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Early Second Free Flap is Required in Osteoradionecrosis-related Nonunion after Primary Mandible Reconstruction

Richard Tee, MBBS, PhD, FRACS (Plast)*
Riccardo Schweizer, MD†‡
Cristina Gomez-Martinez-de-Lecea, MD*
Villiam Vejbrink Kildal, MD*†
Andreas Thor, DDS, PhD*†
Andres Rodriguez-Lorenzo, MD, PhD*†

Background: Osteoradionecrosis (ORN) manifested as symptomatic nonunion between primary free flap and native mandible after primary bony reconstruction of the mandible is an entity not included in current conventional ORN staging guidelines. This article reports on and proposes early management of this debilitating condition using a chimeric scapular tip free flap (STFF).
Methods: A retrospective review was performed examining cases with bony nonunion at the junction of primary free fibula flap (FFF) and native mandible at a single center over a 10-year duration, which required a second free bone flap. Details of each case (patient demographics, oncological details, primary surgery, presentation, and secondary surgery) were documented and analyzed. Outcomes of the treatment were assessed.
Results: Four patients (two men and two women; age range, 42–73 years) out of a total of 46 primary FFF were identified. All patients presented with symptoms of low-grade ORN and radiological signs of nonunion. All cases were reconstructed with chimeric STFF. The duration of follow-up ranged from 5 to 20 months. All patients reported resolution of symptoms and radiological evidence of union. Two of four patients subsequently received osseointegrated dental implants.
Conclusions: Institutional rate of nonunion after primary FFF requiring a second free bone flap is 8.7%. All the patients of this cohort presented with a similar clinical entity easily discounted as an infected nonunion postosseous flap reconstruction. There is no ORN grading system that currently guides the management of this cohort. Good outcomes are possible with early surgical intervention with a chimeric STFF. *(Plast Reconstr Surg Glob Open 2023; 11:e5024; doi: 10.1097/GOX.0000000000005024; Published online 15 June 2023.)*

INTRODUCTION

Nonunion of the primary bone flap for mandible reconstruction is a rather complex subject. Firstly, it is not a standard union of native bone edge to native bone edge (as in a fracture), but rather of the "pseudo-mandible."[1] It is now shown that, in contrast to a fracture site, the duration for complete union between the transplanted bone edge and the native mandible may be up to 3 years.[2] Secondly, the study of bone union is often radiological, and its clinical usefulness is not clear due to different criteria for assessment[3]; as a result, the true rate of nonunion that requires surgical intervention is not clear.

The authors were interested in reviewing and reflecting on cases of patients who received a second bone flap for the reason of nonunion. It was clear, however, during the data collection phase that this cohort of patients was not "simple" nonunion, but rather, a group with Notani grade III osteoradionecrosis (ORN).[4–7] The presence of a cutaneous fistula with nonunion is, technically speaking, an "ORN with skin fistula and pathological fracture," but can easily be discounted as infection after free osseous

*From the *Department of Plastic and Maxillofacial Surgery, Uppsala University Hospital, Uppsala, Sweden; †Department of Surgical Sciences, Uppsala University, Uppsala, Sweden; and ‡Department of Plastic Surgery and Hand Surgery, University Hospital Zurich (USZ), University of Zurich, Zurich, Switzerland.*

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flap nonunion. This is a difficult group of patients to diagnose, as neither Notani nor others who followed include patients who had osseous free flap reconstruction in their original description of ORN gradings.[4–7] Although the association of ORN and bony nonunion was observed in several published case series,[2,8] no in-depth analysis or focused discussion has been conducted on this topic to date. Instead, the studies only reported nonunion as a consequence of radiation. It was not until recently that ORN was discussed in detail in the context of primary bone flap reconstruction, yet the focus was on its predictive factors.[9]

This study began with a retrospective review of the local database, identifying a group of patients who required a second bony free flap after primary mandible reconstruction with free fibula osteocutaneous flap (FFOCF) for nonunion. The article will follow by presentation of a case series outlining the experience and outcomes in using a chimeric scapular tip free flap (STFF) for the management of this group of patients with Notani grade III ORN and radiological nonunion. Finally, the article will conclude with thoughts on this entity, the decision-making process, and technical nuances.

Takeaways

Question: What are the reasons for nonunion between primary fibula flap and native mandible in mandible reconstruction that subsequently require a second free flap in a Swedish microsurgical center?

Findings: All the cases of nonunion between primary fibula flap and native mandible requiring a second free bone flap are due to osteoradionecrosis (ORN). Treating it within less than 6 months of presentation of symptoms can yield good outcomes and limit prolonged suffering of a patient.

Meaning: Although not mentioned in existing ORN classification, ORN of the primary fibula flap and native mandible should be managed as a full-thickness ORN.

MATERIALS AND METHODS

A retrospective study was conducted after obtaining Swedish ethics review board (Etikprövningsmyndigheten) institutional review board approval. Written consent was obtained to use patients' images for publication, and the patients' data were handled in accordance with research ethics policies (ethical approval number Dnr 2019-04910/Dnr 2020-04848). We included all patients who received a second vascularized free osseous flap bone after primary free osseous mandible reconstruction between 2010 and 2020, whose indication is for nonunion.

