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Risk Factors of Free Flap Complications in Reconstruction for Head and Neck Cancer

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ABSTRACT

Background Although head and neck reconstruction using free flaps has become a common procedure, flap complications remain a concern. This study aimed to analyze the risk factors of free flap complications and to identify the causes of these complications.

Methods We studied 97 patients with head and neck cancer with intraoral defects who underwent reconstruction using free flaps at Tottori University Hospital between 2011 and 2020. We used a retrospective cohort study design to investigate whether flap complications, including flap necrosis (total and partial) and flap dehiscence, were related to various factors, including the underlying disease condition, treatment status, and surgical factors.

Results Of the 97 patients analyzed, total flap necrosis was observed in one patient (1.0%). The incidence rate of flap complications, including flap necrosis and flap dehiscence, was 29.9%. When the time taken to perform one vascular anastomosis, including preparation of the recipient vessel and flap vessel, exceeded 30 min, the incidence rates of flap necrosis (total and partial) (odds ratio, 8.30; 95% confidence interval, 1.91–36.00; P = 0.005) and flap dehiscence (odds ratio, 3.46; 95% confidence interval, 1.05–11.36; P = 0.041) increased significantly.

Conclusion The time taken to perform one vessel anastomosis was the factor that contributed the most to the incidence of flap complications. Reconstructive surgeons should reduce the incidence of flap complications by keeping the known risk factors of the surgery in mind and by aiming to complete a vascular anastomosis time, including the time taken for the preparation of vessels, of ≤ 30 min per vessel during surgery.

Key words flap complication; free flaps; head and neck cancer; microsurgery; risk factors

The safety of reconstruction surgery for head and neck cancer using free flap transplantation has been established through advancement in surgical skills and instruments.[1, 2] However, the incidence rate of flap complications (FC) ranges from 1 to 20%,[1–5] indicating that the flap success rate does not reach 100%. Additionally, FC in head and neck cancer may lead to local infections and cause delayed wound healing and deterioration of the patients' general condition, delaying postoperative adjuvant therapy. Consequently, the length of hospital stay may be prolonged, potentially increasing the medical cost.[6, 7] Various reports have analyzed the risk factors of FC in head and neck reconstruction surgery. However, patient-dependent risk factors of FC such as comorbidity, life style and habit, general condition, and history of therapy are often difficult to eliminate at the time of head and neck reconstruction surgery.[1–4, 8, 9] Furthermore, although the patient situation may improve by controlling risk factors such as obesity, malnutrition, drinking, and smoking, it is difficult to delay the treatment of the underlying malignant disease in the interest of such lifestyle management.[1, 3, 10, 11] Therefore, reconstructive surgeons have no choice but to proceed with surgery keeping in mind that these are high-risk patients.[1–4, 8, 9] However, some of the factors reported during surgery, such as ischemia time of flap, operative time, the number of venous anastomoses, and size of flap, may be controlled by the surgeon.[1, 5, 8, 9, 11–16] Although it is the major FC such as total flap necrosis (FN) that the reconstructive surgeons should avoid, there are minor complications underlying

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Abbreviations: ALT, anterolateral thigh flap; ASA, American Society of Anesthesiologists; BMI, body mass index; fibula, fibula osteocutaneous flap; FC, Flap complications; FD, Flap dehiscence; FN, Flap necrosis; latissimus, latissimus dorsi muscle flap; NC, no complications; RAM, rectus abdominal muscle flap; RFF, radial forearm flap; SCC, Squamous cell carcinoma

the major complications. It may be possible to reduce FC by focusing on minor FC and analyzing their risk factors. Therefore, this study aimed to analyze the risk factors of FC, with a focus on minor FC, such as partial FN and flap dehiscence (FD), in addition to total FN in patients with head and neck cancer who have undergone primary reconstruction using free flaps. Moreover, we aimed to analyze the factors caused by the reconstructive surgeon's procedures and to report on the causes of FC that may be avoided during the procedure based on the judgment and technique of the reconstructive surgeon.

SUBJECTS AND METHODS

Ethics statement

This study was approved by the Ethics Committee of Tottori University Hospital (Protocol No.: 20A231). Informed consent was obtained using an opt-out option available on the institution's website. Those who declined were excluded from the analysis.

Study design and population

We enrolled patients with head and neck cancer who underwent reconstruction surgery using free flaps or free bone flaps for defects left after cancer resection at Tottori University Hospital between January 2011 and December 2020. Ninety-seven patients underwent reconstructive surgery using free flaps for head and neck cancer with intraoral defects (tongue, pharynx, floor of the mouth, mandible, buccal mucosa, maxilla, and palate). All operations involved tumor resection performed by head and neck surgeons, followed by reconstructive surgery by two reconstructive surgeons.

