Early and late complications in the reconstructed mandible with free fibula flaps

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\textbf{Background and Objectives:} Evaluation of mandibular reconstructions with free fibula flaps. Identification of factors associated with major recipient site complications, that is, necessitating surgical intervention under general anaesthesia.

\textbf{Methods:} Seventy-nine reconstructions were included. The following factors were analyzed: fixation type, number of osteotomies, site of defect (bilateral/unilateral), surgeon, sex, ASA classification, continuous smoking, pathological N-stage, age, defect size, flap ischemic time, and postoperative radiotherapy. Proportional hazards regression was used to test the effect on the time between reconstruction and intervention.

\textbf{Results:} Sixty-nine (87\%) of the 79 fibula flaps were successful at the last follow-up. Forty-eight major recipient site complications occurred in 41 reconstructions. Nineteen complications required surgical intervention within six weeks and were mostly vascular problems, necessitating immediate intervention. These early complications were associated with defects crossing the midline, with an estimated relative risk of 5.3 (CI 1.1-20, $P = 0.01$). Twenty-nine complications required surgical intervention more than 6 weeks after the reconstruction. These late complications generally occurred after months or years, and were associated with smoking, with an estimated relative risk of 2.8 (CI 1.0-8.3, $P = 0.05$).

\textbf{Conclusions:} Fibula flaps crossing the midline have a higher risk of early major recipient site complications than unilateral reconstructions. Smoking increases the risk of late complications.

\textbf{Keywords:} early complications, free fibula flap, oral cancer, late complications, major recipient site complications, mandibular reconstruction

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1 | INTRODUCTION

Malignant and benign tumors, as well as infectious diseases or trauma can result in segmental defects of the mandible. The interruption of the continuity of the mandible, disruption of muscular attachments and loss of innervation of sensory and motor nerves can cause problems with mastication, swallowing, and speech.\(^1\) If a mandible is not reconstructed, considerable functional, aesthetic and social problems may result with consequently poor health-related quality of life.\(^2\)-\(^4\)

From both a functional and aesthetic point of view, immediate reconstruction is preferable.

The defect in the mandible can be bridged by a reconstruction plate. This is possible if sufficient soft tissue remains for watertight primary closure. Reconstruction plates are easy and quick to apply, but their drawback is the susceptibility for the occurrence of complications such as loosening of screws, plate fracture, plate exposure, and infection.\(^5\) Another way to reconstruct the mandible is by free vascularized osseous or osteocutaneous flaps. These flaps provide bone or bone with soft tissue to fill segmental defects. The functional and aesthetic results are often better than with reconstruction plates alone and free flaps with bone offer the possibility to place dental implants to facilitate dental rehabilitation. The fibula free flap is frequently applied for the reconstruction of segmental defects of the mandible. The fibula flap offers a long vascular pedicle with an adequate vessel diameter, a sufficient length of bone with reliable blood supply enabling multiple osteotomies to shape the transplanted segment, and thin and pliable skin.\(^6\)-\(^12\) However, the procedure is time-consuming and ablation combined with immediate reconstruction requires two surgical teams working simultaneously. The harvest of composite flaps is associated with a certain amount of donor-site morbidity.\(^13\) In addition, medical complications and complications at the recipient site frequently occur.

At our institution fibula free flaps have been used since 1999. The most serious complications require surgical re-intervention under general anaesthesia. These major complications occur mostly at the recipient site. These complications can occur early, within days or weeks after the reconstruction, but also much later, after months or even years. We noticed that early complications mostly are solved relatively quickly and rarely involve the fixation plating, except in extreme cases with flap loss. Late major recipient site complications are often preceded by prolonged attempts at conservative, non-invasive treatment to avoid surgery. These prolonged treatments are a heavy burden for the patient and for the hospital's resources in addition to the final surgical intervention. Late interventions nearly always involve removal of the fixation plating.

Some studies tried to elucidate risk factors for postoperative complications. They describe flap reconstructions of the mandible with other donor sites, such as radial forearm or iliac crest and/or different recipient sites in the head and neck area.\(^11\)-\(^12\) Few articles focused on reconstruction of the mandible with fibula free flaps.\(^9\)-\(^10\),\(^14\) However, these articles do not distinguish between recipient site and donor site complications, between moderate and major complications or between early and late complications.

