

Staged method using antibiotic beads and subsequent autografting for large traumatic tibial bone loss

22 of 23 fractures healed after 5–20 months

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Introduction The vascularity of surrounding soft tissues, which is related to muscle cover, is important for the healing of traumatic bone loss. Muscle cover on the distal tibia is limited compared to the diaphyseal and proximal tibia, and delayed healing of fractures in this area is common. We evaluated the healing of traumatic bone loss in the proximal, diaphyseal, and distal tibia.

Patients and methods 23 open tibial fractures with substantial bone loss (mean 52 (34–104) mm) were treated using a staged method with antibiotic-impregnated beads and later autologous bone grafting at second-stage surgery on average 8 weeks after the injury.

Results 22 fractures healed after mean 40 (20–79) weeks. The average healing time in the distal tibia (mean 30 weeks) was 7 weeks shorter (95% CI: 12–26 weeks) than in the proximal tibia (37 weeks), and 16 weeks shorter (95% CI: 3–29 weeks) than in the tibial shaft (47 weeks). The length of the bone and the type of soft tissue cover (free muscle or secondary suture) had no effect on healing time.

Interpretation Our study suggests that the method we used is applicable in all parts of the tibia, although the healing of bone loss is slower in the diaphyseal tibia than in the proximal and distal tibia.

interventions due to delayed healing are especially common for distal tibial fractures (McFerran et al. 1992, Bone et al. 1993, Teeny et al. 1993, Anglen 1999, Pugh et al. 1999, Ristiniemi et al. 2007). Thus, early or primary bone grafting is recommended as an essential part of treatment of distal tibial fractures (Ruedi and Allgöwer 1969, Teeny et al. 1993, Tornetta et al. 1993, Marsh et al. 1995, Sirkin and Sanders 2001, Pugh et al. 1999, French and Tornetta 2000), whereas diaphyseal fractures usually heal without secondary interventions.

Little is known about the healing of traumatic tibial bone loss, and the available literature has concentrated on loss of bone from the tibial shaft (Christian et al. 1989, Robinson et al. 1995, Watson et al. 1995). Furthermore, there have been no studies comparing healing of traumatic bone loss in different parts of the tibia.

We evaluated the healing of traumatic bone loss first treated with a spacer of antibiotic-impregnated beads and thereafter with cancellous autografting in the proximal, diaphyseal, and distal tibia.

Patients and methods

From 2000 through 2004, 725 tibial fractures (excluding malleolar fractures) were treated in our hospital. Patient records and radiographs were evaluated retrospectively to find the fractures with bone loss exceeding 3 cm. The length of bone loss was measured at the center of the bone. Thus, in wedge-

It has been suggested that the healing potential of fractures differs in different parts of the tibia (Heppenstall et al. 1984, Bilal et al. 1994, Audige et al. 2005). Nonunion and the need for secondary

type bone loss, at least 50% of the circumference of the bone had bone loss at least 3 cm long.

26 open fractures (5 in the proximal tibia, 14 in the diaphyseal tibia, and 7 in the distal tibia) had significant bone loss. More than half of the instances of bone loss (14/26) were located in the tibial shaft, where the proportion of all tibial shaft fractures was 4% (14/351 fractures). The relative proportion of instances of bone loss was highest in the distal tibia (7/123 fractures, 6%) and lowest in the proximal tibia (5/251 fractures, 2%). The overall rate of bone loss in tibial fractures was 3.6%. Bone loss was treated with segment transport in 3 cases of 12-, 15- and 17-cm long diaphyseal bone loss; these patients were excluded from the study. Thus, the final study group consisted of 23 open fractures (Tables 1 and 2).

Fracture location was classified according to AO categories (Müller et al. 1990). In this classification, by definition proximal (zone 41) segments and distal (zone 43) segments comprise the anatomical regions of metaphysis and epiphysis. Proximal and distal segments are defined by squares whose sides are equal in length to the widest part of the epiphysis in question. Zone 43 in the distal tibia, for example, comprises the most distal 5 cm of the length of the tibia. The diaphyseal segment (zone 42) is the part of the tibia between the two aforementioned segments. According to the classification of open tibial fractures of Gustilo et al. (1984), there were 2 type 3C fractures (1 in the proximal segment and 1 in the shaft segment) and 21 type 3B fractures (4 in the proximal segment, 10 in the shaft segment, and 7 in the distal segment).