Data collection

Outcome measures

All items were investigated retrospectively based on digitized medical information. The presence or absence of FC within 30 days of surgery was evaluated. We extracted details regarding FC using the medical chart findings noted by the head and neck surgeons or reconstructive surgeons and photographs of the patients' clinical courses. We classified FC cases into two categories: 1. FN (partial or total necrosis) and 2. FD (flap dehiscence not due to necrosis). If both FN and FD occurred in the flap, their incidences were counted individually.

Risk factors

We collected the patients' basic information, factors related to the treated disease, patients' general preoperative condition, lifestyle habits, and surgical factors. Regarding the patients' basic information, patient age at the time of surgery was determined. Factors related to the treated disease included the lesion site, disease stage, preoperative disease history, preoperative pathological diagnosis, whether the cancer was primary or recurrent, whether the patient received neoadjuvant chemotherapy or radiation therapy, and details about the patient's history of radiation therapy, including recurrence of head and neck cancer after previous irradiation or a history of irradiation for past head and neck cancer. Variables related to the patient's general preoperative condition included the American Society of Anesthesiologists (ASA) physical status score (1, 2, and ≥ 3),[2] body mass index (BMI) (low BMI: <18.5 kg/m^2, median BMI: 18.5–24.9 kg/m^2, and high BMI: ≥ 25 kg/m^2), and comorbidities (hyperlipidemia, hypertension, liver disease, heart disease, respiratory disease, and diabetes). Variables related to lifestyle habits included smoking history (non-smoker, previous smoker who quit smoking, and current smoker) and drinking history (non-drinker, drinks one to two times per week, and drinks daily).

Regarding surgical factors, we extracted data on the type of free flap used; type of recipient vessel; number of venous anastomoses; use/non-use of a venous coupler device; blood loss during surgery; blood transfusion during surgery; operative time; flap ischemia time; total microsurgery time; anastomosis time per blood vessel from the surgical records, anesthesia records, and detailed nursing records during surgery; and intraoperative photographs. The time data were recorded in real time by circulating nurses using surgical progress record forms and included in the electronic medical record for all surgeries. The surgical progress record form contains a detailed description of the surgical process. The operative time (h) was calculated as the time from the start of the incision by the head and neck surgeon to the time of closure of the head and neck and flap donor sites. Furthermore, the ischemia time, total microsurgery time, and vascular time were defined as appropriate (Fig. 1). The flap ischemia time (min) was calculated as the time from ligation and dissection of the flap vascular pedicle to the point when blood flow reperfusion to the flap was enabled after the completion of vascular anastomosis.[5] The flap ischemia time varied depending on the order of the procedure and the number of anastomosed vessels. The total microsurgery time (min) was calculated as the time from the preparation of recipient vessels and flap pedicle under the microscope to the end of vessel anastomosis. The vascular time (min) was defined as the average time, determined by dividing the total microsurgery time by the number of anastomosed vessels.