Data Collection

For the ease of contributing to any future systematic or meta-analysis, the dataset proposed by Brown et al[10] was collected from electronic records and imaging databases. These include patients' demographics (age, comorbidities, smoking status, and preoperative dental status) and oncological details (pathology, staging, levels of cervical lymphadenopathy, and adjuvant therapy). Details of the first bony reconstruction include the laterality of defect, the extent and size of the defect (with anatomical description), recipient vessels, number of osteotomies, type of osteosynthesis, complications (Clavien-Dindo grading), and duration of intensive care unit (ICU) and inpatient stay. The details of the subsequent nonunion presentation (including the timing of presentation, the location of nonunion, and presenting symptoms) and the bone gap present at the first computed tomography (CT) scan postoperatively were measured. The details from the secondary free bony flap reconstruction recorded were components of flap, the dimension of bone required, recipient vessels used and its laterality, type of osteosynthesis, duration of surgery, duration of stay in ICU and as inpatient, and postoperative complications. Finally, various outcome parameters, including the resolution of symptoms, radiological evidence of bone union (as reviewed by a radiologist), and subsequent progression to osseointegrated implant dental rehabilitation were reported.

Surgical Technique

Patients were all positioned supine without position change intraoperatively. However, a two-team simultaneous approach is not usually possible for the reason of uncertain defect size after debridement. Tracheostomies were discussed and considered preoperatively, but the decision is usually made after the patient is in ICU postoperatively.

The nonunion sites were accessed with a submental incision directly over the neomandible. The incision crosses to the contralateral side to allow dissection of nonirradiated recipient vessels. Using this access, both ends of the neomandible were debrided to bleeding bone edge. A template was fabricated to plan the size and orientation of various components of the flap.

The markings and the operative technique used for the dissection of the chimeric STFF were previously detailed.[11] In brief, with the shoulder extended, an incision was made between the lateral border of the scapula and the edge of the latissimus dorsi (LD) muscle. The interval between the LD and teres major muscles was identified. Deep to the interval lies the angular branch of the thoracodorsal vessel, which supplies the scapular tip flap. The surrounding muscle attachments were released. Osteotomy was performed to obtain the desired bone stock. Finally, the LD muscle is harvested with the pedicle dissection into the subscapular system completed to obtain good pedicle length based on the template made. The detached muscles were then reattached using drill holes. Several steps taken to avoid complications in such a complex reoperation were discussed in a previous publication.[12]

RESULTS

Patient Demographics and Oncological Status

Between 2009 and 2020, a total of 46 cases of FFOCF were performed for primary mandibular reconstruction. A total of four patients who underwent free osseous flap

for bony nonunion of the primary reconstruction were identified. These include two men and two women, with a mean age of 56.5 years (range, 42–73 years). Other than patient 1 who had diabetes, the other three patients were relatively free of systemic morbidities that could impact the outcomes of the surgery. All patients were T4 in tumor staging, as expected, and received ipsilateral cervical lymphadenectomies. (**See table, Supplemental Digital Content 1,** which shows the patients' characteristics and oncological details, **http://links.lww.com/PRSGO/C577**.) All patients received standard adjuvant radiotherapy of 66 Gy to the intraoral primary site, and only patient 2 received additional adjuvant chemotherapy.

Primary Reconstruction

All patients were reconstructed with FFOCF in the first operation with the aid of virtual surgical planning. (**See table, Supplemental Digital Content 2,** which shows the details of the first bony free flap reconstruction of the mandible, **http://links.lww.com/PRSGO/C578**.) The defect reconstructed averaged 94.25 mm (range, 58–130 mm). As expected, in the longer defects (115 and 130 mm), two osteotomies were required. Multiple 2.0-mm low-profile titanium plates were used for fixation for all the cases. Two patients had Clavien-Dindo class III complications that required return to the operating room: one was an early abscess that required washout, and the other (patient 3) had a flap-related take-back that required arterial revision. Patients spent one night in ICU (except patient 2), and total inpatient duration averaged 13.25 days (range, 9–16 days). All patients except patient 2 received osseointegrated dental implants at approximately 23.3 months after surgery (range, 15–34 months). (**See table, Supplemental Digital Content 2, http://links.lww.com/PRSGO/C578**.)

Presentation of Symptomatic Nonunion and Details of Secondary Reconstruction

Patients presented with problematic nonunion between 5 and 35 months after the first surgery (Table 1). Interestingly, the patients who received osseointegrated dental implant developed symptoms within a month after placement (Table 1; **See table, Supplemental Digital Content 2, http://links.lww.com/PRSGO/C578**). The symptoms ranged from pain, cutaneous fistulas to exposed bone. The only patient who did not receive dental implants presented a month after completion of radiation therapy (Table 1; **See table, Supplemental Digital Content 1**, **http://links.lww.com/PRSGO/C577**). Other than patient 1, who is the earliest patient of the series, other patients received a chimeric STFF reconstruction within a year of symptomatic presentation (range, 3–7 months). All patients received a chimeric STFF design that includes the LD muscle (Table 1). The bone length harvested averaged 34.5 mm (range, 27–45 mm). All flaps were anastomosed to the contralateral neck recipient vessels. Operation time averaged 8.63 hours (range, 7.5–10 h). Other than patient 2, who had a postoperative tracheostomy that required three nights stay in the ICU, the rest of the patients stayed for one night only in the