All cases were treated with intravenous antibiotics, primary debridement of necrotic soft tissue and bone, and early stabilization. The method and timing of soft tissue cover was dictated by the location and size of the wound (Table 1). Secondary suture was used if the skin could be closed without tension. Split skin grafting was used if the wound was in an area with muscular cover—i.e. the anterior, lateral or posterior leg. Free or local muscle transfer (in 12 cases and 1 case, respectively) was used in cases where the bone was widely exposed, usually at a medial site, and if tension-free suture was not possible. During the wound cover procedure, the bone loss was replaced with gentamicin-impregnated Septopal beads (Merck, Darmstadt,

Germany) to preserve the volume of the bone loss for later insertion of the cancellous bone graft, as described by Christian et al. (1989) (Figure 1).

For stabilization, a locked reamed intramedullary nail was used in all 11 of the diaphyseal fractures (Figure 1); external fixation was used in 2 cases in the proximal tibia and in 6 cases in the distal tibia, and a locking plate was used in 3 cases in the proximal tibia and in 1 case in the distal tibia (Figure 2, Table 1). The adjacent joint line was reconstructed and fixed with screws. In 2 periarticular proximal fractures and 5 distal fractures, temporary external fixation bridging the adjacent joint was used as primary stabilization until soft tissue closure/reconstruction.

At second-stage surgery, mean 8 (3–15) weeks after the injury, the beads were removed and the bone loss was filled with autogenous cancellous bone—harvested from the posterior iliac crest in 14 cases and from the anterior iliac crest in 9 cases. After removal of the spacer, the ends of the bone were refreshed, but the other parts of the foreign body membrane around the beads were preserved. The filling of the bone loss was “oversized” (Figure 1) because the closure of soft tissues tends to press on the graft, leading to an hourglass shape. After filling the bone loss, the membranous and other soft tissues were closed. The limbs were kept elevated for at least 2–3 days postoperatively in order to avoid hematoma formation.

The patients were followed up at the outpatient clinic on a monthly basis until fracture union. Weight bearing was restricted until the graft started to consolidate. The bone loss was considered to have healed when radiography revealed that there was uniform consolidation of the graft without translucent lines in the reconstructed segment or the graft-host interface and corticalization in three out of four cortices, and when there was no pain upon weight bearing. In cases where external fixation was used, the time of the removal of the fixator was based on the following criteria: (1) no mobility of the fracture, and (2) no pain upon walking or pain elicited by stressing the fracture after removal of the connection bars between the rings. The mean follow-up time was 2 (1–6) years.