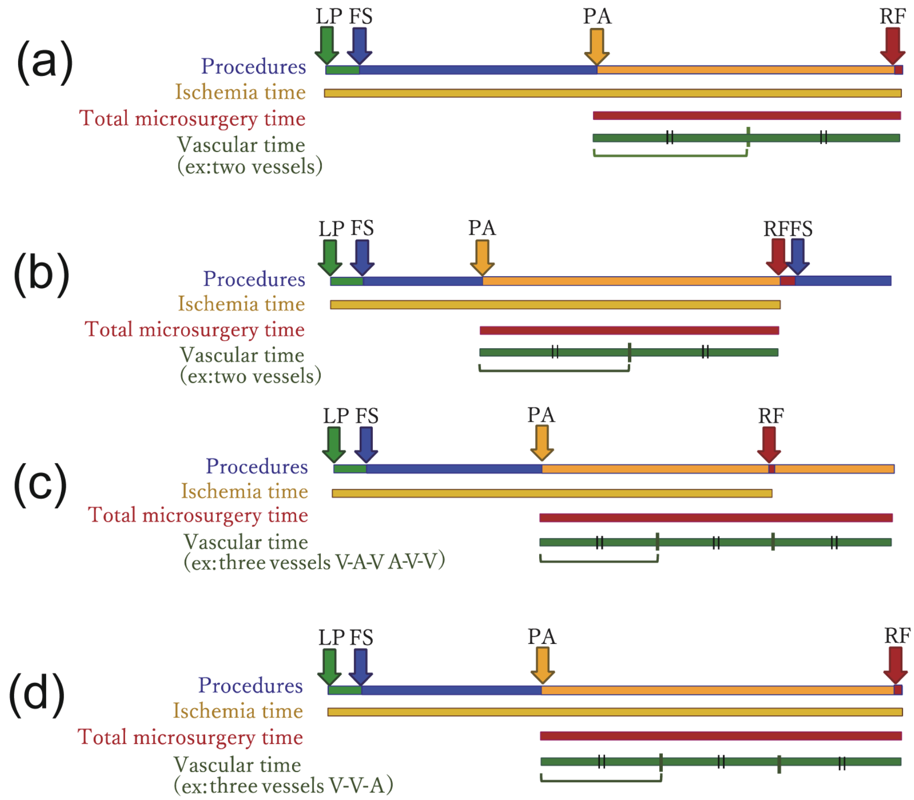

Fig. 1. Defining the time required for microsurgery. Arrows indicate the beginning of each procedure. A, Arterial anastomosis; LP, Ligation of the flap pedicle; FS, Flap suturing to defects; PA, Preparation and anastomosis vessels; RF, Reperfusion to flap; V, Venous anastomosis. Ischemia time was defined as the time from the ligation of the flap pedicle to reperfusion of the flap. Total microsurgery time was defined as the time from the preparation of the recipient vessels and flap pedicle under the microscope to the end of vessel anastomosis. Vascular time (min) = (total microsurgery time) / (no. of anastomosis vessels). **(a)** A case of preparing and anastomosing the flap pedicle and the recipient vessel after suturing the flap. **(b)** A case of preparing and anastomosing the flap pedicle and the recipient vessel after partially suturing the flap. **(c)** A case of three vessels that were anastomosed. One artery and one vein were anastomosed; the flap was reperfused, following which the second vein was anastomosed. **(d)** A case of three vessels that were anastomosed. Two venous anastomoses were followed by an arterial anastomosis, following which the flap was reperfused.

Statistical analyses

Univariate analysis was performed to compare the type of complications as well as preoperative and intraoperative factors between the group of patients without FC (no complications: NC) and that with FC. Continuous variables are presented as means±standard deviations, and categorical variables are expressed as *n* (%). In the univariate analysis, continuous variables were tested using the t-test or Welch's two-sample t-test. Categorical variables were analyzed using the chi-square or Fisher's exact test. Relevant factors identified in the univariate analysis were included as dependent variables in the binomial logistic regression model in which the complications (FC, FN, and FD) were included as dependent variables. The vascular time, identified as being relevant in the univariate analysis, was categorized into 5-min units and entered into the binomial logistic regression model. Furthermore, it was categorized into two groups according to the 80th percentile of the cases (≤ 30 min and >30 min). The binomial logistic regression model was adjusted for age and sex. Statistical significance was determined as $P < 0.05$. All statistical analyses were conducted using SPSS Statistics version 25 (IBM Corp, Chicago, IL).

RESULTS

Ninety-seven free flap transplantation surgeries were conducted in 97 patients [72 males, 25 females; mean age, 64.0 ± 12.6 years (range, 31–85 years)]. There were 29 FC cases (29.9%). FN was observed in 12 cases (12.3%), where 1 (1.0%) had total necrosis and 11 (11.3%) had partial necrosis. The case with total necrosis showed favorable flap color 1 to 2 days after surgery but exhibited FN and local infection on postoperative day 4; the patient underwent salvage surgery using a pectoral major musculocutaneous flap. The cause of FN was unknown. The other 11 cases had partial necrosis in the flap margins. Of the 11 cases of partial necrosis, one patient had combined fistula formation and infection; thus, this patient required additional treatments with a pectoral major musculocutaneous flap. The remaining 10 cases healed conservatively. There were 24 FD cases (24.7%) in which the wound was closed after conservative treatments. Flap engraftment was observed in 96 cases (99.0%).

Table 1 shows a summary of patient demographics and results of the univariate analysis. None of the variables showed any statistically significant correlation with the incidence of complications.

Table 2 shows a summary of the general patient condition before surgery and results of the univariate analysis. Among the FC cases, BMI had a particularly significant correlation with the incidence rate of FN ($P = 0.037$, NC vs. FC; $P = 0.002$, NC vs. FN; $P = 0.20$, NC vs. FD).

Regarding internal comorbidities, liver disease showed a significant association with the incidence rate of FN ($P = 0.024$, NC vs. FN). Other comorbidities, smoking history, drinking history, and ASA physical status showed no statistically significant relationship with the incidence rate of FC.

