Delayed Foreign-body Reaction to Absorbable Implants in Metacarpal Fracture Treatment

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Abstract

Background First-generation bioabsorbable implants have been associated with a high complication rate attributable to weak mechanical properties and rapid degradation. This has led to the development of stronger devices with improved durability. However, the modern implants have raised concerns about potential late-occurring adverse reactions.

Questions/purposes This retrospective study addressed the following questions: Can absorbable implants consisting of trimethylene carbonate, L-lactide, and D,L-lactide provide adequate fixation for healing of a metacarpal fracture? Will these implants obviate a second removal

operation? What complications can occur in the reaction to implant breakdown?

Patients and Methods Twelve unstable, displaced, metacarpal fractures were studied in 10 consecutive patients (seven men, three women; mean age, 36.4 years; range, 18–75 years). The fractures were treated with absorbable plates and screws consisting of the aforementioned copolymers and designed to resorb in 2 to 4 years. Nine patients (10 fractures) were available for clinical and radiographic followups (mean, 45.7 months; range, 34–61 months).

Results Fracture healing was uneventful in all cases. Four patients experienced a foreign-body reaction during the second postoperative year and required surgical débridement to remove implant remnants. Histologic examination confirmed the diagnosis of a foreign-body reaction. Two other patients reported a transient local swelling that subsided without treatment.

Conclusions Our results indicate these absorbable implants for metacarpal fractures achieved adequate bone healing but simply postponed the problem of foreign-body reactions. Patients treated with bioabsorbable implants should be advised of potential late complications and should be followed for at least 2 years, possibly longer.

Level of Evidence Level IV, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

Each author certifies that he or she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

Each author certifies that his or her institution approved the human protocol for this investigation that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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Introduction

Metacarpal fractures are common; they account for nearly 50% of all hand fractures [11]. The majority of metacarpal fractures can be treated successfully without surgery. However, the current general consensus is that comminuted

or grossly displaced fractures must be treated operatively to achieve accurate reduction and stabilization of the fracture and permit early motion [13]. Although the use of metallic implants is considered the gold standard for operative treatment of displaced metacarpal fractures, these implants often are associated with high complication rates. In one series [27] that included open and closed phalangeal and metacarpal fractures, major complications were reported in 36% of patients. The most important complications were delayed union and malunion, stiffness, plate prominence, tendon irritation and rupture, infection, bony atrophy, and osteoporosis attributable to stress shielding. Closed metacarpal fractures appear to have relatively low complication rates [26, 29]. However, these complications, combined with the patient's demand for plate removal, greatly increase the probability that a second operation will be required [27].

During the past decade, bioabsorbable plates and screws have been introduced as a reliable alternative option for treating metacarpal fractures [19]. Various polymers have been shown to lead to lower implant-associated morbidity. These absorbable implants are designed to have several advantages over metallic implants: they are radiolucent and MRI compatible, they limit stress shielding by incrementally transferring load to healing fractures, and they theoretically eliminate hardware removal procedures [19]. The disadvantages of bioabsorbable, compared with metal implants [7, 30], include weakness, rapid loss of initial implant strength, higher refracture rates [30, 31], and foreign-body reactions. The latter range from a synovial reaction to sterile fluid accumulation and sinus formation [19, 28].

First-generation bioabsorbable implants consisting mainly of polyglycolic acid appeared in the 1990 s. They displayed rapid degradation and high rates of subsequent inflammatory reactions [3]. Second-generation implants consisted of poly-L-lactide and showed substantial improvements in degradation rates and foreign-body reactions. Third-generation implants composed of trimethylene carbonate, L-lactide, and D, L-lactide displayed improved strength and slow degradation rates (2–4 years). These were designed to overcome the problems of rapidly diminishing strength and frequent foreign-body reactions [22, 23, 25]. However, the prolonged degradation rate of new implants has raised further concerns. A major concern is whether these materials actually diminish adverse soft tissue reactions or whether the reactions simply are postponed to a later time? These bioabsorbable implants have been studied extensively *in vitro* and in animal models [22, 25], but only few short-term studies were conducted in humans [20, 33].

