 (20%)	11 (20%)	1.000
Recipient artery			0.631
Facial	5 (50%)	28 (50%)	
Superior thyroid	3 (30%)	13 (23.2%)	
Cervical transverse	0	8 (14.3%)	
Other	2 (20%)	7 (12.5%)	
Recipient vein			0.780
Facial	3 (30%)	19 (33.9%)	
External jugular	3 (30%)	20 (35.7%)	
Internal jugular	1 (10%)	8 (14.3%)	
Other	3 (30%)	9 (16.1%)	
Defect region (“CAT” classification)			0.801
Body	3 (30%)	20 (35.7%)	

T	2 (20%)	12 (21.4%)	
A	1 (10%)	7 (12.5%)	
TT’	1 (10%)	5 (8.9%)	
CA	3 (30%)	5 (8.9%)	
CAT	0	4 (7.1%)	
AT	0	2 (3.6%)	
ATT’A’	0	1 (1.8%)	
Time of flap ischemia (min)	46.5 (41.8, 50.8)	48.0 (42.0, 58.3)	0.458
Number of perforators	1 (1, 1)	1 (1, 2)	0.319
Skin paddle size (cm^2)	18.6 (16.4, 22.5)	26.4 (21.8, 32.6)	0.036*
Laterality			< 0.001*
Correct	1 (10%)	42 (75%)	
Incorrect	9 (90%)	14 (25%)	

Data are shown as median (first quartile, third quartile) or n (%).

* Statistically significant ($p < 0.05$)

Table 3. Variables affecting the risk of skin paddle necrosis: multivariate logistic regression analysis

Variables	β	OR	95% CI		*p*-value
			Lower	Upper	
Incorrect laterality	3.09	22.0	2.50	195	0.005*
Skin paddle size	-0.06	0.94	0.85	1.05	0.285
Number of perforators	-0.53	0.59	0.11	3.03	0.525
Time of flap ischemia	0.01	1.01	0.98	1.05	0.521

*Statistically significant ($p < 0.05$)

Abbreviations: OR, odds ratio; CI, confidence interval

Table 4. The relationship among donor-site complications, dominant foot, and skin graft

Leg	Skin graft	Donor-site complications	
		Yes (n = 12)	No (n = 52)
Dominant (n = 20)	With (n = 9)	1	8
	Without (n = 11)	4	7
Non-dominant (n = 44)	With (n = 7)	2	5
	Without (n = 37)	5	32

Table 5. Review of literature related to donor side selection in mandibular reconstruction with free fibula osteocutaneous flap

Study	Total number	Donor side selection ("laterality")	Skin paddle necrosis	Remarks
Wei, et al.[30] (1994)	27 (25 patients)	Not necessary	1 (3.7%)	Large skin paddles were harvested in all patients.
Hidalgo, et al.[14] (1995)	32	Incorrect	-	No details of the skin paddle was provided.
Lorenz, et al.[31] (2001)	29	Correct: 25 (86.2%)	-	The usefulness of preoperative MRA was indicated.
		Incorrect: 4 (13.8%)	-	No details of the skin paddle was provided.
Yagi, et al.[9] (2006)	15	Correct	1 (6.7%)	Small number of cases
Yadav, et al[32] (2010)	386	Not necessary	40 (10.4%)	Large skin paddles were harvested probably.
Kim, et al.[33] (2016)	8	Correct	1 (12.5%)	Small number of cases (all osteoradionecrosis)
Present study	66	Correct: 43 (65.2%)	1 (2.3%)	-
		Incorrect: 23 (34.8%)	9 (39.1%)	