Atrophic Mandible Fractures: Are Bone Grafts Necessary? An Update

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Purpose: The management of atrophic mandibular fractures poses a challenge because of anatomic variations and medical comorbidities associated with elderly patients. The purpose of this article is to review and update the literature regarding the management of atrophic mandible fractures using load-bearing reconstruction plates placed without bone grafts.

Materials and Methods: We performed a review of the English-language literature looking for atrophic mandibular fractures with or without continuity defects and reconstruction without bone grafts. Included are 2 new patients from our institution who presented with fractures of their atrophic mandibles and had continuity defects and infections. Both patients underwent reconstruction with a combination of a reconstruction plate, recombinant human bone morphogenetic protein 2, and tricalcium phosphate. This study was approved as an "exempt study" by the Institutional Review Board at the University of Kentucky. This investigation observed the Declaration of Helsinki on medical protocol and ethics.

Results: Currently, the standard of care to manage atrophic mandibular fractures with or without a continuity defect is a combination of a reconstruction plate plus autogenous bone graft. However, there is a need for an alternative option for patients with substantial comorbidities. Bone morphogenetic proteins, with or without additional substances, appear to be a choice. In our experience, successful healing occurred in patients with a combination of a reconstruction plate, recombinant human bone morphogenetic protein 2, and tricalcium phosphate.

Conclusions: Whereas primary reconstruction of atrophic mandibular fractures with reconstruction plates supplemented with autogenous bone graft is the standard of care, in selected cases in which multiple comorbidities may influence local and/or systemic outcomes, bone morphogenetic proteins and tricalcium phosphate can be used as a predictable alternative to autogenous grafts.
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In 2010 our group published our experience with the management of atrophic mandible fractures (AMFs).[1] We summarized the outcomes of using large load-bearing reconstruction plates placed without the addition of bone grafts for both unilateral and bilateral atrophic edentulous body fractures. Although controversial, we believed that bone grafts were not always necessary to treat these patients. The exception would be patients with severe atrophy or those with a continuity defect.

In our previous article, a bilateral AMF was presented, in which treatment with the off-label use of recombinant human bone morphogenetic protein 2 (rhBMP-2) and a large reconstruction plate was

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successful.[1] The patient, who had several comorbidities, was an elderly woman whose initial injury was the result of a fall.

The use of bone morphogenetic protein (BMP) with or without additional substances for the management of AMFs and/or continuity defects remains controversial. The purpose of this article is to review the literature and present 2 more cases of geriatric patients with AMFs and continuity defects, both of whom had infections and went on to successful healing with a combination of a reconstruction plate, rhBMP-2, and tricalcium phosphate.

Review of Literature

During the past 7 decades, numerous modalities for treating AMFs have been proposed.[1-41] This diversity of techniques is an indication of the difficulties incurred during and after treatment. Surgical management is further complicated by comorbidities, physical and/or mental status, and compromised vascular supply of the atrophic mandible in most of these patients.[2,5,7,12,14] For edentulous mandibles, as with all traumatic injuries, alignment of segments and dental rehabilitation are implicit in the functional restoration to the premorbid state.

The use of reconstruction plates for mandibular defects started in the 1960s[36] and became popular when the titanium-coated hollow screw and reconstruction plate system was developed.[39-41] The universal locking plate appeared later as an improved version. Almost simultaneously, good results using compression plates for the management of AMFs were presented in the late 1990s.[13]

Nonunion and other limitations of the reconstruction plates made surgeons look for alternatives, such as grafting the atrophic mandible using tibia, hip, and particulate autogenous marrow to achieve union and to restore the lost volume of the mandible for strength and future occlusal rehabilitation. Since the 1980s, many surgeons have believed that autogenous grafts are necessary to treat severe AMFs.[6,11,17]

Recombinant Human BMPs

An alternative option to the use of autogenous bone grafts became available with the introduction of BMPs. On the basis of the 1965 findings of Urist,[42] Toriumi et al[43] used recombinant human BMP to reconstruct mandibular continuity defects in a canine model. In several articles, rhBMP-2 was shown to effectively induce bone regeneration in nonhuman primates with mandibular segmental defects.[44-46] In 2001 Seto et al[47] reported successful regeneration of segmental mandibular defects in a primate model with rhBMP-2 in a polyglycolic co-lactic acid carrier when used with different amounts of autogenous bone marrow.

