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External fixation of tibial pilon fractures and fracture healing

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OULUN YLIOPISTO

Thesis

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Thesis at a glance

	Question	Patients and methods	Outcome measures	Results	Answer
I	Which factors affect the healing of distal tibial fractures treated with external fixation?	47 consecutive fractures treated with a two-ring hybrid fixator	1. Time to fracture healing 2. Number of secondary interventions due to delayed healing	Displacement >3mm is predictive of longer healing time and secondary interventions. Fibula fixation is predictive of secondary interventions.	Displacement and fibular fracture fixation have negative impacts, whereas fracture energy, closed/open, fracture morphology and age have no effect.
II	Can the healing of distal tibial fractures treated with external fixation be accelerated by using recombinant human bone morphogenetic protein-7 (rhBMP-7)?	20 fractures treated with osteoinduction with rhBMP-7 and 20 matched controls	1. Time to fracture healing 2. Number of secondary interventions	More fractures in the BMP group healed by 16 and 20 weeks. Shorter union time, sick leave and frame time in the BMP group	Yes
III	What is the role of temporary external fixation prior to definitive non-spanning external fixation?	44 type C fractures, of which 15 were temporarily fixed with a spanning external fixator.	1. Number of complications necessitating reoperations, 2. Time to fracture union, 3. Functional recovery	Better reduction in the proximal fracture line and a tendency towards better fracture healing in patients treated with temporary external fixation. No difference in any other outcome measures.	No effect on healing time. Improves fracture reduction and tends to decrease secondary operations.
IV	Is there a difference in the healing potential of bone defects treated with autogenous bone at different locations of tibia?	23 high-energy open tibial fractures with a significant > 3 cm bone defect	1. Time to the healing of the reconstructed segment, 2. Number of secondary interventions	Fastest healing in distal tibia, slowest in shaft	Yes

Abstract

Distal tibial fractures are rare and difficult to treat because the bones are subcutaneous. External fixation is commonly used, but the method often results in delayed union. The aim of the present study was to find out the factors that affect fracture union in tibial pilon fractures. For this purpose, prospective data collection of tibial pilon fractures was carried out in 1998–2004, resulting in 159 fractures, of which 83 were treated with external fixation. Additionally, 23 open tibial fractures with significant > 3 cm bone defect that were treated with a staged method in 2000–2004 were retrospectively evaluated. The specific questions to be answered were: What are the risk factors for delayed union associated with two-ring hybrid external fixation? Does human recombinant BMP-7 accelerate healing? What is the role of temporary ankle-spanning external fixation? What is the healing potential of distal tibial bone loss treated with a staged method using antibiotic beads and subsequent autogenous cancellous grafting compared to other locations of the tibia?

The following risk factors for delayed healing after external fixation were identified: post-reduction fracture gap of >3 mm and fixation of the associated fibula fracture. Fracture displacement could be better controlled with initial temporary external fixation than with early definitive fixation, but it had no significant effect on healing time, functional outcome or complication rate. Osteoinduction with rhBMP-7 was found to accelerate fracture healing and to shorten the sick leave. A staged method using antibiotic beads and subsequent autogenous cancellous grafting proved to be effective in the treatment of tibial bone loss. Healing potential of the bone loss in distal tibia was at least equally good as in other locations of the tibia.

List of Papers

I Ristiniemi J, Flinkkilä T, Hyvönen P, Lakovaara M, Pakarinen H, Biancari F and Jalovaara P. Two-ring hybrid external fixation of distal tibial fractures: A review of 47 cases. J Trauma 2007; 62: 174-183.

II Ristiniemi J, Flinkkilä T, Hyvönen P, Lakovaara M, Pakarinen H and Jalovaara P. RhBMP-7 accelerates fracture healing in distal tibial fractures treated with external fixation. J Bone Joint Surg (Br) 2007; 89-B (2): 265-272.

III Ristiniemi J, Hyvönen P, Flinkkilä T and Jalovaara P. Role of temporary external fixation in the treatment of tibial pilon fractures. (Submitted to Acta Orthopaedica)

IV Ristiniemi J, Flinkkilä T, Lakovaara M and Jalovaara P. Staged method using antibiotic beads and subsequent autografting for large traumatic tibial bone loss. Acta Orthopaedica. (Accepted)

Abbreviations

AO Arbeitsgemeinschaft für Osteosynthesefragen (The Swiss Association for the Study of the Problems of Internal fixation, ASIF)
BMP Bone morphogenetic protein
CT Computerized tomography
IF Internal fixation
IMN Intramedullary nailing
ORIF Internal fixation with screws and/or plate
OTA Orthopaedic Trauma Association (North America)
ROM Range-of-motion

Introduction

Distal tibial fractures are difficult to treat and often result in permanent disability. These fractures are relatively rare, accounting for only 3% to 10% of all fractures of the tibia and fewer than 1% of all fractures of the lower extremity. (Rüedi & Allgöver1969, Ayeni 1988). After diaphyseal fractures, the highest incidence of open fractures of the tibia and fibula occur in the tibial plafond. In a study from Scotland (Court-Brown 1996), 6% of pilon fractures were open.

The tibia articulates distally with the talar dome, forming a congruent saddle-shaped weight-bearing surface. Under physiological conditions, the ankle joint sustains peak loads of almost four times the body weight (Procter & Paul 1982). Between 80 and 90% of the load is transmitted through the tibial plafond to the dome of the talus (Calhoun et al. 1994) and 17% through the fibula (Lambert 1971). High-energy trauma is usually required to break the articular surface of the tibia and the overlying metaphysis.

Blood supply to the distal tibia is provided by the three main systems: (1) the epiphyseal-metaphyseal; (2) the nutrient (arteria nutricia tibiae); and (3) the periosteal (Nelson et al. 1960). The anterior and posterior tibial arteries together divide into numerous extraosseous branches around the distal tibia. The posterior tibial artery supplies extraosseous branches to the area of the medial malleolus and the posterior aspect of the tibial metaphysis just proximal to the tibial plafond (Borrelli et al. 2002). The skin receives significant blood supply from the underlying fascia by way of small perforating arteries (Tolhurst et al. 1983). In dislocated fractures, endosteal circulation is always disrupted and extraosseous blood supply has a dominant role in fracture healing. Most of the extraosseous blood supply comes from the injured soft tissues adjacent to the fracture (Gothman 1961). The periosteal vessels are important in re-establishing endosteal circulation in the distal fragment after fracture (Macnab 1974). In the lower leg, the tibia and the fibula are mostly subcutaneous and susceptible to degloving injuries of the skin and subcutaneous tissues. These vascular and anatomical features make the treatment of injuries of the distal tibia very challenging.

Mechanism of injury and classification

Distal tibial fractures caused by direct axial loading and ankle fractures caused by indirect trauma are distinct entities. They both involve the same joint, but their treatment and prognosis differ significantly. Rotational ankle fractures are not discussed in this thesis.

The term “tibial pilon” was introduced by the French radiologist Destot in 1911 to describe the distal tibial metaphysis, which is shaped like a pharmacist’s pestle (“pilon”) (Bartlet 1998). Another French term was contributed by Bonin, who used the word “plafond” (’ceiling’) to refer to the horizontal distal tibial articular surface (Bartlet 1998). Kellam and Waddel named this fracture “the distal tibial explosion fracture” (1979).

Tibial pilon fractures involve the weight-bearing articular surface of the distal tibia or the adjacent tibial metaphysis or both (Thordarson 2000). The defining characteristic of a pilon fracture is the involvement of the supra-articular metaphysis, which typically exhibits varying degrees of impaction (Figure 1). Pilon fractures are most commonly caused by a fall from a height or a motor vehicle accident with a sudden stop. Axial compression occurs as the talus is driven into the tibial plafond. The foot position at the time of the injury determines the exact fracture pattern. In a plantarly flexed foot, the posterior lip of the tibial articular surface is separated, while in a dorsiflexed foot, the anterior portion of the tibial surface is disrupted and impacted. In a neutral position of the foot, the typical fracture pattern involves anteromedial, posterolateral, posteromedial and anterolateral (Tillaux) fragments and what is called a dye fragment (Topliss et al. 2005). In 70–85% of the cases, the fibula is also fractured (Mast et al. 1988, Marsh 1995). Pilon fractures can also occur after

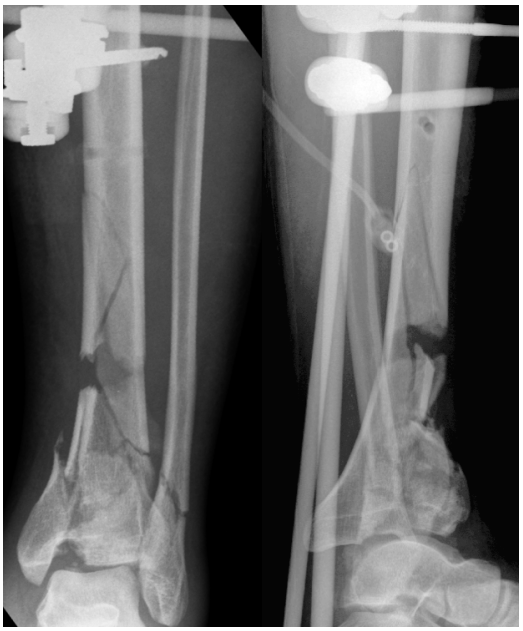

Figure 1. Tibial pilon fracture with impaction of the metaphysis temporarily fixed with external fixator spanning the ankle joint.

low-energy injuries with more rotational and less axial loading, resulting in less comminution and less soft-tissue injury.

Distal tibia fractures can be classified according to the fracture morphology (spiral, transverse, oblique, comminuted) and depending on whether the fracture is open or closed. Fractures can also be categorized according to the degree of soft-tissue damage and the fracture morphology (Oestern et al. 1984).

Rüedi and Allgöwer`s classification of intra-articular distal tibial fractures is based on comminution and dislocation of articular and metaphyseal fractures (Rüedi & Allgöwer 1979). Rüedi type 1 fracture is a low-energy fracture with a simple fracture pattern and no dislocation. In type 2 fracture, the joint line fracture is dislocated, but there is no gross crushing or comminution. Type 3 fracture is a high-energy fracture with impaction and comminution of the articular surface and the overlying metaphysis. Extra-articular fractures are not included in this classification.

The most widely used and comprehensive classification system today is the Orthopaedic Trauma Association (OTA) classification, initially described by the AO group (Müller et al. 1990). The tibia is

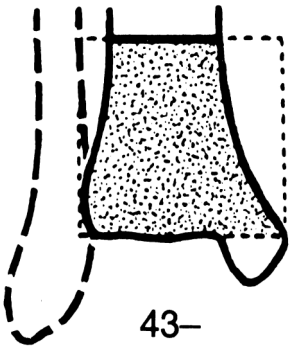

Figure 2. Distal tibia as defined in AO/OTA classification.

divided into three segments: proximal, diaphyseal and distal. The distal segment is defined by squares whose sides are equal in length to the widest part of the epiphysis in question. The distal segment comprises the most distal 5 cm of the tibial length (Figure 2). Distal tibia fractures are divided into type A, B and C fractures (Figure 3). Type A fractures are totally extra-articular fractures with disruption of the metaphysis from the diaphysis. Type B fractures are partially articular fractures. There is a disruption in the joint line, but the metaphysis-diaphysis communication is not disrupted. The most typical pilon fractures are of type C. In type C fractures, the joint surface is fractured and there is metaphyseal-diaphyseal disruption. There are several subclassifications for each fracture type in the AO/OTA classification. Inter- and intraobserver agreement is good at the A-C level, but much less good at the subtitle level (Swiontkowski et al. 1997). Open fractures are almost invariably classified according to Gustilo and Anderson (1976) or Gustilo et al. (1984).

