Delayed Union and Nonunions

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20.1 Introduction

Battlefield injuries, high-speed accidents, and work mishaps may cause fractures of the lower extremities. A limb with a fractured bone leads to significant disability. Generally, this disability is temporary and ends when fracture union is achieved. Delayed union or nonunion, however, may occur significantly more often after high-energy trauma, infection, or multidirectional deformity [16]. Bone is the only tissue that can heal without scar formation. Bone fractures initiate a complex interdependent sequence of events, including inflammation (the cellular and vascular response to injury), repair (the replacement of damaged or necrotic tissue by cell proliferation and synthesis of new matrix), and remodeling (the reshaping, internal reorganization, and replacement of repair tissue) [23]. Knowledge of normal bone healing and the reasons for nonunion may help the surgeon to better plan the management of this complication. The lack of a normal healing process during the inflammation phase leads to an atrophic nonunion, or to a hypertrophic nonunion, if it occurs during the bone healing repair phase.

A fractured bone needs mechanical stability, biological sufficiency, and contact between properly aligned fragments for healing to occur. Bone defects or severe displacement of the fragments, infection, insufficient local blood supply, usage of steroids and non-steroid anti-inflammatories [10], radiotherapy, soft tissue problems, and atrophic muscles and contractures may negatively impact the healing process.

Delayed union is a term used for a fracture that has not united within a period of time that is considered adequate for bone healing; the union is slow but will eventually occur without additional surgical or nonsurgical interventions. Thus, delayed union is mainly a clinical diagnosis [26]. According to the FDA, a diagnosis of nonunion may be established "when a minimum of 9 months has elapsed since injury and the fracture shows no visible progressive signs of healing for 3 months." The time frame, however, is different for different fractures. A fracture of the tibial shaft is not considered a nonunion until at least 9 months, while a fracture of the femoral neck can be defined as a nonunion after just 3 months. Tibial diaphyseal fractures that do not exhibit a bridging callus sufficient to achieve clinical stability by 16 weeks are considered to be delayed union fractures [46]. On the other hand, nonunion refers to a fracture that will not unite without additional surgical or nonsurgical intervention (usually by 6–9 months). Of the long bones, the tibia is the most common site for nonunion development.

20.2 Classification

The most widely used classification is the Weber–Cech system [44] (Figs. 20.1 and 20.2). The nonunion is classified according to the radiographic appearance, which correlates with the fracture biology.

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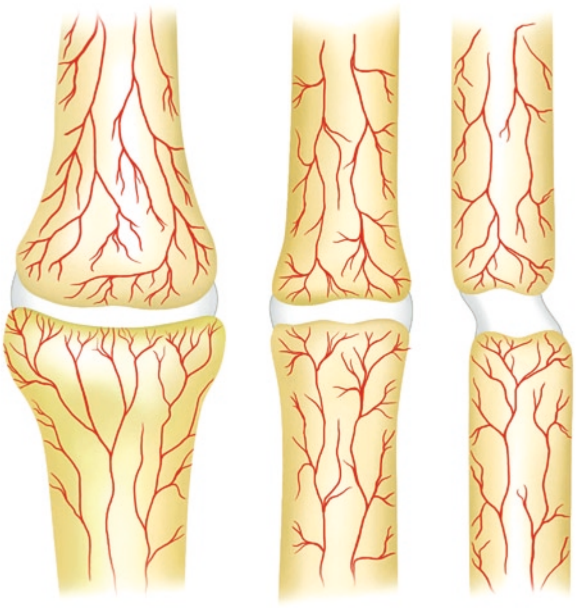


Fig. 20.1 Vascular nonunions according to the Weber–Cech classification: "elephant foot," "horse hoof," and oligotrophic nonunion (from *left* to *right*)