Table 1. Details of Scapular Tip Free Flap Reconstruction for Osteoradionecrosis-related Nonunion

		Nonunion Presentation				Secondary Scapular Tip Free Flap Reconstruction							
Case No.	**Duration since First Surgery, Months (until the Presentation)**	**Location of Nonunion**	**Presenting Symptoms**	**Original Bone Gap after First Surgery**	**Time to Reconstruction**	**Flap Component**	**Length of Bone Required (L × H × Thickness, mm)**	**Recipient Vessel**	**Osteosynthesis**	**Operative Time (h)**	**Duration of Hospital Stay (day/s)**	**Intensive Care Admission (day/s)**	**Postoperative Complications (Clavien-Dindo)**
1	15	Posterior fragment and native mandible	Exposed bone, cutaneous fistula	3 mm	5 y	B,M	45×20×16	Ctr. STA and 1× IJV br.	2.4 mm locking plate	10	8	1	Nil
2	5	Anterior fragment and native mandible	Discharging cutaneous fistula	2.9 mm	7 mo	B,M	31×19.7×12.3	Ctr. FA and 1 × IJV br.	2.0 mm locking plate	7.5	16	3	II (tracheostomy)
3	21	Anterior fragment and native mandible	Swelling, pain cutaneous fistula	1.4 mm	3 mo	B,M	35×16×9.2	Ctr, LA and 1 × IJV br.	2.3 mm locking plate	9.5	12	1	Nil
4	35	Within anterior fragment	Pain at implant site	0 mm	5 mo	B,M	27×15×8.7	Ctr. STA and 1 × VC	2.3 m locking plate	7.5	10	1	Nil

B, bone; br., branch; Ctr, contralateral; FA, facial artery; IJV, internal jugular vein; LA, lingual artery; M, muscle; STA, superior thyroid artery; VC, venae comitantes.

Table 2. Outcomes of Scapular Tip Free Flap Reconstruction

Case No.	Resolution of Symptoms	Radiological Evidence of Bony Union	Osseo-integrated Implants (Y or N, Number of Implants, Time to Implants)	Dental Implant Retention	Duration of Follow-up after Scapular Tip (mo)
1	Y	Y (29 mo)	Y, 2 (38 mo)	Yes	40
2	Y	Y (7 mo)	Y, 3 (17 mo)	Yes	20
3	Y	Y (9 mo)	TBD	Not applicable	12
4	Y	Y (5 mo)	TBD	Not applicable	5

TBD, to be determined.

ICU. The total duration of admission averaged 11.5 days (range, 8–16 d). No patient developed significant surgical complications.

Outcomes of Scapular Tip Reconstruction

The duration of follow-up averaged 19.25 months (range, 5–20 mo) (Table 2). All patients reported complete resolution of symptoms and demonstrated radiological evidence of union (Figs. 1–3). Two of the four patients with longer term follow-up received osseointegrated dental implants and went on to dental rehabilitation (Table 2).

Case 1

A 42-year-old man presented with a right-sided well-differentiated squamous cell carcinoma (T4aN0M0) that requires a mandibular resection creating a 58-mm gap. (**See table, Supplemental Digital Content 1, http://links.lww.com/PRSGO/C577; see table, Supplemental Digital Content 2, http://links.lww.com/PRSGO/C578.**) An FFOCF was performed for the mandible reconstruction (Fig. 2A). Postoperatively, the patient received 66 Gy radiation in fractions of 2 Gy to the oral cavity and 50 Gy to the bilateral neck. Fourteen months after surgery, the patient received four osseointegrated dental implants. However, soon after the implants, the patient presented to clinic with exposed bone, a cutaneous fistula with radiological evidence of nonunion between the posterior fragment of the fibula flap and native mandible (Fig. 1). Two of the implants were removed. Almost a year later, after conservative