Treatment of pilon fractures

The fact that, during rapid axial loading, the energy released from the fractured bone is imparted to the thin soft-tissue cover makes tibial pilon fractures extremely challenging to manage. The energy release injures the vulnerable soft-tissue envelope in an area with no muscle cover, where vascularity is marginal due to the limited anastomoses between the major vessels (Marsh 1999). Soft-tissue injury,

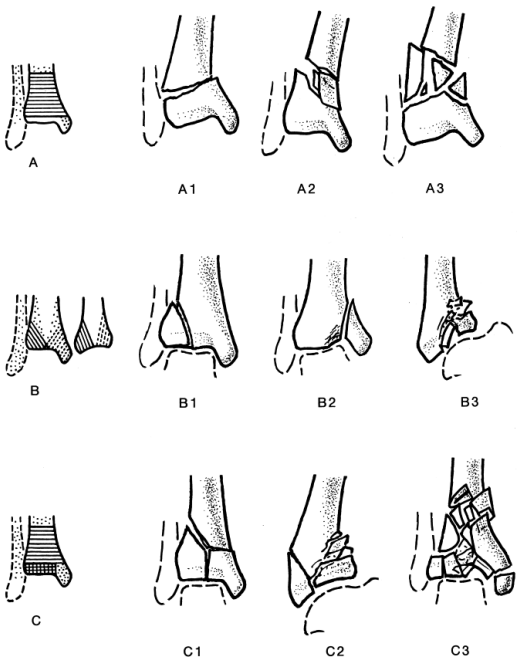

Figure 3. AO/OTA classification of distal tibial fractures.

primary cartilage damage, comminution of the weight-bearing articular surface and metaphysis and displacement of the talus contribute to the uncertain outcome of fractures of the tibial pilon and often result in treatment-related complications (Figure 4).

Conservative treatment

Conservative treatment using closed reduction and a plaster cast usually has a poor outcome, as secondary displacement of the ankle joint cannot be prevented (Rüedi & Allgöwer 1969). Initial calcaneal traction for 3 to 8 weeks followed by a non-weight-bearing plaster cast for six to nine weeks and restricted weight bearing for up to 20 weeks was previously recommended (Scheck et al. 1965, Colton 1976). There are few data on the results of treating pilon fractures closed. Ayeni (1988) reported good results in Rüedi type I fractures and poor results in type II fractures. However, he did not find conservative treatment applicable to type III fractures. Today, conservative treatment is exclusively used for undisplaced type A and C1 fractures.

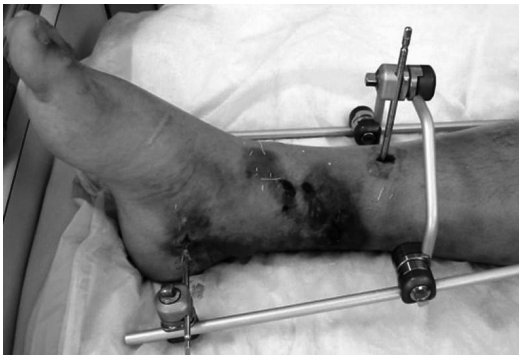

Figure 4. Skin injury related with closed pilon fracture.

Operative treatment

The poor results of the conservative treatment of tibial pilon fractures have prompted most surgeons to seek better methods to control dislocation of the meta-diaphyseal fracture and joint fragments. The current treatment strategies recommend at least some surgical manipulation of the fragments, which requires incision through the soft tissues (Marsh et al. 1999). The basic methods of operative treatment are open reduction and internal fixation with a plate (ORIF) or external fixation combined with minimally invasive joint line reconstruction. Preoperatively, computerized tomography is recommended (Tornetta & Gorup 1996) (Figure 5).

Plate osteosynthesis

The principles of open reduction and internal fixation (ORIF) described by the AO group (Allgöwer et al. 1963, Müller et al. 1979) include initial restoration of fibular length, anatomic reconstruction of the articular surface of the tibia, cancellous bone grafting of any bone defect, application of a T-shaped plate to the medial side of the tibia and early motion of the ankle joint. Good-to-excellent functional results in 80 to 90% of patients with less than 5% infections were reported using the method (Rüedi & Allgöwer 1969 and 1973, Heim& Naser 1976, Kellam& Waddell 1979, Ovadia & Beals 1986). Anatomic reconstruction of the articular surface and early motion were considered the key factors for successful outcome.

Less optimistic reports were published from a more recent series, which included high-energy

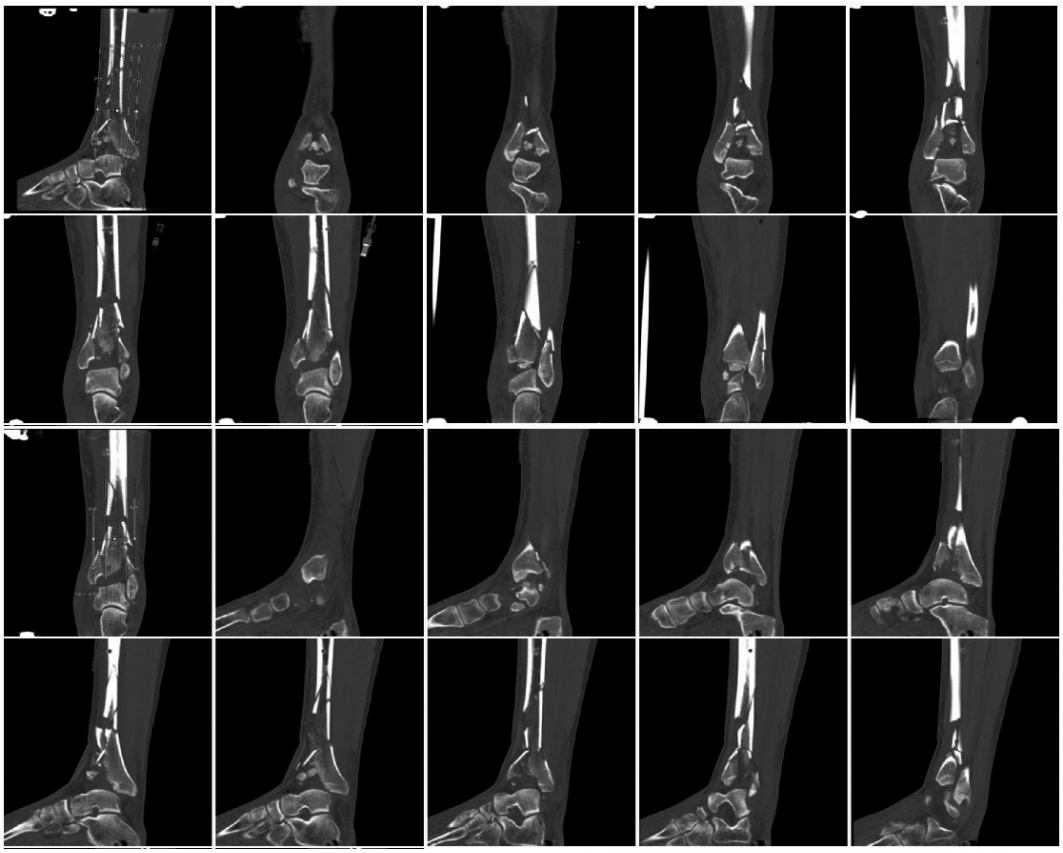

Figure 5. Coronal and sagittal reconstructions of the CT scan of the fracture that was presented in Figure 1.

fractures (McFerran et al. 1992, Teeny& Wiss 1993, Wyrsch et al. 1996). McFerran and co-workers reported 54% complications in severe pilon injuries operated at a university trauma centre (McFerran et al. 1992). Teeny and Wiss diagnosed 37% deep infections in Rüedi type III fractures (Teeny& Wiss 1993). Unacceptable clinical results were reported for 75% of their patients. The presence of wound problems increased the incidence of deep infections sixfold, from 7 to 43%. Arthrodesis was ultimately required in 26% of the cases. Fracture severity and inability to obtain anatomic reduction were the key factors correlating with their poor results.

Wyrsch and colleagues (Wyrsch et al. 1996) performed a prospective study comparing the results of ORIF of pilon fractures versus external fixation with or without limited internal fixation. Although the ankle scores for the two groups were equivalent, complications were more frequent and severe in the patients treated with ORIF. There were 15 complications in 7 out of 18 patients treated with ORIF. Three amputations were performed among the 18 closed fractures. In contrast, only 4 complications occurred in 4 of the 20 patients treated with external fixation. The study was prematurely aborted because of ethical concerns, when it became apparent that there were more complications in the group treated with plate osteosynthesis (Wyrsch et al. 1997).

Sirkin et al. (1999) postulated that the poor results in the series of Wyrsch and co-workers (1997) may have been due to surgical timing rather than the technique, because the internal fixation was performed at the worst possible time, namely 3 to 5 days post-injury. Temporary external fixation prior to definitive ORIF is recommended by many authors, and remarkably low deep infection rates have been reported (Sirkin et al. 1999, Anglen & Aleto 1998, Patterson & Cole 1999, Watson 2000A, Blauth et al. 2001).

One disadvantage of open reduction and plate osteosynthesis is the extensive dissection and devascularization of the underlying tibia (Teeny & Wiss 1993, Wyrsch et al. 1997). In a cadaver study, it was shown that traditional open plating of the distal tibia caused more disruption of the metaphyseal extraosseal blood supply compared to percutaneous plating (Borrelli et al. 2002). A low rate of soft-tissue complications have been reported using percutaneous, minimally invasive submuscular and subcutaneous plating mainly in low-energy type A fractures (Helfet et al. 1997, Oh et al. 2003).

External fixation

To avoid complications associated with traditional ORIF, many surgeons have turned to external fixation, usually combined with limited internal fixation provided by lag screws that are used to stabilize the joint surface. Three categories of fixator design are available: the joint-spanning rigid fixator (Bone et al. 1993, Pugh et al. 1999), the joint-spanning articulated fixator (Bonar & Marsh 1993, Marsh et al. 1995), and the non-joint-spanning fixator (Tornetta et al. 1993, Barbieri et al. 1996). The joint fragments are usually reduced using minimally invasive methods and fixed with lag screws (Tornetta et al. 1993). The external fixator is placed to bridge the ankle joint and the diaphysis or metaphysis and diaphysis. In the non-spanning "hybrid" technique, the distal segment is fixed with tensioned wires attached to a fully circular ring. The diaphysis is fixed with half pins, and these are connected to a distal ring with a monolateral fixator (Tornetta et al. 1993, Barbieri et al. 1996). To avoid cantilever bending forces and the possibly increased risk of non-union, a full ring construct has been recommended (Watson et al. 2000 A). In this technique, diaphyseal half pins as well as distal wires are connected to a full ring (Figure 6).

External fixation gives a lower complication rate than traditional plating. Bonar and Marsh (Bonar & Marsh 1993) had 0/15 wound infections, Tornetta et al. (1993) had 1/26, Marsh et al. (1995) had 0/47, Barbieri et al. (1996) had 3/37, Court-Brown et al. (1999) had 1/24, and Bone et al. (1993) had 0/20. Good-to-excellent functional results have been reported in more than two thirds of patients (Tornetta et al. 1993, Bone et al. 1993, Barbieri et al. 1996) Bone et al. (1993) reported on severely comminuted open pilon fractures undergoing ankle-spanning external fixation combined with limited internal fixation. Range of motion (ROM) was excellent or good in 15/20 patients. Overall functional results were similar compared to ORIF, but complications were less severe (Marsh 1999). The main problem is due to pin-related infections, which are reported to occur in 10 to 20% of patients (Gaudinez et al. 1996, Marsh et al. 1995, Tornetta 1993). These are rarely severe and mostly manageable with oral antibiotics.

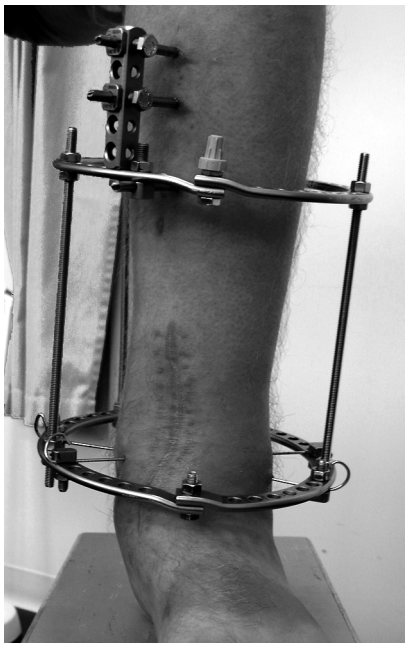

Figure 6. Two-ring hybrid external fixator.

Fixation of associated fibular fracture

Some authors have fixed associated fibular fractures in conjunction with the external fixation of distal tibial fractures (Bone et al. 1993, Saleh et al. 1993, Tornetta et al. 1993), but there are no unambiguous recommendations for this in the clinical reports. Williams et al. (Williams et al. 1998) found significantly more serious complications in the cases where the fibular fracture was fixed compared to those where it was not fixed. They did not find any significant differences in the mean union times of tibial fractures, regardless of whether the fibular fracture was fixed or not.