This study aims to identify risk factors associated with early and late major complications at the recipient site after reconstruction of the mandible with fibula free flaps. For this we looked at complications with early and late interventions separately. We set the demarcation at 6 weeks, which is the time it takes for the free vascularized flap to integrate into the recipient bed, resulting in a stable union between the flap and graft.\(^1\),\(^15\)

2 | MATERIALS AND METHODS

The study was carried out at the Department of Oral and Maxillofacial Surgery, of the University Medical Center Utrecht, The Netherlands. The institutional medical ethical committee approved this retrospective study, the written informed consents were not required. All segmental mandibular defects reconstructed with free fibula flaps between September 1999 and June 2013 were identified from the departmental database. Clinical data were retrieved from the medical records.

Four maxillofacial head and neck surgeons (RvE, AR, RK, and EVC) performed the surgical procedures. Unlike the other three surgeons, RK was not involved in the reconstructive surgery, but only in the ablative surgery, while RvE, AR, and EVC performed both ablative and reconstructive procedures. In three cases a fellow in head and neck surgical oncology harvested the flap under supervision. Ablation was combined with immediate reconstruction and carried out by two teams working simultaneously. In all cases pre-operative angiography and Doppler examination of the lower leg was performed to assure adequate blood supply to the flap and its accompanying skin. The reconstructive team performed harvesting, contouring, and inset of the fibula flap. The minimum size of the fibula fragments measured 2.0 cm, as described by Bähr.\(^16\) Fixation of the fibula fragments was achieved with titanium fixation plates, type KLS Martin®. The type of fixation plate was determined by the preference of the surgeon responsible for the reconstruction. Three types were used: 2.7 mm locking reconstruction plates (n = 24); rigid 2.3 mm non locking plates (n = 13); and malleable 2.0 mm non locking miniplates (n = 42). The 2.3 plates were used from 2006 on. Fixation of the fibula fragments was performed before the microvascular anastomoses. The microvascular surgery was performed by the reconstructive surgeon, assisted by the ablative surgeon or a fellow. Low molecular weight heparin was given as deep venous thrombosis prophylaxis. Antibiotics were administered for at least 3-7 days postoperatively.

Major recipient site complications were defined as necessitating surgical intervention under general anaesthesia. The time between the reconstruction and surgical intervention was registered as well as the duration of the conservative treatment preceding the intervention, that is, the time between the first observation of the complication in the outpatient department and the surgical intervention. We also registered any manipulation of the fixation plating in the intervention, that is, whether it was removed, replaced, or otherwise adjusted. Follow-up was registered. To prevent bias by complications caused by (pre)prosthetic surgery follow-up stopped at the time of surgery for
the purpose of dental rehabilitation. At the last review appointment the fibula was examined by clinical examination and often by imaging. Success was defined as continuity of the bone in the absence of infection or plate related problems.

The following categorical factors potentially associated with the occurrence of complications were scored: type of fixation plate, number of osteotomies in the fibula, site of the mandibular defect, the reconstructive surgeon, sex, American Society of Anaesthesiologists classification, smoking, that is, continuous smoking during the follow-up; other patients were regarded as non-smokers. The \( (p)N \) stage was registered for cancer related mandibular defects. We registered the following continuous factors: age, size of the mandibular defect, ischaemic time of the fibula during surgery and total operative time.

Postoperative radiotherapy, if indicated, started within 6 weeks after the reconstructive surgery and lasted 6 weeks. To identify the effect of radiotherapy on major recipient site complications, we included only the complications later than 9 weeks after surgery, which is on average halfway the course of the radiotherapy.

For the analysis of the categorical factors we determined per category the number of reconstructions with which a (one or more) major complication occurred. For the continuous factors we determined their average values in the reconstructions with and without such complications. For the factor analysis we looked at major recipient complications with early interventions and late interventions separately. For this we registered the interventions within 6 weeks and also the interventions later than six weeks after the reconstruction of the mandible. Binary logistic regression was used to test whether the factors affected the occurrence of the complications. (IBM SPSS Statistics, version 21). A two tailed \( P \)-value equal or less than 0.05 was considered as statistically significant.

3 | RESULTS

Seventy-nine free fibula flaps were used to reconstruct the mandible in 76 patients, between September 1999 and June 2013. Cancer surgery was performed in 76 cases (74 squamous cell carcinomas, one chondrosarcoma, and one osteosarcoma), for osteoradionecrosis in one case and for osteomyelitis in two cases. Three patients had a second fibula flap after 15, 37, and 107 months, respectively, and were twice included in this study. One of these patients had a residual odontogenic carcinoma, one a second primary oral squamous cell carcinoma, and one had extensive oral field cancerization. In six cases osseous free fibula flaps without skin paddle were used. All other cases were osteocutaneous free fibula flaps. Follow-up ranged from 2 to 148 months with a median of 27 months. Two-year survival was 59%. In 16 cases without major recipient site complication follow-up stopped 4-30 months after the reconstruction because the patient died after the last visit. Seven patients were censored when they underwent (pre) prosthetic surgery, 17-37 months after the reconstruction. Of the 79 fibula flaps, 69 (87%) were successful at the last review appointment and 10 (13%) failed.

