

Multiple Free Flap Reconstructions of Head and Neck Defects Due to Oral Cancer

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Objective: We studied complications following multiple free flap reconstructions in the head and neck.

Methods: In this cohort, 26 patients (14 men and 12 women) who underwent multiple microvascular free flap reconstructions were included in the study. The reasons for secondary reconstruction were recurrence of tumor (12 cases), necrosis of transferred skin and/or bone (6 cases), reconstruction plate fracture or exposure (4 cases), and others (4 cases). A third reconstruction in 4 cases and a fourth reconstruction in 1 case were performed.

Results: No flap necrosis occurred. Postsurgical infections occurred at only secondary reconstructions in 7 patients. Although 4 cases with a history of external radiation therapy were anastomosed at contralateral side, those 4 cases suffered from severe pre-and postsurgical infection of the ipsilateral side. Postsurgical infection occurred in 2 cases with anastomoses at the ipsilateral side of the neck and required drainage after secondary surgery.

Conclusions: A history of external radiation therapy and the existence of severe preoperative infection affected complications after multiple reconstructions. (*Plast Reconstr Surg Glob Open* 2017;5:e1337; doi: 10.1097/GOX.0000000000001337; Published online 13 June 2017.)

INTRODUCTION

Multiple free flap reconstructions are required in the surgical management of a second primary tumor, tumor recurrence, and complications, or in cases of previous flap failure.¹ Thus, multiple free flap reconstructions in the head and neck present a distinct technical challenge.² Difficulties can occur because of prior surgical scarring, postsurgical alteration of anatomy, intraoral or extraoral soft-tissue defects,³ and complications such as infection, draining fistulae, and poor vascularity of local tissue.¹ Also, in multiple reconstructive cancer surgeries, limitation of selective recipient vessels by previous neck dissection or radiotherapy hampers successful reconstruction.⁴

Previously, some researchers reported according to the recipient vessels, surgical conditions of side of the neck for vascular anastomosis and surgical complications following multiple free flap reconstructions. However, the

success rate of multiple flap reconstructions reportedly ranges from 28% to 95%^{1,5-7} in the literature with conflicting suggestions.⁸ Moreover, there have been few detailed studies on the complications associated with multiple free flap reconstructions in patients with a history of external radiation therapy to the head and neck.²

Surgeons should carefully consider the complications, quality-of-life outcomes, and especially the survival prognosis for the various treatments of advanced cancer before surgery.^{1,9} The objective of this study was to reassess the relationship between previous treatments, anastomosed vessels, side of the neck where anastomosis was performed, and complications following multiple free flap reconstructions in the head and neck.

MATERIALS AND METHODS

We retrospectively reviewed the medical records of 524 patients who underwent flap reconstruction for oral carcinoma at the Department of Oral and Maxillofacial Surgery, Tokyo Medical and Dental University Hospital between January 2004 and December 2016. In this cohort, 26 patients (14 men and 12 women) who underwent multiple microvascular free flap reconstructions were included in the study. The diagnoses were oral cancer in 25 cases and odontogenic tumor in 1 case. Secondary

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reconstruction was performed in 26 cases; a third reconstruction was performed in 4 cases, and a fourth reconstruction in 1 case. The observation endpoint was set as January 31, 2017. The median duration of follow-up was 84.5 months (range, 21–106 months). The median age at the time of the first reconstruction was 64.0 years (range, 47–87 years). The mean interval between the first and second reconstructions was 12.0 months (range, 1 day to 221 months), between the second and third reconstructions, 20.0 months (range, 7–138 months), and between the third and fourth reconstruction, 18.0 months.

The following factors were analyzed: the type of free flap, the side of the neck for vascular anastomosis (ipsilateral to the intraoral reconstruction side or contralateral), anastomosed vessels, history of neck dissection of the neck side for vascular anastomosis, and history of external radiation therapy of the anastomosed neck side. All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was performed with the approval of the ethics committee of Tokyo Medical and Dental University Faculty of Dentistry (number 1235).

