

Original Article

Using of injectable bio-degradable calcium sulfate as bone graft substitute in the treatment of periarticular fractures

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Abstract: Although the use of calcium sulfate has been used as a bone graft substitute in the treatment of fractures for more than a century, few studies investigate the use of recently developed injectable calcium sulfate-based bone graft substitute with high compressive strength after curing in situ. In this study, we evaluated preliminary results of a high compressive strength calcium sulfate-based bone graft substitute used in the treatment of periarticular fractures. Eighty-five patients with periarticular fractures who were treated with an injectable bio-degradable calcium sulfate cement (BCSC) (MIIG X3, Wright Medical Technology, Inc, Arlington, TN, USA) between October 2005 and June 2012 were included in this study. The fracture location distribution was as follows: Fourteen proximal humeral fractures, eight acetabular fractures, thirty-six tibial plateau fractures, seventeen distal tibial fractures and ten calcaneal fractures. Postoperative roentgenologic study was adapted to evaluate the congruity of the articular surface, bone replacement profile and the resorption process of the bone substitute. The postoperative joint function recovery assessment was achieved with Neer's score system, modified D'Aubigne and Postel hip scale, Rasmussen's functional and anatomical grading score system and Mazur ankle score correspondingly to the shoulder, hip, knee and ankle joints. The Maryland Foot Score Profile was adapted for the postoperative evaluation of calcaneal fractures. Seventy-seven of the 85 patients were followed-up successfully. The average length of follow-up was 20.2 months (range: 12-27 months). Fractures healed uneventfully in all patients without infection. According to the corresponding functional score system in each location, joint function was excellent or good. Two patients with tibial plateau fractures had an articular subsidence of 2 mm showed by X-ray film one year after operation without joint dysfunction. Four weeks after surgery, partial absorption of BCSC was evident on radiographs. Six months postoperatively, radiographs showed areas previously filled with BCSC with the same bone density as normal cancellous bone. This study showed that the use of a high compressive strength calcium sulfate-based bone graft substitute to fill metaphyseal defects in the treatment of periarticular fractures can provide adequate immediate stability and strength for fracture reduction while improving the safety of early stage joint motion in functional rehabilitation.

Keywords: Calcium sulfate, bone graft substitute, periarticular fractures

Introduction

Despite many advances in the management of fractures, periarticular fractures continue to be a great challenge to orthopedic surgeons because of articular surface depression and compaction into the subchondral cancellous bone. To acquire optimal joint function, intra-articular fracture fragments must be anatomically reduced to guarantee the congruity of the articular surface, and initial stability is necessary for early stage rehabilitation. After articu-

lar surface reduction, the periarticular metaphysis is often left with significant bone loss. This intraosseous void may need to be filled with a bone graft to provide mechanical support to the articular surfaces during healing.

Autogenous bone, typically harvested from the iliac crest, traditionally remains the standard of bone grafting. It can be associated, however, with an inadequate amount of material and donor-site morbidity, including chronic pain and wound complications [1, 2]. Alternative graft

materials for filling fracture voids include allograft bone and synthetic bone graft substitute. While the use of allograft avoids the donor-site morbidity associated with the use of autograft, it may also lead to complications, including potential disease transmission, slower incorporation, and possibly lower union rates [3-6]. Therefore, structural bone graft substitutes, such as calcium sulphate, calcium phosphate, porous coralline ceramics and tricalcium phosphate, appear to be an attractive alternative because they lack the disadvantages of autografts and allografts [7-9].

Calcium sulfate (CaSO_4) has been used, researched, and reviewed as a bone void filler for over 100 years, and has been well-researched and thoroughly-reviewed by a many of investigators [7, 10-13]. In 1892, Dreesmann reported on results from CaSO_4 used to fill osseous cavities in tuberculosis patients [14]. Since that time, there have been numerous human clinical and animal model-based reports on the effectiveness of CaSO_4 as a bone graft substitute in fields such as otolaryngology, dentistry, and orthopedics, animal models and clinical applications [15]. Although the exact mechanism of action remains unknown, CaSO_4 appears to function as resorbable osteoconductive scaffold and space filler, not only providing the structural framework necessary for angiogenesis and osteogenesis but also preventing soft tissue invasion [16]. It is hypothesized that increased local acidity during CaSO_4 resorption may result in demineralization of adjacent bone. This demineralization would release matrix-bound morphogenetic proteins that have a stimulatory effect on bone formation [17].