A total of 48 major recipient site complications occurred in 41 reconstructions (Table 1). In five fibula flaps, two or three complications occurred, the first of which always involved an early vascular problem. Nineteen complications required surgical intervention within 6 weeks. These early complications were mostly vascular problems, such as hemorrhage or venous congestion that necessitated immediate intervention. Insufficient blood supply of the skin island in five cases led to skin necrosis and surgical intervention, four of which within six weeks. One miniplate fractured and was removed with refixation of the flap 17 days after the reconstruction. Otherwise the fixation plating was involved in early interventions when the flap failed and was removed. This occurred in three cases (4%), respectively 7, 8, and 14 days after the reconstruction.

Twenty-nine complications required surgical intervention more than 6 weeks after the mandibular reconstruction. These complications were mostly infection or wound dehiscence. One case showed nonunion of the transplanted bone, 507 days after the reconstruction, and refixation was carried out. Osteoradionecrosis was observed in four cases. Another three fractured miniplates were discovered and removed. In one case the plate fracture had caused problems leading to

| Complications                  | N  | Intervention (weeks) | Time to intervention (days) | Conservative treatment (days) | Flap loss (days) |
|-------------------------------|----|----------------------|-----------------------------|------------------------------|-----------------|
|                               |    | ≤6                   | >6                          | Mean                         | Range           | Mean                         | Per flap |
| Arterial insufficiency/Venous congestion | 8  | 8                    | 0                           | 1.25                         | 0-3             | 0                            | 7, 8, 14 |
| Hemorrhage/hematoma           | 3  | 3                    | 0                           | 2.33                         | 1-5             | 0                            | 0        |
| Skin island necrosis          | 5  | 4                    | 1                           | 24                           | 13-52           | 13.4                         | 0        |
| Extraoral wound dehiscence    | 5  | 1                    | 4                           | 114.4                        | 28-374          | 28.6                         | 0        |
| Intra- and extraoral wound dehiscence | 4  | 0                    | 4                           | 203.5                        | 78-281          | 190.25                       | 202, 415 |
| Infection                     | 14 | 2                    | 12                          | 248.5                        | 16-1028         | 56.14                        | 150      |
| Plate fracture                | 4  | 1                    | 3                           | 649.5                        | 17-2100         | 141.75                       | 268      |
| Osteonecrosis                 | 4  | 0                    | 4                           | 663.5                        | 227-1070        | 76.75                        | 527, 986, 1070 |
| Nonunion                      | 1  | 0                    | 1                           | 507                          | 507             | 0                            | 0        |
| Total                         | 48 | 19                   | 29                          | 224.2                        | 0-2100          | 54.8                         | 10 flaps |
flap loss. In seven cases (9%) late surgical intervention led to flap removal. These flap failures were due to osteonecrosis (after 527, 986, and 1070 days), wound dehiscence (202 and 415 days), infection (150 days) and plate fracture (268 days). In nearly all late interventions the fixation plating was removed as by then bony union had been established.

Table 2 shows the effect of the categorical factors on the early complications that required intervention within 6 weeks. It shows per category the number of fibula flap reconstructions and the number of reconstructions in which a major recipient site complication occurred. Furthermore, it shows for each factor the results of a binary logistic regression analysis. The site of the defect (unilateral/bilateral; ie, crossing the midline) was significantly associated with the occurrence of these early complications ($P = 0.01$). The estimated relative risk of early surgical intervention in a fibula crossing the midline was 5.3 (CI 1.1-20) compared to a fibula not crossing the midline. The other categorical factors did not reach significance. None of the continuous factors; age, size of defect, ischaemic time during the surgical procedure, and total operative time, were associated with the early complications (Table 3).

Table 4 shows the effect of the categorical factors on the late complications that required intervention later than 6 weeks after the reconstruction. For the late complications we evaluated 76 fibula flap reconstructions, as three flaps had been lost due to early complications. Only continuous smoking was significantly associated with these late complications ($P = 0.05$). The estimated relative risk in smokers was 2.8 (CI 1.0-8.3) compared to non-smokers. None of the continuous factors was associated with the late complications (Table 5).