Table 3 shows the intraoperative factors. The type of flap, type of recipient vein, use/non-use of a venous coupler device, blood loss during surgery, and blood transfusion during surgery did not affect the incidence rate of any of the complications. When the number of veins anastomosed was two or more, the incidence rate of FD was significantly lower than that when only one vein was anastomosed ($P = 0.045$, NC vs. FD). The operative and ischemia times did not affect the incidence rate of the complications. However, the total microsurgery time was significantly longer in the FN group than that in the NC group ($P = 0.045$, NC vs. FN). The vascular time was associated with the incidence rate of FC and showed a particularly significant relationship with the incidence rate of FN ($P = 0.047$, NC vs. FC; $P = 0.003$, NC vs. FN; $P = 0.066$, NC vs. FD).

Table 4 shows the results of the logistic regression analysis of complications by the vascular time categorized per 5 min. The risk of incidence for FC, FN, and FD significantly increased along with increases in vascular time [odds ratio (OR), 1.46; 95% confidence interval (CI) 1.05–2.02; $P = 0.024$; OR, 2.31; 95% CI, 1.28–4.16; $P = 0.005$; and OR, 1.47; 95% CI, 1.05–2.07; $P = 0.026$, respectively].

Table 5 shows the results of the logistic regression analysis of complications by the vascular time and number of anastomosed veins. The risks of FC, FN, and FD were significantly higher when the vascular time was > 30 min than when it was ≤ 30 min (OR, 3.75; 95% CI, 1.22–11.53; $P = 0.021$; OR, 8.30; 95% CI, 1.91–36.00; $P = 0.005$; and OR, 3.46; 95% CI, 1.05–11.36; $P = 0.041$, respectively). No significant difference was observed in the risk of any of the complications depending on whether the number of veins anastomosed was two or more, or only one. However, the incidence rate of FD tended to be higher when only one vein was anastomosed than when two or more veins were anastomosed (OR, 2.64; 95% CI, 0.94–7.42; $P = 0.065$).

DISCUSSION

We showed that the vascular time per vessel is the most important factor related to FC, including FN and FD, which was not reported previously. This information may contribute to the reduction of both minor and major FC in the future.

Total flap failure was observed in 1% of cases, and the incidence rate of FC was 29.9%. The prevalence of total flap failure is consistent with that reported previously, which is between 1–10%.[1, 2, 4, 5] Furthermore, the incidence rate of FC, albeit varying between reports, ranges from 1 to 20%.[1–5] The incidence of FC in this study was higher than that reported previously. This may be explained by the fact that minor FN and FD cases were also considered when calculating the incidence rate of FC in this study.

Numerous previous reports have suggested that prolonged flap ischemia time and operative time lead to flap failure.[1, 8, 9, 11–16] In this study, no significant difference in FC was found in flap ischemia time and operative time. The flap ischemia time varies depending on the order of the procedure and the number of anastomosed vessels (Table 1). Further, operative time varies with the time required for resection and other factors. Herein, we defined total microsurgery time as the net time the reconstructive surgeon is in direct contact with vessels under the microscope, and vascular time as the time per vessel. In other words, vascular time is not affected by the number of anastomotic vessels or other procedure or factors. Prolonged contact with blood vessels causes vascular spasm, increased direct vascular endothelial damage, swelling of the endothelial cells, narrowing of the capillary diameter due to edema of the stroma, and microthrombosis due to platelet aggregation.[17–20] Additionally, the concentration of superoxide involved in tissue damage, which is generated after flap reperfusion, increases depending on the tissue damage during ischemia.[21] Therefore, prolonged vascular time is thought to cause partial FN through microvessel dysfunction in flaps and the formation of microthrombi.