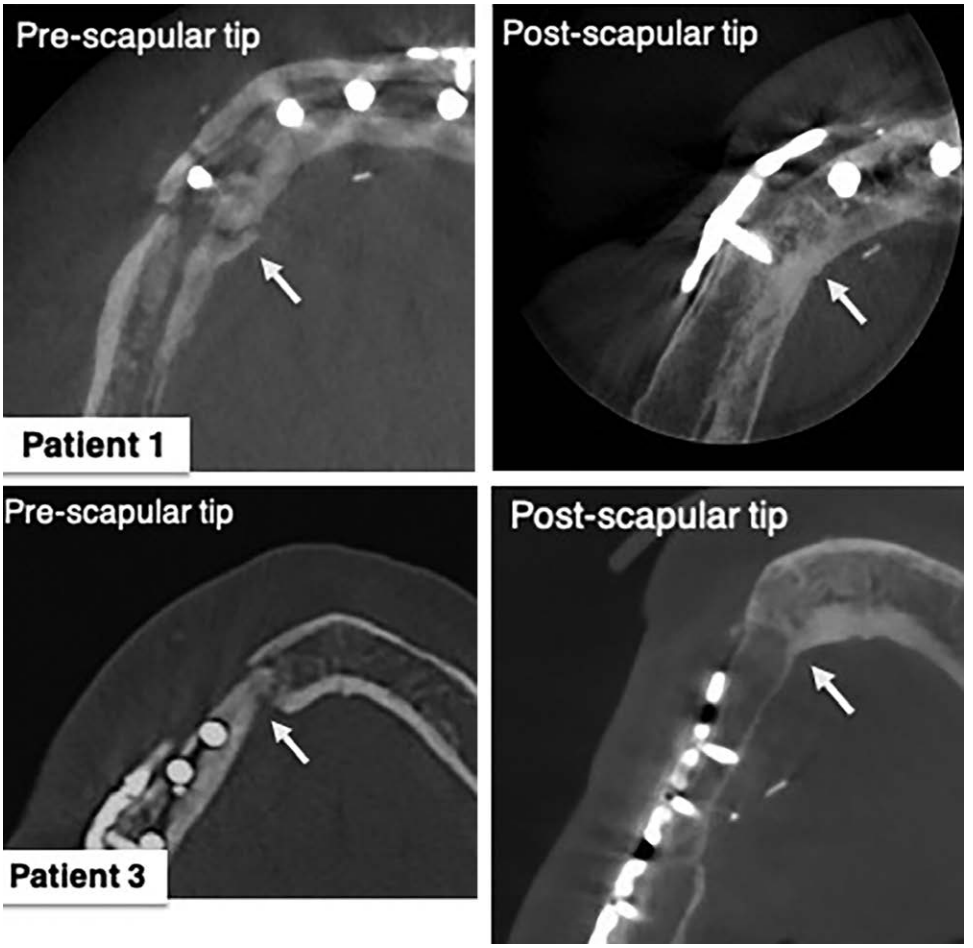

Fig. 1. Axial CT images of patients 1 and 3 pre- and postscapular tip free flap showing bone union.

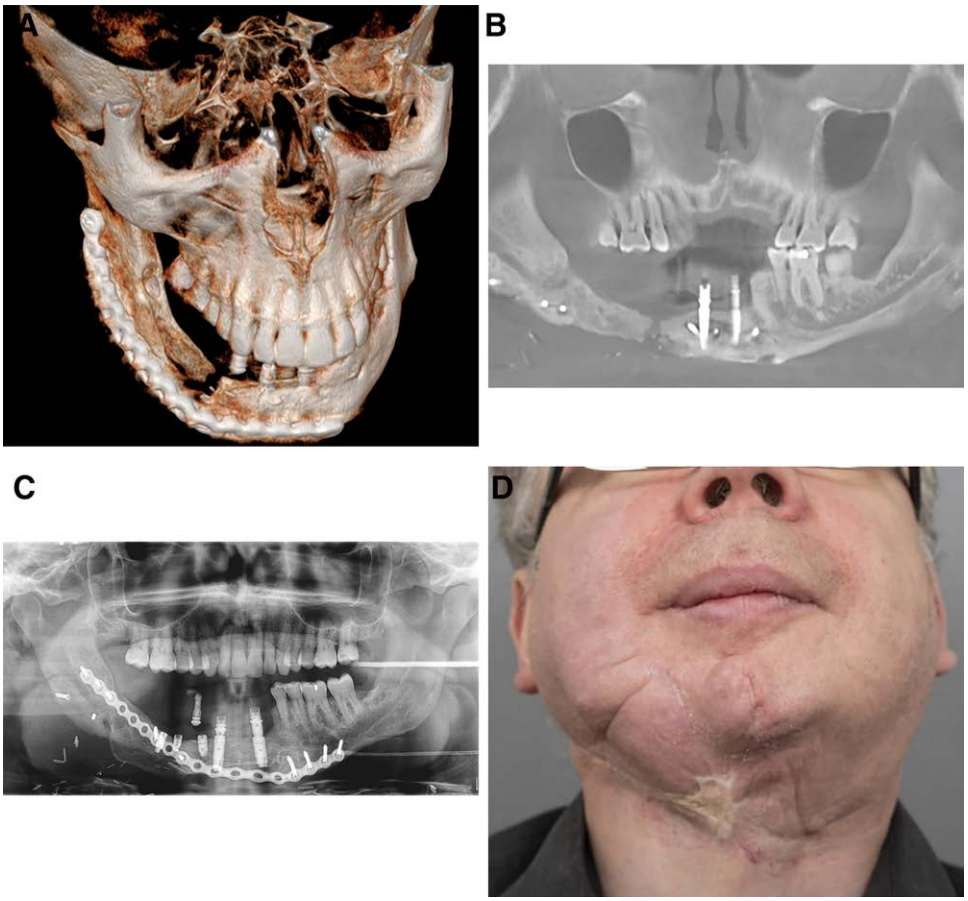

Fig. 2. Representative images for case 1. A-B, A 43-year-old patient with SCC (T4N0M0) of the right gingiva who underwent wide local excision, segmental mandibulectomy and level I-III neck dissection with a 58 mm bony defect reconstructed with a free fibula osteocutaneous flap. After postoperative radiotherapy, osteoradionecrosis of the fibula developed. This was first debrided, and non-vascularised bone graft was placed, which subsequently resorbed; two dental implants were lost in the process. C, After scapular tip bone flap salvage, bony union was achieved and two dental implants were successfully placed. D, The orocutaneous fistula was closed with acceptable aesthetic outcome.