Statistics

For the group comparisons, differences between

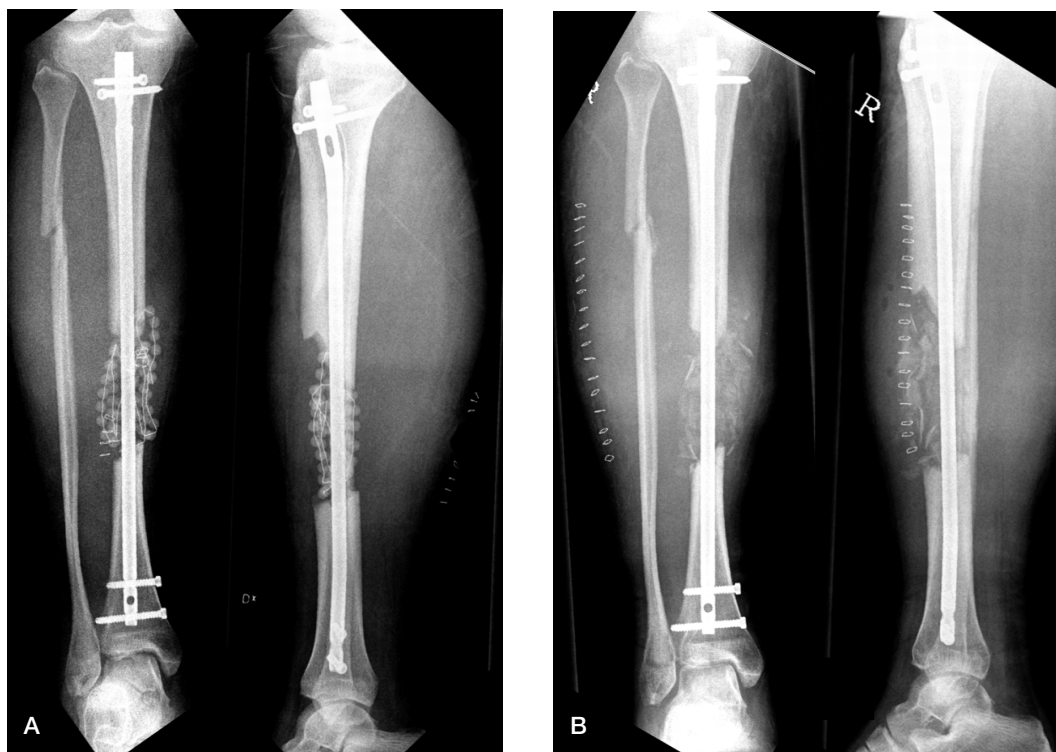


Figure 1. An open fracture of tibial diaphysis with bone loss treated with a reamed intramedullary nail. The defect was filled with antibiotic-impregnated beads (A). 6 weeks later, the beads were removed and the defect was filled with "oversized" cancellous autograft bone (B). Additional bone grafting was required at 6 months. Healing time was 79 weeks (C).

means with 95% confidence intervals (CI) are presented. SPSS version 10.0.5 was used for all analyses. Post hoc power analyses for the hypothesis that the mean values are different were calculated for healing time with (two-tailed) $\alpha = 5\%$.

Results

All but 1 of the 23 fractures healed in a mean time of 40 (20–79) weeks (Table 1 and Figure 2). The average healing time in the distal tibia was 7 weeks shorter (95% CI: 12–26 weeks) than in the proximal tibia, and 16 weeks shorter (95% CI: 3–29 weeks) than in the tibial shaft. The post hoc power analysis for the differences gave 14% (i.e. beta error = 86%) and 74% (beta error = 26%), respectively. The mean bone loss in the distal tibia was shorter than





Figure 2. An open pilon fracture with partial loss of articular surface (A) 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 has been sealed off by foreign body membrane, which is forming around the antibiotic-impregnated beads. This enabled cancellous autografting 8 weeks after the injury. Healing time was 20 weeks (D).

that in the proximal and diaphyseal tibia, but there was no significant correlation between the extent of bone loss and healing time (Spearman correlation, $r = 0.16$, $p = 0.5$). The patients with diaphyseal bone loss were younger than those with proximal and distal bone loss, but there was no correlation between healing time and age of the patient (Spearman correlation, $r = 0.092$, $p = 0.7$).

The healing time was 9 weeks longer (95%CI: 6–23) when muscle flap was used than when secondary suture/SSG was used (post hoc power 26%, beta error = 74%).

14 cases of bone loss healed without secondary intervention, whereas 8 patients needed an additional operation to promote healing (Table 1). Exchange nailing was done in 2 cases of diaphy-

seal bone loss, and additional cancellous autografting was done in 1 case in the proximal tibia, 3 cases in the diaphyseal tibia (1 case twice), and 2 cases in the distal tibia (1 case twice). Altogether, there were soft tissue complications related to the primary wound or flap, necessitating 17 reoperations.

1 failure occurred in the proximal tibia, which necessitated a change of the method of treatment. The autograft bone became infected, and the bone loss was eventually treated successfully with segment transport.

Discussion

Fractures with bone loss are rare. In a prospective

Table 1. Clinical, treatment, and outcome data in the groups based on the location of the fracture and the degree of bone loss ^a