Intramedullary nailing

Nork et al. (Nork et al. 2005) treated 36 fractures that involved the distal 5 cm of the ankle joint with reamed intramedullary nailing. Ten fractures had articular extension and were treated with supplementary screw fixation prior to the intramedullary nailing. Thirty patients were followed. All of the fractures united in an average of 23.4 weeks. Seven fractures needed secondary operation to promote healing. There was only 1 deep infection. Using modern outcome evaluation methods, the patients were found to have several limitations in physical functioning, which improved over time.

Factors affecting outcome

Although anatomic reduction of the articular surface has been considered the key factor for successful outcome by many clinicians (Rüedi& Allgöver 1969 and 1979, Heim& Naser 1976, Kellam& Waddell 1979, Ovadia & Beals 1986), the effects of injury to the articular cartilage sustained during articular fracture and the effect of treatment interventions on joint function and preservation are poorly understood (Marsh et al. 2002). There is no evidence to show that improved articular reduction leads to better outcomes (Wyrsch et al. 1996, DeCoster et al. 1999, Etter & Ganz 1991, Marsh 1999). Many authors think that the most important determinant for outcome is the severity of the articular injury (Etter & Ganz 1991, Crutchfield et al. 1995, Marsh et al. 1995). It is, however, difficult to measure the relative importance of articular reduction and injury severity because the quality of reduction is closely associated with the severity of the original injury (Marsh et al. 2003).

In recent studies, neither the quality of articular reduction nor the severity of the injury was found to have any correlation with the ankle score or any of the categories of the SF-36 quality of life survey. (Williams et al. 2004, Marsh et al. 2003). Williams et al. reported that surgical assessment of injury severity and the quality of reduction were less important predictors of outcome than patient demographic factors (gender, age, level of education and whether or not the injury was work-related) (Williams et al. 2004).

Intra-articular fractures of the tibial plafond, especially ones caused by high energy, have a negative effect on ankle function, pain and general health (Marsh et al. 2003, Pollack et al. 2003, Williams et al. 2004) The damage of the articular cartilage by the acute injury may be the most important determinant of outcome, as it may lead to joint degeneration despite accurate reduction (Marsh et al. 2003).

Several systemic and pharmacological factors have been recognized as risk factors for delayed healing of fractures. These are: age and gender (Kyrö et al. 1993), malnutrition (Hulth et al. 1989), diabetes mellitus (Macey et al. 1989), corticosteroids (Cruess & Sakai 1972), non-steroidal anti-inflammatory drugs (Giannoudis et al. 2000, Aspenberg 2002) and smoking (Kyrö et al. 1993, Schmitz et al. 1999).

The following injury-related factors have been documented to have prognostic value for delayed healing or non-union of tibial fractures in clinical series: mechanism and energy of the injury (Karladani et al. 2001, Bhandari & Tornetta 2003), fracture morphology (Tonnesen et al. 1975, Bhandari & Tornetta 2003), degree of soft tissue injury (Nicoll 1964, Tonnesen et al. 1975, Court-Brown & McQueen 1987, Gaston et al. 1999, Audigé et al. 2005), vascular injuries (Brinker & Bailey 1997) and location of the fracture (Heppenstall et al. 1984, Bilat et al. 1994, Audigé et al. 2005).

Some aspects of fracture care, such as motion at the fracture site (Sarmiento et al. 1977), surgical delay (Smith et al. 1974, Coutts et al. 1982), type of fixation (Claes et al. 2006) and periosteal stripping during open reduction (Hayda et al. 1998), have been shown to affect fracture union.

Most of the data currently available come from experimental or clinical studies, where univariate statistics have been used, and controversy remains regarding the relative importance of prognostic factors. Audigé et al. used statistical multivariate analysis and a logistic regression model to assess the probability of delayed union or non-union of operatively treated tibial fractures from 41 different centres (Audigé et al. 2005). The most important predictors of delayed healing were the severity of skin injury, postoperative diastasis between the fracture fragments and the location of the fracture. Fractures occurring in the distal 1/3 of the

tibia were twice as likely to proceed to delayed healing or non-union compared with other shaft fractures. Surgical treatment methods appeared to have an influence on the occurrence of delayed union through their effects on the occurrence of diastasis. Fractures treated by intramedullary nailing or external fixation were more likely to have postoperative diastasis than those treated by plating. Distal location of the tibial shaft fracture was also shown to be prognostic of delayed union in other studies (Heppenstall et al. 1984, Bilat et al. 1994). On the other hand, good results of conservative treatment using functional bracing were reported in a large series of 450 closed fractures of the distal third of the tibia (Sarmiento et al. 2004).

Osteoinduction

Osteoinduction is a process whereby primitive, undifferentiated and pluripotent cells are stimulated by some osteoinductive signals to develop into a bone-forming lineage and, ultimately, to enable remodelling of new bone tissue.

Bone morphogenetic proteins (BMPs) are members of the TGF-β superfamily of growth and differentiation factors, which induce bone formation by promoting the differentiation of mesenchymal cells into chondrocytes and osteoblasts (Dimitriou et al. 2005). At least 16 different BMPs are known, of which BMP-2 and BMP-7 are currently commercially available (Cook et al. 1996, Matthews et al. 2005, Einhorn 2003, Termaat et al. 2005). The different BMPs are structurally and functionally closely related. Each has a unique role as well as a distinct temporal expression pattern during the fracture repair process (Dimitriou et al. 2005). Cheng et al. suggested that BMP-2, -6 and -9 may be the most potent proteins to induce osteoblast differentiation of mesenchymal progenitor cells, whilst most BMPs (except BMP-3 and -13) can promote the terminal differentiation of committed osteoblastic precursors and osteoblasts (Cheng et al. 2003).

Recombinant human BMP-7 (RhBMP-7), also known as osteogenic protein-1 (OP-1), is strongly osteoinductive (Cook et al. 1996). Its clinical efficacy has been shown in spinal fusion (Johnsson et al. 2002, Vaccaro et al. 2005) and tibial non-union (Friedlaender et al. 2001). Geesink and co-workers harvested critical-sized (mean 15 mm) circular defects from human tibias during high tibial osteotomy, which were filled with either rhBMP-7 and carrier (collagen) or carrier alone. Significantly better bone healing was observed in the rhBMP-7-treated patients, indicating that rhBMP-7 can be used to heal critical-sized bone defects (Geesink et al. 1999). A preliminary report showed stimulated healing in human open tibial fractures (McKee et al. 2003).

Delayed healing of distal tibial fractures

Delayed union or non-union and need for secondary interventions due to delayed healing have been common in the treatment of distal tibial fractures (Teeny & Wiss 1993, Anglen et al. 1999, Pugh et al. 1999, French & Tornetta 2000, Nork et al. 2005) (Table 1). Therefore, early or primary bone grafting is recommended in the treatment (Rüedi & Allgover1969, Teeny&Wiss 1993, Tornetta et al. 1993, Marsh et al. 1995, Sirkin et al. 1999, Pugh et al. 1999, French&Tornetta 2000). According to French & Tornetta, the potential need for bone grafting can be predicted by the amount of bone loss or comminution on the original radiographs (French & Tornetta 2000). The proportion of bone loss is only mentioned by Nork et al. (2005). Three out of 33 fractures were associated with bone loss, all of which were open.

In the treatment of tibial shaft fractures, external fixators have a reputation of being "non-union machines" (Court-Brown 2001 A). Clinical studies have shown that the quality of reduction, especially the avoidance of a fracture gap, is extremely important (Court-Brown&Hughes 1985, Helland et al. 1996, Audigé et al. 2005). This fact has received little attention in the literature on distal tibial fractures. The published series on hybrid (Tornetta et al. 1993, Anglen 1999Barbieri et al. 1996) or ankle-bridging external fixation (Bone et al. 1993, Marsh et al. 2003) show a tendency for delayed union and a need for additional operations, especially in meta-diaphyseal fractures.

Table 1. Reported bone grafting and healing rates of tibial pilon fractures

A	B	C	D	E	F	G	H
Teeny 1990	ORIF	60	28	10	38	10	NA
McFerran 1992	ORIF	52	NA	6	NA	6	NA
Tornetta 1993	Hybrid EF	26	11	0	11	0	18
Bone1993	Spanning EF	20	NA	NA	NA	3	19
Marsh 1995	Articulated EF	49	14	1	15	2	NA
Barbieri 1996	Hybrid EF	37	11	1	12	3	20
Gaudinez 1996	Hybrid EF	14	0	0	0	0	13
Wyrsch 1996	ORIF	19	10	1	11	1	14
	EF	20	8	2	10	2	15
Pugh 1999	ORIF	24	6	4	10	8	21
	Unilateral EF	21	9	4	13	33	31
	Hybrid EF	15	1	7	8	40	26
Anglen 1999	Hybrid EF	29	5	4	9	7	20
	ORIF	19	8	0	0	0	15
Watson 2000	ORIF	36	5	5	10	5	NA
	Hybrid EF	58	9	NA	NA	2	NA
Oh 2003	ORIF	21	0	0	0	0	15
Nork 2005	IMN	36	3	NA	NA	7	23
Total		556	128 (23%)	45 (8%)	147 (26%)	129 (23%)	Mean 19

NA = Data not available.
A. First author, year
B. Fixation method:
ORIF=internal fixation,
EF= external fixation,
IMN= internal fixation
C. Number of fractures
E. Number of secondary autograftings
F. Total number of autograftings
G. Number of fractures that had had delayed or non-union
H. Union time in weeks

Aims of the present study

The main purpose of the present study was to identify the factors that affect fracture union in tibial pilon fractures, and to find out if osteoinductive materials can be used to enhance fracture union. The specific questions to be answered were:

1. What are the risk factors for delayed union of tibial pilon fractures treated with two-ring hybrid external fixation?
2. Can the healing of tibial pilon fractures be accelerated using recombinant human BMP-7?
3. What is the role of temporary ankle-spanning external fixation in the treatment of tibial pilon fractures?
4. Is the healing potential of traumatic bone loss treated with the staged method using antibiotic beads and subsequent autogenous cancellous bone inferior in the distal tibia compared to other locations of the tibia?

Patients

Data collection

Data from consecutive patients with distal tibial pilon fractures concerning the mechanism of injury, the AO/OTA fracture classification, the grade of open fractures, operative notes and post-operative recovery were prospectively collected by specialists of orthopaedic traumatology on a special form in 1998–2004. Oulu University Hospital is the only hospital treating high-energy trauma for a population of 376 000 and a referral centre for a population of 760 000. 159 patients were identified, accounting for 5% of the patients with tibial and malleolar fractures. A flow chart showing patient selection for the different treatment methods is shown in Figure 7. The annual incidence of tibial pilon fractures was 4.4/100 000. The incidence of AO/OTA type C fractures was 3/100 000 per year. Forty-two patients were referred to us from other hospitals. The patients referred to us for the treatment of complications, non-union, etc., were not included. Clinical and outcome data are shown in Table 2 and clinical data in the Studies I, II and III in Table 3 and in the Study IV in Table 4.

Study I

Forty-seven consecutive patients with tibial pilon fractures treated with two-ring hybrid external fixation were included.

Study II

Twenty consecutive patients with tibial pilon fractures received osteoinduction treatment with rhBMB-7 and bovine collagen (BMP group) (Figure 8). The fractures were treated with two-ring hybrid external fixation. Fracture union time, fixator time and the length of sick leave were compared with a matched group of 20 patients. The matched group consisted of the 20 patients selected from 47 patients who were treated with a similar method but without osteoinduction. Each patient was assigned an appropriate pair by matching for the type of fracture, the shape of the

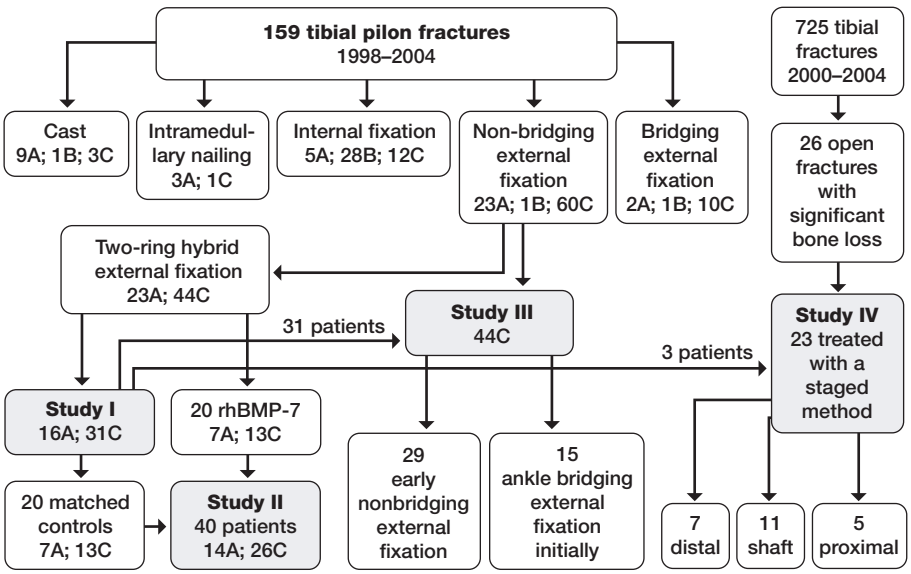

Figure 7. Flow chart showing patient selection into different treatment methods. A, B, C= AO fracture types (Müller et al. 1990). Number of patients is presented.