The effect of radiotherapy on the complications was analysed in 75 of the 79 reconstructions as three had failed before 9 weeks after the reconstructive surgery and in one patient the follow-up time was too short due to oncological reasons. Sixty-seven of the 75 reconstructions (87%) received radiotherapy and eight did not (13%). In 23 of the irradiated reconstructions (34%) a major complication occurred, and in just one of the reconstructions that was not irradiated (13%). The significance of the overall score of the logistic regression analysis was 0.211 with an estimated hazard ratio for postoperative radiotherapy of 3.7 (CI 0.4-32).

An example of a panoramic radiograph of a reconstruction of the right mandible, one year postoperatively, is shown in Figure 1.

### Table 2

Effect of categorical factors on early recipient site complications (within 6 weeks), requiring intervention

| Categorical factors | Categories | Number of flaps | Flaps with intervention ≤6 weeks (%) | $P$-value$^a$ | Rel. risk (CI) |
|---------------------|------------|-----------------|--------------------------------------|--------------|---------------|
| Fixation type       | 2.0 plate  | 42              | 8 (19)                               | 0.26         |               |
|                     | 2.3 plate  | 13              | 5 (39)                               |              |               |
|                     | 2.7 plate  | 24              | 4 (17)                               |              |               |
| # Osteotomies       | 0          | 28              | 5 (18)                               | 0.73         |               |
|                     | 1          | 33              | 7 (21)                               |              |               |
|                     | 2          | 18              | 5 (28)                               |              |               |
| Site of defect      | Unilateral | 36              | 3 (8)                                | 0.01*        |               |
|                     | Bilateral  | 43              | 14 (33)                              | 5.3 (1.1-20) |               |
| Surgeon             | 1          | 30              | 6 (20)                               | 0.77         |               |
|                     | 2          | 27              | 6 (22)                               |              |               |
|                     | 3          | 19              | 5 (26)                               |              |               |
|                     | Other      | 3               | 0 (0)                                |              |               |
| Sex                 | Male       | 51              | 8 (16)                               | 0.09         |               |
|                     | Female     | 28              | 9 (32)                               |              |               |
| ASA score           | 1          | 31              | 5 (16)                               | 0.12         |               |
|                     | 2          | 45              | 10 (22)                              |              |               |
|                     | 3          | 3               | 2 (67)                               |              |               |
| Smoking             | no         | 29              | 7 (24)                               | 0.67         |               |
|                     | yes        | 50              | 10 (20)                              |              |               |
| pN stage            | 0          | 30              | 6 (20)                               | 0.54         |               |
|                     | 1          | 15              | 5 (33)                               |              |               |
|                     | 2          | 30              | 6 (20)                               |              |               |
|                     | n/a        | 4               | 0 (0)                                |              |               |

$^a$Binary logistic regression, significance of overall statistics.
DISCUSSION

At the end of our observation 69 (87%) of 79 fibula flap reconstructions of the mandible were still in function and ten flaps (13%) were lost. A total of 48 major recipient site complications occurred in 41 reconstructions, meaning that some patients had 2 or even 3 surgical interventions. Seventeen flaps needed early surgical intervention within 6 weeks. Two of these even twice, but both flaps survived. Twenty-nine flaps needed surgical intervention later than 6 weeks after the reconstruction. Five of these flaps had survived early major complications and also survived the late intervention.

Fifteen of the early complications, about three-quarters, were of vascular origin, such as bleeding, venous congestion and insufficient perfusion of the skin island. Bleeding and venous congestion occurred within days after the reconstruction and necessitated immediate intervention. In three of these patients (4%) the flap could not be saved and had to be removed within two weeks after the reconstruction. Insufficient perfusion of the skin island was initially treated

| Continuous factors     | Range     | Intervention ≤ 6 weeks | Intervention >6 weeks | P-valuea |
|------------------------|-----------|------------------------|------------------------|----------|
| Age at surgery (yrs)   | 26.0-81.4 | 61.1 ± 11.3            | 62.2 ± 8.1             | 0.72     |
| Defect size (cm)       | 4.5-14.0  | 8.36 ± 2.18            | 8.05 ± 2.15            | 0.19     |
| Ischaemia (hrs)        | 1.5-5.0   | 2.82 ± 0.71            | 2.59 ± 0.39            | 0.58     |
| Operation (hrs)        | 7.0-15.5  | 10.6 ± 1.8             | 11.0 ± 1.7             | 0.38     |

*Binary logistic regression, significance of overall statistics.