therapy failed, a nonvascularized iliac crest bone graft was performed, which eventually failed with total bone resorption (Fig. 2A, B). Three years after primary procedure, after multidisciplinary head and neck meeting deliberation, consensus was reached for a secondary vascularized bony reconstruction. A chimeric STFF was performed, harvesting a 45×20×16 mm scapular bone and LD muscle for the soft tissue defect. The patient was admitted to the ICU overnight and discharged after 8 days of inpatient stay. At postoperative follow-up, the patient reported complete resolution of symptoms, and repeat CT scan showed bony union (Fig. 1). Thirty-eight months after scapular tip procedure, the patient received osseointegrated dental implants for the two previously lost (Fig. 2C, D).

Case 3

A 62-year-old woman presented to us with a well-to-moderately differentiated squamous cell carcinoma (T4aN0M0) on the right-sided alveolus, requiring a resection with a bone gap of 115 mm. (**See table, Supplemental Digital Content 1**, **http://links.lww.com/PRSGO/C577**; and **table, Supplemental Digital Content 2, http://links.lww.com/PRSGO/C578**.) An FFOCF was performed for the mandible reconstruction, two osteotomies (Fig. 3A). Postoperatively, the patient received adjuvant radiotherapy of 66 Gy in two fractions to the intraoral region. Eight months later, the patient developed a recurrence in the ipsilateral neck that required a radical neck dissection. Twenty-one months from the first surgery, the patient received three osseointegrated dental implants only to present within the same month with swelling, pain, and cutaneous fistula with subtle radiological evidence of nonunion between the anterior fragment and the native mandible (Figs. 1, 3B). An 18F-fluoride-labeled positron emission tomography/computed tomography was performed but showed viable bone (Fig. 3C). As the patient's symptoms persisted, the multidisciplinary team proposed a second bone flap for reconstruction. A chimeric STFF with 35×16×9.2 mm segment of bone and LD muscle was harvested (Fig. 3D–F). The patient was admitted to the ICU overnight with a tracheostomy and discharged

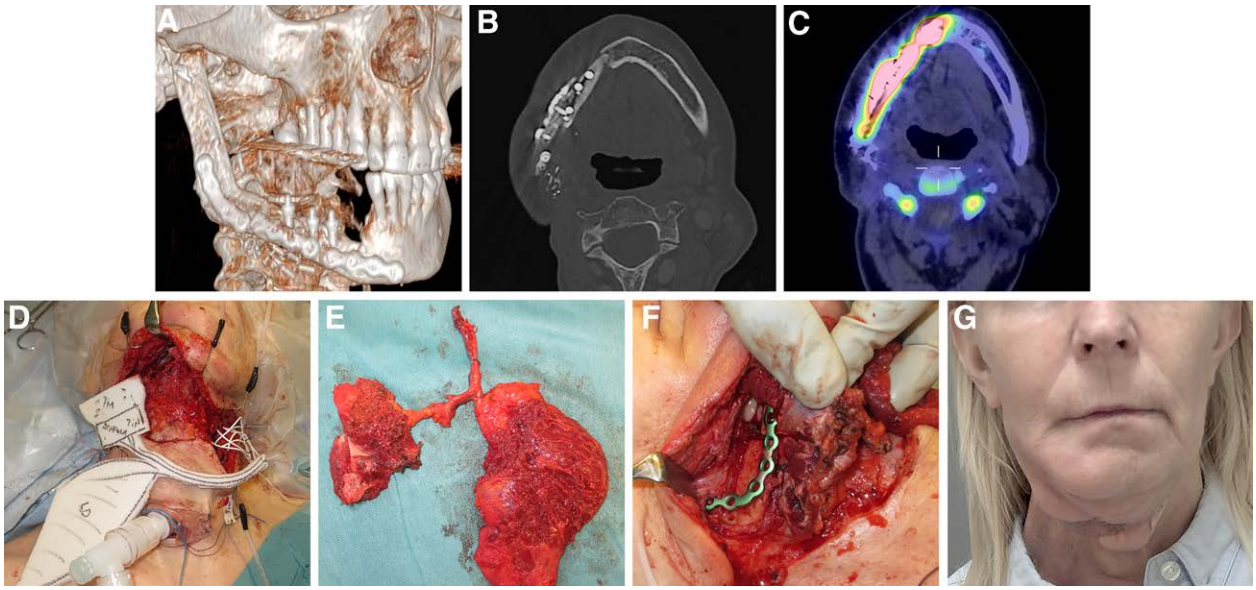

Fig. 3. Representative images for case 3. A, Dental implants were placed in a 62 year-old with SCC (T4aN0M0) of the premolar region after a segmental mandibulectomy defect reconstructed with a free fibula osteocutaneous flap 21 months post irradiation. B, An osteoradionecrosis related non-union developed at the juncture of the native mandible and fibula flap. C, 18Fluoride based PET showed viable bone around non-union site despite the clinical findings. D-F, A 35-mm chimeric scapular tip bone and latissimus dorsi muscle flap was performed. G, Appearance at 9 months. Radiological evidence of bony union was observed on CT (See Figure 1).

after 12 days of inpatient care. At 9-month follow-up, the patient reported complete resolution of symptoms and CT evidence of bone union (Fig. 1). The patient had follow-up at 12 months after surgery and has yet to decide on proceeding with dental rehabilitation.

