

Fibula Free Flap for Mandibular Reconstruction using Simulation Surgery in Bisphosphonate related Osteonecrosis of the Jaw

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Purpose Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is an emerging problem. Extensive osteonecrosis of the jaw needs free flap reconstruction. Free fibular flap is the most useful flap for maxilla-mandibular hard and soft tissue reconstruction. The advantages of fibular free flap are simultaneous soft and hard tissue reconstruction and placing implant in reconstructed mandible and maxilla. In this study, four consecutive BRONJ patients who underwent fibula free flap reconstruction using simulation surgery were reviewed.

Materials and Methods Four BRONJ patients who underwent free fibula reconstruction between May 2006 and September 2014 were included in this study. Male to female ratio was 1:3 and average age was 67.3 years old (62-70). All patients need mandibular bone reconstruction. Three patients suffered from osteoporosis and one male patient had multiple myeloma. Postoperative flap survival, functional reconstruction, esthetic results, food taking were evaluated.

Results Three osseous flaps and one osteocutaneous flap were used. All the fibular flaps were survived and patients were recovered without complications. Oro-cutaneous fistula was resolved after operation. All patients were satisfied with the esthetic results. Patients reported improved solid food intake after operation with partial denture. One fully edentulous patient had semi-fluid diet after operation.

Conclusion Treatment of the BRONJ is difficult due to lack of standard protocol. Fibular free flap using simulation surgery is the workhorse flap for mandibular hard and soft tissue reconstruction, especially in stage III BRONJ patient. In this study, functional and esthetic results were successful in all patients. Normal diet was possible with partial dentures.

Key Words 3D RP model · Simulation surgery · Fibula free flap · Reconstruction · BRONJ.

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Introduction

Bisphosphonates-related osteonecrosis of the jaw (BRONJ) is an emerging problem and it was first reported in 2003 (1). The typical signs of BRONJ are exposed bone over 8 weeks, pus discharge, formation of sequestrum, skin fistula and pathologic fracture of the jaw bone. Initiation of BRONJ is related with dental procedures such as dental extraction, preprosthetic procedure, dental implant surgery and denture wearing (2). However, BRONJ could be occurred without any evident causes. Bisphosphonates are world widely prescribed drugs for osteoporosis, metastatic cancer from breast and prostate cancer, hy-

percalcemia and multiple myeloma patients (3, 4). Intravenous bisphosphonates has a 100-10,000 fold potency compared with oral drugs. Most of the BRONJ patients received intravenous bisphosphonates. Common symptoms of BRONJ are teeth mobility, pain and swelling. Treatment protocol has been suggested from American association of oral and maxillofacial surgeons to improve patients' quality of life (5, 6). The first step is to stop using bisphosphonates and conservative treatment. Mouth gargle with chlorohexidine and periodic dental care is the first aid for BRONJ. However, BRONJ has been progressed to the basal bone; resection of the sequestrum is needed for reducing pain and further pathologic fracture (4).

Extensive osteonecrosis of the jaw needs segmental resection of the jaw bone and free flap reconstruction. Free fibular flap is the most useful flap for maxilla-mandibular hard and soft tissue reconstruction (7-11). The advantages of fibular free flap are simultaneous soft and hard tissue reconstruction and placing implant in reconstructed mandible and maxilla. However, it takes many hours to adapt straight fibular bone into the jaw bone with segmentation. Because extended ischemic time is related with flap failure, it is mandatory to expedite the operation and reduce surgical time for re-anastomosis.

One of the most efficient ways to reduce operation time is simulation surgery (12). Surgical stent and 3D RP model give lots of clue and ideas before surgery. Prebended titanium reconstruction plate could be easily adapted after mandibular resection during surgery. In this study, 4 consecutive BRONJ patients who underwent fibular free flap reconstruction using simulation surgery were reviewed.

Materials and Methods

Four consecutive BRONJ patients who underwent free fibular reconstruction between May 2006 and September 2014 were included in this study. Inclusion criteria for free fibula reconstruction are stage III BRONJ patients who have signs of pathologic fracture of the mandible, destruction of mandibular inferior border or extraoral skin fistula. Stages of BRONJ are described in Table 1.