RESULTS

Clinical Findings of 26 Cases

Reconstructions and Types of Flap

Among the 26 patients, the locations of excision were 17 cases of the lower gingiva, 1 case of the mandible, 4 cases of the buccal mucosa, 3 cases of the tongue, and 1 case of the floor of mouth. Histopathological diagnoses of surgical specimens at the first surgery were 23 cases of squamous cell carcinoma, 1 case of mucoepidermoid carcinoma, 1 case of low-grade myofibroblastic sarcoma, and 1 case of keratocystic odontogenic tumor (Table 1). Ten patients (10/26; 38.5%) who had undergone a first surgery at other institutions were referred to our department for secondary reconstruction (Table 1).

Secondary reconstruction was performed in 26 cases. Of these, there were 12 cases with tumor recurrence, and 12 cases had a failed first free flap requiring a second salvage free flap reconstruction (due to necrosis of the skin and/or bone in 6 cases, reconstruction plate fracture or exposure in 4 cases, and orocutaneous fistula in 2 cases). Also, modification surgery was performed in 1 case, and

secondary carcinoma was diagnosed in 1 case. The case of secondary carcinoma was diagnosed as squamous cell carcinoma of the lower gingiva after a left side segmental mandibulectomy and reconstructive surgery with a vascularized fibular osteocutaneous flap for keratocystic odontogenic intraosseous tumor of the mandible. A third reconstruction was performed in 3 cases with tumor recurrence and in 1 case with modification surgery, and a fourth reconstruction was performed in 1 case of tumor recurrence. The types of flaps were summarized in Table 1.

In this analysis, we excluded the 5 cases with a pedicle flap (4 cases of pectoralis major muscle and 1 case of latissimus dorsi muscle flaps) and analyzed 21 cases.

External Radiation Therapy

Preoperative external radiation was performed in 9 cases. Four cases received external radiation (mean dose, 52.5; range, 40.0–70.0 Gy), and 5 cases received chemoradiotherapy (cisplatin and Fluorouracil (5-FU), 2 cases; 5-FU, 1 case; others, 2 cases; dose of external radiation, 40.0 Gy; mean dose, 52.5; range, 40.0–50.0 Gy).

History of Prior Neck Dissections

The ipsilateral side had a history of suprahyoid neck dissection (cervical lymph node levels I, II) in 3 cases, supraomohyoid neck dissection (SOHND, levels I–III) in 3 cases and modified radical neck dissection (mRND, levels I–V) in 4 cases. The contralateral neck side had a history of suprahyoid neck dissection in 2 cases, SOHND in 2 cases, and mRND in 1 case.

Conditions of the Side of the Neck with Vascular Anastomosis

The details of anastomosed vessels at the second, third, and fourth reconstruction are shown in Tables 2–4, respectively.

At the second reconstruction, 9 of the 21 cases were anastomosed at the ipsilateral side. Of these 9 cases, 8 had a history of neck dissection (Table 2). At the second reconstruction, 12 of the 21 cases were anastomosed at the contralateral neck side. Of these 12 cases, 4 had a history of neck dissection (Table 2). In the “unknown” case of anastomosed cervical artery in Table 2, anastomosis at the second reconstructive surgery was performed using the radial artery, which had also been used at the first reconstructive surgery. The name of the cervical artery anastomosed to the radial artery was unavailable from the surgical reports.

Table 1. Types of Flap

Type of Flap	Operation			
	First	Second	Third	Fourth
Scapular osteocutaneous flap	9 (0)	8	1	
Scapular osteocutaneous flap + deltopectoral flap		1		
Scapular osteolattissimus dorsi myocutaneous flap			1	
Forearm flap	9 (6)	6		
Fibula osteocutaneous flap	4 (1)			
Rectus abdominis myocutaneous flap	2 (1)	6	2	
Latissimus dorsi myocutaneous flap	1 (1)	1		
Pectoral major musculocutaneous flap		4		
Anterolateral thigh flap	1 (1)			1

Values in parenthesis indicate cases where the first reconstruction was performed at other institutions.