Table 2. Clinical and outcome data on all patients in the Studies I–IV

A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W
1	1	28	3	A1	0	0	0	2	0	0	0	1	1	0	0	15	0	12	10	2	I,II	M1
2	1	26	3	A1	0	0	0	2	1	0	0	0	0	0	0	9	0	NA	9	2	II	B1
3	2	57	3	A1	0	0	0	2	0	0	1	0	0	0	0	21	0	NA	21	2	I,II	M2
4	1	24	3	A1	0	0	0	2	0	0	0	0	0	0	0	16	0	6	20	2	II	B2
5	2	47	3	A1	0	0	0	2	0	0	1	0	0	0	0	35	1	9	38	1	I,II	M3
6	2	46	3	A1	0	0	0	2	1	0	1	0	1	0	0	12	0	5	12	1	II	B3
7	2	51	3	A1	0	0	0	2	0	1	0	0	0	0	0	21	1	10	17	3	I,II	M4
8	2	79	3	A1	1	0	1	2	0	0	1	0	0	0	0	13	0	3	18	NA	II	B4
9	1	42	3	A1	0	0	0	2	0	1	0	0	0	0	0	23	0	NA	24	NA	I,II	M5
10	2	66	3	A2	0	0	0	2	1	0	1	0	1	0	0	13	0	NA	17	1	II	B5
11	2	78	3	A2	0	0	0	2	0	1	1	0	0	0	1	63	1	NA	26	2	I,II	M6
12	1	39	3	C1	0	0	0	2	0	0	0	0	1	0	0	7	0	5	11	1	II	B6
13	2	63	3	A3	0	0	0	2	0	0	0	0	0	0	0	19	0	NA	12	NA	I,II	M7
14	2	48	3	C1	0	0	0	2	1	0	0	0	1	0	0	16	0	NA	15	2	II	B7
15	1	41	3	C1	0	0	0	2	1	0	0	0	0	0	0	21	0	NA	13	1	I,II,III	M8
16	2	41	3	C1	0	0	0	2	1	0	1	0	1	0	0	14	0	6	15	2	II	B8
17	2	46	3	C1	0	0	0	2	0	0	0	0	0	0	0	21	0	6	22	2	I.II.III	M9
18	2	28	3	C1	0	0	0	2	0	1	0	0	0	0	0	9	0	3	12	1	II	B9
19	1	32	3	C1	1	0	1	2	0	0	0	0	0	0	0	14	0	7	14	2	I,II	M10
20	1	56	3	C2	0	0	0	2	1	0	0	0	0	0	0	13	0	3	9	3	II	B10
21	1	36	3	C1	0	0	0	2	1	0	0	0	1	0	0	26	0	9	27	4	I.II.III	M11
22	1	48	3	C2	0	0	0	2	1	0	0	0	1	0	0	8	0	5	14	2	II	B11
23	2	44	3	C1	0	0	0	2	0	0	1	0	1	0	0	20	0	7	12	1	I.II.III	M12
24	2	46	3	C2	0	0	0	2	0	0	1	0	0	0	0	16	0	13	16	2	II	B12
25	2	44	3	C2	0	0	0	2	0	0	0	0	0	0	0	15	1	NA	28	1	I.II.III	M13
26	1	31	3	A3	0	0	0	2	1	0	1	0	0	0	0	23	0	NA	18	2	II	B13
27	1	49	3	C2	0	0	0	2	0	0	1	0	0	0	0	29	1	11	29	1	I.II.III	M14
28	1	59	3	A3	0	0	0	2	1	1	1	0	0	0	0	22	0	6	22	1	II	B14
29	2	55	3	C2	1	0	1	2	1	1	0	0	0	0	0	23	1	7	24	2	I.II.III	M15
30	1	37	3	C2	1	0	1	2	1	0	0	0	0	0	0	17	0	5	21	2	II	B15
31	1	35	3	C3	1	1	1	2	1	0	0	1	0	0	0	25	0	15	24	4	I.II.III	M16
32	2	52	3	C3	0	0	0	2	1	1	0	0	0	0	0	13	0	5	13	2	II	B16
33	2	44	3	C2	0	0	0	2	1	0	0	0	0	0	0	14	0	4	13	1	I.II.III	M17
34	1	25	3	C3	0	0	0	2	1	0	1	0	0	0	1	13	0	7	14	3	II	B17
35	1	57	3	C2	0	0	0	2	0	0	0	0	1	0	0	11	0	NA	15	1	I.II.III	M18
36	2	23	3	C3	0	0	0	2	0	1	1	0	0	0	1	17	0	12	12	2	II	B18
37	1	52	3	C3	1	0	1	2	1	1	0	0	1	0	0	23	0	NA	22	4	I.II.III	M19
38	2	23	3	C3	1	1	1	2	1	1	0	0	0	0	0	22	1	6	24	3	II	B19
39	1	44	3	C3	0	1	0	2	0	1	1	0	1	0	1	40	1	12	40	4	I,II,III,IV	M20
40	1	29	3	C3	1	1	1	2	1	1	0	0	1	0	0	43	1	13	37	3	II	B20
41	1	44	3	A1	0	1	0	2	0	0	0	1	1	0	0	21	0	11	22	1	I	
42	1	15	3	A2	0	1	0	2	0	0	0	0	1	0	0	8	0	NA	8	3	I	
43	1	44	3	A1	0	0	0	2	0	0	0	0	1	0	0	21	0	12	10	1	I	
44	1	31	3	A1	0	0	0	2	0	0	0	1	0	0	0	10	0	5	10	1	I	
45	2	16	3	A1	0	0	0	2	0	0	0	0	0	0	1	19	0	2	16	2	I	
46	1	15	3	A3	0	1	0	2	0	0	0	1	1	0	0	21	0	NA	9	NA	I,IV	
47	2	75	3	C3	0	1	0	2	1	0	0	0	0	0	0	20	0	NA	17	NA	I,IV	
48	1	59	3	C1	0	0	0	2	1	0	0	0	1	0	1	18	0	10	14	3	I	
49	1	66	3	A1	0	0	0	2	0	1	1	0	0	0	0	37	0	NA	19	1	I	
50	1	51	3	A2	0	0	0	2	0	1	1	0	0	0	0	17	1	8	16	4	I	
51	1	62	3	A2	1	0	1	2	1	0	1	0	0	0	0	60	1	NA	20	3	I	
52	2	35	3	C3	1	0	0	2	1	1	0	0	0	0	0	24	0	NA	22	NA	III	
53	1	51	3	C2	0	0	0	2	1	1	0	0	0	0	0	20	0	NA	20	NA	III	
54	1	39	3	C3	0	1	0	2	0	0	0	0	0	0	0	25	0	NA	21	NA	III	
55	1	42	3	C2	0	0	0	2	0	0	0	0	1	0	0	17	0	NA	16	NA	III	
56	1	51	3	C2	0	0	0	2	0	0	0	1	0	0	0	35	0	NA	22	NA	III	
57	2	47	3	C1	0	0	0	2	0	0	0	0	0	0	0	21	0	7	8	1	III	
58	1	59	3	C2	0	0	0	2	1	0	0	0	1	0	1	18	0	10	14	3	III	
59	2	63	3	C3	1	0	1	2	0	0	0	0	0	0	0	30	0	NA	24	2	III	
60	2	55	3	C1	0	0	0	2	0	1	0	0	1	0	0	16	0	NA	16	NA	III	

61	2	67	3	C3	1	0	0	2	1	0	0	0	1	0	0	20	0	NA	20	NA	III
62	1	44	3	C3	0	1	0	2	1	1	0	0	1	0	0	39	0	11	22	2	III
63	1	49	3	C3	1	0	0	2	0	0	0	0	1	0	0	27	1	NA	23	NA	III
64	1	51	3	C2	0	1	0	2	0	0	1	0	0	0	0	25	0	NA	20	1	III
65	1	52	3	C2	0	0	0	2	0	0	1	0	0	0	0	16	0	NA	16	NA	III
66	1	41	3	C1	1	0	1	2	0	1	1	0	0	0	0	17	1	8	16	4	III
67	2	50	3	C3	0	0	0	2	0	0	1	0	1	0	1	68	1	NA	20	NA	III
68	2	56	3	C2	0	0	0	2	0	0	0	0	0	0	0	18	0	3	15	1	I,III
69	1	59	3	C3	0	0	0	2	0	0	0	0	1	0	0	19	0	5	19	1	I,III
70	1	66	3	C3	0	1	0	2	0	0	0	0	0	0	0	22	0	NA	20	3	I,III
71	1	49	3	C2	0	1	0	2	1	0	0	0	1	0	0	23	0	9	19	1	I,III
72	2	49	3	C2	0	0	0	2	1	1	0	1	0	0	0	19	0	NA	19	NA	I,III
73	1	55	3	C3	0	1	0	2	1	0	0	0	0	0	0	15	0	NA	13	4	I,III
74	2	66	3	C1	0	0	0	2	0	0	0	0	1	0	0	18	0	NA	17	2	I,III
75	1	35	3	C1	0	0	0	2	0	0	0	0	0	0	0	13	0	6	12	2	I,III
76	2	44	3	C2	0	0	0	2	0	0	0	0	0	0	0	21	0	NA	25	NA	I,III
77	2	55	3	C1	0	0	0	2	0	1	0	1	0	0	0	20	0	5	14	1	I,III
78	2	58	3	C2	0	0	0	2	0	1	0	0	0	0	0	14	0	NA	15	NA	I,III
79	1	74	3	C2	0	0	0	2	0	0	1	0	0	0	0	12	0	NA	18	4	I,III
80	1	57	3	C3	0	0	0	2	0	1	1	0	0	0	0	30	0	30	26	4	I,III
81	1	40	3	C3	1	0	1	2	0	0	1	0	1	0	0	43	1	NA	21	4	I,III
82	1	47	3	C3	0	1	0	2	0	1	1	0	0	0	0	38	1	18	38	4	I,III
83	1	61	3	C3	0	0	0	2	1	1	1	1	0	1	0	30	1	8	31	4	I,III
84	2	42	3	A3	1	1	1	2	0	1	0	0	0	0	0	42	0	NA	38	NA	IV
85	1	15	1	A3	NA	1	1	2	1	0	0	1	1	1	1	53	0	NA	48	NA	IV
86	1	39	1	C3	NA	1	1	2	1	0	0	0	1	0	1	47	0	NA	40	NA	IV
87	2	50	1	C3	NA	1	1	1	1	0	0	0	NA	0	0	22	0	NA	NA	NA	IV
88	1	26	2	C2	NA	1	1	3	0	0	0	1	NA	0	0	63	1	NA	NA	NA	IV
89	1	63	2	C3	NA	1	1	3	0	0	0	0	NA	0	0	55	1	NA	NA	NA	IV
90	1	33	2	C3	NA	1	1	3	0	1	0	1	NA	0	0	44	0	NA	NA	NA	IV
91	1	53	3	C3	1	1	1	2	1	1	0	0	1	0	0	23	0	NA	22	52	IV
92	2	60	3	C3	0	1	1	1	1	0	0	0	NA	0	1	20	0	NA	NA	NA	IV
93	1	55	1	C3	NA	1	1	3	0	0	0	0	NA	0	0	44	0	NA	NA	NA	IV
94	1	19	1	A3	NA	1	1	1	0	0	0	0	NA	0	0	19	0	NA	NA	NA	IV
95	1	45	2	C3	NA	1	1	3	0	0	0	0	NA	0	0	54	1	NA	NA	NA	IV
96	2	14	2	C3	NA	1	1	3	0	0	0	1	NA	0	0	33	0	NA	NA	NA	IV
97	1	15	2	C3	NA	1	1	3	0	0	0	0	NA	0	0	25	1	NA	NA	NA	IV
98	2	16	2	C2	NA	1	1	3	0	0	0	0	NA	0	0	40	1	NA	NA	NA	IV
99	1	37	2	C3	NA	1	1	3	0	0	0	0	NA	0	0	79	1	NA	NA	NA	IV
100	1	24	2	C3	NA	1	1	3	0	0	0	1	NA	0	0	40	1	NA	NA	NA	IV
101	1	15	2	C3	NA	1	1	3	0	0	0	0	NA	0	0	24	0	NA	NA	NA	IV
102	1	15	2	C3	NA	1	1	3	0	0	0	0	NA	0	0	51	0	NA	NA	NA	IV
103	2	21	3	C3	1	1	1	2	1	1	0	0	0	0	0	22	1	6	24	74	IV