Male to female ratio was 1:3 and average age was 67.3 years old (62-70). All patients need mandibular bone reconstruction.

Three patients suffered from osteoporosis and one male patient had multiple myeloma. Patient's demographic data and bisphosphonate usage are described in Table 1. Postoperative flap survival, function such as speech, mastication, swallowing and esthetic results were evaluated. The study was conducted in accordance with the ethical principles provided by the Declaration of Helsinki and the principles of good clinical practice. Because of the retrospective study with de-identification of the patient's data, Asan medical center IRB(Institutional review board) exempted ethical review of this study.

Results

Flap survival

Three osseous fibula flaps and one osteocutaneous fibula flap were used for mandibular bone defect. All the fibula flaps were survived and patients were recovered without complications. Oro-cutaneous fistula was resolved after operation. Patients with dentition had maintained intermaxillary fixation (IMF) for 4 weeks. One edentulous patient did not receive IMF. Liquid and soft diet had been taken for 4 weeks. Mouth opening exercise was started 4 weeks after operation.

Functional results and esthetics

Gait exercise was started 1 week after operation. All patients could walk as before 4 weeks after operation. Mouth opening exercise was encouraged 4 weeks after operation in dentate patients. Edentulous patient could open his mouth right after operation. All patients were satisfied with the esthetic results. Ex-

Table 1. Stages of bisphosphonate related osteonecrosis of the jaw

Stages	Description
At risk	No apparent necrotic bone in patients who have been treated with either oral or intravenous bisphosphonates.
Stage 0	There is no clinical evidence of necrotic bone, but there are nonspecific clinical findings and symptoms such as swelling of the soft tissue, fistula formation.
Stage 1	There is exposed and necrotic bone in asymptomatic patients but there is no evidence of infection
Stage 2	There is exposed and necrotic bone associated with infection as evidenced by pain and erythema in region of exposed bone with or without purulent drainage
Stage 3	There is exposed and necrotic bone with pain, infection and one or more of the following: exposed and necrotic bone extending beyond the region of alveolar bone resulting in 1) pathologic fracture, 2) extraoral fistula, 3) oral antral/oral-nasal communication or 4) osteolysis extending to the inferior border of the mandible or sinus floor.

Table 2. Patient characteristics

Sex/age	Diagnosis	Bisphosphonate usage	Stage	Fracture
F/69	Osteoporosis	AD p.o. for 4 Years	3	No
F/68	Osteoporosis	AD, RD p.o. for 2 Years	3	No
F/62	Osteoporosis	PD injection. 1 time	3	Yes
M/70	MM	ZD & PD injection for 2.5 Years	3	No

AD: alendronate, RD: risedronate, PD: pamidronate, ZD: zoledronate, p.o.: per os, MM: multiple myeloma

Table 3. Postoperative complications and follow-up periods

	Recipient site complications	Post op Prosthodontics/Diet	Other complications	Follow-up
1	None	Denture (RPD)/Soft Diet	Fracture of plate	8 Y 3 M
2	None	Denture (RPD)/Soft Diet	None	1 Y 6 M
3	None	Denture (RPD)/Soft Diet	None	12 M
4	None	None/Liquid Diet	None	7 M

traoral fistula was disappeared after operation and no patient reported recurrence of cutaneous fistula during follow-up period. Patients reported improved solid food intake after operation with partial denture. Two patients had reported preoperative malocclusion which was resolved after operation. One fully edentulous patient had semi-fluid diet after operation. No patient showed dysphasia after operation. One patient showed fracture of the miniplate during follow-up. Occlusion was the same as before, so no further treatment had been performed. (Table 3) There was no problem for swallowing in all patients.