The aforementioned results were confirmed clinically during the past 2 decades.[48-50] In 2001 Moghadam et al[51] published a report on the reconstruction of a 6-cm mandibular defect with a poloxamer-based gel containing BMPs isolated and partially purified from allogeneic bone. Osteogenesis was documented radiographically at 3 and 9 months. A bone biopsy performed at 9 months documented the presence of healthy osteocytes. Since then, several articles have described the use of recombinant human BMPs for the reconstruction of human mandibular defects.[15,18,48,52-61]

Case Presentation

Two elderly, medically compromised patients with AMFs, osteomyelitis, and continuity defects underwent debridement, alignment of segments, and placement of load-bearing reconstruction plates. The continuity defects were reconstructed with a combination of rhBMP-2 and tricalcium phosphate.

CASE 1

In December 2012, a 78-year-old female patient presented with pain and swelling in the lower left side of the face associated with a recently placed dental implant. She had undergone an immediate replacement of a failing implant in her lower mandible on the left side 1 month before presentation. Clinically, she had a draining fistula, pain, edema, and erythema in the submental region. There was an implant-supported fixed lower denture in place. Her mandible was atrophied, measuring 10 mm in the symphyseal region. The medical and surgical history included acute myocardial infarction, atrial fibrillation, colon polyps, hiatal hernia, cervical surgery, colon surgery, spinal fusion, and a hysterectomy. The clinical diagnoses were wound infection and osteomyelitis of the lower jaw (Fig 1).

With the patient under general anesthesia, her hybrid appliance was removed, a bone biopsy was performed, and cultures were obtained. The mandible had a wormian appearance but appeared intact. The pathology report indicated focal necrosis, granulation tissue, and focal acute and chronic inflammation. A peripherally inserted central catheter was placed to administer intravenous antibiotics for 6 weeks. Two weeks later, the patient returned complaining of her mandible "moving around." A panoramic radiograph confirmed a pathologic fracture of the left side of the mandible.

During general anesthesia on the second occasion, the patient underwent open reduction via an extraoral approach. A 2.2-mm-thick titanium locking