DISCUSSION

Secondary bone flap reconstruction for long-term complications after primary bony reconstruction of the mandible is seldom reported.[13–16] This may be explained by a high success rate with a low nonunion rate reported.[10] However, it may also reflect the heterogeneity, the complexities, and the lack of a consistent approach to these secondary problems.[8,14–17] In the current article, the authors identified a small cohort of patients who required a second bony free flap for treatment of bony nonunion after primary FFOCF mandibular reconstruction (8.7%). Careful scrutiny of the data suggests that no patient received surgical intervention purely for nonunion without concurrent symptoms. All patients exhibited symptoms of pain/cutaneous fistula and radiological nonunion of the pseudomandible. All cases underwent successful secondary reconstruction with free chimeric STFF, achieving complete resolution of symptoms and radiological evidence of union. Two cases even proceeded to receive dental rehabilitation. The following discussion intends to document this clinical entity not clearly covered under existing ORN guidelines and outline some key experience obtained in the management of these patients and the versatility of the chimeric STFF in secondary reconstruction.

Upon reviewing the presentation and management of the patients presented, we observed that this group of patients all presented with ORN[7] (Fig. 4) with nonunion as the only radiological sign. This subset of patients was clearly not an ORN of the transplanted fibula, which subsequently fractured pathologically, but rather, the end of the fibular flap never unites across to the native mandible (or vice versa, or both). The presenting complaints were preceded, within a month, by either placement of osseointegrated implants or completion of adjuvant radiation, both known causes or predisposing factors for ORN.[6]

Based on current ORN classifications commonly cited,[4,6,18] unless full-thickness mandible is involved, a free bone flap is not indicated.[4,6,7,17] Some may even consider hyperbaric oxygen therapy (HBOT) as an option,[18,19] but its role (both primary or adjuvant) in both prevention and treatment of mandible ORN is questionable.[19] One of the reasons some may consider HBOT is the failure of existing ORN classification (Fig. 5) to include a nonunited free bone flap and native mandible juncture with ORN features. A critical review by Sultan et al[19] showed that the best evidence for HBOT for grade I and II Notani ORN of the mandible is limited. In our patient cohort, a nonunion site at this juncture should be considered full-thickness bone involvement (Notani grade III). However, the evidence behind this entity is even more lacking, and in view of cost and prolonged suffering of the patient, HBOT was not considered in our patient series. The necrotic material discharging out of the location of nonunion reflects active necrosis and poor vascularity. Considering that the healing of a pseudomandible is already tenuous,[1,2] healing is unlikely to be achieved when managing as a Notani low-grade ORN or as an infection. Furthermore, in light of the recent understanding of the natural history of pseudomandible bone union, this may be interpreted as an expected benign finding.[2] The first case was managed as such, until debridement revealed a

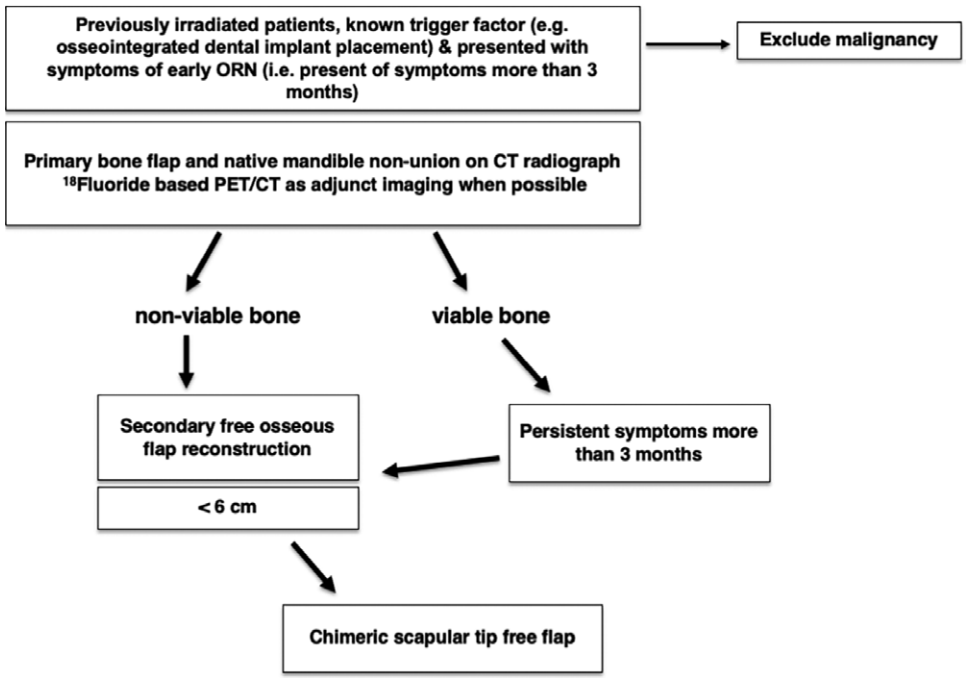

Fig. 4. Flow chart summarizing the common thread of the case series. The authors proposed early intervention with a secondary free bone flap in a patient with this characteristic.