Table 2. Conditions of the Anastomosed Neck Side (Analysis of 21 Vascularized Free Flaps at the Secondary Reconstruction)

Anastomosed Side (Cases)	Previous Neck Dissections (Cases)	Anastomosed Cervical Artery (Cases)	Anastomosed Cervical Vein (Cases)
Ipsilateral side (9)	○ 8	Transverse cervical (5) Superior thyroid (2) Unknown (1)	External jugular (4) Facial (2) Transverse cervical (1) Superior thyroid (1)
Contralateral side (12)	× 1	Facial (1)	External jugular (1)
	○ 4	Facial (2) Superior thyroid (2)	Facial (2) Internal jugular (1) External jugular (1)
	× 8	Superior thyroid (5) Facial (3)	Facial (4) Superior thyroid (2) External jugular vein + facial (2)

○, yes; ×, no.

Table 3. Conditions of the Anastomosed Neck Side (Analysis of 4 Vascularized Free Flaps at the Third Reconstruction)

Anastomosed Side (Cases)	Previous Neck Dissections (Cases)	Anastomosed Cervical Artery (Cases)	Anastomosed Cervical Vein (Cases)
Ipsilateral side (1)	○ 1	Facial (1)	External jugular (1)
	× 0		
Contralateral side (3)	○ 2	Facial (1) Superior thyroid (1)	Internal jugular (1) External jugular (1)
	× 1	Facial (1)	Facial (1)

○, yes; ×, no.

Table 4. Conditions of the Anastomosed Neck Side (Analysis of 1 Vascularized Free Flap at the Fourth Reconstruction)

Anastomosed Side (Cases)	Previous Neck Dissections (Cases)	Anastomosed Cervical Artery (Cases)	Anastomosed Cervical Vein (Cases)
Ipsilateral side (1)	○ 1	Facial (1)	External jugular (1)
Contralateral side (0)	× 0		

○, yes; ×, no.

In 8 cases anastomosed at the ipsilateral side with a history of neck dissection, the transverse cervical artery was used in 5 cases and the external jugular vein was used in 4 cases (Table 2). In the cases anastomosed at the contralateral side with a history of neck dissection, regardless of the frequency of reconstruction times including third and fourth reconstructions, the facial artery or the superior thyroid artery was selected for anastomosis (Table 3).

In cases anastomosed at the contralateral side with a history of neck dissection, various veins were used for anastomosis (Table 3).

All cases of external radiation therapy were anastomosed at the nonirradiated side of the neck.

Postsurgical Complications

Postsurgical complications occurred at sites of secondary vascularized free flap reconstructions in 7 patients with 8 complications. There were no postsurgical complications in the cases that had third and fourth reconstructions. The details are shown in Table 5.

In 2 flaps anastomosed at the ipsilateral side, infection occurred that required drainage. One case with a recurrence of lower gingival carcinoma had previously been diagnosed with oropharyngeal carcinoma and external radiation (70 Gy) was performed before the second re-

constructive surgery. Pathological fracture of the mandible and preoperative infection due to osteoradionecrosis had occurred before the secondary reconstruction in this case (patient 1). Another case was combined mandibular reconstruction plate exposure and presurgical infection (patient 2).

Composite subtotal mandibulectomy and resection of facial skin was performed in 1 case (patient 3) of recurrent lower gingival cancer with contralateral neck dissection. The oral mucosal and bone defect was reconstructed with a scapular osteocutaneous flap, and the middle facial skin defect was reconstructed with a deltopectoral flap. This case had venous thrombosis in branches of the internal jugular, which was salvaged with reanastomosis. Also, there was dead space between the scapular reconstructed bone, and the deltopectoral flap was infected and required drainage.