Currently, surgical grade CaSO_4 is available in multiple forms such as Osteoset (Wright Medical Technology, Inc., Arlington, TN), BonePlast (Interpore Cross, Irvine, CA), Calceon 6 (Synthes, Paoli, PA), MIIG 115 (Wright Medical Technology, Inc., Arlington, TN), MIIG X3 (Wright Medical Technology, Inc., Arlington, TN), MIIG X3 HiVisc (Wright Medical Technology, Inc., Arlington, TN). Among them, the recently developed MIIG X3 (BCSC) series is designed to be injectable and will harden in situ several minutes after injection with high compressive strength. The authors report on the preliminary result of this new bone graft substitute for the treatment of periarticular fractures.

Materials and methods

Eighty-five patients with periarticular fractures who were treated with BCSC (Wright Medical Technology, Inc, Arlington, TN) between October 2005 and June 2012, were included in this study. The patient population was comprised of 56 males and 29 females whose mean age at surgery was 52.3 years (range 26-77 years). The patients sustained injuries in 56 road traffic accidents, 15 falls from height, 10 simple falls, and 4 sports injuries. According to fracture location, appropriate preoperative radiographs were acquired in every patient (**Figure 1A**). A computed tomography (CT) scan was acquired to determine the displacement and extent of the depressed articular surface (**Figure 1B**). The fracture location distribution is as follows: 14 proximal humeral fractures, 6 Neer type III, 8 Neer type IV; 8 acetabular fractures, 6 posterior column and posterior wall fractures, 2 posterior wall fractures; 36 tibial plateau fractures, according to Schatzker classification, 24 Schatzker II, 7 Schatzker III, 1 Schatzker IV, 2 Schatzker V, 2 Schatzker VI; 17 distal tibial fractures, 10 Ruedi-Allgowe type II, 7 Ruedi-Allgowe type III; 10 calcaneal fractures, 4 Sanders type II, 5 Sanders type III, 1 Sanders type IV. Postoperative roentgenologic study was adapted to evaluate the congruity of articular surface, bone replacement profile and resorption process of bone substitute. The postoperative joint function recovery was assessed with Neer's score system [18], modified D'Aubigne and Postel hip scale [19], Rasmussen's functional and anatomical grading score system [20] and Mazur ankle score [21] correspondingly to the shoulder, hip, knee and ankle joints. The Maryland Foot Score Profile was adapted for the postoperative evaluation of calcaneal fractures [22].

Surgical techniques

According to the fracture location, adequate anesthesia was acquired. The fracture site was exposed and temporary reduction was achieved with K-wires and reduction clamps. The delivery needle was placed in the deepest zone of the defect under fluoroscopic guidance. With the use of the vacuum mixing machine, the dry CaSO_4 powder and the solution were mixed. After mixing, the paste like bone graft was placed in a syringe and injected into the intraos-

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Figure 1. A and B: Preoperative anteroposterior radiographs and axial CT scan revealing a Schatzker classification II fracture in right tibial plateau. C: The radiopaque zone indicates the distribution of graft material on the immediate postoperative anteroposterior radiographs. D: The 4-week postoperative radiograph exhibited resorption of the margin of the graft material. E: Nearly half of the graft material was absorbed at 8 weeks postoperatively on anteroposterior radiograph. F: Full bone graft incorporation was observed on the radiograph at 12-14 weeks postoperatively. G: Six month after operation, radiograph demonstrated equivalent bone density in the previous area of graft material as surrounding cancellous bone.