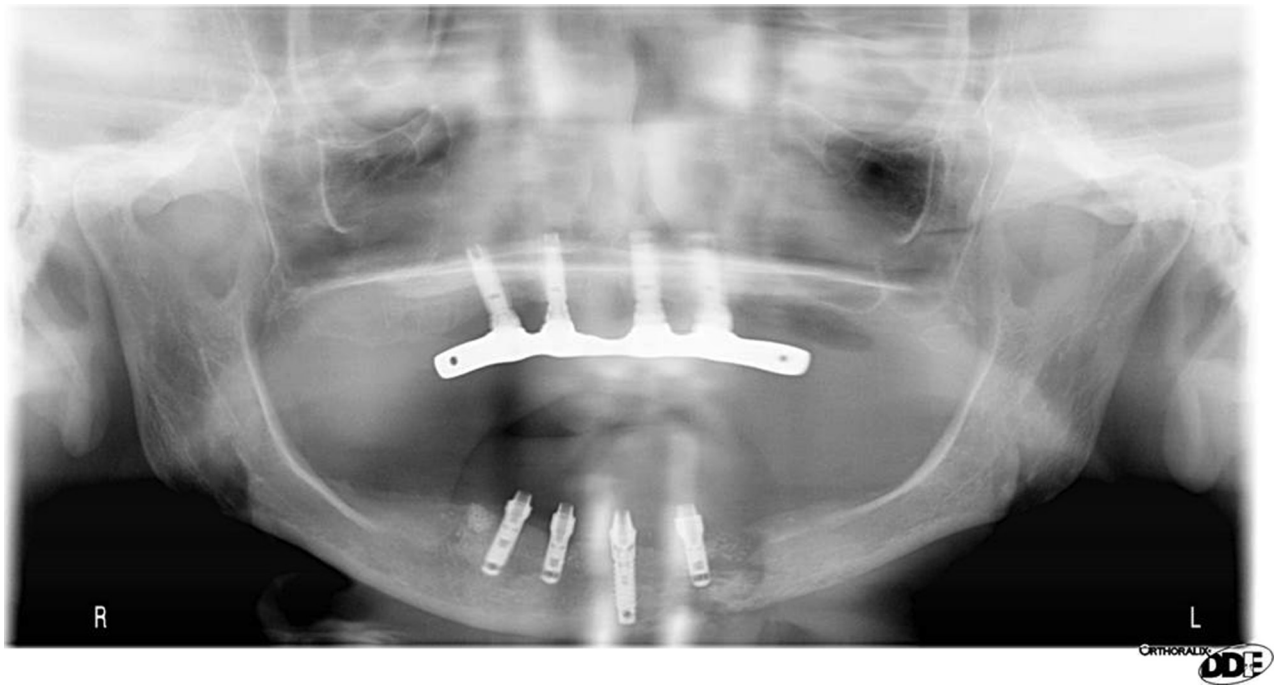


FIGURE 1. A failing implant placed in the area of the lower left canine caused a bone infection and, eventually, a mandibular fracture. L, left; R, right.
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reconstruction plate with 6 bicortical screws (Fig 2) was placed. After debridement, a 1-cm defect of the bone was reconstructed with rhBMP-2 (Infuse Bone Graft; Medtronic, Fridley, MN) wrapped over tricalcium phosphate. Two of the patient's implants had failed and were removed. Bone specimens were submitted to pathologic analysis, which confirmed the diagnosis of osteomyelitis.

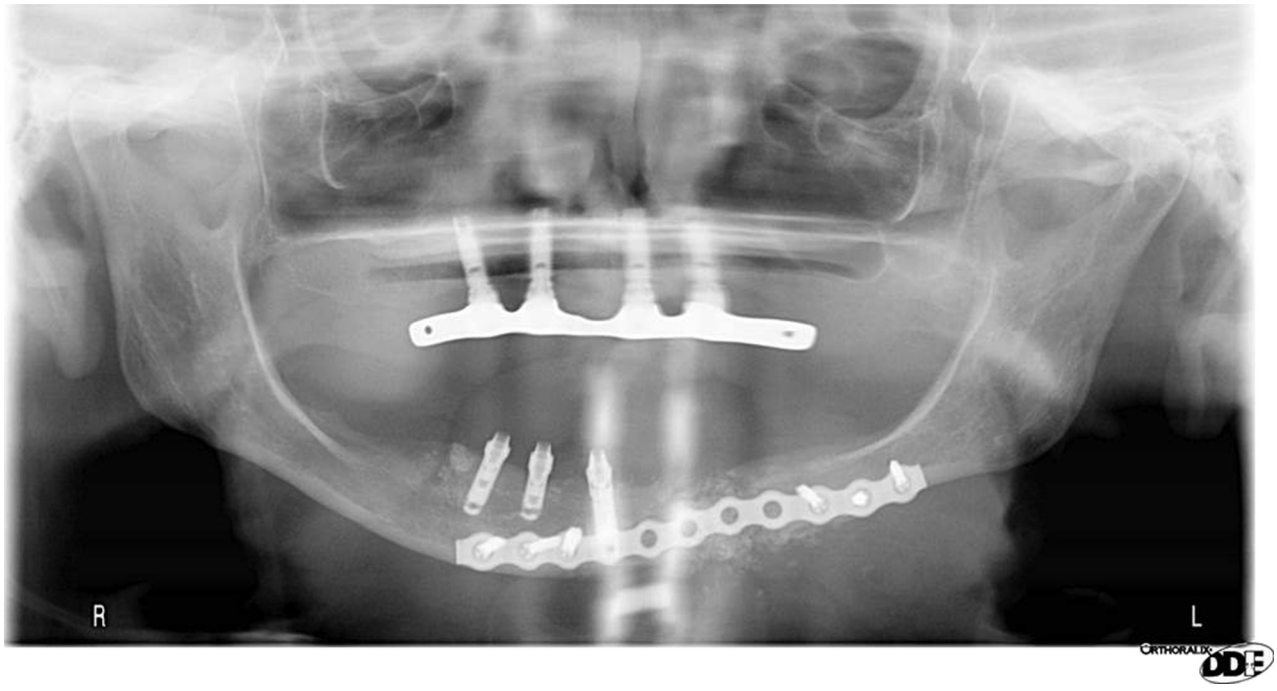


FIGURE 2. Reconstruction of a 1-cm bony defect by placing tricalcium phosphate and bone morphogenetic protein. L, left; R, right.
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Two months postoperatively, the patient reported a substantial reduction of pain, no signs of infection, and a return to normal function with a maximum interincisal opening of 50 mm. She had decreased sensation of the lower lip on the left side. Two years after reconstruction, the continuity defect has healed and the patient has returned to normal function with an implant-supported prosthetic device (Fig 3).