In flaps anastomosed at the contralateral side with no history of neck dissection, infection occurred in 3 cases (patients 4–6), and orocutaneous fistula occurred in 1 case (patient 7). Secondary scapular reconstructive surgery was performed in 1 case (patient 4) of postsurgical infection because of mandibular osteoradionecrosis after brachytherapy (total, 97.5 Gy) for cancer of the floor of the mouth. Three cases of postsurgical infection had a history of external radiation before the second reconstructive surgery (patients 5–7).

Table 5. Postoperative Complications

Patients	Anastomosed Neck Side	Postoperative Complication	Tumor Locations	Using Flap at Secondary Reconstruction	History of Neck Dissection at Anastomosed Neck Side	History of External Irradiation Therapy	History of Brachytherapy	Preoperative Infection	Cases Where First Reconstruction Was Performed at Other Institutions or by Previous Surgeons	
									○	○
1	Ipsilateral side (L)	Postoperative infection	Lower gingival (L)	Rectus abdominis myocutaneous flap	○ Level I-IV	70 Gy* (R)		○	○	
2	Ipsilateral side (R)	Postoperative infection	Lower gingival (R)	Rectus abdominis myocutaneous flap	○ Level I-V			○	○	
3	Contralateral side (L)	Vein thrombosis† Postoperative infection	Lower gingiva (R)	Scapula osteocutaneous flap + Deltopectoral flap	○ Level I-III			○	○	
4	Contralateral side (L)	Postoperative infection	Floor of mouth (R)	Scapula osteocutaneous flap	×	97.5 Gy		○	○	
5	Contralateral side (R)	Postoperative infection	Buccal mucosa (L)	Scapula osteocutaneous flap	×	40 Gy (L)		○	○	
6	Contralateral side (L)	Postoperative infection	Lower gingiva (R)	Scapula osteocutaneous flap	×	40 Gy (R)		○	○	
7	Contralateral side (R)	Orotocutaneous fistula	Tongue (L)	Forearm flap	×	50 Gy (L)		○	×	

*External irradiation for right-side oropharyngeal carcinoma.

†In branches of the internal jugular.

○, yes; ×, no; L, left; R, right.

Four of 7 cases were patients who received preoperative external irradiation therapy. No significant differences between preoperative external irradiation therapy and postsurgical complications were found (chi-square test, $P = 0.83$).

Prognosis

During follow-up, 19 patients (73.1%) remained alive and disease free, 6 patients had died (23.1%), and 1 patient was lost to follow-up. The disease-specific survival rate was 60.2% at 5 years.

CASE REPORTS

Case 1

A 62-year-old man was treated at the first surgery for lower gingival squamous cell carcinoma. The UICC TNM Classification of Malignant Tumours at the first diagnosis was T3N2b.

After induction chemoradiotherapy using a combination of a dose of 1,000 mg/m² of tegafur/gimeracil/oteracil (S-1) and 40-Gy radiation, ipsilateral lateral mRND and segmental mandibulectomy were performed and the bone defect was reconstructed with a vascularized fibular osteocutaneous flap. At this reconstructive surgery, the peroneal artery was anastomosed to the facial artery and the peroneal vein was anastomosed to the facial vein at the ipsilateral side. The bone paddle of the fibular flap became necrotic, and the necrotic fibular osteocutaneous flap was removed at postoperative day 28; a pedicled pectoralis major flap was successfully used for secondary reconstruction of the defect. At 1.5-year postoperative follow-up period, the mandibular bone defect was reconstructed by a scapular osteocutaneous flap for the third reconstructive surgery. At this surgery, the circumflex scapular artery and vein were anastomosed to the facial vein and artery, respectively, from the contralateral side of the neck. No perioperative complications occurred. Removable dental prosthesis was made, and masticatory ability for solid foods and satisfaction of oral functions improved.

Panoramic radiographs before and after the third reconstructive surgery and oral photographs before the third reconstructive surgery are shown in Figure 1.