We addressed the following questions in humans: Can third-generation bioabsorbable implants consisting of

trimethylene carbonate, L-lactide, and D,L-lactide provide adequate mechanical stability and guarantee uneventful healing of displaced metacarpal fractures? Is it feasible to use these implants to obviate a second operation for implant removal? Finally, what complications are associated with the reaction to the breakdown of these materials?

Patients and Methods

This retrospective case series study was approved by our hospital's ethical committee for clinical studies and was in accordance with the Greek guidelines for clinical studies. Between December 2004 and March 2007, 12 displaced, unstable, metacarpal fractures with rotational and angular deformities were studied in 10 consecutive patients (seven men, three women). The fractures were treated with open reduction and internal fixation with absorbable plates and screws (Fig. 1). The mean age of the patients was 36.4 years (range, 18–75 years) (Table 1).

Fig. 1A–D The images show metacarpal fractures treated with absorbable plates. (A) AP and (B) oblique radiographs show a displaced and angulated oblique fracture of the fifth metacarpal treated with absorbable plates and screws. (C) AP and (D) oblique radiographs show a perfect reduction was achieved with the use of bioabsorbable implants.

Table 1. Patient demographics, fracture and implant characteristics, and followup data

Patient	Gender	Age (years)	Metacarpal number (hand)	Plates used	Followup (months)	Remarks
1	Male	32	Third (fourth*) (left)	6-hole plate	61	Implant removal (18 months PO) attributable to FBR (15 months PO)
2	Male	18	Fifth (right)	6-hole plate	55	Transient local swelling (22 months PO)
3	Male	27	Fifth (left)	6-hole plate	50	Implant removal (22 months PO) attributable to FBR (19 months PO)
4	Female	56	Fourth (left)	6-hole-plate	49	No reported complications
5	Male	18	Fourth, fifth (right)	6-hole and 4-hole plates		Died in a car accident
6	Male	29	Fifth (right)	6-hole plate	47	No reported complications
7	Female	75	Second (left)	6-hole plate	45	Implant removal (17 months PO) attributable to FBR (14 months PO)
8	Male	57	Fourth (left)	6-hole plate	35	Transient local swelling (13 months PO)
9	Female	20	Fourth (third*) (left)	6-hole plate	35	No reported complications
10	Male	32	Fourth, fifth (right)	6-hole and 4-hole plates	34	Implant removal (18 months PO) attributable to FBR (15 months PO)

* Metacarpal fracture not fixed; FBR = foreign-body reaction; PO = postoperatively.

Nine patients with 10 fractures were available for followup (mean, 45.7 months; range, 34–61 months); one patient had died in a car accident shortly after surgery (Table 1).

Absorbable four- and six-hole plates and 2.0- or 2.5-mm screws from the Inion® OTPS™ Biodegradable Mini Plating System (INION, Tampere, Finland) were used for internal fixation of the metacarpal fractures (Table 1). The implant copolymers were amorphous and consisted of trimethylene carbonate, L-lactide, and D, L-lactide. According to the manufacturer, after 18 to 36 weeks in vivo, the implants would gradually lose strength, and in 2 to 4 years, complete strength loss and resorption would occur.

All patients were anesthetized with either brachial plexus or general anesthesia, and all surgeries were performed with the aid of a tourniquet by the senior author (PKG). A longitudinal dorsal incision was performed centered over the metacarpal, followed by dissection through the subcutaneous and fascial layers. In two cases where two adjacent metacarpals were fixed, the incision was placed between the involved metacarpals. Extensor tendons were mobilized and displaced to reveal the fracture site. After reduction of the fracture, an absorbable plate was placed on the dorsal cortex, and screw holes were created with the appropriate drill bit. The screw holes were tapped manually and the screws were inserted carefully to avoid head breakage. Before application, the plates were placed in sterile warm normal saline (Inion® thermo water bath, 55°C). This rendered them malleable for contouring to the exact shape of the metacarpal bone (Fig. 2). After plate implantation, the extensor tendons were put back into place and the wound was closed in layers. Fracture

Fig. 2 An intraoperative photograph shows placement of the bioabsorbable plates and screws.

reduction and stabilization were confirmed with intraoperative radiographs. A splint was applied postoperatively, with the metacarpophalangeal joints flexed at 70° and the interphalangeal joints at 0° (hand safe position). The splint was maintained for 2 weeks until suture removal. Afterward, the patients were encouraged to commence active motions of the carpus, metacarpus, and fingers, but load-bearing was delayed for another 2 weeks.