seous void with steady pressure. The injection of the BCSC was started from the deepest recesses of the defect toward superficial areas by withdrawing the canula in a retrograde fashion. With the assistance of fluoroscopy, appropriate positioning of the graft material was monitored in real time. Extra caution should be taken when treating severely comminuted fractures or fractures with cartilage defects to avoid extravasation of the graft material into the joint space. It's not necessary to remove the graft from the joint space or soft tissues since it will be resorbed without affecting the local tissues. KELLY reference the paste like graft materials (MIIG X3) must be injected within 3 minutes. The MIIG X3 HiVisc will be injectable up to 10 minutes. To prevent the contact between the blood and the graft material, which may interfere with the set time, after injection the outer surface of the graft materials was covered with dry gauze until it hardened completely. Complete set time was about 9-11 minutes after mixing began. For the tibial plateau fractures, distal tibial fractures and acetabular fractures, the injection of the graft was commonly performed prior to definitive hardware placement and stabilization. Five minutes after thorough hardening of the graft material, internal fixation devices were applied with standard techniques. The placement of screws across the hardened bone graft materials provided increased screw purchase and intraoperative stability. The thread of the screws should traverse the hardened graft material to contralateral cancellous bone or penetrate the contralateral cortex. Thus, the anti-pullout and support strength of the screws was maintained throughout the process of graft resorption and host bone replacement. For proximal humeral fractures and calcaneal fractures, we performed the internal fixation first.



Figure 2. The comparison of sequential radiographs at follow-up the distal tibia showed no significant difference in the incorporation rate of the graft material. A: Preoperative, B: Postoperative, C: 12 weeks after operation, D: Six months after operation.

Postoperative management

Proximal humeral fractures: The pendulum exercises are usually initiated on the second day postoperative. Gently active, and assisted, range-of-motion exercises are started approximately 2 weeks after the surgery when the soft tissues healed. A sling is worn for 4 to 6 weeks. Active motion is commenced after discontinuation of the sling. Strengthening exercises are delayed until 12 weeks after operation.

Tibial plateau fractures: Post-operatively the limb is placed in a hinged brace. Continuous passive motion from full extension to flexion of 30° is started on postoperative day 1. The rate and the degree of flexion are increased as tolerated. Active motion of the knee is initiated once the wound healed without complications. Partial weight bearing of up to 50% of body weight is begun at 8 to 10 weeks. Full weight bearing is not allowed in 10-12 weeks until the follow-up x-rays show complete union of fracture.

Distal tibial fractures: The ankle is maintained in a neutral position with a posterior plaster slab splint and the lower extremity is elevated to reduce swelling. Active range of motion of the ankle, subtalar joint, and foot/toes is initiated on the second postoperative day. When the patient is not exercising, the right-angled splint is applied again to prevent equinus deformity. Partial weight bearing with the aid of crutches is advanced at the 6 weeks. Usually the patients are allowed to full weight bearing at 10-12 postoperative weeks with the evidence of bone union.

Calcaneal fractures: The patient is placed in a well-padded soft bandage with a posterior plaster slab at 90°. At the second postoperative week, active

range of motion of the ankle and subtalar joint is instituted. No weight bearing is allowed for 8 weeks. Minimal toe-touch weight bearing with crutches is started at 8-10 weeks. Full weight bearing is commenced at 10-12 weeks.

Results

Seventy-seven of the 85 patients have sufficient follow up. One proximal humeral fracture and 3 tibial plateau fractures were lost postop-