4 | TABLE 3  Effect of continuous factors on early recipient site complications (within 6 weeks), requiring intervention

| Categorical factors     | Categories | Number of flaps | Flaps with intervention >6 weeks (%) | P-valuea | Rel. risk (CI) |
|-------------------------|------------|-----------------|--------------------------------------|----------|----------------|
| Fixation type           | 2.0 plate  | 42              | 15 (36)                              | 0.84     |                |
|                         | 2.3 plate  | 11              | 5 (46)                               |          |                |
|                         | 2.7 plate  | 23              | 9 (39)                               |          |                |
| # Osteotomies           | 0          | 26              | 8 (31)                               | 0.60     |                |
|                         | 1          | 32              | 14 (44)                              |          |                |
|                         | 2          | 18              | 7 (39)                               |          |                |
| Site of defect          | Unilateral | 36              | 12 (33)                              | 0.41     |                |
|                         | Bilateral  | 40              | 17 (43)                              |          |                |
| Surgeon                 | 1          | 29              | 11 (38)                              | 0.77     |                |
|                         | 2          | 25              | 8 (32)                               |          |                |
|                         | 3          | 19              | 9 (53)                               |          |                |
|                         | Other      | 3               | 1 (33)                               |          |                |
| Gender                  | Male       | 49              | 16 (33)                              | 0.18     |                |
|                         | Female     | 27              | 13 (48)                              |          |                |
| ASA score               | 1          | 31              | 13 (42)                              | 0.35     |                |
|                         | 2          | 44              | 15 (34)                              |          |                |
|                         | 3          | 1               | 1 (100)                              |          |                |
| Smoking                 | No         | 26              | 6 (23)                               | 0.05*    |                |
|                         | Yes        | 50              | 23 (46)                              |          | 2.8 (1.0-8.3)  |
| pN stage                | 0          | 27              | 12 (44)                              | 0.69     |                |
|                         | 1          | 15              | 6 (40)                               |          |                |
|                         | 2          | 30              | 10 (33)                              |          |                |
|                         | n/a        | 4               | 0 (0)                                |          |                |

*Binary logistic regression, significance of overall statistics.
conservatively, but led in five cases (6%) to skin necrosis and surgery to remove dead skin, 13–52 days after the reconstruction. The fibula flap is known to have a rather unreliable skin island, which depends on small and few septocutaneous and musculocutaneous perforating vessels.11,17 Our 4% early flap loss and 6% cases of skin island necrosis are similar to numbers reported in the literature.11,18 Reconstructions crossing the midline of the mandible appeared to have a significantly greater risk of early complications necessitating surgical intervention within 6 weeks (P = 0.01). The estimated relative risk of such early complications for a fibula flap crossing the midline was 5.3 (CI 1.1–20) compared to a unilateral fibula flap reconstruction. This finding is consistent with Lodders et al.,14 who described an increased risk for postoperative complications in continuity defects of the anterior mandible in reconstruction with fibular free flaps. The fact that the early complications were mostly of vascular origin suggests that it is harder to realize a stable blood supply in bilateral reconstructions than in unilateral reconstructions of the mandible. This may be explained by the increased complexity of bilateral reconstructions. They are often combined with a bilateral neck dissection necessitating a larger surgical wound than a unilateral neck dissection. Also in a bilateral defect a larger surgical defect is necessary for access to the mandible compared to true lateral defects. Furthermore, bilateral defects require detachment of the digastric muscle. Other studies have associated longer operation time (exceeding 10 h) with surgical complications.18–21 In our study cohort, the complexity of the bilateral reconstructions indeed led to significantly longer operative time than the unilateral reconstructions, 11.3 versus 9.9 h, P < 0.001. However, the total operative time was not significantly associated with major complications, early or late.