NA = not applicable or data not available
A. Patient number
B. Sex, 1= male, 2= female
C. Age in years
D Location of the tibial fracture 1= proximal tibia, 2= tibial shaft, 3= distal tibia
E. AO fracture class (Müller et al. 1990)
F. Diaphyseal extension of tibia fracture, 0= no, 1= yes
G. Closed (=0) or open (=1) nature of the fracture
H. Significant bone defect: 0= no, 1= yes
I. Type of the definitive fixation, 1= internal fixation, 2= external fixation, 3= locked intramedullary nailing
J. Temporary ankle spanning external fixation used, 0= no, 1= yes
K. Fibula fracture fixed, 0= no, 1= yes
L. Postreduction displacement ≥ 3 mm, 0= no, 1= yes
M. Major complication necessitating reoperation, 0= no, 1= yes
N. Pin tract infection, 0= no, 1= yes
O. Deep infection of the fracture, 0= no, 1= yes
P. Malunion, 0= no, 1= yes
Q. Union time of the tibia fracture in weeks
R. Delayed fracture union requiring reoperation, 0= no, 1= yes
S. Length of sick leave in months
T. Time spent in external fixation in weeks
U. Functional recovery (Merchant et al. 1989), 1= excellent, 2=good, 3= fair, 4= poor
V. The study in which the patient was included
W. The pairs in the Study II, B=patient who received osteoinduction with rhBMP- 7, M= Matched pair

Table 3. Clinical data on patients in the Studies I, II and III

	Study I		Study II		Study III	
	A (n=35)	B (n=12)	C (n=20)	D (n=20)	E (n=29)	F (n=15)
Age in years	49	50	41	47	51	49
range	(15–75)	(40–78)	(23–79)	(28–78)	(35–74)	(35–67)
Men	22	7	11	10	17	10
Smokers	9	7	10	8	6	4
Patients with multiple injuries	3	4	3	1	3	5
Significant bone defects	4	2	3	6	2	5
Fibula intact or fibular fracture fixed	7	7	6	6	7	7
AO fracture type:						
A1	8	2	4	5		
A2	1	3	1	1		
A3	2		2	1		
C1	9		4	5	8	2
C2	8	3	4	5	11	6
C3	7	4	5	3	10	7
Configuration of the proximal tibial fracture						
Spiral	10	2	7	7	3	2
Oblique	4	2	0	1	3	1
Transverse	3		1	0		1
Wedge	5	5	5	6	5	2
Complex	13	3	7	6	8	6
Tibial fractures with diaphyseal extension	3	3	4	4	3	2
Open fractures	8	2	2	2	5	4
Secondary suture	3		2		1	
Split skin graft	1					
Muscle flap	4	2		2	4	4
Time delay in closure of open fractures in days	10 (6–27)	6 (4–9)	7 (7–7)	5 (4–6)	7 (6–9)	7 (4–10)
Median time delay to definitive fixation in days	3 (0–16)	2 (0–27)	6 (0–14)	2 (0–12)	2 (0–8)	9 (2–27)
Postreduction displacement in millimetres	0 (0–7)	4 (0–7)	3 (0–7)	0 (0–7)	3 (0–13)	0 (0–5)

Continuous values are medians and (range).
A= fractures that united without additional operation,
B= delayed union requiring reoperation,
C= patients who received osteoinduction with recombinant human BMP-7,
D= matched patients,
E= the patients who had early non-spanning external fixation,
F= the patients who had temporary external fixation.

proximal fracture, the tibial defect, the diaphyseal extension, the fixation of the associated fibula fracture, the closed or open nature of the fracture, the postreduction displacement and the patient's smoking status, gender and age.

Study III

Forty-four consecutive patients operated on for type C tibial pilon fracture by using non-bridging external fixation (two-ring hybrid external fixation in 31 and a half-pin fixator in 13) as definitive treatment. The initial treatment was early definitive external fixation (EF group, 29 patients) or temporary external fixation spanning the ankle joint (TEF group, 15 patients).

Study IV

In 2000–2004, 725 tibial fractures, excluding malleolar fractures, were treated in Oulu University Hospital. Patient records and radiographs were retrospectively evaluated to find the fractures with bone loss exceeding 3 cm. Twenty-six patients were identified. Twenty-three open fractures, in which bone loss was treated with staged cancellous autografting, were selected for further analysis. Healing of the reconstructed segment was compared in different locations of the tibia.

Table 4. Clinical and outcome data in the groups based on the location of the fracture and bone loss (Study IV)

Location of the fracture	Proximal	Diaphysis	Distal	All
Number of fractures with bone loss	5	11	7	23
Age in years	36 (15–55)	28 (14–63)	46 (15–75)	35 (14–75)
Women	1	2	4	7
Fixation:				
Reamed IMN		11		11
Locking plate	3		1	4
External fixation	2		6	8
Open fractures	5	12	6	23
Soft tissue cover:				
Free flap	3	6	3	12
Local flap		1		1
Skin graft		2	1	3
Secondary suture	2	4	3	9
Delay in coverage in days	8 (2–14)	5 (0–9)	9 (4–16)	7 (0–16)
Bone loss				
Length (mm)	70 (46–74)	45 (38–100)	40 (35–60)	52 (35–100)
Delay in bone grafting				
(= antibiotic beads time) in days	50 (46–60)	63 (38–108)	46 (23–63)	52 (23–108)
Healing time in weeks	37 (20–53)	47 (24–79)	30 (20–42)	40 (20–79)
Delayed healing				
(secondary intervention)	1	5	2	8

Continous valus are mean and (range)

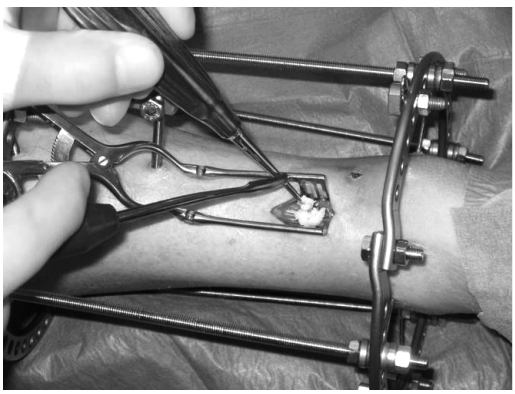

Figure 8. RhBMP-7 application.

Methods

Classifications, measurements and assessment of functional recovery

The fractures were classified according to the AO/OTA classification (Müller et al. 1990), open fractures according to Gustilo et al. (1984) and bone loss in the Studies I, II and III according to a modified Winquist-Hansen classification (Robinson et al. 1995). In Study IV, the length of the bone loss was measured at the centre of the bone. The range of motion of the ankle joint was measured according to the method described by Lindsjö et al. (1985). Functional recovery was assessed using the IOWA ankle score (Merchant & Dietz 1989) (Studies I, II, III) and self-administered RAND 36-Item Health Survey (Aalto et al. 1999, Hays & Morales 2001) (Study I). An IOWA ankle score of 90 to 100 points was considered excellent; 80 to 89 points good; 70 to 79 points fair; and < 70 poor. Sex- and age-matched (in ten-year intervals) representatives of the Finnish general population were used as controls for the RAND 36-Item Health Survey scores.

Operative treatment

Primary treatment

Twenty-five closed fractures were initially treated with ankle-spanning external fixation (Hoffman II, Stryker, Geneva, Switzerland). Whether or not an ankle-spanning fixator was used was decided by the attending surgeon. Definitive non-spanning external fixation was done within a median of 8 (2–27) days from the injury. Other fractures had definitive early non-spanning external fixation in a median time of 2 (0–7) days from the injury. The method of initial treatment was decided by the attending surgeon.

Joint surface reconstruction was conducted using minimally invasive open reduction as described by Tornetta et al. (1993) or percutaneously. Joint fragments were fixed with 3.5 mm screws. A two-ring hybrid external fixator (Ilizarov, Smith & Nephew, Memphis, Tennessee, USA) (Fig 6) was used as a neutralization device in 67 cases (Studies I, II and III) and a Hoffman II (Hoffman II, Stryker, Geneva, Switzerland) half-pin fixator in 13 cases (Study III).

Protocol for the treatment of open fractures

All open fractures were treated according to a staged protocol with intravenous antibiotics (cefuroxime + metronidazole until 24 hours from the wound closure), immediate debridement, primary stabilization, second looks and early soft-tissue coverage when the wound was clean in a median time of 7 (2 to 30) days from the injury.

Two-staged treatment of bone loss

Associated bone loss was treated with a staged method as described by Christian et al. (1989). During the wound cover procedure, the bone loss was filled with gentamicin-impregnated Septopal (Merck, Darmstadt, Germany) beads to preserve the bone loss volume for later insertion of a cancellous bone graft. In second-stage surgery at a median of 52 (23–108) days after the injury, the beads were removed, and the bone loss was filled with autogenous cancellous bone harvested from the posterior or anterior iliac crest. After careful removal of the spacer, the bone ends were refreshed, but the other parts of the foreign body membrane around the beads were carefully preserved. The filling of the bone loss was "oversized" because the closure of soft tissues tends to press on the graft, leading to an hourglass shape. After the filling procedure, the membranous and other soft tissues were closed.

Rehabilitation

Physiotherapy was started 3 to 5 days after the operation to maintain ankle and knee movements, and it was continued until the healing of the fracture. The patients were followed up monthly at the outpatient clinic. Partial weight bearing was

allowed until the wound had healed. After healing, full weight bearing was gradually allowed as tolerated. The patients were scheduled for frame removal as soon as there was radiographic evidence of bridging callus or disappearance of the fracture lines and no abnormal mobility or pain upon walking or in response to pressure applied to the fracture after the removal of the connecting bars between the rings.

Osteoinduction

Osteoinduction was performed with rhBMP-7 (with bovine collagen as a carrier: Osigraft, Stryker Biotech, Limerick, Ireland) in a median time of 18 (5–47) days from the injury (Study II). In type C fractures the application was done during the joint surface reconstruction, while in type A fractures it was done through a small incision (Figure 8). One polytrauma patient with a high-energy open pilon fracture and severe bone loss had two units of Osigraft mixed with cancellous autograft, and each of the other 19 patients had one unit of Osigraft. The application time was dictated by the condition of the soft tissues.

Radiological studies and assessment of fracture union

Antero-posterior and lateral digital radiographs were taken at the follow-up visits. At the final follow-up visit, standing antero-posterior and lateral radiographs were taken of both legs, including both knees and subtalar joints. Displacement of the meta-diaphyseal fracture was measured from the follow-up radiographs after reduction using the method described by Green and Gibbs (1994). Joint line orientation was assessed using the method described by Paley and Tetsworth (1992). The fracture was considered malunited if there was at least a 10° difference in either the anterior distal tibial angle or the lateral distal tibial angle compared with the uninjured tibia.

The fractures were considered united when antero-posterior and lateral radiographs showed bridging of 3 out of 4 cortices or when the fracture lines disappeared, and there was no pain in the fracture upon weight bearing. Fracture union was defined as “delayed” when an additional operation was required to promote fracture union. The decision to reoperate was made by the attending surgeon based on his estimation of the capacity of the fracture to heal.

The bone loss was considered to have healed when radiography revealed uniform consolidation of the graft without any translucent lines in the reconstructed segment or the graft-host interface and corticalisation in three out of four cortices, and when there was no pain upon weight bearing.