CASE 2

A 70-year-old female patient was referred for definitive treatment of chronic osteomyelitis, orocutaneous fistula, and pathologic mandibular fracture. She presented with a draining orocutaneous fistula in the submental area that communicated intraorally. The mandibular body on the left side was mobile, and her chin deviated 2 cm to the left. She had less than 10 mm of bone in the site of the fracture. Cone beam computed tomography was performed. When her mandible was aligned in its ideal position, the images showed a 4-cm continuity defect of the left-sided body (Fig 4).

The patient's comorbidities included chronic obstructive pulmonary disease, mitral valve prolapse, coronary artery disease, gastroesophageal reflux disease, anxiety, depression, gait disturbance, and malnutrition. In addition, she had an internal demand pacemaker for a rhythm disturbance. She had a peripherally inserted central catheter line and was undergoing 12 weeks of intravenous daptomycin and ertapenem prescribed by an outside institution. On finishing 12 weeks of intravenous antibiotic therapy, she was prescribed oral sulfamethoxazole and trimethoprim and amoxicillin/clavulanic acid until the time of surgery. Because of her complicated medical status and difficulty ambulating, an autogenous hip graft was ruled out. Therefore, it was decided to debride the mandible and reconstruct it with a locking reconstruction plate with placement of rhBMP-2 (Infuse Bone Graft) plus tricalcium phosphate.

With the patient under general anesthesia, a transcervical approach was used to access the mandible. Debridement of the fibrous callus and a minimal amount of bone was performed. The soft tissue scars were released, the bony segments were placed near their normal position, and the prefabricated 2.5-mm-thick locking reconstruction plate was secured with 11 bicortical screws. The bony defect was replaced with alloplastic material and placement of a mixture of rhBMP-2 and β-tricalcium phosphate (Fig 5). The tissue was undermined to allow for soft tissue coverage over the plate. The 6-week postoperative image shows good restoration of the segments with the defect filled with a bone-like substance (Fig 6). At present, 9 months after surgery, despite resumption of the patient's smoking habit, her wounds have healed and her mandible remains stable.

Discussion

The purpose of this article was to review the literature regarding the management of AMFs and present 2 cases of elderly patients with AMFs and continuity defects treated with a combination of a reconstruction