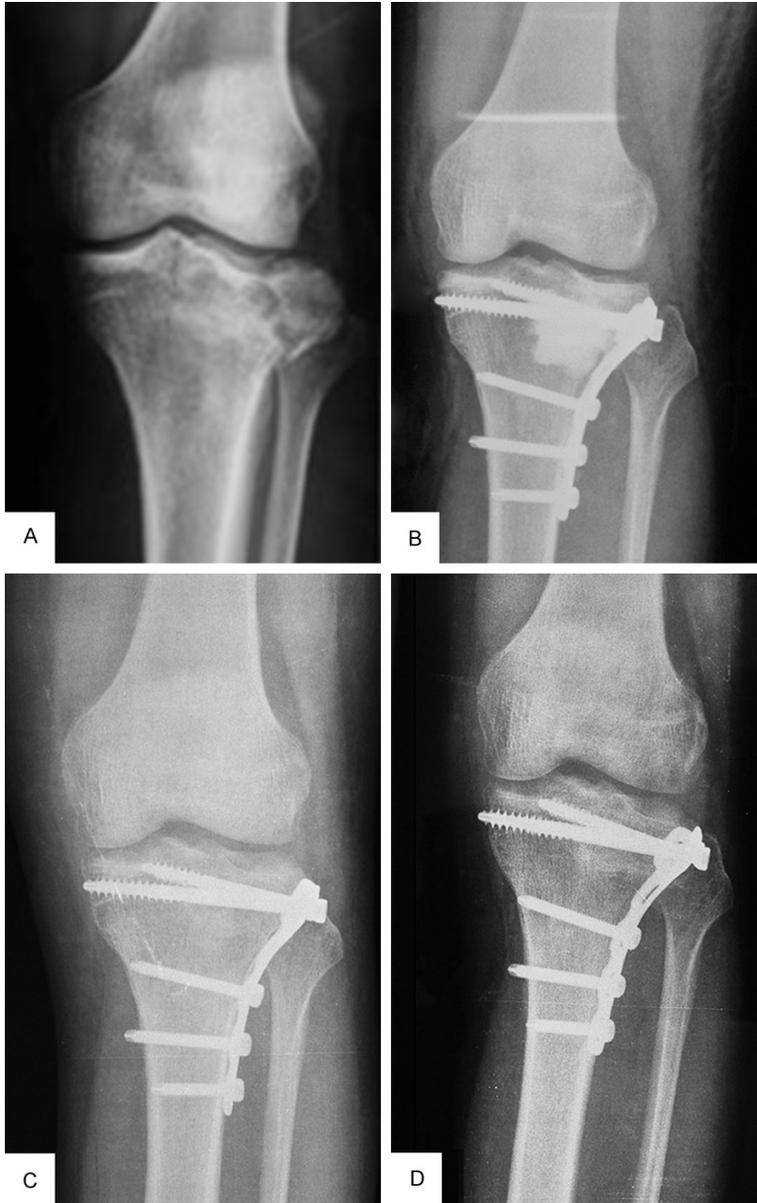


Figure 3. The comparison of sequential radiographs at follow-up tibial plateau showed no significant difference in the incorporation rate of the graft material. A: Preoperative, B: Postoperative, C: 12 weeks after operation, D: Six months after operation.

eratively. The average length of follow-up was 20.2 months (range: 12-27 months). Postoperative radiographs were taken to assess the reduction of the articular surface, bone healing and the incorporation of bone graft and new bone. Four week postoperative radiographs exhibited resorption of the margin of the graft material compared with the immediate postoperative radiographs (**Figure 1C, 1D**), however,

no obvious radiolucent line was identifiable. The graft material resorbed 67% (range: 50%-75%) on the 8-week postoperative radiographs with the formation of trabecula in the early absorption area (**Figure 1E**). Full bone graft incorporation was observed on the radiograph at 12-14 weeks postoperatively (**Figure 1F**). In young patients, the rate of bone-ingrowth was faster than that in elderly patients. Six months after operation, areas previously grafted demonstrated equivalent bone density with the surrounding cancellous bone as determined by radiographs (**Figure 1G**). There's no significant difference of the incorporation rate between different sites (**Figures 1-3**). Only two patients with tibial plateau fractures had radiographically evident articular subsidence of 2 mm at one year after operation. Neither patient had joint dysfunction. Fractures healed uneventfully in all the patients. The average time for fracture healing is 8.2 (range: 7-10) weeks in proximal humeral fractures, 10.5 (range: 9-12) weeks in tibial plateau fractures, 12 (range: 10-14) weeks in distal tibial fractures and 11.3 (range: 10-12) weeks in calcaneal fractures. There were no infections. Wound exudations were observed in two cases of tibial plateau

fractures. The cultures were taken and the results were negative. With empirical oral antibiotics (Cephadrine) and standard dressing change, the wounds healed in 2-3 weeks.