Twenty-nine fibula flaps needed surgical intervention later than 6 weeks after the reconstruction. These interventions took place months or years later, often following long periods of conservative treatment. Seven of these flaps (9%) were lost. These late interventions were due to other types of complications than the early interventions, as acute bleeding, thrombo-embolic complications and necrosis of the skin island no longer occurred. Twenty of the late interventions, about two-thirds, were due to infection or wound dehiscence. Three of these flaps could not be saved. Three more fractured miniplates were discovered and were removed, which in one case led to flap loss. Osteonecrosis occurred in four fibula flaps, three of which failed. Smoking appeared the only factor associated with late complications requiring surgical intervention (P = 0.05). The estimated relative risk of smoking was 2.8 (CI 1.0–8.3) compared to non-smoking. Cigarette smoke contains toxic constituents, like nicotine and other toxins such as carbon monoxide and hydrogen cyanide. These by-products cause an environment of relative tissue hypoxia, abnormal cellular function and thrombogenesis. Vasoconstriction is mediated directly and indirectly by nicotine, decreasing the available oxygen in tissues. The tobacco by-products interfere with the dynamics of normal wound repair. Smoking is also a risk factor for complications in head and neck reconstructions.22 Continuous smoking after reconstruction of the mandible causes a reduction in tissue perfusion, further amplified by diminished vascularization in case of postoperative radiotherapy. The authors believe that the vascular deprived reconstructed mandible, especially in postoperative, irradiated, continuous smokers is prone to complications, possibly even caused by invisible micro-damage. Cigarette smoking and tobacco use have been associated as contributing factors for postoperative surgical complications in head and neck free flap reconstruction.12,14,23 The necessity of smoking cessation is evident. More efforts should be made to stress the importance of smoking cessation. Physicians should support patients to quit smoking and/or refer patients to smoking cessation programs.

The late recipient site complications nearly always involved the fixation plating, which was removed or sometimes refixated in the intervention. It is not clear to what extent the fixation plating is affected by the complication or contributes to its origin. Our results do not indicate that the choice of fixation plating affects the risk of major

### TABLE 5 Effect of continuous factors on late recipient site complications (later than 6 weeks), requiring intervention

| Continuous factors     | Range     | Mean ± sd   | Mean ± sd   | P-value*  |
|------------------------|-----------|-------------|-------------|-----------|
| Age at surgery (yrs)   | 26.0–81.4 | 61.4 ± 11.8 | 61.3 ± 9.4  | 0.97      |
| Defect size (cm)       | 4.5–14.0  | 8.39 ± 2.12 | 8.21 ± 1.92 | 0.70      |
| Ischaemia (hrs)        | 1.2–5.0   | 2.78 ± 0.70 | 2.78 ± 0.63 | 0.99      |
| Operation (hrs)        | 7.0–15.5  | 10.5 ± 1.9  | 10.8 ± 1.6  | 0.44      |

*Binary logistic regression, significance of overall statistics.
recipient site complications. Two studies on free fibular reconstructions of mandibular defects showed no differences in complication rates between fixation with miniplates (≥2 mm) and reconstruction plates (≥2.7 mm).\textsuperscript{24,25} Plate fracture occurred in seven cases and always concerned miniplates located in the angle of the mandible. Four of these necessitated surgical intervention and were scored as major recipient site complications. Three plate fractures were incidental findings on a panoramic radiograph and were managed conservatively. Miniplates are easier to use than larger reconstruction plates. They are thinner and more pliable, but may be too weak to use in the mandibular angle region.

We expected postoperative radiotherapy to be associated with major complications of the fibula flap. The blood supply of the neomandible depends on relatively few vessels in the periosteum. This makes the neomandible particularly susceptible to irradiation that causes inflammation an endarteritis of blood vessels. However the association was not statistically significant. This is probably due to the case mix in our cohort, with only eight cases (11%) that were not irradiated. Conflicting data are reported regarding the effect of radiotherapy on late complication rates of free flaps in head and neck cancer patients. Choi et al\textsuperscript{26} and Deutsch et al\textsuperscript{27} found no significant differences in complications when comparing cases without radiotherapy with preoperative or postoperative irradiation. Shaw et al\textsuperscript{24} studied 143 mandibular reconstructions with flaps from various donor sites and found that postoperative radiotherapy strongly correlated with complications involving plate fixation.

In this study only 7 of 76 patients underwent (pre)prosthetic surgery for the purpose of dental rehabilitation. Six patients underwent dental implant surgery, with or without removal of fixation plates, and one patient had a vestibuloplasty in the neo-mandible. Three of these seven patients developed a major complication after the (pre)prosthetic surgery. In one case dental implants in the neomandible were lost due to peri-implantitis and dental rehabilitation could not be restored. In another case progressive disease (osteosarcoma) prevented further treatment. In the third case wound dehiscence caused loss of one implant, but a prosthesis could be placed on the remaining implants. Patients with advanced stages of oral cancer and reconstructed mandibles are nearly always additionally treated with radiotherapy and/or chemotherapy. The combination of these treatment modalities form an increased risk for impaired wound healing after secondary (pre)prosthetic surgery, despite precautions such as hyperbaric oxygen therapy. Therefore, the patient’s need and desire for dental rehabilitation must be weighed against the risk of complications after (pre)prosthetic surgery. This must be extensively discussed with the patient. Other studies show that a minority of patients with fibula flap reconstructed mandibles reach implant supported dental rehabilitation.\textsuperscript{9,28–30}