Table 1. Summary of patient demographics and results of the univariate analysis

	Total		All patients					Types of flap complications					
			No flap complications (NC)		Flap complications (FC)		NC vs. FC	Flap necrosis (FN)		NC vs. FN	Flap dehiscence (FD)		NC vs. FD
	n = 97	%	*n* = 68	%	*n* = 29	%	*P*	*n* = 12	%	*P*	*n* = 24	%	*P*
Age (years)							0.370†			0.228†			0.537†
Mean (±SD)	64.0±12.6		64.7±12.1		62.2±13.5			60.1±12.6			62.9±14.5		
Sex							0.439‡			0.483§			0.583‡
Male	72	74.2	52	76.5	20	69.0		8	66.7		17	70.8	
Female	25	25.8	16	23.5	9	31.0		4	33.3		7	29.2	
Location of the cancer							0.700‡			0.764‡			0.701‡
Tongue	42	43.3	30	44.1	12	41.4		5	41.7		9	37.5	
Pharynx	21	21.6	14	20.6	7	24.1		2	16.7		6	25	
Floor of the mouth	13	13.4	8	11.8	5	17.2		3	25		4	16.7	
Mandible	11	11.3	7	10.3	4	13.8		2	16.7		4	16.7	
Buccal mucosa	6	6.2	6	8.8	0	0		0	0		0	0	
Maxilla	3	3.1	2	2.9	1	3.4		0	0		1	4.2	
Palate	1	1	1	1.5	0	0		0	0		0	0	
Type of cancer													
SCC	93	95.9	64	94.1	29	100		12	100		24	100	
Others	4	4.1	4	5.9	0	0		0	0		0	0	
Classification of T (TNM)							0.429‡			0.533‡			0.397‡
T1	1	1	0	0	1	3.4		0	0		1	4.2	
T2	24	24.7	17	25	7	24.1		4	33.3		5	20.8	
T3	17	17.5	11	16.2	6	20.7		3	25		4	16.7	
T4	55	56.7	40	58.8	15	51.7		5	41.7		14	58.3	
Classification of N (TNM)							0.744‡			0.199‡			0.522‡
N0	41	42.3	29	42.6	12	41.4		6	50		9	37.5	
N1	14	14.4	9	13.2	5	17.2		4	33.3		5	20.8	
N2	38	39.2	28	41.2	10	34.5		2	16.7		8	33.3	
N3	4	4.1	2	2.9	2	6.9		0	0		2	8.3	
Classification of M (TNM)													
M0	97	100	68	100	29	100		12	100		24	100	
M1	0	0	0	0	0	0		0	0		0	0	
Primary or recurrence							1.000§			0.587§			0.717§
Primary	87	89.7	61	89.7	26	89.7		12	100		21	87.5	
Recurrence	10	10.3	7	10.3	3	10.3		0	0		3	12.5	
Preoperative chemotherapy							0.194‡			0.495§			0.213‡
Yes	66	68	49	72.1	17	58.6		7	58.3		14	58.3	
No	31	32	19	27.9	12	41.4		5	41.7		10	41.7	
Preoperative irradiation							0.272§			0.599§			0.437§
Yes	9	9.3	8	11.8	1	3.4		0	0		1	4.2	
No	88	90.7	60	88.2	28	96.6		12	100		23	95.8	
History of irradiation							0.881‡			0.442§			0.768‡
Yes	11	11.3	15	22.1	6	20.7		1	8.3		6	25	
No	86	88.7	53	77.9	23	79.3		11	91.7		18	75	

Statistically significant ($P < 0.05$, **$P < 0.01$, ***$P < 0.001$); †: *t*-test; ‡: χ2 test; §: Fisher's exact test. FC, Flap complications; FD, Flap dehiscence; FN, Flap necrosis; NC, no complications; SCC, Squamous cell carcinoma.

Table 2. Summary of the general patient condition before surgery and results of the univariate analysis

	Total		All patients: No flap complications (NC)		Flap complications (FC)		NC vs. FC	Types of flap complications: Flap necrosis (FN)		NC vs. FN	Flap dehiscence (FD)		NC vs. FD
	n = 97	%	*n* = 68	%	*n* = 29	%	*P*	*n* = 12	%	*P*	*n* = 24	%	*P*
BMI							0.037‡*			0.002‡**			0.205‡
< 18.5 kg/m^2	22	22.7	12	17.6	10	34.5		5	41.7		8	33.3	
18.5–24.9 kg/m^2	59	60.8	47	69.1	12	41.4		2	16.7		12	50	
≥ 25 kg/m^2	16	16.5	9	13.2	7	24.1		5	41.7		4	16.7	
Comorbidities													
Hyperlipidemia	52	53.6	37	54.4	15	51.7	0.808‡	3	25	0.115§	14	58.3	0.74‡
Hypertension	40	41.2	29	42.6	11	37.9	0.666‡	5	41.7	1.00§	10	41.7	0.933‡
Liver disease	35	36.1	21	30.9	14	48.3	0.102‡	8	39.7	0.024§*	10	41.7	0.337‡
Cardiac disease	28	28.9	19	27.9	9	31	0.758‡	4	33.3	0.736§	7	29.2	0.909‡
Pulmonary disease	23	23.7	15	22.1	8	27.6	0.558‡	2	16.7	1.00§	7	29.2	0.483‡
Diabetic mellitus	20	20.6	15	22.1	5	17.2	0.785§	3	25	1.00§	4	16.7	0.771§
Smoking							0.67‡			0.379‡			0.861‡
Non-smoker	28	28.9	19	27.9	9	32.1		4	33.3		7	30.4	
Ex-smoker	27	27.8	18	26.5	9	32.1		5	41.7		7	30.4	
Smoker	41	42.3	31	45.6	10	35.7		3	25		9	39.1	
Alcohol consumption							0.082‡			0.47‡			0.064‡
None	21	21.6	14	20.6	7	25		2	16.7		6	26.1	
1–2 drinks/week	16	16.5	8	11.8	8	28.6		3	25		7	30.4	
Everyday	59	60.8	46	67.6	13	46.4		7	58.3		10	43.5	
ASA physical status							0.706‡			0.649‡			0.699‡
1	16	16.5	10	14.7	6	20.7		2	16.7		5	20.8	
2	59	60.8	43	63.2	16	55.2		6	50		13	54.2	
≥ 3	22	22.7	15	22.1	7	24.1		4	33.3		6	25	