According to Neer's functional score system, at one year the postoperative average score of fourteen proximal humeral fractures were 91 (range: 89-93).

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For the 8 acetabular fractures, the rating according to the Modified D'Aubigne and Postal scale was excellent in 6 at one year and good in 2 at one year follow-up.

For the thirty-three patients with tibial plateau fractures, the postoperative knee function was good according to Rasmussen's functional and anatomical grading score system. Six months after surgery, the mean function score was 25.2 (range: 20-30) and the mean fracture anatomic reduction score was 16.8 (range: 14-18) in the 33 patients available. One year after the operation, the thirty-three patients' mean function score reached 26.6 (range: 24-30) and the mean anatomic reduction score was 16.5 (range: 14-18).

In the distal tibial fracture group, Mazur ankle scores were excellent in 10, good in 6, and fair in 1 at six months follow-up. One year after surgery, ratings were excellent in 15 patients; good in 2 patients.

The Maryland Foot Score Profile was adapted to evaluate the function recovery of the patients with calcaneal fractures. At the 6 month follow-up timepoint, 7 patients had an excellent rating with a mean score of 92.6 (range: 90-95), 2 patients had a good rating with a mean score of 81.2 (range: 75-89), and one patient had a fair rating with a score of 68. The one year postoperative rating was excellent in all 7 patients with a mean score of 93.4 (range: 90-95), good rating was acquired in two patients with a mean score of 84.5 (range: 75-89), fair rating in one patient with a score of 71.

Discussion

For periarticular fractures, several issues need to be taken into consideration. It is imperative that the articular surface be anatomically reduced to decrease the chance of long term complications such as pain or traumatic arthritis. In order to avoid joint stiffness, adequate bone-implant construct strength must be achieved to permit early rehabilitation. Periarticular fracture internal fixation success, however, is always challenged by two factors. The first factor is the subchondral cancellous bone defect presented after elevation of depressed articular fracture fragments. Filling of such defects with a structural material is necessary to provide initial mechanical support to the

reduction and prevent subsidence of the articular surface during joint loading before bone healing. The second factor is osteoporosis. Insufficient screw purchase in weak osteoporotic bone increases the risk of internal fixation failure and loss of reduction. In osteoporotic patients, bone graft is especially important for good fracture and hardware stabilization.

Bone grafts usually serve one or both of two main functions, as a resource of osteogenetic cells and as a mechanical support [23]. Autogenous bone graft with the ability of osteogenesis and osteoconduction capabilities is well known as the standard means of bone grafting despite the limitations such as donor site morbidity and inadequate amount. Autogenous cancellous bone has greater potential for bone formation and very limited structural strength as compared to autogenous cortical bone [24]. Frozen cortical allograft bone is only osteoconductive, and has the same structural support strength as the autogenous cortical bone [5]. However, cortical bone is very slow to incorporate [6, 25, 26]. Both autograft and allograft share one drawback. It is difficult to fill voids well in irregularly shaped defects with both types of graft. Collectively, the drawbacks of autograft and allograft materials impel scientists and medical companies to develop additional bone graft substitute materials.