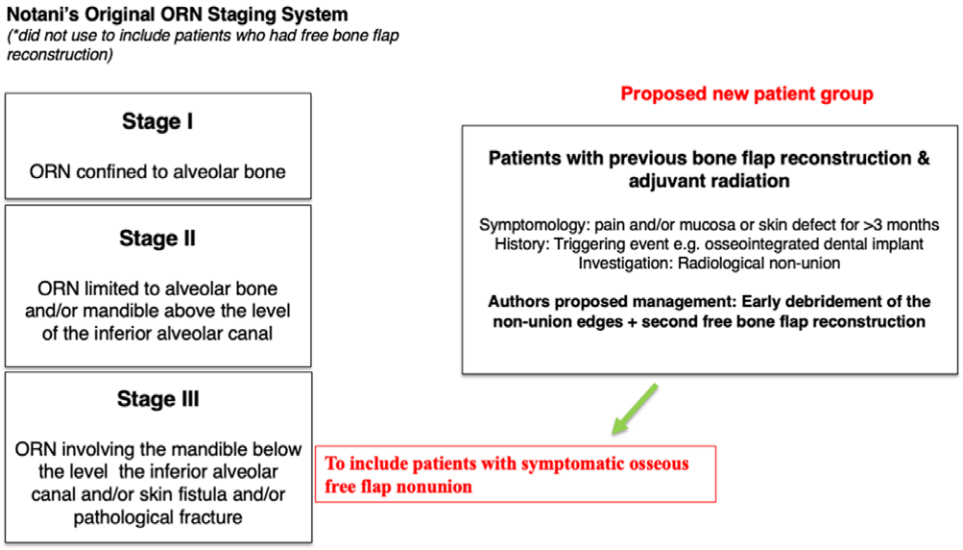

Fig. 5. Original Notani et al three stages of ORN of the native mandible did not include patients with free bone flap reconstruction. This current case series argues that this small subset of patients with symptomatic nonunion at the interface of native and transplanted bone flap, practically speaking, belongs to stage III, which is essentially a "fractured" mandible and will need a second bony free flap reconstruction.

wider extent of poorly perfused bone, in which treatment with a nonvascularized bone graft subsequently failed.[20] It is interesting to find this unique entity (consisting of radiological nonunion and symptoms of early ORN) mentioned in several case series previously, albeit in small numbers, but its association has never been drawn.[8,9,17] Successful management of these patients with vascularized chimeric STFF led the authors to consider patients with this profile as a different entity and to propose a more aggressive treatment pathway to avoid prolonged suffering (Figs. 4, 5). Thus, cases 2–4 were managed with a second free flap as soon as possible.

Interestingly, although earlier experience of 18F-fluoride-based positron emission tomography/computed tomography imaging[21] seemed promising in detecting and defining the extent of ORN,[22] it was not effective

in the third patient (Fig. 3C). Because ORN is a diffuse process, it is likely that the density threshold was not reached for it to be radiologically apparent,[5] despite a debridement to bleeding edge still yielding a 35-mm bone gap. A clinical decision should thus be made based on clinical symptoms (Fig. 5). However, understanding the postulated disease process as described earlier aided in intervening at an earlier disease stage. Bone gap will likely be shorter (27–35 mm), and delivery of external biological source for vascularization could potentially salvage the adjacent bone from deterioration.

Several factors usually deter surgeons from proceeding with surgical intervention. These factors include reoperating in an irradiated primary surgical field, patient morbidity,[12,23] and limitations/morbidity of a second bone flap.[24] Furthermore, these are usually deconditioned,[25] demanding, and frustrated patients who have endured prolonged symptoms with no improvement, giving strength to the authors' proposal for early intervention. This case series illustrates how the chimeric STFF appears to be an ideal flap for such complex secondary surgery that can reduce the weight of the aforementioned deterrents. The STFF is based on the thoracodorsal vessel, which is a long pedicle that can reach healthy recipient vessels in the contralateral neck, with no vein grafts were required in this series. A chimeric STFF can include the LD muscle and/or a fasciocutaneous component, with great mobility independent of the bone, if desired. This can cover the expected soft tissue defect on both the irradiated neck[8,12,15] and inevitable intraoral tear of the friable mucosa during the manipulation of the resected nonviable mandible. Figure 6 shows the author's technique of addressing both defects using only a single LD muscle. The harvest is technically easy and morbidity free.[23,26] In addition, the risk of atherosclerosis is less common in the subscapular system compared with the peroneal artery, making it more appealing in the older population.[27] In complex secondary defects, this removes several aspects of the complexity, with a robust flap conducive to uneventful healing.