Maintenance of reduction and fracture healing were evaluated on radiographs taken at 6 weeks, 6 months, 1 year, during any returns to the outpatient clinic owing to the appearance of soft tissue reactions, and at the final followup. The appearance of callus or the presence of bony trabeculae that formed across the fracture line seen on radiographs was considered evidence of fracture healing.

Radiographic data were assessed by two independent observers (SIS, PJP) not involved in the initial surgical treatment. The final assessment was taken as the concurrence of the two observers after reading the films together in a conference.

The patients were examined clinically and interviewed for any appearance of soft tissue reactions at the above-mentioned times or when they returned to the clinic for a suspected reaction.

The indications for a reoperation to remove the implants were defined as follows: (1) clinically apparent, tender, local swelling over the implant site with a positive ballotement sign indicating contained fluid accumulation; (2) pain that interfered with everyday living; to evaluate pain, we used a visual analog scale (VAS) for pain (0–10; where 0 represented no pain and 10 represented the worst imaginable pain); (3) symptoms and signs refractory to oral medication and limitation of activity; and (4) persistence of signs and symptoms for at least 2 months. All of these criteria had to be present before we proposed a reoperation for implant removal. According to prior studies, this type of clinical presentation was indicative of a foreign-body reaction to absorbable implants and was considered to be clinically significant [5, 6].

Four patients required reoperation. The minimum followup after the second operation to the last followup was 16 months (mean, 28.75 months; range, 16–43 months). After implant removal surgery, sutures were removed at 2 weeks, and the patients were examined clinically and radiographically at 6 weeks and at the final followup.

In cases of reoperation, two separate culture samples were collected intraoperatively; the first was either from the aseptic pus or reaction fluid, and the second was from the metacarpal surface immediately after removal of the implant remnants. Removed implant remnants also were sent for culturing and the reactive tissue was prepared for histologic examination. The samples were cultured for aerobic and anaerobic bacteria, fungi, and mycobacterium tuberculosis. Histologic analysis of all tissue samples was performed by the same senior pathologist (SP) from the Department of Pathology in our hospital. Tissue samples from all patients were fixed in 10% formalin and embedded in paraffin wax. The blocks were sectioned in 4- μ m-thick slices. The slices were stained with hematoxylin and eosin, and analysis was performed with a light microscope. A semiquantitative analysis was performed to assess the extent of the foreign-body reaction.

Results

For all patients, the fracture healed uneventfully within 6 weeks. There were no incidences of malunion, delayed

union, pseudarthrosis, osteolysis, deformity, loss of reduction, or implant failure. Additionally, none of the cases of foreign-body reactions showed any radiographic or intraoperative evidence of bone resorption, osteolysis, or bone involvement.

Of the nine patients available for followup, six showed evidence of postoperative soft tissue reactions. Two patients reported the appearance of a painless local swelling without further signs of inflammation. In one case, the swelling appeared approximately 13 months postoperatively and, in the other case, 22 months postoperatively. In both cases, the swelling lasted for approximately 2 weeks and disappeared spontaneously. Neither patient had sought medical assistance owing to the complete lack of accompanying symptoms. Therefore, the reported complications could not be evaluated. Four patients experienced a foreign-body reaction during the second postoperative year (mean, 15.7 months; range, 14–19 months). In all cases, the same clinical symptoms were present, and the patients sought medical assistance after the swelling and symptoms had persisted for at least 1 month (Table 1). At clinical examination, the implantation site showed local swelling and tenderness (Fig. 3), with a positive ballotement sign, indicative of a contained fluid accumulation. The patients reported, after the initial appearance of the swelling, it gradually increased in size over a few weeks. All patients complained of an accompanying mild continuous ache at rest (mean VAS score, 2.25; range, 2–3) that was exacerbated by finger motion and impeded everyday activities.

