Atrophic Nonunion of Humeral Diaphysis Treated With Locking Plate and Recombinant Bone Morphogenetic Protein: Nine Cases

Charles H. Crawford III, MD, and David Seligson, MD

Abstract

Nonunions of the humerus are debilitating for patients and challenging for surgeons. We retrospectively reviewed our first 9 humeral nonunions treated with a locking plate and commercially available recombinant bone morphogenetic protein. At latest follow-up, 8 patients showed clinical and radiographic signs of union. One patient had a persistent (11-year) nonunion that failed to unite at 1 year, despite new bone formation, and underwent revision with the same technique. The reported technique is a useful part of the surgeon's armamentarium in treating difficult humeral nonunions. We found a high union rate with an acceptably low complication rate in this difficult population.

Reported nonunion rates for humeral shaft fractures range from 2% to 30%.[1,2] Humeral nonunions are associated with pain and loss of upper extremity function.[1,2] Reported treatment options include external fixation, intramedullary nailing, and plate fixation.[1,2] Recently, several authors have supported open reduction and plate fixation with bone grafting as the preferred method of treatment.[1-7] Autogenous cancellous bone graft is most commonly used, though recent literature suggests bone graft substitutes may be adequate.[1-6] Other authors advocate free vascularized bone grafts for recalcitrant humeral nonunions, while yet others have reported acceptable results with structural allografts.[7,8] Recent advances in bone morphogenetic protein (BMP) research support use of BMPs in nonunion treatment, but further investigation is needed.[9-11]

Dr. Crawford is Assistant Professor, and Dr. Seligson is Professor, Vice Chair, and Chief of Fracture Service, Department of Orthopaedic Surgery, University of Louisville, Louisville, Kentucky. Dr. Crawford was an orthopedic resident at the time the article was written.

Address correspondence to: Charles H. Crawford III, MD, Department of Orthopaedic Surgery, University of Louisville, 210 E Gray St, Suite 1003, Louisville, KY 40202 (tel, 502-852-5319; fax, 502-852-7227; e-mail, chcraw01@louisville.edu).

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Now available locking plate technology has had promising results in osteopenic bone, which is often encountered in cases of atrophic humeral nonunion. Patient comorbidities, prior surgical procedures, and disuse all lead to poor-quality, osteopenic bone.[4] Locking plates are internal fixators that stabilize the bone—in contrast to plating, which applies traditional compressive forces. The result is an angle-stable construct that may not interfere with the local, compromised vascularity of the bone.

Here we report our first 9 cases of atrophic nonunion of the humeral diaphysis treated with locking plate fixation and recombinant human BMP (rhBMP).

Materials and Methods

With approval from our human studies committee and in accordance with HIPPA (Health Insurance Portability and Accountability Act) regulations, we retrospectively performed a clinical and radiographic review of our first 9 patients treated for humeral diaphyseal nonunion with a locking plate and BMP. Data were collected for previous treatments, radiographic characteristics, operative details, complications, successful union, and failures and were analyzed and compared with the data of historical controls from the literature.

Patients

All 9 patients (8 women, 1 man) were diagnosed with an atrophic nonunion. Mean age was 60.4 years (range, 41-69 years). Patients had multiple comorbidities, including obesity, tobacco use, diabetes, and rheumatoid arthritis. Three patients had preoperative radial nerve palsies. One patient had a history of infected nonunion, successfully treated with débridement and antibiotics. All patients had previous operative treatment, ranging from 1 to 18 prior surgeries. The majority of the patients had been referred after failed initial treatment elsewhere. Three patients had failed delayed intramedullary nailing after failed nonoperative treatment. Two patients had failed primary intramedullary nailing, and 1 of these had failed additional exchange nailing with bone grafting. Four patients had failed primary plate fixation, and 2 of these had failed an additional revision plate fixation with bone grafting (Table).