Statistically significant ($P < 0.05$, **$P < 0.01$, ***$P < 0.001$); †: *t*-test; ‡: $\chi 2$ test; §: Fisher's exact test. ASA, American Society of Anesthesiologists; BMI, body mass index.

Further, it is surmised that prolonged anastomosis enhances tissue edema and contributes to FD.[17, 21]

As the number of anastomosed vessels increases, the operative time and ischemia time, which are regarded as risk factors according to previous reports, may be prolonged.[1, 8, 9, 11–16] We found that the incidence rates of all complications were not significantly different depending on the number of anastomosed veins. Reports have shown a relationship between the operative time and the number of anastomosed veins: anastomosis of two veins prolonged the operative time significantly compared to anastomosis of one vein, although the flap engraftment rate was high and vascular insufficiency was significantly lower in the former than in the latter.[22] Hence, we believe that even if the operative time is prolonged due to an increase in the number of anastomosed veins, FC will not be more prevalent as long as each individual vessel is anastomosed quickly. Furthermore, though no significant difference was observed, our study showed that anastomosis of two or more veins tended to decrease the risk of FD. Multiple reports have suggested that venous reperfusion in the flap is ameliorated when two or more veins are anastomosed than when only one vein is anastomosed.[22–24] Anastomosis of two or more veins may reduce flap tissue edema that increases due to the invasiveness of procedure.[17, 21] Analysis with additional cases and homogenization of the flap types may produce a significant difference in the incidence rate of FD according to the difference in the number of anastomosed veins.

Table 3. Results of the univariate analysis of the intraoperative factors

	Total		No flap complications (NC)		Flap complications (FC)		NC vs. FC	Flap necrosis (FN)		NC vs. FN	Flap dehiscence (FD)		NC vs. FD
	n = 97		*n* = 68		*n* = 29		*P*	*n* = 12		*P*	*n* = 24		*P*
No. (%) of flaps							0.739†			0.392†			0.229†
RAM	47	(48.5)	32	(47.0)	15	(51.7)		3	(25.0)		15	(62.5)	
ALT	38	(39.2)	28	(41.2)	10	(34.5)		7	(58.3)		6	(25.0)	
RFF	6	(6.2)	5	(7.4)	1	(3.4)		1	(8.3)		0	(0)	
Latissimus	4	(4.1)	2	(2.9)	2	(6.9)		0	(0)		2	(8.3)	
Fibula	2	(2.1)	1	(1.5)	1	(3.4)		1	(8.3)		1	(4.2)	
Recipient vessel, n (%)							0.854†			0.313†			0.643†
Internal jugular vein	42	(43.3)	28	(41.2)	14	(48.3)		6	(50.0)		11	(45.8)	
External jugular vein	23	(23.7)	16	(23.5)	7	(24.1)		1	(8.3)		7	(29.2)	
Both (internal+external)	22	(22.7)	17	(25.0)	5	(17.2)		5	(41.7)		3	(12.5)	
Others	10	(10.3)	7	(10.3)	3	(10.3)		0	(0)		3	(12.5)	
No. (%) of vein anastomoses							0.096†			0.851†			0.045†*
1 vein	51	(52.6)	32	(47.1)	19	(65.5)		6	(50.0)		17	(70.8)	
≥ 2 veins	46	(47.4)	36	(52.9)	10	(34.5)		6	(50.0)		7	(29.2)	
Use of a coupler device							0.518†			0.367‡			0.562†
Yes	45	(46.4)	33	(48.5)	12	(41.4)		4	(33.3)		10	(41.7)	
No	52	(53.6)	35	(51.5)	17	(58.6)		8	(66.7)		14	(58.3)	
Blood loss, mean (SD), mL	471.4	(291.2)	470.5	(274.6)	473.6	(332)	0.962	518	(406.1)	0.614§	463.5	(306.0)	0.918§
No. (%) of blood transfusions	13	(13.4)	8	(11.8)	5	(17.2)	0.521‡	1	(8.3)	1.00‡	5	(20.8)	0.298‡
Operative time, mean (SD), h	11.5	(1.7)	11.6	(1.7)	11.4	(1.9)	0.618§	10.8	(1.6)	0.122§	11.6	(1.7)	0.951§
Ischemia time, mean (SD), min	124.1	(33.6)	122.5	(35.2)	127.9	(29.7)	0.473§	127	(21.0)	0.551‖	128.6	(31.6)	0.456§
Total microsurgery time, mean (SD), min	62.6	(21.2)	61.6	(20.6)	64.9	(22.6)	0.486§	74.6	(20.9)	0.045§*	63.3	(23.1)	0.735§
Vascular time, mean (SD), min	25.3	(7.3)	24.1	(5.8)	28.1	(9.7)	0.047‖*	30	(7.6)	0.003§**	28.3	(10.2)	0.066‖