We rarely reconstruct the mandible with a free vascularized flap in patients with ASA classification 3. The poor physical condition of these patients increases the odds of developing postoperative adverse events.\textsuperscript{14,21} Nevertheless we did a fibula flap reconstruction of the mandible in three ASA 3 patients. We felt that in these cases there was no reasonable alternative with less chance of complications. In these patients there was not sufficient soft tissue to close the wound primarily with an acceptable functional outcome. A plate reconstruction in combination with a fasciocutaneous free flap is also prone to complications.\textsuperscript{30} A pedicled transposition flap to close a segmental mandibular defect is not an acceptable alternative anymore. Unfortunately, in all three ASA 3 cases the fibula flap failed. In two patients an early vascular complication occurred that led to flap loss after 7 and 14 days, respectively. In the third ASA 3 patient, osteonecrosis led to flap loss after 1070 days.

The retrospective design and the limited number of cases, 79 in 13 years, are limitations of this study. Larger sample numbers might reveal additional factors associated with recipient site complications. The small number of non-irradiated patients may have prevented to show more clearly the detrimental effect of radiotherapy on the healthy tissue of the neomandible. Cost effectiveness is of increasing importance in medicine, but was not taken into account in this study. It would be interesting to know, for example, the extra costs of the prolonged attempts to conservative treatment preceding late surgical interventions. Our institution is a university, teaching hospital. Participation of fellow head and neck oncology surgeons may have influenced surgical procedures and this could have influenced the results.

5 CONCLUSIONS

Major recipient site complications in mandibular reconstruction with free fibula flaps are common. Early complications, necessitating intervention within 6 weeks, are mainly of vascular origin. We found that they are associated with defects crossing the midline of the mandible that need relatively complex reconstructions. The later surgical interventions are predominantly caused by infection, wound dehiscence, osteonecrosis and plate fracture. These interventions are often preceded by months or even years of conservative treatment of the complications, that are associated with continued smoking. Smoking cessation will reduce the incidence of particularly late recipient site complications and should start immediately at the time of diagnosis and before surgical oncologic treatment.\textsuperscript{32} The different influence of risk factors on early and late complications in mandibular reconstruction with free fibula flaps has not been described before. The type of fixation plating appeared to have little effect on the occurrence of major recipient site complications. However, we advise against the use of miniplates in the angular region, because they may fracture during normal function of the jaw, when applied at that location.