Case Presentation

A 70-year-old male was referred from department of hemato-oncology for treating exposed bone in the mandible (Fig. 1). Patient had suffered from multiple myeloma for 7 years. His past medical history included diabetes mellitus for 10 years. He found multiple myeloma during regular follow-up laboratory examination. After bone marrow aspiration, plasmacytic type multiple myeloma was diagnosed. He received pamidronate and zoledronate for 2.5 years every 4 weeks. Symptoms of BRONJ started from January 2013 such as teeth loosening, mandibular bone exposure and pus discharge. He visited our department in July 2013. Anterior mandibular bone was exposed and anterior teeth of the mandible were extracted spontaneously. Patient complained about teeth loss, pus discharge, foul odor and pain. After consultation with hemato-oncologist, he was recommended to receive symptomatic treatment for BRONJ. On 22th July 2013, debridement of the anterior mandible and extraction of the remaining teeth was performed under general anesthesia. Patient reported decreased pain after operation for 10 months; however mandibular basal bone was exposed during follow-up periods. Patient presented pus discharge and extraoral fistula in September 2014.

BRONJ was progressed to the basal bone of the mandible and oro-cutaneous fistula was occurred (Fig. 2, 3). BRONJ stage III was diagnosed and extensive surgery was planned after medical consultation and patient's consent.

3D RP model was made before surgery (Fig. 4). Simulation surgery was performed to confirm the extent of the mandibular resection and reconstruction plate bending before surgery.



Fig. 1. Anterior mandibular bone necrosis due to intravenous bisphosphonate injection.



Fig. 2. Progression of the BRONJ to the basal bone of the mandible.



Fig. 3. Extraoral discharge of pus in the lower mandible.

Mandibular angle to angle was planned to resect (Fig. 5). Reconstruction plate (Leibinger, San Diego, USA) was bent according to the ideal contour of the mandible. Baseplate wax was designed for fibula free flap.

Operation was performed under general anesthesia on 24th

September 2014. Skin incision was made in the neck including skin fistula. Mandible was exposed and resected according to the simulation surgery. Reconstruction plate was applied and fixed with bicortical screws.

Left side fibular was harvested (Fig. 7). Free osseous flap was elevated without skin paddle. A total of 13 cm was harvested

and osteotomized according to the simulation surgery. Two sites were cut and bent according to the contour of the mandible.

Free fibula flap was inserted into the mandibular defect and fixed with bicortical screws (Fig. 8). Righth side superior thyroid

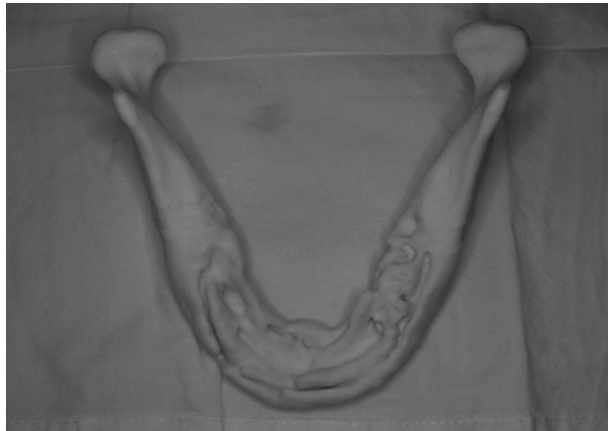


Fig. 4. 3D RP model of the mandible.



Fig. 5. Simulation surgery of mandibular resection and fibula free flap reconstruction.



Fig. 6. Reconstruction plate was fixed after mandibular resection.



Fig. 7. Elevation of the free fibula flap in the left side.



Fig. 8. Free fibula flap fixed with bicortical screws.



Fig. 9. Comparison of the resected mandible and simulated 3D RP model.



Fig. 10. Intraoral photograph showing complete healing of the mucosa without bone exposure.

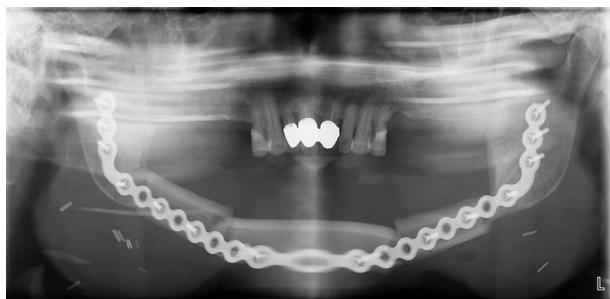


Fig. 11. Postoperative panoramic radiography showing reconstructed mandible from mandibular angle to angle.

artery was used for feeding artery and two branches of the internal jugular vein were anastomosed with venae comitantes.