Location of fracture	Proximal	Diaphysis	Distal	All
Number of fractures with bone loss	5	11	7	23
Age (years)	36 (15–55)	28 (14–63)	46 (15–75)	35 (14–75)
Women	1	2	4	7
Fixation				
Reamed intramedullary nail	–	11	–	11
Locking plate	3	–	1	4
External fixation	2	–	6	8
Time to definitive fixation (days)	1 (0–3)	1 (0–2)	5 (0–16)	2 (0–16)
Soft tissue cover				
Free flap	3	6	3	12
Local flap	–	1	–	1
Skin graft	–	2	1	3
Secondary suture	2	2	3	7
Delay in coverage (days)	7.5 (2–14)	4.5 (0–9)	9.4 (4–16)	6.7 (0–16)
Length of bone loss (mm)	62 (46–74)	54 (38–100)	43 (35–60)	52 (35–100)
Delay in bone grafting (=days with antibiotic beads)	52 (46–60)	63 (38–108)	45 (23–63)	54 (23–108)
Healing time (weeks)	37 (20–53)	47 (24–79)	30 (20–42)	40 (20–79)
Delayed healing (secondary intervention)	1	5	2	8

^a Continuous variables are presented as mean and rangeTable 2. Clinical and outcome data in the groups based on the type of soft tissue cover ^a

	Muscle flap (n = 13)	Secondary suture or SSG ^b (n = 10)	Difference between means (95% CI)
Age of the patients	37 (14–67)	33 (19–79)	-4 (-13–21)
Bone loss			
Length (mm)	50 (34–74)	54 (34–104)	4 (-10–20)
Delay in bone grafting (=days with antibiotic beads)	60 (40–108)	50 (23–72)	-10 (-7–26)
Healing time (weeks)	43 (20–63)	34 (19–79)	9 (-6–23)
Delayed healing (secondary intervention) (n)	5	3	
Location of fracture			
Proximal / Shaft / Distal	3 / 7 / 3	2 / 4 / 4	
Type of definitive fixation			
Reamed locking intramedullary nail	7	4	
Locking plate	2	2	
External fixation	4	4	
Mechanism			
Fall from a height (> 2 m)	2	2	
Traffic accident	7	8	
Industrial accident	3	–	
Gun shot injury	1	–	
Patients with multiple injuries	6	7	

^a Continuous variables are presented as mean and range.^b SSG: split skin graft.

study from Scotland (Keating et al. 2005), they for only 0.4% of all fractures in patients admitted to hospital. The lower extremities were mostly

involved—the tibia in two-thirds of the cases and the femur in one-fifth. This in accordance with the results of our series, where 4% of tibial fractures

were associated with substantial bone loss. In our series most of the fractures with bone loss were located in the tibial shaft, but the rate of bone loss was highest in the distal tibia.

Christian et al. (1989) were the first to describe the method of using antibiotic-impregnated beads as a spacer. Masquelet (2003) used methylmethacrylate cement for the same purpose. Both the beads and the cement spacer induce development of a surrounding synovium-like foreign body membrane, which has both a mechanical and a biological role. It prevents 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 revascularization and corticalization (Pelissier et al. 2002). In an experimental study by Pelissier et al. (2004), the membrane was found to secrete vascular endothelial growth factor, transforming growth factor- β 1, and bone morphogenetic protein 2 (BMP-2). The maximum BMP-2 production was measured 4 weeks after implantation of the cement spacer.

The staged method of using spacers and cancellous autografting seems to be a successful technique of treating bone loss in fractures up to 10 cm in length. Segmental bone loss exceeding 4 to 6 cm has been considered unsuitable for cancellous bone grafting in some reviews (Decoster et al. 2004, Keating et al. 2005). There have been a few small series, however, in which tibial bone loss up to 25 cm in length has been treated successfully with cancellous bone grafting (Christian et al. 1989, Watson et al. 1995, Masquelet 2003, Schlötte et al. 2005). In the study of Masquelet (2003), the time of bone healing was found to be independent of the extent of the bone loss, and our results are in accordance with this.

Cancellous autografting can be considered the golden standard for most surgeons in the treatment of tibial fractures with bone loss, since no special skills or equipment are needed. Cancellous autograft bone is an ideal material since it is both osteoinductive and osteoconductive. It also has osteogenic capacity because at least some of the cells remain viable after transfer. The major restriction is the availability of cancellous bone in massive bone loss and donor site complications (Friedlaender et al. 2001).