Statistical methods

Statistical analysis was performed with the help of a statistician using the SPSS statistical software (SPSS v. 10.0.5, SPSS Inc., Chicago, Ill., USA). Continuous variables were reported as median and range or mean and standard deviation (SD) The chi-square test and Fisher’s exact test were used for univariate analysis of categorical data. The Mann-Whitney and Kruskall-Wallis tests were used to assess the distribution of continuous variables in the different subgroups. Spearman’s test was used to evaluate the correlation between continuous variables. The receiver operating characteristics (ROC) curve was used to identify the best cut-off value of the degree of translation predisposing to delayed union requiring reoperation in Study I. Linear and logistic regressions with the help of backward selection were used for multivariable analysis. Only preoperative variables whose p-values in univariate analysis were <0.05 were considered for inclusion in the regression model. The Wilcoxon signed-rank test was used to compare fracture healing times, and the McNemar test was used to compare the number of healed fractures at different time points in Study II. Two-tailed p-values were reported. Post hoc power analyses for the hypothesis that the mean values were different were calculated for healing time with (two-tailed) alpha=5% in Study IV. For the group comparisons, the differences between the mean 95 confidence intervals (95% CI) were presented.

Results

Study I – Risk factors for delayed union of tibial pilon fractures

The median time for fracture union was 24 weeks (8–60). Twelve patients required reoperation because of delayed union within a median time of 21 (16–24) weeks from the injury. Eventually, all fractures united.

Risk factors predicting delayed union

According to linear regression analysis, the degree of translation was the only independent predictor of longer union time (regression coefficient 3.9 95%CI 2.1–5.7; p<0.001).

The degree of translation (OR 2.1; 95% CI 1.3–3.5; p=0.004) and fibular fracture fixation (OR 19.4; 95% CI 1.1–340; p=0.043) increased the risk for reoperation. Reoperation was performed on 50% of the patients who underwent fibular fixation and on 15% of the patients who did not undergo fibular fixation (Figure 9).

The cut-off value for translational displacement in ROC curve analysis was 3 mm (sensitivity 83.3%, specificity 94.3%), under which value (translation <3 mm) the rate of reoperation was 6%, whilst above that value (translation ≥ 3 mm) it was 83% (p<0.001). Fifty percent of the patients with a translation ≥ 3 mm had fibular fixation, and 22.9% of those with a translation < 3 mm had fibular fixation (p=0.14). There were no differences between the high- and low-energy fractures in the number of cases with translation ≥3 mm (42% vs. 58%, p=0.56) or fibular fixation (43% vs. 57%, p=0.59).

Clinical ankle scores and RAND 36-Item Health Survey scores are presented in Table 5. Overall, there were no significant differences in the RAND 36-Item Health Survey scores between our series and the general Finnish population aged 18 - 64 years. The patients with AO/OTA type C fractures, open fractures and complex metaphyseal fractures had lower scores on some of the subscales compared to the other patients and the general population. Delayed union had no negative influence on the functional outcome. Four cases had malunion. One corrective osteotomy was done, but the other patients refused further operations. None of the patients in the follow-up study had a shortening of more than 10 mm compared to the uninjured leg.

One patient with type C3 fracture, comminution and a bone defect due to impaction had a deep infection after joint line reconstruction and primary bone grafting. The infection resolved and the fracture united after 7 revisions, treatment with intra-

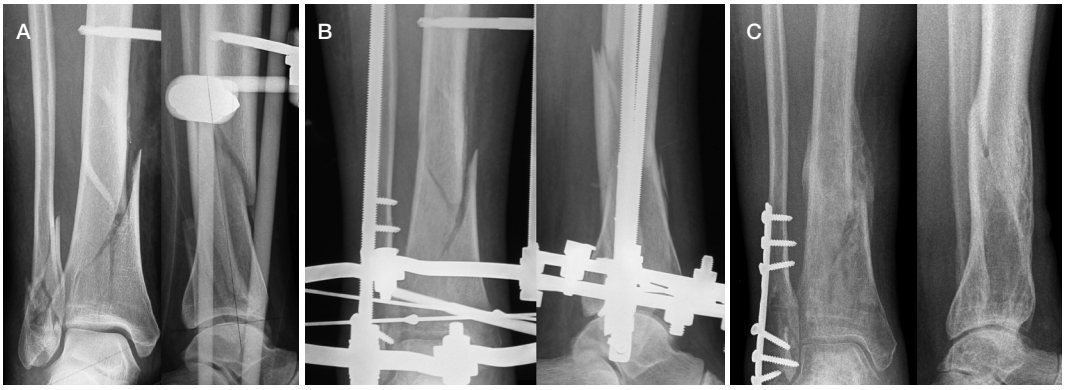

Figure 9. Low energy C1 type fracture was temporarily fixed with external fixator crossing the ankle joint (A). The fracture was fixed with non-spanning external fixator. There was 4 mm of posterior displacement and fibula was plated. At three months from the injury there were no clinical or radiological signs of union in metadiaphyseal fracture (B). After cancellous autografting the fracture united (C). Union time was 24 weeks.

Table 5. Comparison of IOWA ankle scores and RAND 36-Item Health Survey scores between different subpopulations in the Study I

Subscale	IOWA	PF	RP	RE	VT	MH	SF	BP	GH
General population (n=1529)		90	74	78	65	81	83	78	68
Our series (n=38)	79 (19)	78 (23)	76 (37)	84 (31)	71 (21)	75 (20)	84 (19)	74 (27)	64 (22)
Age- and sex-adjusted difference (Rand-36)		-3.6 (24)	4.9 (37)	1.4 (19)	7.1 (22)	1.5 (20)	2.7 (19)	0.7 (27)	3 (19)
AO/OTA class A fract. (n=10)	87 (11)	10 (21)	24 (22)	-19 (16)	18 (15)	7.7 (14)	12 (18)	15 (12)	9.4 (11)
AO/OTA class C fract. (n=28)	75 (21)	-7.6 (24)	-1.3 (39)	-7.2 (35)	3.5 (24)	-0.5 (21)	-0.5 (21)	-3.9 (29)	0.9 (21)
Closed fracture (n=30)	82 (17)	3.1 (20)	9.6 (32)	-9.6 (31)	13 (18)	4.8 (17)	6.2 (18)	3.2 (26)	5.7 (19)
Open fracture (n=8)	64 (23)	-27 (25)*	-1. 3 (49)	-13 (35)	-12 (25)*	-11 (24)	-9.9 (20)	-8.3 (32)	-6.9 (19)
Low-energy fracture (n=19)	85 (17)	5.6 (18)	14 (31)	-13 (29)	14 (17)	6.7 (15)	11 (15)	9 (20)	5.2 (14)
High-energy fracture (n=19)	72 (20)	-12 (26)*	-3.5 (41)	-7.6 (35)	0.8 (25)	-3.6 (23)	-4.7 (21)*	-7.2 (31)	1 (23)
Union (n=27)	81 (18)	-6 (22)	-1.3 (37)	-8.7 (32)	8.8 (20)	1.8 (20)	3.1 (20)	1.4 (26)	3.4 (22)
Delayed union (n=11)	74 (22)	3.1 (30)	22 (33)	-14 (34)	2.8 (29)	0.5 (21)	1.7 (20)	-1.2 (32)	1.8 (14)
Simple metaphyseal fracture (n=26)	84 (15)	3.3 (20)	14 (27)	-13 (28)	4.2 (19)	4.2 (19)	9 (17)	4.5 (28)	5.5 (16)
Complex metaphyseal fracture (n=12)	65 (23)*	-19 (27)*	-15 (46)	-5.6 (39)	1.4 (22)	-4.2 (20)	-10 (19)*	-7.2 (25)	-2.4 (25)

The general population consisted of the Finnish population aged 18–64 years. IOWA: IOWA ankle score, PF: physical functioning, RP: role limitations due to physical health, RE: role limitations due to emotional problems, VT: vitality, SF: social functioning, P: somatic pain, GH: general health. The bolded numbers indicate the differences between our series and the age- (10 years interval) and sex-adjusted general Finnish population. *: $p < 0.05$. Values are mean (SD) or age- and sex-adjusted mean difference

venous vancomysin 2 g twice daily (Vancosin) and delayed bone grafting.

Fifteen patients had at least one pin tract infection. Four pins were replaced, and one was removed. One patient, who had the frame and all pins removed due to fulminant pin infection 8 weeks after the injury already, displayed bridging callus, and the infection healed rapidly after the procedure. Other pin tract infections resolved after local pin care, dressing changes and oral cefalexine (750 mg 3 times/day). There were 6 other complications and 10 reoperations due to hardware problems.

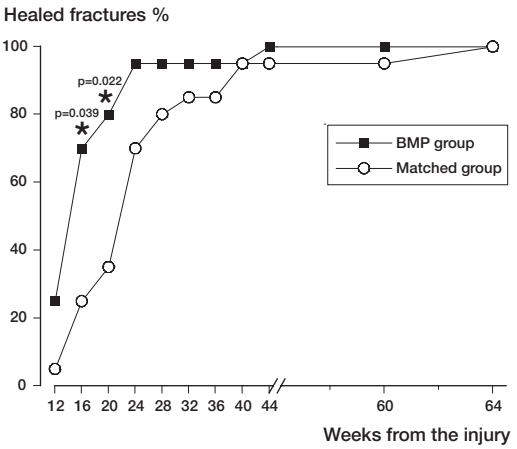

Figure 10. Healing rates of the fractures.

Study II – Acceleration of fracture union by rhBMP-7

All fractures united in both groups. Significantly more fractures had healed by 16 ($p = 0.039$) and 20 ($p = 0.022$) weeks in the BMP group than in the matched group (Figure 10). Accelerated bone healing was also seen in perfectly reduced fractures without bone defects. Significantly more of these had healed by 20 weeks in the BMP group ($p = 0.016$) than in the matched group (Figure 11). Outcome data is presented in Table 6.

Sixteen patients in the BMP group and 13 in the matched group were employed at the time of the injury. Of these, 14 and 12, respectively, regained their preinjury working capacity. Sick leaves ($p = 0.018$) and frame times ($p = 0.037$) were sig-

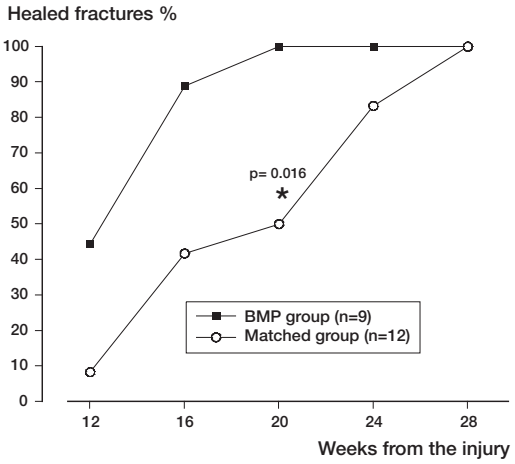

Figure 11. Healing rates of the anatomically reduced fractures (displacement < 3mm) without significant bone defects.

nificantly longer in the matched group than in the BMP group.

There were no deep infections. Six patients in the BMP group and 4 in the matched group had one-pin-tract infections, which were diagnosed based on discharge, redness, swelling and pain at the pin site and verified by bacterial culture. One patient in the BMP group had 3 infected pin tracts. In the BMP group, all of the infections resolved after local revision and oral cefalexine (750 mg two times/day). One patient in the matched group had the frame and all of the 5 pins removed due to fulminant pin tract infection 8 weeks after the injury, but already displayed bridging callus at that time, and the infection healed rapidly after the procedure. In the BMP group, normal remodelling of the fracture had started by the 1-year follow-up visit, and no excessive callus formation was seen (Figure 12). One patient in the BMP group displayed calcification in the wound in follow-up radiography, but no symptoms related to the finding were registered.

Study III – Temporary external fixation of pilon fractures

All fractures eventually united within a median time of 21 (11–80) weeks The patients in the TEF group had less post-reduction displacement (median 0, 0–5 mm) than those in the EF group (median 3, 0–7mm) (95% CI -0.48 to 2 mm) and tended to have fewer secondary interventions due to delayed healing of the meta-diaphyseal fracture than those in the EF group (2/15 vs. 7/29, RR 0.5, 95% CI 0.1–2.1). Five cases of delayed union in the EF group and 2 cases in the TEF group were treated with bone grafts, and 2 cases in the EF group were treated with locked intramedullary nailing after the intra-articular fractures had healed. There was no significant difference in the median healing time (23 (14–39) weeks in the TEF group and 21 (11–68) in the EF group) between the groups. One

Table 6. Outcome data in the Study II

	BMP [a]	Matched	p–value
Union time in weeks	14 (7–43)	21 (11–63)	0.002
Fixator time in weeks	15 (9–37)	21 (10–40)	0.04
Length of sick leave, months	6 (3–13)	9 (4–15)	0.02
Follow up duration, months	12 (11–13)	32 (12–45)	
Median ankle score	84 (70–100)	84 (46–98)	0.9
Excellent	5	7	
Good	10	6	
Fair	4	1	
Poor	0	4	
Restriction in range of motion			
Dorsiflexion (°)	-12 (-42 to 5)	-8 (-33 to 6)	0.7
Plantar flexion (°)	-10 (-50 to 5)	-6 (-20 to 8)	0.3
Secondary intervention			
due to delayed healing	2	7	0.1

[a] BMP, bone morphogenetic protein.
Continuous values are medians and (range).