One could argue that a second fibula flap may be an option. Indeed, if the subsequent ORN defect exceeds 6 cm, a free fibula flap may be more appropriate (Fig. 4). However, it is clear in the literature, although low in general, a free fibula flap is not without its morbidity,[28] particularly in an older head and neck oncology population.[12] Using a scapular flap preserves the future option of a free fibula flap. In addition, it allows for early mobilization of the patient without restrictions, avoiding risk of thromboembolic complications. The argument of having a two-team approach in a secondary reconstruction is less persuasive, because the process of defining the defect of ORN is not as arduous as primary resection of the tumor. Furthermore, in the authors' experience, the scapular tip can be harvested in a supine position without requiring a position change.

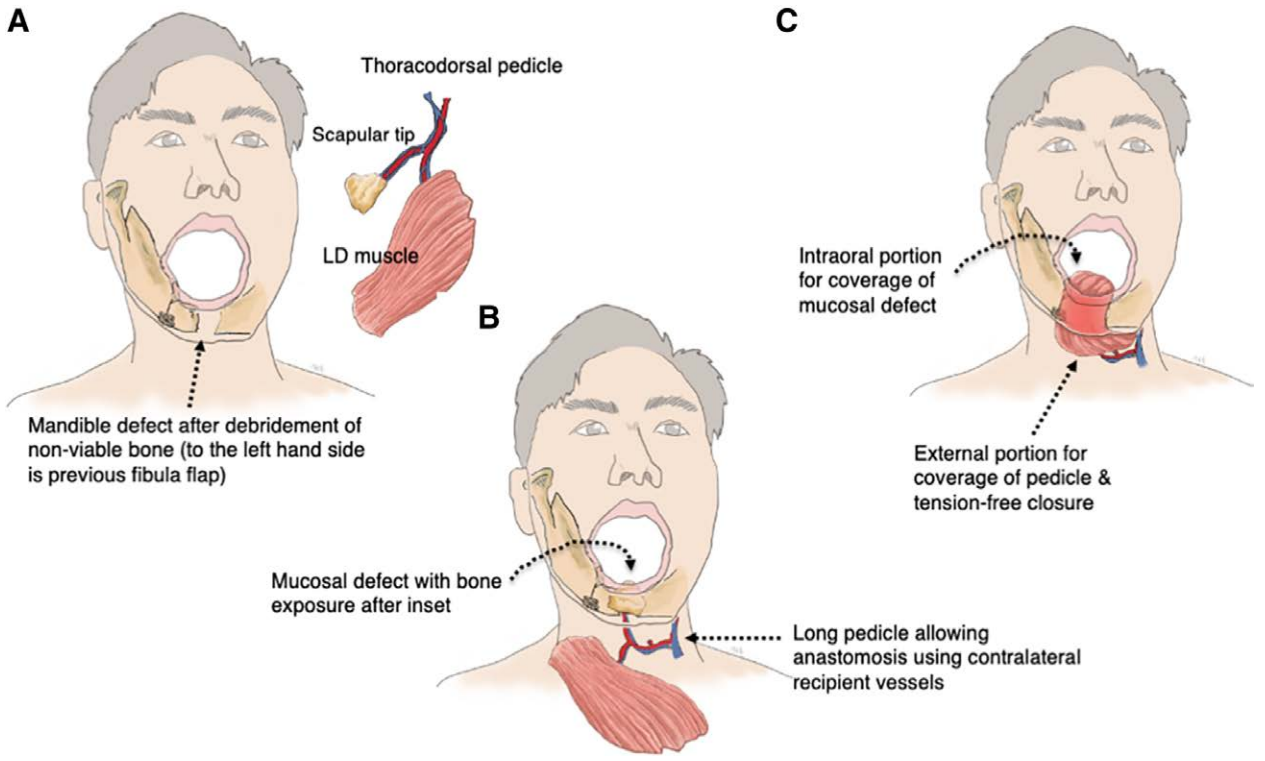

Fig. 6. Authors' technique to obtain coverage of external skin and intraoral mucosal defect with single LD muscle. A, Adequate debridement of the non viable bone at the bone flap and native mandible junction. B, After bone flap inset, there is usually a mucosal defect and external skin defect. C, The single LD muscle can cover both the external skin defect and intraoral inset avoiding tension closure and simply the inset in an already complex case.

The limitations of the study are the small number of patients and its retrospective nature. However, in an era of reconstructive microsurgery when success rates of reconstruction are high overall, a small number of difficult cases will need to be pooled for worthwhile discussion. ORN may still occur years after reconstruction, and currently, duration of follow-up does not preclude the possibility of ORN recurring,[25] but with clear evidence of bone union (Fig. 1), it is unlikely.

CONCLUSIONS

The head and neck surgical team should be mindful of the association of symptomatic nonunion and low-grade ORN symptoms, as highlighted in the case series presented. Based on this case series, clinical suspicion should prompt further investigations and multidisciplinary discussion with the goal of early surgical intervention. Chimeric STFF is an ideal flap for these complex secondary reconstructions and has produced good outcomes for the patients in all four cases.

Richard Tee, MBBS, PhD, FRACS (Plast)
Ingang 85, 3 tr
Uppsala, Sweden
E-mail: richard@prsmelbourne.com.au

DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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