The role of soft tissue injury in the healing of tibial fractures has been documented earlier (Nicoll 1964, Gustilo and Anderson 1976, Gaston et al. 1999). Many authors believe that the vascularity of surrounding soft tissues is one of the key factors that promote successful healing of fractures, especially ones with bone loss (Christian et al. 1989, Robinson et al. 1995, Watson et al. 1995, Pelissier et al. 2002). This assumption has also been supported by an experimental study (Richards et al. 1991), where healing of the devascularized segment of canine tibia was superior when soft tissue was covered with a free muscle flap rather than covered with a skin graft. In our series, the type of soft tissue cover had no effect on the healing of the reconstructed segment. Measurement of the severity of the fracture is difficult, and it is possible that the fractures that were covered with muscle flap were more severe than the other fractures. However, there was no significant difference in the extent of bone loss, the mechanism of the injury was not remarkably different, and there was similar number of multiply injured patients in both groups, indirectly indicating that the fracture severity was similar. Although we agree with the other authors that the extent of soft tissue injury is an important predictor of union time, the type of soft tissue cover may not be predictive of healing as long as the basic principles of tension-free skin closure and avoidance of infection are followed.

The fixation method differed in different locations, as did the healing times. All of the diaphyseal fractures were nailed. Autograft was applied around the nail in these cases, whereas in proximal and distal fractures the area of bone loss was completely filled with autograft. The bone loss in the tibial shaft healed more slowly than in other locations. Whether or not the findings would have been similar if type of fixation had been the same can only be speculated upon. There have been no studies comparing different fixation methods in the treatment of traumatic bone loss.

The healing time of the reconstructed segment was shortest in the distal tibia, where the extent of bone loss was also somewhat less than for the other locations, which may play some role. It seems, however, that the healing potential of a reconstructed segment in the distal tibia is at least equally as good as at other tibial locations. This finding is clinically

important, since high-energy pilon fractures often result—even in closed fractures—in stripping of the periosteum in metaphyseal bone. The question of whether or not to remove devascularized cortical fragments arises during the operation of such fractures. Our findings encourage removal of the fragments and filling of the resultant bone loss with spacer. Bone loss can be treated effectively with a cancellous autograft using the staged method with antibiotic beads as spacer. Contamination of the avascular cortical fragments and possible infection of the fracture can be minimized.

In conclusion, traumatic tibial bone loss can be treated in most cases with a simple staged method using antibiotic beads as a spacer, and with subsequent autografting when the soft tissues have healed. The method appears to be at least as effective in the proximal and distal tibia as in the tibial shaft.

Contributions of authors

JR: practical execution of the study, writing of the manuscript, analysis of the data, and surgical treatment of the patients. TF: critical analysis of the manuscript. ML: critical analysis of the data, radiographic evaluation of the fracture healing, and surgical treatment of the patients. PJ: critical revision of the manuscript and participation in the design of the study.

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Anglen J O. Early outcome of hybrid external fixation for fracture of the distal tibia. *J Orthop Trauma* 1999; 3 (2): 92-7.

Audigè L, Griffin D, Bhandari M, Kellam J, Ruedi T P. Path analysis of factors for delayed healing and nonunion in 416 operatively treated tibial shaft fractures. *Clin Orthop* 2005; (438): 221-32.

Bilat C, Leutenegger A, Ruedi T. Osteosynthesis of 245 tibial shaft fractures: early and late complications. *Injury* 1994; 25 (6): 349-58.

Bone L, Stegeman P, McNamara K, Seibel R. External fixation of severely comminuted and open tibial pilon fractures. *Clin Orthop* 1993; (292): 101-7.

Christian E P, Bosse M J, Robb G. Reconstruction of large diaphyseal bone loss, without free fibular transfer, in Grade-IIIB tibial fractures. *J Bone Joint Surg (Am)* 1989; 71 (7): 994-1004.

DeCoster T A, Gehlert R J, Mikola E A, Pirela-Cruz M A. Management of posttraumatic segmental bone loss. *J Am Acad Orthop Surg* 2004; 12 (1): 28-38.

French B, Tornetta P 3rd. Hybrid external fixation of tibial pilon fractures. *Foot Ankle Clin* 2000; 5 (4): 853-71.

Friedlaender G E, Perry C R, Cole J D, Cook S D, Cierny G, Muschler G F, Zych G A, Calhoun J H, LaForte A J, Yin S. Osteogenic protein-1 (bone morphogenetic protein-7) in the treatment of tibial nonunions. *J Bone Joint Surg (Am)* (Suppl 1) 2001; 83: S151-8.