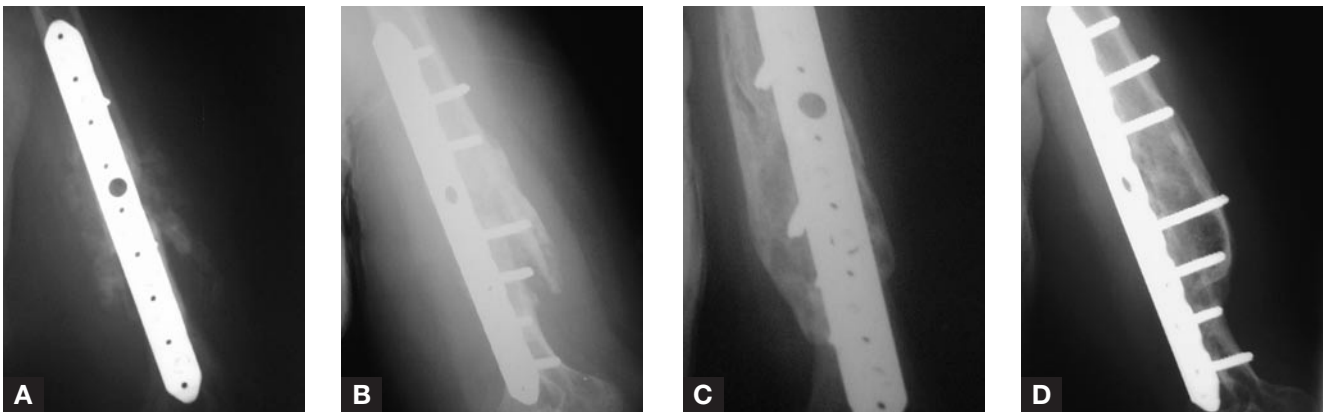

Figure 1. Sixty-nine-year-old woman with nonunion after failed intramedullary nail for failed functional brace treatment. (A,B) Immediate postoperative radiographs show locking plate and graft. (C,D) Follow-up radiographs show abundant bony union.

Surgical Technique

Standard surgical principles for treatment of nonunions were followed. All patients had prior surgery, and therefore existing incisions were used. Four patients had previous posterior approaches, and 5 had previous anterolateral approaches. All patients received perioperative antibiotics. Care was taken to preserve soft-tissue viability and vascularity. Unnecessary bone stripping and electrocautery were avoided. Prior implants were removed, and the nonunion site was exposed. Fibrous scar and nonviable tissue was débrided from the nonunion site. Bone ends were freshly cut, as needed. After adequate bone preparation and reduction, locking plates were applied. Minimal plate contouring was needed. Plates were chosen on the basis of preoperative planning and availability. Six to 8 cortices were used on either side of the nonunion site. Autogenous cancellous bone grafting was performed in 5 patients. Four patients had cancellous bone taken from the proximal tibia, and 1 had cancellous bone take from the iliac crest. All patients received a commercially available rhBMP preparation. Eight received rhBMP-2 with a collagen carrier and a ceramic bulking agent (commercially available as Infuse and Mastergraft, respectively; Medtronic, Minneapolis, Minn), and 1 received rhBMP-7 with a collagen carrier (commercially available as OP-1; Stryker Biotech, Hopkinton, Mass).

Results

All patients were followed until healing or failure, and none was lost to follow-up. Mean follow-up was 16 months (range, 10-31 months). Eight patients showed clinical and radiographic union at latest follow-up (Figure 1). One patient, who had 18 prior surgeries for a persistent (11-year) pseudarthrosis, failed to unite after 1 year, despite some bone formation, and required revision with the same technique (Figure 2). Two patients had postsurgical superficial erythema that resolved after a short course of antibiotics. One patient had a postsurgical partial radial nerve palsy that resolved completely under observation.

Discussion

Humeral nonunions are notoriously difficult to treat.[1-8] The clinical situation can be complicated by previous surgical attempts and comorbidities such as obesity and osteopenia. Patients with inherent difficulties (eg, those already mentioned here) are often treated by fracture specialists at referral centers. Likewise, there are many reported treatment approaches because of the inherent difficulty of these nonunions.[1-8]

The nonunions of our patients were considered exceptionally difficult. In all 9 cases, previous operative treatment had failed. All patients had age-and comorbidity-related osteopenia and atrophic nonunions.