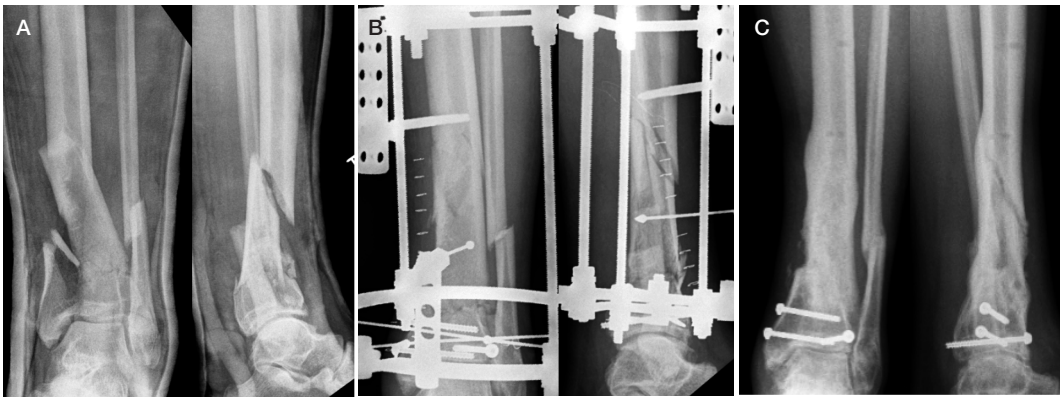

Figure 12. A high energy C2 type fracture (A) was treated with joint-line reconstruction and external fixation. During joint-line reconstruction, rhBMP-7 was introduced into the fracture gap and over the proximal fracture (B). By 20 weeks the fracture had united without secondary interventions (C).

fracture in the EF group and 2 in the TEF group malunited, but none of these patients wanted corrective osteotomy. There were no significant differences in the ankle score or the ankle ROM between the groups (Table 7).

Major complications

Three of the 29 patients in the EF group and 3/15 in the EF group had major complications necessitating 2 and 8 reoperations, respectively (p=0.677).

In the EF group, one failed half-pin fixation of a C1 type fracture was replaced by two-ring hybrid fixation, after which the fracture united without additional measures. In another case with a C1 type fracture, the distal pins were replaced because they penetrated the extensor tendons, and in another case of C1 type fracture, there was an injury of the superficial peroneal nerve during plating of the associated fibular fracture.

In the TEF group, one deep infection developed after joint line reconstruction, primary bone grafting of the metaphyseal defect and non-spanning external fixation of a closed C3 type fracture. The infection was treated with revisions and intravenous antibiotics. This fracture united in 20 months. Broken distal wires were replaced in a non-cooperative female patient. One patient had a pin tract infection of the temporary external fixator, which developed into *Staphylococcus aureus* sepsis and was treated successfully with intravenous antibiotics.

Table 7. Functional recovery in Study III

Group	EF [a]	TEF [b]	p-value
Ankle score	86 (28–100)	78 (52–98)	0.3
Excellent	6	4	
Good	4	2	
Fair	2	1	
Poor	5	5	
Restriction in range of motion (°)	14 (0–48)	22 (0–49)	0.5
Dorsiflexion (°)	9 (0–33)	13 (0–25)	0.4
Plantarflexion (°)	7 (0–32)	7 (0–32)	0.8

[a] Early external fixation
[b] Temporary external fixation spanning the ankle joint
Continuous values are medians and (range)

Study IV – Treatment of traumatic bone loss in different locations of tibia

All but one of the 23 bone losses healed in a median time of 40 (20–79) weeks, indicating that the staged method can be successfully applied to bone loss up to 100 mm in length (Table 4, Figure 13). The average healing time in the distal tibia was 7 weeks shorter than in the proximal tibia (95% CI -12 to 26 weeks) and 16 weeks shorter than in the tibial shaft (95% CI 3–29 weeks). The results of the post hoc power analysis of the differences were 14% (i.e. beta error = 86%) and 74% (beta error = 26%), respectively. The bone loss in the distal tibia was shorter than those in the proximal and diaphyseal tibia, but the length of the bone loss

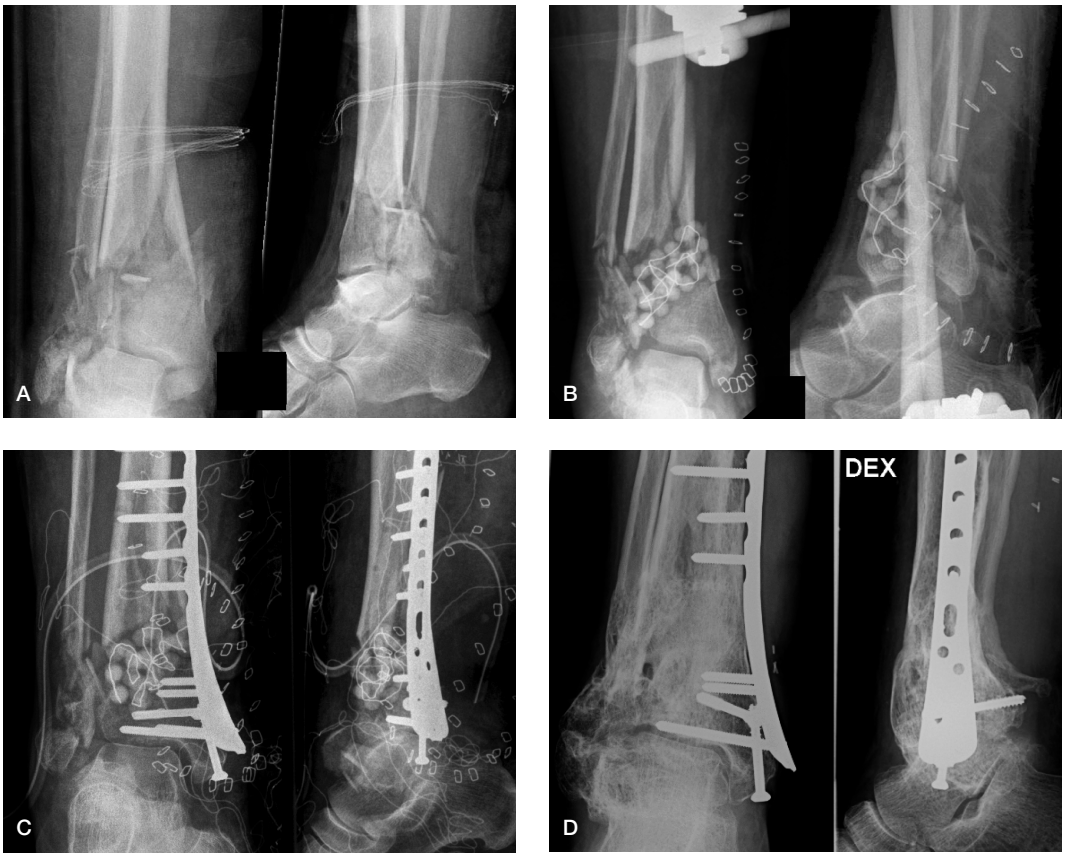

Figure 13. An open pilon fracture with partial loss of articular surface (A) was temporarily fixed with spanning external fixation after debridement (B). Before wound reconstruction the fracture was fixed with a medial locking plate (C). The interconnection between the joint space and the epi-metaphyseal defect was sealed off by foreign body membrane which is forming around antibiotic-impregnated beads. This enabled cancellous autografting 8 weeks after the injury. Healing time was 20 weeks (D).

did not correlate significantly with healing time (Spearman's correlation, r 0.156, p 0.469).

Healing time was 9 weeks (95%CI -6 to 23) longer when a muscle flap was used compared to secondary suture/SSG (post hoc power 26%, beta error = 74%) (Table 8).

There was one failure in the proximal tibia that necessitated a change of the method of treatment. The autograft bone was infected, and the bone loss was eventually treated successfully with segment transport. This was the only deep infection in this series. There were no other wound complications related to bone grafting operations.

Fourteen of the remaining 22 cases of bone loss healed without secondary intervention, whereas 8 patients needed an additional operation to promote healing. Exchange nailing was done in 2 cases and additional cancellous autografting in 6 (in 2 cases twice). There were 5 soft tissue complications related to the primary wound or flap, necessitating 17 reoperations.

Table 8. Clinical and outcome data in the groups based on the type of soft tissue cover in the Study IV

	Soft tissue cover		
	Muscle flap	Secondary suture or SSG	Difference between means (95% CI)
Number of patients	13	10	
Age of the patients	37 (14–67)	33 (19–79)	-4 (-13 to 21)
Length of bone loss (mm)	50 (34–74)	54 (34–104)	4 (-10 to 20)
Delay in bone grafting (=antibiotic beads time) in days	60 (40–108)	50 (23–72)	-10 (-7 to 26)
Healing time (weeks)	43 (20–63)	34 (19–79)	9 (-6 to 23)
Delayed healing (secondary intervention) (n)	7	3	
Location of the fracture:			
Proximal	3	2	
Shaft	7	4	
Distal	3	4	
Type of definitive fixation:			
Reamed locking intramedullary nail	7	4	
Locking plate	2	2	
External fixation	4	4	
Mechanism:			
Fall from height (>2 metres)	2	2	
Traffic accident	7	8	
Industrial accident	3		
Gun shot injury	1		
Patients with multiple injuries	6	7	

Continuous variables are presented as mean and range.
SSG = split skin graft.

General discussion

In the present study, two-ring external fixation with mini-invasive articular osteosynthesis of pilon fractures resulted in acceptable functional results and a low deep infection rate. Although internal fixation may involve an acceptable rate of complications in very expert hands (Sirkin et al. 1999, Anglen & Aleto 1998, Patterson & Cole 1999, Watson 2000 A, Blauth et al. 2001), significantly fewer wound infections have been reported using techniques of external fixation (Bonar & Marsh 1993, Tornetta et al. 1993, Marsh et al. 1995, Bone et al. 1993, Barbieri et al. 1993, Griffiths & Thordarson 1996) compared with traditional plating (McFerran et al. 1992, Teeny & Wiss 1993, Wyrsch et al. 1997). There was only one deep infection in this series, where 83 pilon fractures were treated with external fixation. We agree with J.L.Marsh that external fixation is the treatment of choice for most surgeons in the treatment of pilon fractures (Marsh 1999).

Intra-articular fractures of the tibial plafond, especially those caused by high energy, have a negative effect on ankle function, pain and general health (Marsh et al. 2003, Pollak et al. 2003, Williams et al. 2004) The factor that may be most important in determining outcome is the damage caused by the acute injury to the articular cartilage, which may lead to joint degeneration despite accurate reduction (Marsh et al. 2003). The functional results of the present study appear to be more related to the original injury than the timing of the operation or the type of definitive fixation. The patients with a more severe fracture pattern and soft tissue injury had the worst functional results and scored lowest on the RAND-36 subscales measuring physical functioning.

Temporary external fixation prior to definitive internal fixation in the treatment of complex high-energy fractures has been used by many authors, and reductions of severe complications have been reported (Anglen & Aleto 1998, Patterson & Cole 1999, Sirkin et al. 1999, Watson et al. 2000 A, Blauth 2001). The influence of the timing of definitive fixation on the outcome is not clear. We were unable to find any difference in either function or infection rate based on whether or not temporary external fixation had been used. We found temporary external fixation to result in better reduction of the proximal fracture line of the pilon fracture. This may be due to reduced soft tissue swelling during temporary fixation, which allows for better reduction at the time of definitive fixation, increased planning time for definitive fixation, or easier definitive reduction if the alignment of the fracture is restored as soon as possible.

We found delayed union of meta-diaphyseal fracture to be a common finding, which is also seen in other studies on pilon fractures (Teeny & Wiss 1993, Anglen et al. 1999, Pugh et al. 1999, French & Tornetta 2000, Nork et al. 2005) and fractures of the distal tibial shaft (Heppenstall et al. 1984, Bilat et al. 1994, Audigé et al. 2005). The reason for the delayed union of distal tibial fractures is poorly understood.