Gaston P, Will E, Elton R A, McQueen M M, Court-Brown C M. Fractures of the tibia. Can their outcome be predicted? *J Bone Joint Surg (Br)* 1999; 81 (1): 71-6.

Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. *J Bone Joint Surg (Am)* 1976;58 (4): 453-8.

Gustilo R B, Mendoza R M, Williams D N. Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. *J Trauma* 1984; 24: 742-6.

Heppenstall R B, Brighton C T, Esterhai J L Jr, Muller G. Prognostic factors in nonunion of the tibia: an evaluation of 185 cases treated with constant direct current. *J Trauma* 1984; 24 (9): 790-5.

Keating J F, Simpson A H, Robinson C M. The management of fractures with bone loss. *J Bone Joint Surg (Br)* 2005; 87 (2): 142-50.

Marsh J L, Bonar S, Nepola J V, Decoster T A, Hurwitz S R. Use of an articulated external fixator for fractures of the tibial plafond. *J Bone Joint Surg (Am)* 1995; 77 (10): 1498-509.

Masquelet A C. Muscle reconstruction in reconstructive surgery: soft tissue repair and long bone reconstruction. *Langenbecks Arch Surg* 2003; 388 (5): 344-6. Epub 2003 Sep 11.

McFerran M A, Smith S W, Boulas H J, Schwartz H S. Complications encountered in the treatment of pilon fractures. *J Orthop Trauma* 1992; 6 (2): 195-200.

Müller M E, Nazarian S, Koch P, Schatzker J. The comprehensive classification of fractures of long bones. New York: Springer 1990.

Nicoll E A. Fractures of the tibial shaft. A survey of 705 cases. *J Bone Joint Surg (Br)* 1964; 46: 373-87.

Pelissier P, Martin D, Baudet J, Lepreux S, Masquelet A C. Behaviour of cancellous bone graft placed in induced membranes. *Br J Plast Surg* 2002; 55 (7): 596-8.

Pelissier P, Masquelet A C, Bareille R, Pelissier S M, Amedee J. Induced membranes secrete growth factors including vascular and osteoinductive factors and could stimulate bone regeneration. *J Orthop Res* 2004; 22 (1): 73-9.

Pugh K J, Wolinsky P R, McAndrew M P, Johnson K D. Tibial pilon fractures: a comparison of treatment methods. *J Trauma* 1999; 47 (5): 937-41.

- Richards R R, McKee M D, Paitich C B, Anderson G I, Bertoina J T. A comparison of the effects of skin coverage and muscle flap coverage on the early strength of union at the site of osteotomy after devascularization of a segment of canine tibia. *J Bone Joint Surg (Am)* 1991; 73 (9): 1323-30.
- Ristiniemi J, Flinkkilä T, Hyvönen P, Lakovaara M, Pakarinen H, Biancari F, Jalovaara P. Two ring external fixation of distal tibial fractures – a review of 47 cases. *J Trauma* 2007; 62(1):174-83.
- Robinson C M, McLauchlan G, Christie J, McQueen M M, Court-Brown C M. Tibial fractures with bone loss treated by primary reamed intramedullary nailing. *J Bone Joint Surg (Br)* 1995; 77 (6): 906-13.
- Ruedi T P, Allgöwer M. Fractures of the lower end of the tibia into the ankle-joint. *Injury* 1969; 1: 92-9.
- Schlötte P B, Werner M ., Dumont C E. Two-stage reconstruction with free vascularized soft tissue transfer and conventional bone graft for infected nonunions of the tibia. *Acta Orthop* 2005; 76 (6): 878-83.
- Sirkin M, Sanders R. The treatment of pilon fractures. *Orthop Clin North Am* 2001; 32 (1): 91-102.
- Teeny S M, Wiss D A. Open reduction and internal fixation of tibial plafond fractures. Variables contributing to poor results and complications. *Clin Orthop* 1993; (292): 108-17.
- Tornetta P 3rd, Weiner L, Bergman M, Watnik N, Steuer J, Kelley M, Yang E. Pilon fractures: treatment with combined internal and external fixation. *J Orthop Trauma* 1993; 7 (6): 489-96.
- Watson J T, Anders M, Moed B R. Management strategies for bone loss in tibial shaft fractures. *Clin Orthop* 1995; (315): 138-52.