Table. Patient Data

Case	Age (y)	Sex	Prior Surgery	Time of Nonunion	Existing Complication	Comorbidities
1	61	F	Primary ORIF × 1	3 mo[b]	Radial nerve palsy	Obesity, RA[c]
2	59	F	Primary ORIF × 1	16 mo	—	Smoker
3	69	F	Delayed IMN × 1	6 mo	Radial nerve palsy	Obesity
4	67	M	Delayed IMN × 1	12 mo	—	—
5	52	F	ORIF × 18 prior surgeries	11 y	—	Obesity, smoker, DM
6[a]	41	F	ORIF × 2	21 mo	Radial nerve palsy	Obesity
7	67	F	Delayed IMN × 2	34 mo	—	Obesity, smoker, DM
8	66	F	IMN × 1	6 y	Infection (resolved)	Obesity, smoker
9	62	F	IMN × 2	7 y	—	Obesity, DM, psoriasis

Abbreviations: ACBG, autogenous cancellous bone graft; ORIF, open reduction and internal fixation; IMN, intramedullary nail; RA, rheumatoid arthritis; DM, diabetes mellitus; S&N, Smith & Nephew. [a]Recombinant human bone morphogenetic protein 7 (rhBMP-7) was used in this case; rhBMP-2 was used in all other cases. [b]Loose plate. [c]Currently taking infliximab, prednisone, and methotrexate.

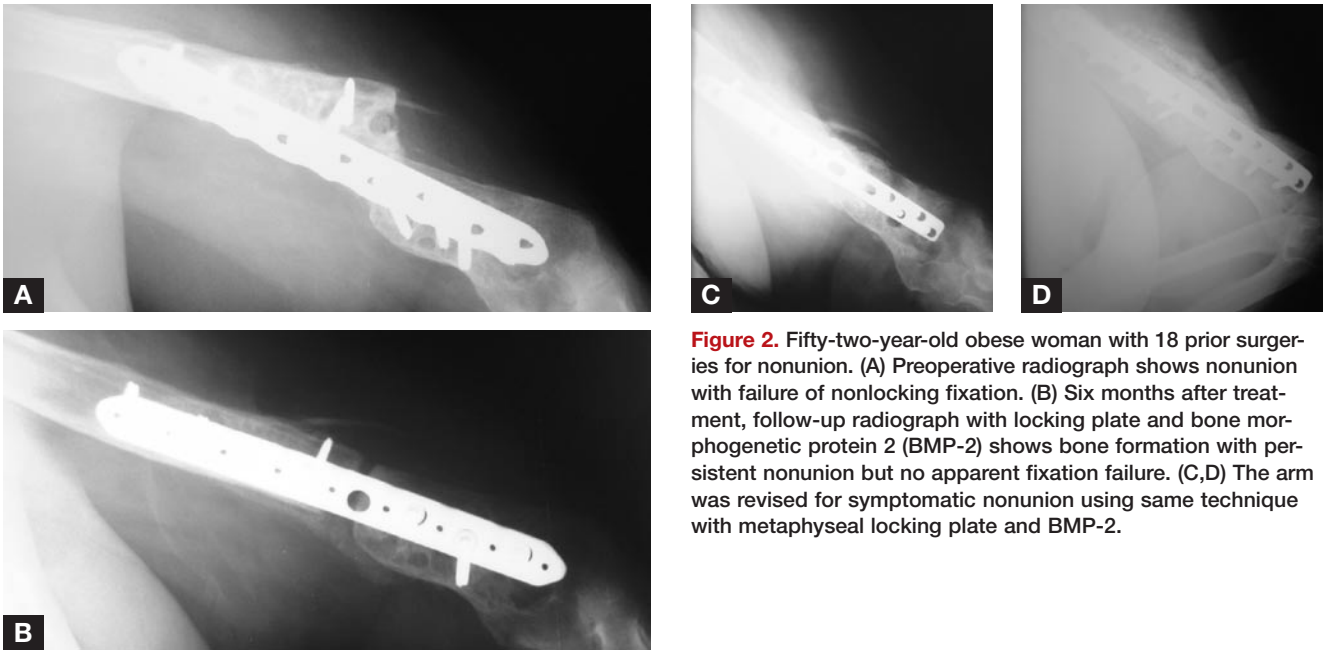

Figure 2. Fifty-two-year-old obese woman with 18 prior surgeries for nonunion. (A) Preoperative radiograph shows nonunion with failure of nonlocking fixation. (B) Six months after treatment, follow-up radiograph with locking plate and bone morphogenetic protein 2 (BMP-2) shows bone formation with persistent nonunion but no apparent fixation failure. (C,D) The arm was revised for symptomatic nonunion using same technique with metaphyseal locking plate and BMP-2.