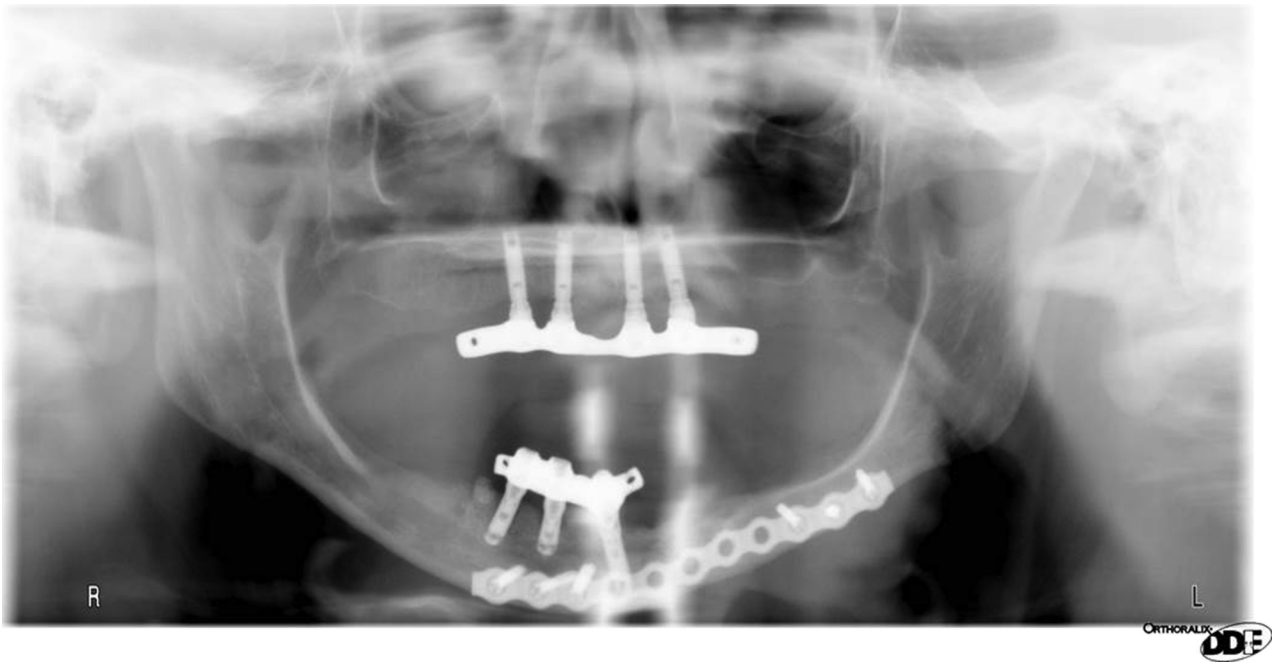


FIGURE 3. A 2-year follow-up radiograph shows successful reconstruction of the case. L, left; R, right.

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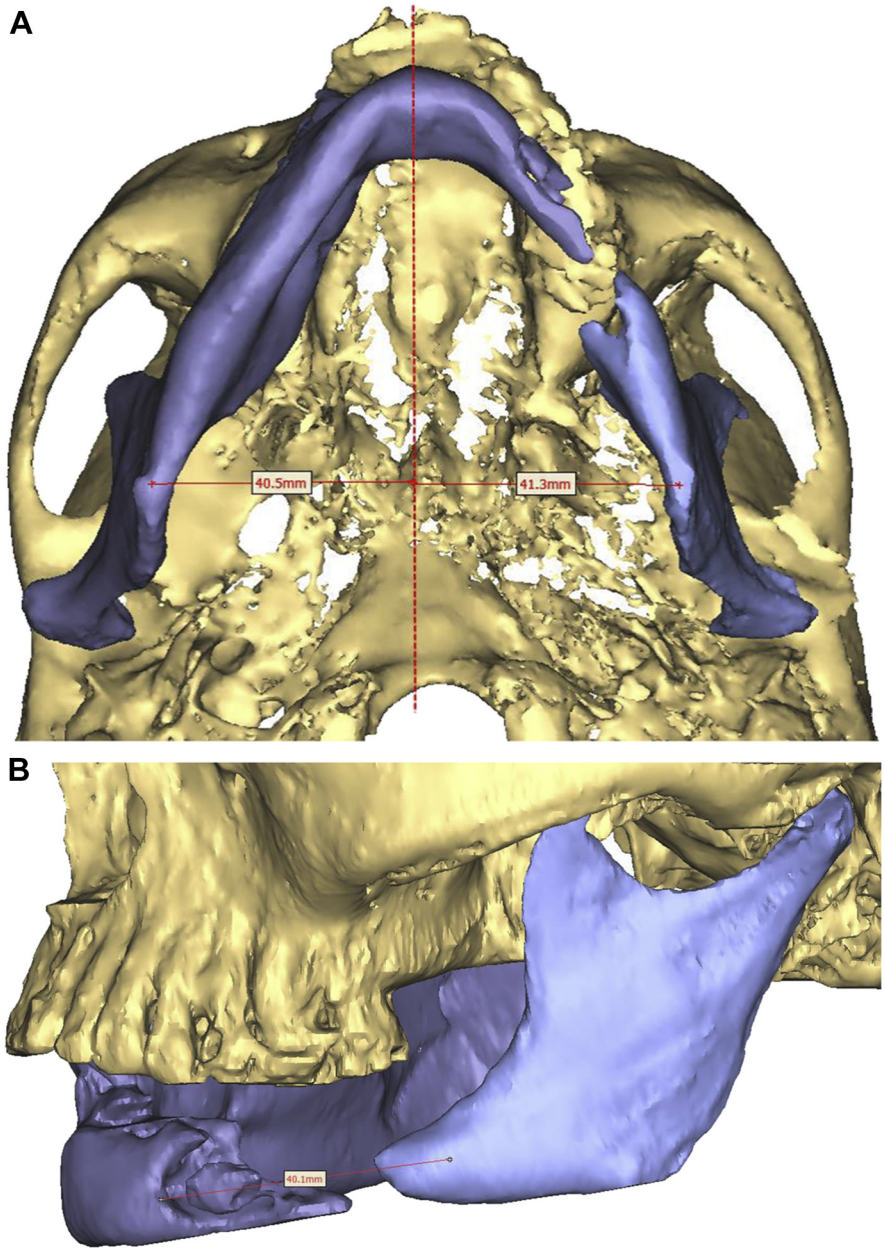


FIGURE 4. Continuity defect on imaging (Materialise USA, Plymouth, MI). *A*, Inferior view. *B*, Lateral view.