Case 2

A 54-year-old man for whom the first surgery performed involved a left side segmental mandibulectomy and reconstruction with a vascularized fibular osteocutaneous flap for keratocystic odontogenic intraosseous tumor of the mandible. At this reconstructive surgery, the peroneal artery was anastomosed to the superior thyroid artery and the peroneal vein was anastomosed to the internal jugular vein at the left side of the neck. At 2 years and 3 months after reconstruction, 4 implants were replaced at the middle of the mandible. At the age of 58 years, a squamous cell carcinoma of the right side of the lower gingiva was diagnosed. At the second surgery, ipsilateral lateral mRND (right side), segmental mandibulectomy, and partial glossectomy of the right side were

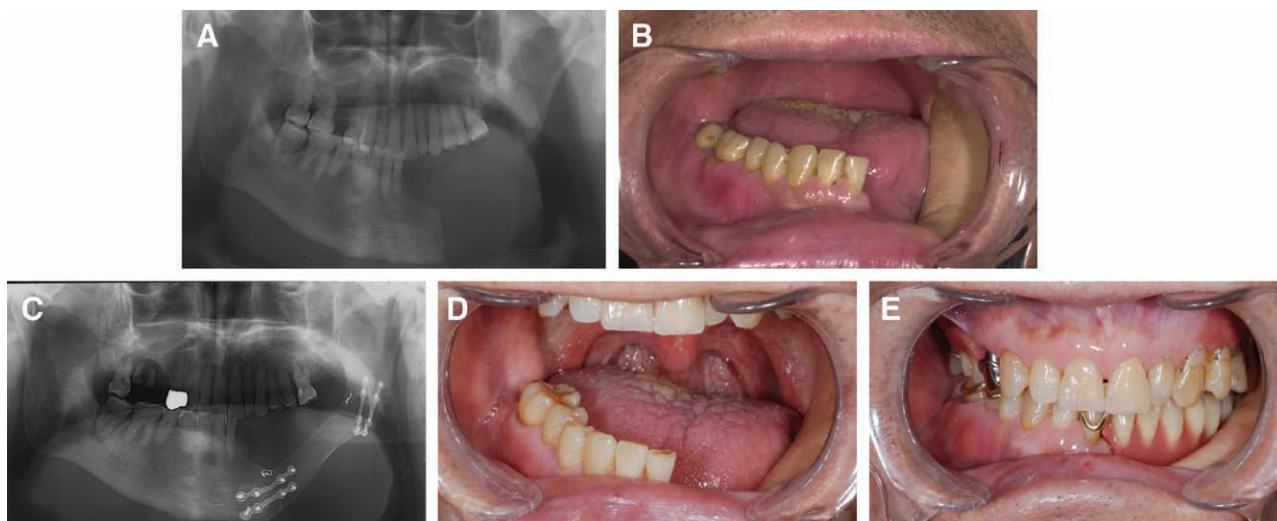


Fig. 1. Pre- and postoperative images of a third reconstructive surgery with a vascularized osteocutaneous scapular flap after the secondary surgery showing movement of necrotic fibular osteocutaneous flap and a pedicled pectoralis major flap. A, Panoramic radiograph before the third reconstructive surgery showing a mandibular defect of the left side. B, Oral photographs before the third reconstructive surgery showing displacement of the left lower teeth toward the lingual side. C, Panoramic radiograph after the third reconstructive surgery with a scapular osteocutaneous bone flap to the mandibular defect. D, Oral photographs after the third reconstructive surgery showing modification of the left side of the lower teeth position (at denture removal). E, Oral photographs after third reconstructive surgery showing normal occlusal position with denture in situ.

performed with reconstruction of the bone defect using a right-side vascularized scapular osteopectoralis major myocutaneous flap. The circumflex scapular artery was anastomosed to the superior thyroid artery, and the circumflex scapular vein was anastomosed to the common facial vein at the right side of neck. Adjuvant chemoradiation therapy (2 cycles of cisplatin and 5-FU2; dose of external radiation therapy to the right side of the neck, 50 Gy) was administered. At the age of 71 years, a lower gingival carcinoma of the mid-mandible reappeared. At the third surgery, SOHND at the left side of the neck, segmental mandibulectomy of the mid-mandible, and reconstruction of the bone defect with the left side of a vascularized scapular osteocutaneous flap were performed. The subscapular artery was end-to-end anastomosed to the facial artery, and the subscapular vein was end-to-side anastomosed to the internal jugular vein at the left side of the neck. There has been no evidence of tumor recurrence or cervical lymph node metastasis during the observation period.