Recent advances in locking plate technology have allowed surgeons to work with the principles of biologic fixation. Locking plates are angle-stable constructs that mechanically function as "internal fixators," which allow for stable fixation without the plate compressing directly against the bone. Locking plates also perform well in osteopenic bone.[4] We used locking plates for the patients in this series because of their poor bone quality, resulting from age and from disuse osteopenia from long-standing nonunions.

Recombinant BMPs are now commercially produced and available for clinical use. Several basic science and clinical studies have demonstrated their efficacy in the treatment of nonunions.[9-11] Comparison with cancellous autograft has shown similar union rates but decreased donor-site morbidity.[9] We used rhBMP in our study both as a single grafting agent and as an adjunct to autogenous graft. The choice depended on several factors, including prior autografting procedures and patient preference. During surgery, we did find the autogenous graft unsatisfactory in several patients with fatty, osteopenic marrow at the donor site.

Limitations of this study include small sample size, retrospective analysis, and some heterogeneity of treatment techniques. Five of the patients in this series received autograft in addition to BMP, though in our experience the autograft is unsatisfactory in this older group of patients and may not be a necessary addition. Although there was some heterogeneity of the plates used with respect to length and manufacturer, all the plates were 4.5-mm locking plates used as angle-stable constructs, and therefore they can be assumed to function in the same biomechanical fashion.

This new technique, which combines locking plate technology and rhBMP, appears to be useful in the treatment of difficult humeral nonunions. We observed a high rate of healing (89%, 8 of 9 patients) and a low rate of complications in this difficult population. The precise role of locking plates and rhBMP in the treatment of humeral nonunion requires further investigation. The increased costs associated with this new technology must be justified by improved outcomes when compared with traditional plating and bone grafting techniques. It is unlikely that

Locking Plate	ACBG	Approach	New Complication	Follow-Up (mo)	Final Outcome
S&N 11 hole, 4.5 mm	Proximal tibia	Posterior	—	21	Union, radial nerve palsy resolved
S&N 8 hole, 4.5 mm	Proximal tibia	Anterolateral	—	10	Union
S&N 8 hole, 4.5 mm	—	Posterior	—	20	Union, radial nerve palsy resolved
Zimmer proximal humerus plate 4.5 mm	—	Anterolateral	Partial radial palsy	10	Union, radial nerve palsy resolved
S&N 8 hole, 4.5 mm	—	Posterior	Superficial erythema	10	Revised for nonunion, no infection
Synthes 9 hole, 4.5 mm	Proximal tibia	Posterior	—	31	Union, radial nerve palsy resolved
S&N 8 hole, 4.5 mm	—	Anterolateral	—	10	Union
Synthes metaphyseal 8 hole, 4.5 mm	Iliac crest	Anterolateral	—	16	Union
Synthes metaphyseal 4.5 mm	Proximal tibia	Anterolateral	Superficial erythema	16	Union, erythema resolved

all patients with humeral nonunions will benefit from this technique, but certain patients who are more likely to have treatment fail because of comorbidities such as osteopenia and recalcitrant nonunion may benefit from the stability of locking plates and the biologic potential of rhBMP. The need for more aggressive grafting procedures, such as free vascularized grafts, may be decreased. The increased monetary costs of this new technology may be balanced by decreased failure rates, which would result in less patient disability and fewer reoperation expenses.

Surgeons should be aware that this use of rhBMP-2 is considered "off-label," as it is not currently one of the indications approved by the US Food and Drug Administration (FDA). The FDA has given rhBMP-7 Humanitarian Device Exemption (HDE) approval as an alternative to autograft in recalcitrant long bone nonunions where use of autograft is not feasible and alternative treatments have failed.

Authors' Disclosure Statement

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This paper will be judged for the Resident Writer's Award.