The role of soft tissue injury in the healing of tibial fractures has been documented earlier (Nicoll 1964, Tonnesen et al. 1975, Gustilo & Anderson 1976, Gaston et al. 1999, Audigé 2005). Many authors believe that the vascularity of surrounding soft tissues is one of the key factors promoting successful healing of fractures (Robinson et al. 1995, Watson et al. 1995, Christian et al. 1989, Pelissier et al. 2002), but the present findings are somewhat conflicting. Soft tissue injury or the energy of injury was not predictive of healing time or the need for secondary interventions due to delayed healing of pilon fractures. The type of soft tissue cover had no effect on the healing of the reconstructed segment in high-energy open tibial fractures with bone loss, and the reconstructed segment in the distal tibia healed at least equally well as similar reconstructions in the other parts of the tibia. These findings may be biased by the fact that there were relatively few patients, and that there is a continuum of fracture severity within the groups (open/closed fractures, low/high-energy injuries). On the other hand, Claes et al. (2006) found that, although soft tissue injury had a negative impact on initial fracture healing in an experimental model, recovery took less than one month.

An interesting finding in the present study was the relatively high number of delayed unions in simple (spiral, oblique or simple wedge) metaphyseal fractures (Study I). About one third of simple metaphyseal fractures displayed delayed union. Half of these fractures were relatively low-energy injuries. This reflects the difficulties in controlling translational displacement in simple fractures, which may be due to the relatively intact soft tissue envelope resisting reduction. The tolerance for displacement is small, only 3 millimetres. Thus, even the fracture haematoma may block closed reduction. Metaphyseal fracture is mostly obliquely or spirally oriented. In the external device used here, interfragmentary movement mostly consists of shearing rather than axial loading, which is generally thought to be beneficial for fracture healing.

Translational displacement has been recognized as a risk factor for delayed union in the treatment of tibial shaft fractures (Helland et al. 1996, Audigé 2005, Drosos 2006), but it has received no attention in tibial pilon fractures. Our findings on displacement are consistent with those of Drosos et al., who found that a post-reduction fracture gap of ≥ 3 mm with a statically locked nail was associated with a significantly longer time to union than a gap of < 3 mm (Drosos et al. 2006). The degree of comminution was also significantly associated with healing, and there was a tendency towards slower healing in distal fractures compared to midshaft and proximal fractures. Audigé et al. found that, in addition to skin injury, distal location of the tibial shaft fracture and postoperative diastasis were risk factors for fracture healing (Audigé 2005).

Fixation of an associated fibular fracture did not help to achieve better contact in the metaphyseal fracture of the tibia. In fact, fixation of the fibular fracture was associated with delayed union. The literature concerning the fixation of associated fibular fractures is controversial. In experimental studies, the fixation of associated fibular fractures has been shown to add structural stability when external fixation of the tibial fracture is used (Weber et al. 1997, Williams et al. 1998). The other theoretical benefits are that the length of the extremity can be preserved and the rotation of the tibial fracture controlled. Some authors have fixed associated fibular fractures in conjunction with the external fixation of distal tibial fractures (Bone et al. 1993, Saleh et al. 1993), but there are no unambiguous recommendations for this in the clinical studies. Williams et al. (Williams et al. 1998) found that there were significantly more complications in the cases where the fibular fracture was fixed compared to those where it was not fixed. Contrary to our study, they did not find any significant differences in the mean union times of tibial fractures.

In our series, fibular fixation was an independent factor leading to additional operations due to delayed fracture union. We hypothesise that fibular fixation might delay the healing of a tibial metaphyseal fracture by keeping the fibula at full length and not permitting axial loading of the tibial fracture. This hypothesis was supported by some experimental and clinical studies (Morrison et al. 1991, Weber et al. 1997, Watson et al. 2000B), which showed that axial loading of the tibia is significantly decreased when the fibular fracture is stabilized.

Our study was the first clinical survey in which rhBMP-7 was applied to one of the therapeutically most challenging fractures, the distal tibial fracture. We observed that osteoinduction with rhBMP- 7 significantly accelerated the healing of distal tibial fractures treated with external fixation. This finding is in line with the reported observations on the effect of rhBMP-2 on open tibial fractures treated with intramedullary nailing (Govender et al. 2002) and also with the results of an experimental study on goat tibial fractures treated with external fixation (den Boer et al. 2002). These findings suggest that rhBMPs can accelerate the healing of fresh fractures. On the other hand, the study by Maniscalco et al. (Maniscalco et al. 2002) could not demonstrate any difference in healing time between seven tibial fractures treated with rhBMP-7 (OP 1) plus external fixation and seven cases treated with external fixation alone.

The mechanism by which BMPs accelerate the union of fresh fractures is not completely understood. It is generally known that the main action of BMPs is to promote the differentiation of mesenchymal cells to osteoblastic cells, but there is only marginal evidence that this process can be accelerated by BMPs in fresh fractures. RhBMP-7 is known to be able to bridge defects of long bones (Geesink et al. 1999), and we initially assumed that the acceleration of bone healing observed here was

caused by the ability of rhBMP-7 to bridge critical-sized defects, without any direct effect on bone healing. However, when we analysed the perfectly reduced fractures without bone defects separately, we saw accelerated bone healing in those cases as well. It thus seems that rhBMP-7 may directly contribute to bone healing by accelerating the differentiation of stem cells into osteoblasts. Furthermore, Ramoshebi and Ripamonti have shown that BMP-7 stimulates angiogenesis (Ramoshebi & Ripamonti 2000). Thus, acceleration may also be due to the ability of BMP-7 to improve and thus to ensure the initial induction of bone formation in fractures with impaired healing capacity due to insufficient blood supply and soft tissue cover.

The timing of the rhBMP application may be important. Based on animal experiments, BMP-7 shows a restricted period of expression from day 14 to day 21 of fracture healing (Cho et al. 2002). Cheng et al. (2003) suggested that BMP-2, -6 and -9 may be the most potent agents to induce osteoblast differentiation of mesenchymal progenitor cells, whilst BMP-7 can stimulate osteogenesis in mature osteoblasts. RhBMP-7 was applied in our series within a mean time of 18 days from the injury, i.e. at the time when BMP-7 is normally expressed. It can be speculated that rhBMP-7 may not have a similar effect if applied earlier (day 1–3).

Failure to perform early bone grafting has been regarded as a major reason for delayed/non-union and malunion of the meta-diaphyseal fracture (Watson 2000B, Pugh 1999). In clinical series, autogenous cancellous autografting has been performed in 30 to 56% of the cases (Marsh et al. 1995, Tornetta et al. 1993 Barbieri 1996, Wyrsch et al. 1996, Anglen 1999). Only 3/36 patients in the series of Nork et al. had bone loss (Nork et al. 2005). This is accordant with our series, where 10% of the patients had significant bone loss. Although it is not clearly explained in earlier reports, it seems that autografting has been performed to induce fracture union rather than to fill metaphyseal defects.

In this study, the staged method was effective in the treatment of pilon fractures with bone loss, although the muscle cover in the distal leg is limited. Christian et al. (Christian et al. 1989) were the first to describe the method of using antibiotic-impregnated beads as a spacer. Masquelet (Masquelet 2003) used methylmetacrylate cement for the same purpose. The beads as well as the cement spacer induce a synovium-like foreign body membrane around them. This induced membrane has both a mechanical and a biological role. It obviates fibrous tissue invasion at the recipient site and preserves the necessary space for the cancellous graft. It also protects the graft material from resorption and promotes its revascularisation and corticalisation (Pelissier et al. 2002). In an experimental study (Pelissier et al. 2004), the membrane was found to secrete vascular endothelial growth factor, transforming growth factor-ß1 and bone morphogenetic protein 2 (BMP-2). The maximum BMP-2 production was measured 4 weeks after the implantation of the cement spacer.

It seems that osteoinduction with cancellous autogenous bone grafting effectively stimulates fracture union in the distal tibial metaphysis. On the other hand, the soft tissue cover of the distal tibia is limited, and bulky autogenous bone material may endanger the patient by risking wound dehiscence and infection. There is level 1 evidence from clinical studies that BMP-7 is comparable to autogenous bone in stimulating bone growth (Johnson et al. 2002, Friedlaender et al. 2001). In a study by Friedlaender et al. (2001), autograft bone was compared to rhBMP-7 in the treatment of non-union. The risk of infection at the implantation site was significantly lower in the rhBMP-7 group. Early stimulation of bone formation at the fracture site results in increased stability of the fracture and is important in reducing infections (Worlock et al. 1994). Thus, the use of rhBMP-7 in distal tibial fractures as a less bulky material becomes an attractive option. Another benefit is that the complications of graft harvesting can be avoided. In the study of Friedlaender et al. (2001), 20% of the patients in the autografting group had chronic pain at the donor site.

It is noteworthy that some patients in the matched group without significant bone defects required a secondary intervention, while none in the BMP group did (Study II). Two patients in the BMP group had secondary interventions due to delayed healing. Both patients had significant bone defects. In a study by Watson et al. (1995) on tibial fractures with bone loss treated with external fixation, as many as 40% of the fractures needed at least one additional secondary bone grafting to promote

fracture union. It seems that, in cases of massive bone defects, a rhBMP implant alone is not sufficient but should be combined with bone grafting. On the other hand, four fractures with minor bone defects in the BMP group healed without additional measures, indicating that rhBMP-7 with carrier may be sufficient to heal wedge type (> 50% but < 100%) defects less than 2 cm in length.

In Finland, primary hospital costs account for only an average of 13% of the total economic burden caused by injuries, the main burden being caused by indirect costs and loss of working days (Vuoriainen et al. 2000). Here, the use of rhBMP-7 shortened the sick leave by an average of almost 3 months. This indicates that this treatment, despite the high price of the implant, is cost-effective. Based on the present findings osteoinduction with rhBMP-7 is indicated in pilon fractures with significant metaphyseal comminution and also in simple fractures where postreduction radiographs show more than 3 mm displacement.

The number of cases in each substudy was rather small, which impairs the reliability of the conclusions. It must be emphasized that tibial pilon fracture is a relatively rare injury, and that the sizes of the present series are comparable to the biggest series so far reported in the literature. For the level of evidence, a study design with a randomised treatment protocol would have been preferable, especially in the studies II and III. In order to overcome this weakness, matched controls were used in study II to assess whether the use of BMP-7 provided accelerated bone healing compared to fractures treated with hardware alone. Although the data on pilon fractures was prospectively collected, this was an observational clinical study and suffers from some inherent limitations. Even though we tried to provide good matching, using the basic variables described in the summary, there is always a risk for confounding factors in a study design of this kind. Adequate randomisation is nearly impossible due to the limited number of patients if the study is carried out in one centre, as here. Most of the treatment modalities were chosen by the treating surgeon, and no fixed protocols were used. Furthermore, the findings in this type of study can always be biased by patient selection, although we tried to control the variables as far as possible. Despite the limitations in the study design and the possibility of confounding factors, we believe that our findings are relevant.

In conclusion, the healing of tibial pilon fractures can be enhanced by using rhBMP-7. External fixation of tibial pilon fractures results in acceptable clinical result with few serious complications. The method is, however, related to delayed healing of the meta-diaphyseal fracture, primarily due to a post-reduction fracture gap of > 3mm. Significant bone loss can be effectively treated with the staged method using cancellous autografting.

Future

Many questions concerning the treatment of this challenging fracture remain open. Although hybrid external fixation was here shown to be safe in the most severely comminuted fractures with soft tissue injury, its applicability can be questioned in the treatment of simple metaphyseal fractures. The development of devices for internal fixation may produce solutions superior to external fixation. For example, the modern intramedullary nails enable the fixation of very distal tibial fractures, and low-profile locking plates provide angular stability to comminuted fractures. I think it would be valuable to compare these techniques with external fixation.

The introduction of osteoinductive materials into the treatment arsenal of fresh fractures has opened up new vistas. As such, this type of injury may be a good indication for such novel treatment, but it may not be ideal scientifically, since there are so many confounding factors. We showed that rhBMP-7 accelerates the healing of tibial pilon fractures in general. However, it remains to be seen how these materials work in different fracture types. Furthermore, we do not know anything about the optimal timing of treatment or the effects of different application modalities. It would also be interesting to know how they perform in tibial bone loss. I believe that these future improvements of the treatment of distal tibial fractures will improve the outcome to a new level.

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