Statistically significant ($P < 0.05$, **$P < 0.01$, ***$P < 0.001$); †: $\chi 2$ test; ‡: Fisher's exact test; §: *t*-test; ‖: Welch two sample test. Operative time was defined as the time from the start to the end of the surgery. Ischemia time was defined as the time from the ligation of the flap pedicle to reperfusion of the flap. Total microsurgery time was defined as the time from the preparation of the recipient vessels and flap pedicle under the microscope to the end of vessel anastomosis. Vascular time (min) = (total microsurgery time)/ (no. of anastomosis vessels). ALT, anterolateral thigh flap; fibula, fibula osteocutaneous flap; latissimus, latissimus dorsi muscle flap; no., number; RAM, rectus abdominal muscle flap; RFF, radial forearm flap.

Table 4. Results of the logistic regression analysis of complications by vascular time (per 5 min)

	No. of cases –	No. of cases +	Odds ratio	(95% CI)	*P*
Flap complications (FC)					
Vascular time (/5 min)	*n* = 68	*n* = 29	1.46	(1.05–2.02)	0.024*
Flap necrosis (FN)					
Vascular time (/5 min)	*n* = 68	*n* = 12	2.31	(1.28–4.16)	0.005**
Flap dehiscence (FD)					
Vascular time (/5 min)	*n* = 68	*n* = 24	1.47	(1.05–2.07)	0.026*

All covariates were adjusted for sex and age. *Statistically significant (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$). For every additional 5 min of vascular time, the risk of flap complications increases 1.46 times, that of flap necrosis increases 2.31 times, and that of flap dehiscence increases 1.47 times. CI, confidence interval; no., number; –, group without flap complications; +, group with flap complications.

Table 5. Results of the logistic regression analysis of complications by vascular time and number of anastomosed veins

		No. of cases –	No. of cases +	Odds ratio	(95% CI)	*P*
Flap complications (FC)		*n* = 68	*n* = 29			
Vascular time (min)	≤ 30	60	19	Reference		
	> 30	8	10	3.75	(1.22–11.53)	0.021*
No. of veins	≥ 2	36	10	Reference		
	1	21	19	2.06	(0.81–5.26)	0.131
Flap necrosis (FN)		*n* = 68	*n* = 12			
Vascular time (min)	≤ 30	60	6	Reference		
	> 30	8	6	8.3	(1.91–36.00)	0.005**
No. of veins	≥ 2	36	6	Reference		
	1	32	6	1.01	(0.26–3.88)	0.988
Flap dehiscence (FD)		*n* = 68	*n* = 24			
Vascular time (min)	≤ 30	60	16	Reference		
	> 30	8	8	3.46	(1.05–11.36)	0.041*
No. of veins	≥ 2	36	7	Reference		
	1	32	17	2.64	(0.94–7.42)	0.065

All covariates were adjusted for sex and age. *Statistically significant (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$). CI, confidence interval; no., number; –, group without flap complications; +, group with flap complications.