The foreign-body reactions initially were treated non-operatively. Patients were given oral analgesics (NSAIDs) and told to limit activity. After 2 months of nonoperative treatment, no improvement was observed in symptoms or signs; therefore, surgery was indicated for these four patients. An average of 3 months passed between the initiation of symptoms and the surgical procedure.

The surgery for all four patients included débridement and implant removal. In two cases, a quantity of thick, yellowish fluid (aseptic pus) was present during surgery. In the other two cases, a small quantity of serum was present. In all four cases, solid remnants of the plate and screws were present (Fig. 3). The implant remnants were enveloped in reactive tissue, but the extensor tendons showed no signs of tendon irritation or inflammation. Free remnants of implanted plates and screw heads were removed, but screw parts inside the bone were left in place.

All culture samples were negative. Histologic examinations of the tissue samples collected intraoperatively from all patients confirmed the diagnosis of a foreign-body reaction. Microscopic examination showed pieces of synovial membranes with extensive foreign-body reaction. The infiltrate comprised predominately histiocytes and foreign-body multinucleated giant cells (Touton type)

Fig. 3A–D A second operation was required after treating a metacarpal fracture with absorbable implants. (A) A foreign-body reaction occurred 15 months after fixation of the third metacarpal. Intraoperatively, (B) a quantity of yellowish, thick fluid was present, and (C) solid remnants of the plate and screws were observed. (D) The solid remnants are shown.

surrounding the implant particles (Fig. 4). This histologic picture was typical for a foreign-body reaction and was found consistently in all cases examined. Semiquantitative analyses showed, among all the tissue samples, 70% to 90% of the tissue section surface showed signs of a foreign-body reaction.

The surgical wound healing was uneventful in all cases. All patients reported a direct clinical improvement, and symptoms subsided as early as 2 weeks postoperatively. None of the patients experienced a recurrence of any type of soft tissue reaction between the reoperation and the final followup.

Discussion

Although bioabsorbable implants have been used increasingly in recent years, there are few studies regarding the long-term effects of these implants for treatment of metacarpal fractures. Our study addressed the following questions: Do third-generation bioabsorbable implants consisting of trimethylene carbonate, L-lactide, and D,L-lactide provide adequate mechanical stability and uneventful healing of displaced metacarpal fractures? Is it feasible to use these implants to obviate a second removal operation? What are the complications associated with reactions to the breakdown of these materials? We found, although fracture healing occurred uneventfully, clinically significant foreign-body reactions did occur in four of nine

patients, and they required a second procedure for implant removal.

The relatively small number of patients could be considered a limitation of our study. Moreover, we did not use a control group treated with metallic implants. However, there is a sufficient body of published information to serve as a solid baseline for the use of metal plates in metacarpal fractures; moreover, metal plates currently constitute the gold standard. The only issue for discussion is the need for a removal operation. As this is the theoretical advantage offered by absorbable implants, we focused on this issue.

Bioabsorbable implants have been shown to provoke an adverse tissue response characterized as an inflammatory, abacterial, foreign-body reaction [2–4]. This reaction represents an inherent biologic tissue response to implant degradation and absorption [5, 28]. The clinical spectrum of these tissue responses is broad, ranging from mild reactions that are considered clinically insignificant and heal uneventfully to severe, inflammatory foreign-body reactions that require surgical débridement [5].

In our study, two patients experienced a painless local swelling that disappeared spontaneously; these might have represented mild soft tissue reactions.