Most of the current available synthetic bone graft substitutes can be grouped into hydroxyapatite products, soluble calcium-based blocks and granules, or injectable cements [15]. Among them, injectable cements with adequate compressive strength that harden in situ have been used to augment internal fixation during fracture surgery. The use of Polymethylmethacrylate (PMMA) was recommended in several studies to enhance fracture stability in the treatment of osteoporotic fractures [27, 28]. Because of its exothermic curing, and inability to be absorbed and the risk of non-union, PMMA is no longer used in fracture treatment. Injectable calcium phosphate cements have been applied in the treatment of metaphyseal fractures for a number of years [8, 29-33]. The mechanical characteristics of calcium phosphate cements vary in different forms. In general, cured calcium phosphate cements have a compressive strength between that of cancellous bone and cortical bone. Resorption

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of calcium phosphate cement has been shown to occur very slowly. In a study by Kopylov et al. calcium phosphate remained in the distal radius two years after implantation [30]. Although Cassidy has reported no adverse sequelae despite intra-articular extrusion into the wrist joint [34], the hardened calcium phosphate cement may cause serious complications such as traumatic arthritis in weight bearing joints. The calcium phosphate cement presents some handling difficulties since the internal fixation hardware must be placed before the injection of graft materials, especially in severely comminuted fractures [35].

An injectable biodegradable CaSO_4 based bone graft substitute, BCSC (Minimally Invasive Injectable Graft (MIIG) Wright Medical Technology, Inc, Arlington, Tenn) was manufactured from a surgical grade CaSO_4 that is uniform in shape and size, contrary to the plaster of Paris used historically. The biodegradable cement was designed to harden with the defect and provide intraoperative stabilization. It can be drilled through and receive self-tapping screws after hardening without hindering material strength or integrity properties. BCSC are recently developed products in the series. In vivo studies showed that the compression strength of BCSC [11, 36] may achieve 40 MPa one hour after preliminary set, and reached levels approximately equal to reported PMMA values after 24-48 hours [37]. The adequate immediate stability and high compressive strength is important to maintain the reduction and prevent subsidence of the articular surface.

Watson reported on the use of an injectable CaSO_4 in the treatment of five patients with tibial plateau fracture and three patients with tibial pilon fractures. All patients had excellent outcomes. In these patients, 90%-100% absorption of the graft materials was observed by 12 weeks postoperatively. Three patients sustained extravasation of graft material into the joint space. These intra-articular materials were completely absorbed at an average length of 15 days. They conclude the injectable CaSO_4 was sufficient for intraoperative support and screw placement [13]. In our study, a graft material with higher compressive strength BCSC (MIIG X3, WMT, ArlingtonTN) was used in the periarticular fractures. According to the

Rasmussen's knee functional score system and the Mazur ankle score system, the weight bearing joint function in this series was good. Only two patients with tibial plateau fractures had the articular subsidence of 2 mm without joint dysfunction, indicating that the postoperative reduction was well maintained from initial hardening to complete incorporation of the graft. The incorporation rate of the graft material was similar between the proximal tibia and distal tibia, which may imply that graft remodeling is predictable and mainly determined by cement microstructure rather than defect location [10, 13].

Moed et al. reported on the use of CaSO_4 pellets (Osteoset, WMT, Arlington, TN) in 32 patients with acetabular fractures who had intraarticular comminution or marginal impaction. Follow-up CT scans showed good (>90%) bone ingrowth in 22 of the 31 patients studied. However, five patients had <50% bone ingrowth, including one in whom there was no bone formation. The authors theorized that synovial fluid contact was responsible for pellet resorption without bone formation in these cases since the pellets were in direct communication with the joint space [11]. In our study, good bone ingrowth was observed in all four acetabular fracture cases. This may be attributed to better void-filling characteristics of injectable CaSO_4 cement over CaSO_4 pellets in irregularly formed defects. The small population of patients with acetabular fractures in this series could be another factor.

In our opinion, this injectable calcium sulfate-based bone graft substitute with high compressive strength is a promising alternative for the treatment of periarticular fractures. The utility of this material is of particular interest in weight-bearing joints where reduction maintenance and an ability to fill irregularly shaped defects are important for great prognosis.

Conclusion

This study showed that the use of a high compressive strength calcium sulfate-based bone graft substitute to fill metaphyseal defects in the treatment of periarticular fractures can provide adequate immediate stability and strength for fracture reduction while improving the safety of early stage joint motion in functional rehabilitation.

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Disclosure of conflict of interest

None.

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