Regarding the other factors, univariate analysis identified a significant difference in the incidence rate of FN depending on the BMI and presence of liver disease. There is no consensus regarding whether a high BMI affects FN.[1, 3, 25] Furthermore, some reports have indicated that the incidence rate of local complications, including FN and local fistula, increases significantly during anterior cranial base reconstruction in patients with a low BMI,[26] while patients with low BMI who have experienced recent weight loss reportedly develop complications due to the decline in the body's reserve capacity.[1, 11, 27] Although the incidence of complications may be reduced through dietary management aiming for a normal BMI before surgery, this may be difficult because of the patient's condition. Additionally, it is necessary to consider delaying the surgery for a malignant tumor to correct the BMI.[11] The reconstructive surgeon needs to proceed carefully with the surgery and recognize that patients with a low BMI are particularly at a high risk of complications. Concerning liver disease, a report on the incidence rate of complications after free flap surgery in patients with head and neck cancer showed a high score on the Model for End-Stage Liver Disease scoring system, indicating that the degree of severity of liver dysfunction is associated with a greater prevalence of FN.[28] However, as the severity of liver disease in the eight patients in this study varied and the number of cases was small, it is difficult to consider liver disease as a risk factor for FC. Further cases should be investigated to verify this in the future.

Our study demonstrated that anastomosing a blood vessel in ≤ 30 min reduces the incidence of FC. We also observed that every 5-min prolongation of the anastomosis time increased the incidence rates of FC, FN, and FD by 1.46, 2.31, and 1.47 times, respectively. In this study, the factors that prolonged the vascular time are unclear; however, performing the vessel anastomosis, including preparation in ≤30 min can be controlled by the reconstructive surgeon, unlike the preoperative physical factors and treatments. Improving the skill levels of the surgeons, assistants, and nurses as well as preparing the instruments and surgical materials in advance are important for ensuring a vascular time of ≤ 30 min. Even a seasoned surgeon requires a longer time to perform vessel anastomosis in patients with severe conditions, such as vessels with severe atherosclerosis, a history of previous surgeries, or few available recipient vessel options due to neck dissection or tumor invasion. It is important to choose the simplest anastomosis technique; select appropriate recipient vessels[29]; reduce the number of anastomosis sutures; employ protective operations, such as applying additional sutures while maintaining blood flow if there is anastomotic leakage; and use minimum procedures. If there are multiple veins in the flap, it is advisable to perform maximum vein anastomoses. Prolongation of the operative time resulting from this should be permissible as long as the vascular time per vessel is ≤ 30 min. Additionally, the coupler device causes less damage to the intima in both venous and arterial anastomoses, improves the flap engraftment rate,[23, 30–32] and shortens the operative time by an average of 7 min during anastomosis of two veins.[32] It is important for the reconstructive surgeon to focus on shortening the vascular time through training, devising the procedure in advance, and utilizing a coupler device. In this study, no significant difference in ischemia time was observed. However, these are not excluded as risk factors, and factors such as the small number of cases may have obscured significant differences in ischemia time. Therefore, shortening ischemic time should always be kept in mind. When multiple veins are anastomosed, in addition to using a coupler device, it is necessary to devise a way to shorten the ischemic time by first anastomosing one artery and one vein, and then anastomosing the remaining veins after reperfusion, as shown in Figure 1(c).

In addition to the BMI, which was found to be significantly different in this study, various risk factors of FC have been reported, including a history of radiotherapy, lifestyle habits, and comorbidities that reconstructive surgeons cannot avoid.[1–4, 8, 9, 26, 27, 33] The reconstructive surgeon needs to predict the vulnerability of a patient to complications by sufficiently considering the apparent risk factors. Thereafter, the reconstructive surgeon and their surgical staff should study the case and prepare to shorten the vascular time and proceed with the surgery. Further, the reconstructive surgeon should ensure that any FC is not taken lightly. Therefore, we believe that the incidence rate of complications may be reduced. The clinical significance of our study is that it revealed the vascular time as a risk factor for FC. Reconstructive surgeons should be aware of this factor because they can control it.

The limitations of this study include its retrospective design and the small number of cases. There is a limit to the number of factors that can be analyzed due to the small number of cases. Since no previous studies have evaluated the vascular time, we anticipate that meta-analyses focusing on the vascular time and prospective studies will be conducted in the future.

In conclusion, although the use of a free flap in head and neck reconstructive surgery is recognized as a safe technique, it is important to shorten the vascular time to reduce the incidence rate of complications associated with the procedure. We believe that the FC incidence rate may be reduced if reconstructive surgeons maintain the vascular time per vessel within ≤ 30 min using careful surgical techniques and keeping in mind the various risk factors that apply to each patient.

The authors declare no conflict of interest.

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