Panoramic radiographs before and after the third reconstructive surgery are shown in Figure 2A–C. Oral photographs after flap modification at the fourth reconstructive surgery are shown in Figure 2D, and facial photographs after flap modification of at the fourth reconstructive surgery are shown in Figure 2E.

DISCUSSION

Anastomosed Vessels

Due to surgical resection of the cervical vessels during prior neck dissection and tissue fibrosis, the vessels in the ipsilateral neck were frequently not available.¹

When finding suitable vessels is difficult, the transverse cervical vessels in the ipsilateral side of the neck could be safely used as an alternative recipient site in some patients.¹⁰ In our cases, the transverse cervical vessels in the ipsilateral side of the neck were the most used, and all cases had no complications. If these ipsilateral vessels were not available, the contralateral neck vessels were evaluated, and alternatives such as the contralateral facial vessels, or the superior thyroid vessels were used.¹ The facial vessels and the superior thyroid vessels in the contralateral side of the neck were the most used with no flap complications in our cases.

Success Rate

In a previous study, flap success rate decreased as the number of reconstructive procedures with free flaps increased.⁸ In our study, 33.3% (7/21) of minor complications were observed at only the second reconstruction. Furthermore, at the third and fourth reconstruction, no complications occurred. As a result, we considered that the flap complication rate had no relation to the number of reconstructive procedures.

A previous study reported that among 71 cases of multiple flap reconstructions dehiscence/fistula occurred in 14 (20%), infection requiring treatment in 6 (8.5%), bleeding requiring reoperation in 2 (2.8%), among 28 cases (39.7%) of postsurgical complications.² In contrast to this report, the rate of minor complications in our study was not especially high.

Alam and Khariwala¹ recommended that anastomosed cervical vessels should be used from the noninfected side of the neck to prevent infection of the operative field because active infections and open wounds do not have