The four patients in our study with foreign-body reactions showed the typical clinical manifestation; a painful, erythematous, fluctuating papule that emerged over the implant [5]. In contrast, none of our patients exhibited osteolysis, which appears in approximately 50% of patients [1, 12]. The clinical and histologic features of adverse

Fig. 4A–B Histologic examination confirmed the diagnosis of a foreign-body reaction. **(A)** Reactive tissue was built around the particles (*) derived from implant degradation (Stain, hematoxylin and eosin; scale bar, 400 µm). **(B)** The rectangle in illustration **(A)** delineates the area shown magnified in **(B)**. Arrowheads (<) indicate the typical multinuclear giant cells found in close proximity to the foreign bodies (Stain, hematoxylin and eosin; scale bar, 100 µm).

tissue reactions to polyglycolide and polylactide implants appear to be quite similar, except that discharging sinuses are common with the former and rare with the latter implants [5]. We used polylactide implants, and none of our patients had discharging sinuses.

Our histologic findings were in accordance with those typically seen with foreign-body reactions: a rather uniform histopathologic picture of nonspecific inflammation and abundant polymeric particles surrounded by mononuclear phagocytes and multinucleated foreign-body giant cells [2, 3, 8].

The risk of foreign-body reaction appears to be independent of age and gender [5]. Of the four foreign-body reactions in our study, three occurred in young men and one in an older woman.

The most demanding phase of implant resorption is the decomposition stage, when the gross geometry of the

implant is rapidly lost. When debris particles are produced rapidly, the clearing capacity of the tissue may become taxed, and there is an increased risk for adverse tissue reactions [5, 24]. In our series, the timing of the adverse reaction and the intraoperative findings of grossly fragmented implants indicated the foreign-body reaction occurred in this sensitive phase, after a resting period of more than 1 year. The immediate postoperative subsidence of symptoms and signs further supported the notion that the implant caused the foreign-body reaction.

Several studies have reported on adverse tissue reactions to Inion® biodegradable implants. In animal models, these implants showed normal inflammatory sequelae [22, 25]. Similarly, the incidence of foreign-body reactions was extremely low in some clinical applications, including maxillofacial surgery [20, 21, 33] and in a series of pediatric patients [23].

Only one short-term study has described metacarpal fractures treated with bioabsorbable plates. In that study, no foreign-body reactions were observed after a 6-month followup [10]. However, that interval was considerably shorter than that observed in our study for the occurrence of foreign-body reactions. This suggests future studies should include at least a 2-year followup.

Recently, two cases of a severe foreign-body reaction requiring implant removal were observed with a bioabsorbable spacer used for treating thumb basal arthritis [9, 15]. In one case, the inflammation recurred and was attributed to residual microfragments, which required a second débridement [9]. That case suggests the possibility of recurrent foreign-body reactions. In our series, no patients showed signs of recurrent inflammation for more than 1 year after implant removal.

The anatomic location of a fracture appears to influence the susceptibility to adverse reactions. Adverse tissue reactions occurred in 22.5% to 40% of wrist fractures compared with 4% to 14.6% of ankle fractures treated with the same polyglycolic acid implant [8, 14, 17, 18], 25% of scaphoid fractures [6], and only 1.8% of elbow fractures [6]. We previously used bioabsorbable pins to treat radial head fractures and did not observe any foreign-body reactions [16].

Foreign-body reactions can be provoked with implant volumes that exceed the capacity of the surrounding soft tissues [32]. Recent recommendations suggest using the minimum possible implant size to reduce the amount of breakdown products [33]. Moreover, an increased frequency of adverse soft tissue reactions may occur owing to poor vascularity of the implantation site and an insufficient layer of soft tissue [5, 22]. Thus, the relatively high intensity and frequency of foreign-body reactions in the metacarpals may be attributable to the proximity of avascular tendons, relative paucity of subcutaneous fat, and

insufficient muscle vascularity for efficient clearance of large implants and abundant degradation products.

Our results call into question one of the primary theoretical advantages of absorbable implants. We found a relatively high incidence of foreign-body reactions requiring a removal procedure. Our findings suggest modern absorbable implants with slow degradation rates have not eliminated the problem of foreign-body reactions but simply postponed the occurrence of reactions to a later postoperative time. Patients treated with bioabsorbable implants should be advised of this possible complication and should be followed for at least 2 years, possibly longer.

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