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DISCLOSURE

The authors have no conflicts of interest to declare.
REFERENCES

1. Disa JJ, Cordeiro PG. Mandible reconstruction with microvascular surgery. Semin Surg Oncol. 2000;19:226–234.
2. Rogers SN, Lowe D, Fisher SE, et al. Health related quality of life and clinical function after primary surgery for oral cancer. Br J Oral Maxillofac Surg. 2002;40:11–18.
3. Rogers SN. Quality of life perspectives in patients with oral cancer. Oral Oncol. 2010;46:445–447.
4. Van Cann EM, Dom M, Koole R, et al. Health related quality of life after mandibular resection for oral and oropharyngeal squamous cell carcinoma. Oral Oncol. 2005;41:687–693.
5. Goh BT, Lee S, Tideman H, Stoelinga PJ. Mandibular reconstruction in adults: a review. Int J Oral Maxillofac Surg. 2008;37:597–605.
6. Wang KH, Inman JC, Hayden RE. Modern concepts in mandibular reconstruction in oral and oropharyngeal cancer. Curr Opin Otolaryngol Head Neck Surg. 2011;19:119–124.
7. Disa JJ, Hidalgo DA, Cordeiro PG, et al. Evaluation of bone height in osseous free flap mandible reconstruction: an indirect measure of bone mass. Plast Reconstr Surg. 1999;103:1371–1377.
8. Zoumalan RA, Hirsch DL, Levine JP, Saadeh PB. Plating in microvascular reconstruction of the mandible: can fixation be too rigid? J Craniofac Surg. 2009;20:1451–1454.
9. López-Arcas JM, Arias J, Del Castillo JL, et al. The fibula osteomyocutaneous flap for mandible reconstruction: a 15-year experience. J Oral Maxillofac Surg. 2010;68:2377–2384.
10. González García R, Naval Gisas L, Rodríguez Campo FJ, et al. Vascularized free fibular flap for the reconstruction mandibular defects: clinical experience in 42 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;106:191–202.
11. Urken ML, Buchbinder D, Costantino P, et al. Oromandibular reconstruction using microvascular composite flaps. Arch Otolaryngol Head Neck Surg. 1998;124:46–55.
12. Haughey BH, Wilson E, Kluwe L, et al. Free flap reconstruction of the head and neck: analysis of 241 cases. Otolaryngol Head Neck Surg. 2001;125:1057–1066.
13. Ling XF, Peng X, Samman N. Donor-site morbidity of free fibula and DCIA flaps. J Oral Maxillofac Surg. 2013;71:1604–1612.
14. Lodders JN, Schulten EAJM, de Visscher JGAM, et al. Complications and risk after mandibular reconstruction with fibular free flaps in patients with oral squamous cell carcinoma: a retrospective cohort study. J Reconstr Microsurg. 2016;32:455–463.
15. Taylor GI, Corlett RJ, Ashton MW. The evolution of free vascularized bone transfer: a 40-year experience. Plast Reconstr Surg. 2016;137:1292–1305.
16. Bähr W. Blood supply of small fibula segments: an experimental study on human cadavers. J Craniofac Surg. 1998;26:148–152.
17. Schusterman MA, Reece GP, Miller MJMD, Harris S. The osteocutaneous free fibula flap: is the skin paddle reliable? Plast Reconstr Surg. 1992;90:787–793.
18. Rosenberg AJ, Van Cann EM, Van der Bilt A, et al. A prospective study on prognostic factors for free-flap reconstructions of head and neck defects. Int J Oral Maxillofac Surg. 2009;38:666–670.
19. Serletti JM, Higgins JP, Moran S, Orlando GS. Factors affecting outcome in free-tissue transfer in the elderly. Plast Reconstr Surg. 2000;106:66–70.
20. Singh B, Cordeiro PG, Santamaria E, et al. Factors associated with complications in microvascular reconstruction of head and neck defects. Plast Reconstr Surg. 1999;103:403–411.
21. Eckardt A, Fokas K. Microsurgical reconstruction in the head and neck region: an 18-year experience with 500 consecutive cases. J Craniofac Surg. 2003;13:197–201.
22. Brands MT, Van den Bosch SC, Dieleman FJ, et al. Prevention of thrombosis after microvascular tissue transfer in the head and neck. A review of the literature and the state of affairs in Dutch Head and Neck Cancer Centers. Int J Oral Maxillofac Surg. 2010;39:101–106.
23. Van der Rijt EE, Noorlag R, Koole R, et al. Predictive factors for premature loss of Martin 2.7 mandibular reconstruction plates. Br J Oral Maxillofac Surg. 2015;53:121–125.
24. Shaw RJ, Kanatas AN, Lowe D, et al. Comparison of miniplates and reconstruction plates in mandibular reconstruction. Head Neck. 2004;26:456–463.
25. Robey AB, Spann ML, McAluliff TM, et al. Comparison of miniplates and reconstruction plates in fibular flap reconstruction of the mandible. Plast Reconstr Surg. 2008;122:1733–1738.
26. Choi S, Schwartz DL, Farwell DG, et al. Radiation therapy does not impact local complication rates after free flap reconstruction for head and neck cancer. Arch Otolaryngol Head Neck Surg. 2004;130:1308–1312.
27. Deutsch M, Kroll SS, Ainsle N, Wang B. Influence of radiation on late complications in patients with free fibular flaps for mandibular reconstruction. Ann Plast Surg. 1998;42:662–664.
28. Iizuka A, Häfliger J, Seto I, et al. Oral rehabilitation after mandibular reconstruction using an osteocutaneous fibula free flap with endosseous implants: factors affecting the functional outcome in patients with oral cancer. Clin Oral Implants Res. 2005;16:69–79.
29. Hundepool AC, Dumas AG, Hofer SOP, et al. Rehabilitation after mandibular reconstruction with fibula free-flap: clinical outcome and quality of life assessment. Int J Oral Maxillofac Surg. 2008;37:1009–1013.
30. Van Gemert JT, Van Es RJ, Rosenberg AJ, et al. Free vascularized flaps for reconstruction of the mandible: complications, success, and dental rehabilitation. J Oral Maxillofac Surg. 2012;70:1692–1698.
31. Piazza C, Grammatica A, Paderno A, et al. Microvascular head and neck reconstruction in the elderly: the University of Brescia experience. Head Neck. 2015;38:E1488–E1492.
32. Krueger JK, Rohrich RJ. Clearing the smoke: the scientific rationale for tobacco abstention with plastic surgery. Plast Reconstr Surg. 2000;108:1063–1073.

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