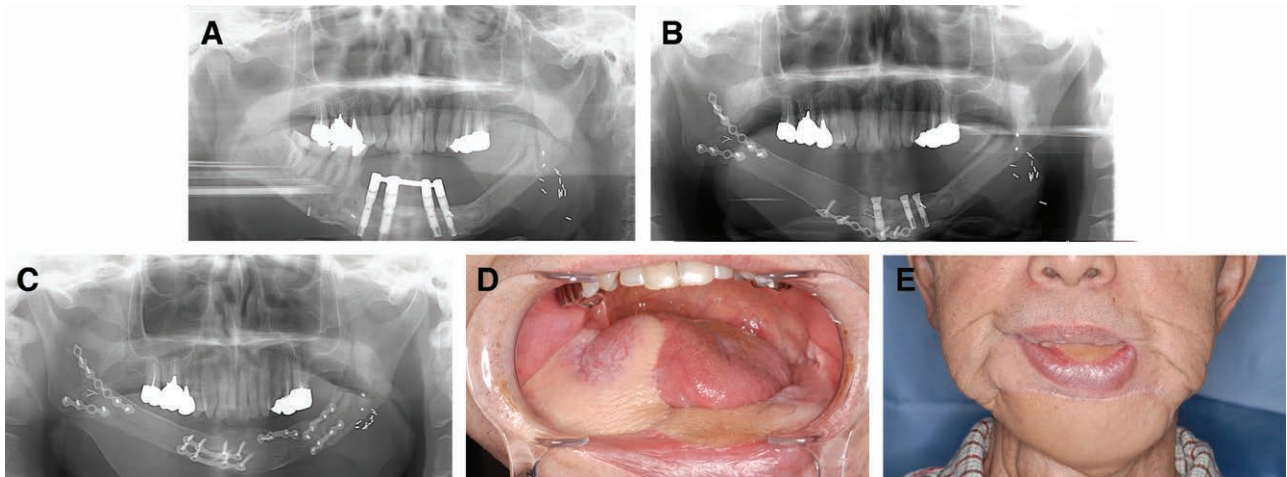


Fig. 2. Pre- and postoperative images of a third reconstructive surgery with vascularized scapular osteopectoralis major myocutaneous flap. A, Panoramic radiograph after the first reconstructive surgery showing a reconstructed fibular bone of the left side. Implants were replaced in the middle of the mandible. B, Panoramic radiograph after the second reconstructive surgery showing an initial reconstructed fibular bone of the left side and a secondary reconstructed scapular bone of the right side. Implants are removed. C, Panoramic radiograph after the third reconstructive surgery showing a reconstructed scapular bone after segmental mandibulectomy of mid-mandible. D, Oral photograph after the third reconstructive surgery showing scapular flap from the right side of the lower gingival mucosa to the right side of the lingual mucosa reconstructed at second reconstructive surgery and from the left side of the lower gingival mucosa to the left side of the lingual mucosa at third reconstructive surgery. E, Facial photograph after the third reconstructive surgery showing a reconstructed mental skin by pectoralis major myocutaneous flap.

healthy vessels. In our series, postsurgical infection occurred in 2 cases with anastomoses at the ipsilateral side of the neck and required drainage after secondary surgery. Because these 2 cases suffered from severe infection before secondary surgery, it is important to aggressively treat such infections with preoperative debridement and antibiotics pre- and postoperatively.

Radiotherapy induces interstitial and perivascular fibrosis,¹¹ and dissection of recipient vessels in irradiated tissue is difficult.^{11,12} Furthermore, microvascular anastomoses in irradiated vessels are occasionally not secure because of progressive intima fibrosis and arteriosclerosis of irradiated vessels.^{13,14} In our cases, all 9 cases that had received external radiation at the ipsilateral side of the neck were anastomosed at the nonirradiated side. This selection prevented from complications such as thrombosis and flap necrosis associated with anastomosed vessels. However, although statistical significance was not observed, 4 of 9 cases with a history of external radiation therapy and severe preoperative infection also suffered from severe postsurgical infection requiring drainage.

It has been reported that persistent infection in radiation-compromised tissue^{11,15,16} and complications after radiation therapy occur in up to 60% of surgical patients.¹¹

In cases with a history of preoperative radiation therapy and preoperative infection, the risk of wound infection might be high even if cervical vessels are anastomosed at the contralateral side because of the susceptibility of irradiated tissue and the dead space in the contralateral side of the wound.

There are few detailed studies on the complications of multiple free flap reconstructions in patients with a history of external radiation therapy to the head and neck^{2,17} and further detailed studies are needed.

Treatment Outcomes

Alam and Khariwala¹ reported that 63% of patients with cancer recurrence requiring a second free flap remained disease free and alive at a mean follow-up of only 13 months. However, as far as we detected, there were no reports on the disease-specific survival rate of free flap reconstructions in the head and neck. In our cases, the disease-specific survival rate was 60.2% at 5 years.

If improvements of patient survival prognosis and their oral functional problems by secondary reconstructions are expected, both patients and surgeons should carefully consider and discuss the process of flap reconstruction as previously suggested.^{1,9} Accumulation of such cases and further studies are needed.

CONCLUSIONS

We retrospectively studied patients who underwent multiple free flap reconstructions and assessed the surgical treatments, neck condition, and surgical outcomes following multiple free flap reconstructions in the head and neck.

In the cases with preoperative severe infection and with a history of preoperative external radiation therapy, surgeons should aggressively treat with preoperative debridement, pre- and postoperative antibiotic treatment, and prevention of dead space.

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