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plate, rhBMP-2, and tricalcium phosphate. Both patients presented with active infection and, after treatment, went on to successful healing without further complications.

The alveolar bone maintains its height owing to the forces exerted by the teeth. Their loss decreases the physiological stimulus, which in turn causes bone atrophy. It is this decreased bone volume that makes the mandible less resistant to traumatic forces and, consequently, more susceptible to fracture. The more severe the atrophy, the higher the probability to fracture. A classification of mandibular atrophy is shown in Table 1.

The management of AMFs is complicated, especially when they occur in older patients. Nonunions have been associated with closed reduction, and such treatment is no longer advocated.[62] According to Buchbinder,[5] it was Prein who advocated the use of long, rigid reconstruction plates along with immediate reconstruction with bone grafting of corticocancellous bone. Two questions remain: Are bone grafts necessary? Is rhBMP-2 a reliable alternative?

The transforming growth factor β (TGF-β) superfamily is currently known as a superfamily of structurally related dimeric disulfide-linked receptor ligands.[63,64] Its first member, TGF-β1, was described in 1983.[65]

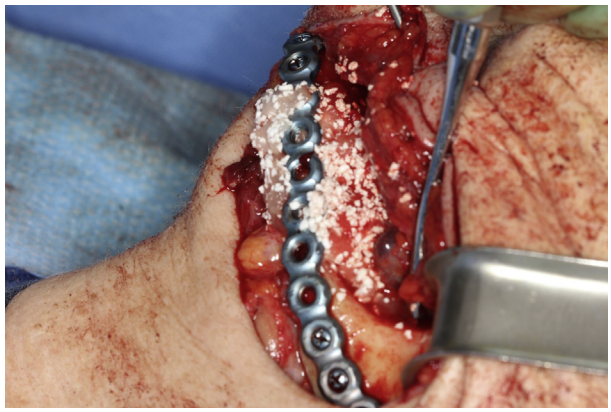


FIGURE 5. The bony defect was covered with alloplastic material and placement of a mixture of recombinant human bone morphogenetic protein 2 and β-tricalcium phosphate.

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The TGF-β superfamily (Table 2) includes proteins such as BMPs, involved in embryogenesis; organogenesis; and cell differentiation, growth, and proliferation. Changes in the expression of these proteins are associated with normal and pathologic processes.[66,67] The end result of these molecular mechanisms is the transcription of runt-related transcription factor 2 (RUNX2), which induces osteoblastic differentiation.[68-71]

Although more than 20 BMPs have been discovered since the late 1980s, osteoinductive properties have been attributed mainly to BMP-2 and BMP-7.[72] In 2000 the US Food and Drug Administration approved rhBMP-2 as an alternative to autografts in lumbar and cervical spine fusions. In 2004 it was approved for tibial surgery. In 2007 approval was given for maxillary sinus augmentation and for localized alveolar ridge augmentation.[73] In 2002 the commercial form of rhBMP-2, Infuse Bone Graft, was released. In 2006 the brand name of rhBMP-7, OP-1 (Stryker Biotech, Hopkinton, MA), became available.

Table 1. CLASSIFICATION OF EDENTULOUS MANDIBLE FRACTURES OF LUHR ET AL[13]

Class	Mandibular Height at Fracture Site
I	16-20 mm
II	11-15 mm
III	≤10 mm

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Repaired mandibular defects have been documented by use of BMPs. This includes defects created by ablative surgery,[15,51] other continuity defects,[42,44-46] and AMFs.[1] Carter et al[56] published the off-label use of rhBMP-2 (with and without allogeneic bone grafts) for reconstructing continuity defects. On the basis of clinical and radiographic evaluations, 3 of 5 patients were successfully treated. Using rhBMP-2 impregnated on a collagen carrier, Herford and Boyne[57] were able to perform reconstruction in 14 patients with continuity defects ranging from 4 to 8 cm. In the same year, Clokie and Sándor[15] reported successful reconstruction in 10 patients with major mandibular defects due to ameloblastoma or osteomyelitis by use of rhBMP-7.