Resected mandible was compared with simulation surgery (Fig. 9). The dimension was nearly same with the simulated 3D RP model. Total length of the resected mandible was 13 cm.

Intraoral fistula and exposure of the bone was resolved and there was no skin fistula in the neck (Fig. 10). Patient was satisfied with the result about esthetics. Patient could not wear denture in the mandible and wanted implant-supported prosthodontics. Patient could eat soft diet without any dysphasia.

Panoramic radiograph showed reconstructed mandible with fibula flap fixed with reconstruction plate and bicortical screws (Fig. 11).

Discussion

Bisphosphonates are a potent drug which is effective in treating metastatic bone lesion, Paget's disease, multiple myeloma and osteoporosis (4). Bisphosphonate reduces pathologic fracture, hypercalcemia and bone pain. Bisphosphonates are related with inhibition of osteoclast through RANKL receptor binding. The early symptoms consist of bone exposure, pain

and swelling of the inflamed mucosa. When BRONJ progressed into the basal bone, pathologic fracture, pus discharge and cutaneous fistula could be formed. The incidence of the BRONJ has been reported as between 0 to 28% (13-17). The incidence of the BRONJ in oral bisphosphonates were reported as a minimal risk. BRONJ is more commonly associated with intravenous injection; however, in this report, three patients mainly took oral bisphosphonates. Oral bisphosphonates has been taken once in a week or a month. Oral bisphosphonates are prescribed to treat pain in osteoporosis patients. The potency of oral bisphosphonates is far less than intravenous bisphosphonates. It has been recommended to prescribe less than 3 years in the clinical base, however, two of our patients received for 4 years and 10 years. It has been known that the risk of BRONJ is increased 3 years after prescription. The risk of BRONJ should be recognized by medical doctors who prescribe bisphosphonates for osteoporosis and warned patients for long-term use.

BRONJ could be occurred without any surgical interventions, however, most of the BRONJ is associated with invasive dental procedure such as dental extraction, surgical removal of the bone exostosis and dental implant surgery (2). Patient who is scheduled to use bisphosphonates should visit dental clinic before medication. Hopeless teeth and causes of periodontal disease should be treated before bisphosphonates medication. Regular follow-up of the patient is required who regularly receives intravenous bisphosphonates.

Surgical intervention of BRONJ should be approached prudently. Debridement is easy with surgical bur, however primary closure is hard to achieve. The inflamed tissues are not easy to suture and usually shortage of the soft tissue always cause re-exposure of the bone. In the maxilla, buccal fat could be lined over the bone and layered suture is possible. In the mandible, usually primary suture is not easy and exposure of the bone causes progression of BRONJ.

Stage I and II BRONJ should be treated conservatively. Even in stage III patient, to reconstruct with free flap has rise a controversy because of possible delayed healing in the donor site (8, 9, 18, 19). Bone flaps such as iliac crest free flap, fibular free flap and scapular flap expose normal bone tissue which has a possibility to cause BRONJ in other bones. Especially in multiple myeloma, the possibility of malignant cell transfer to the reconstructed mandible raises a concern. However, there are no report about BRONJ in the donor site and progression of the multiple myeloma in the grafted area. Long-term follow-up of the patient is required to confirm progression of the disease.

Complication rate of the fibula free flap reconstruction in BRONJ patient is higher than other oncologic patients. Hanasano et al. reported 46% (11). In our study, there was no compli-

cations after operation. Patients were all satisfied with their results and function of the mandible was restored. Malocclusion was the chief complaint in one patient who showed pathologic fracture of the mandible. Restoring occlusion require meticulous design of the surgical resection margin and reconstruction plate application. One millimeter gap results in postoperative discomfort of the patient. IMF with arch bar and mouth opening exercise with guidance are mandatory for dentate patient.

Conclusion

Fibula free flap is the workhorse flap for maxilla-mandibular hard and soft tissue reconstruction. Simulation surgery using 3D RP model makes operation efficient and reduces operation time. In this study, functional and esthetic results were successful in all patients. Normal diet was possible with partial dentures.

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