The use of BMPs is appealing when dealing with AMFs because no donor site is needed, thus minimizing morbidity associated with harvesting an autogenous graft and surgical time. According to Herford

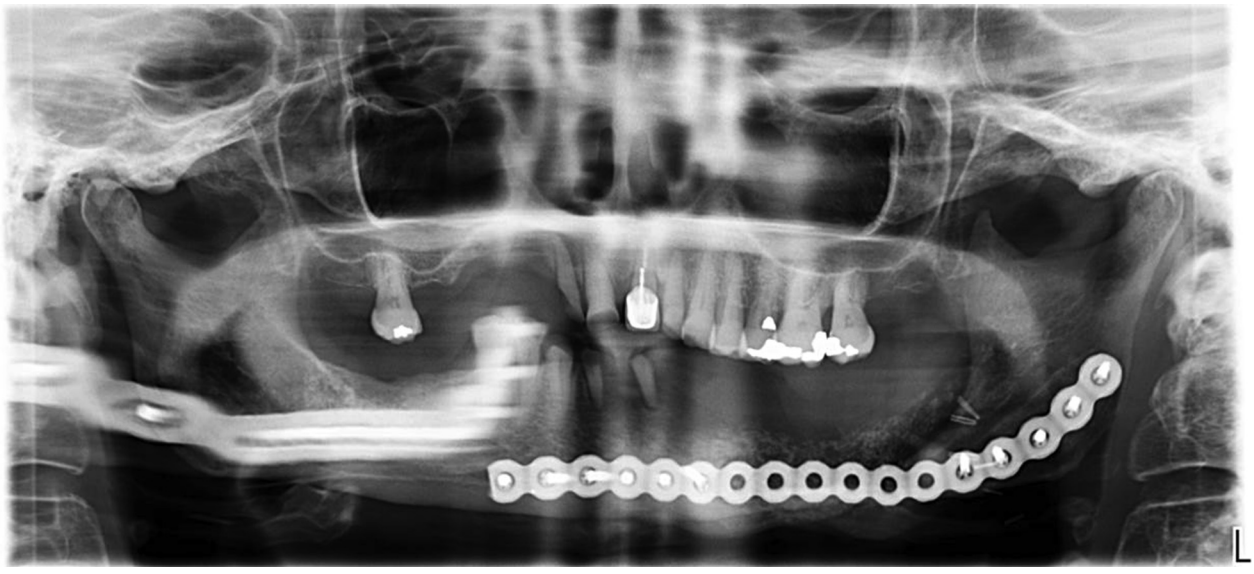


FIGURE 6. The 6-week postoperative image shows good restoration of the segments with the defect filled with a bone-like substance.

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Table 2. GROUPING OF TGF-β SUPERFAMILY

Group	Example
TGF-β subfamily	TGF-β1, TGF-β2, TGF-β3
Decapentaplegic vegetal–related subfamily	BMPs: around 20 members Growth and differentiation: around 9 members
Activin and inhibin subfamily	Activins: A, AB, B Inhibins: A, B
Glial cell–derived neurotrophic factor subfamily	GDNF, artemin, neurturin
Several additional divergent members	Antimüllerian hormone, nodal

Abbreviations: BMPs, bone morphogenetic proteins; GDNF, glial cell-derived neurotrophic factor; TGF-β, transforming growth factor β.

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and Boyne,[57] an ideal grafting method should be a bone inductive material that would be reliable, biocompatible, long-lasting, and capable of restoring mandibular continuity with minimal morbidity. Although particulate marrow and cancellous autogenous bone qualify, they have to be harvested and thus increase a patient's discomfort and costs in operating time. The development of effective reconstruction procedures using BMPs, without using conventional bone grafting, has been playing a substantial role in reconstructive surgery.

In our cases the use of rhBMP-2 and tricalcium phosphate allowed reconstruction of form and function in 2 patients in whom an iliac crest graft would have posed additional surgical risks because of advanced age and comorbidities. Although autogenous bone grafts are the standard of care, it appears that BMPs can be safely used as an alternative for reconstruction in selected cases.

Primary reconstruction of AMFs using reconstruction plates supplemented with autogenous bone graft is the standard of care today. In selected cases in which multiple comorbidities may influence local and/or systemic outcomes, BMPs and tricalcium phosphate can be used as a predictable alternative to autogenous grafts.

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