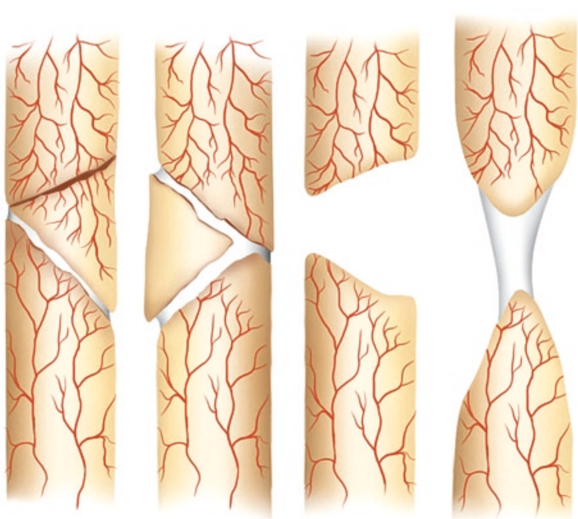


Fig. 20.2 Avascular nonunions according to the Weber–Cech classification: torsion wedge, comminuted, defect, and atrophic nonunion (from *left* to *right*)

- Hypertrophic nonunions are characterized by abundant callus formation. These nonunions are hypervascular and offer excellent healing potential, given the right environment (Fig. 20.3, *right*). They result from insufficient mechanical stability. Hypervascular nonunions are subdivided into three forms: "elephant foot," "horse hoof," and oligotrophic (Fig. 20.1). Elephant foot nonunions are hypertrophic and rich in callus, and result from insecure fixation, insufficient immobilization, or premature weight bearing. Horse hoof nonunions are mildly hypertrophic and poor in callus, and result from unstable osteosynthesis. Oligotrophic nonunions are not hypertrophic but are vascular with no callus, and result from distraction of the bony fragments.

Fig. 20.3 A patient x-ray showing atrophic nonunion of the tibia (*left*). Another patient x-ray exhibiting hypertrophic nonunion of the femur (*right*)

- Atrophic nonunions are characterized by an absence of callus and atrophic bone ends, which may be tapered and osteopenic or sclerotic (Fig. 20.3, *left*). Bone vascularity is deficient and the bone suffers from poor healing potential. If there is a fibrous capsule around a freely mobile nonunion, filled with a viscous fluid and creating the appearance of a joint, then it is referred to as a *pseudarthrosis*. Atrophic nonunions result from insufficient blood supply to the bone fragments. Reed et al. showed that the number of blood vessels in atrophic nonunions reaches the same level as in healing bone but at a later time-point. Diminished vascularity within

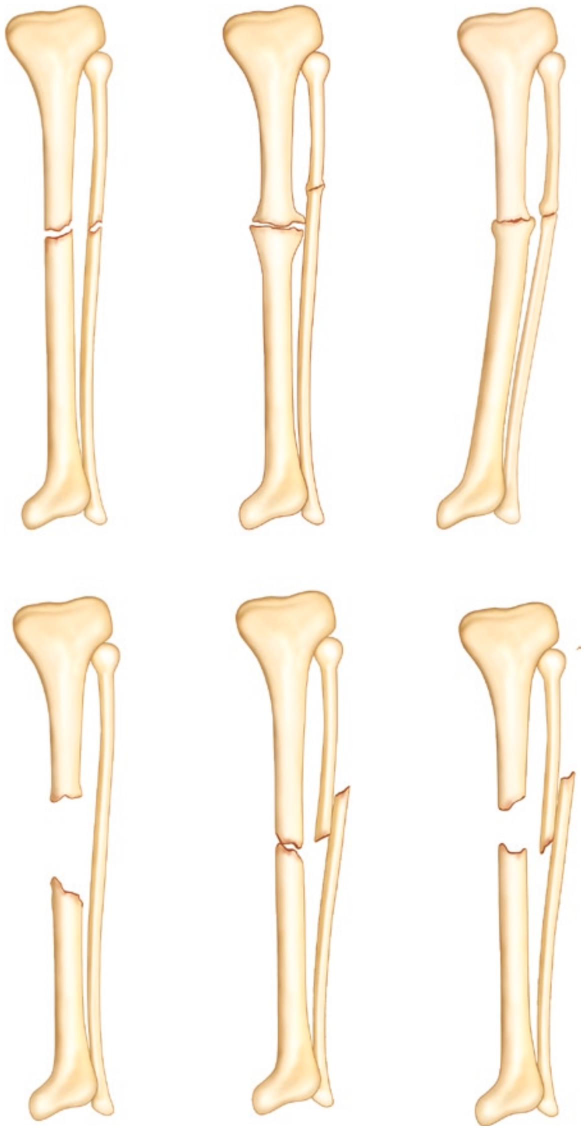


Fig. 20.4 Tibial nonunion classification described by Paley: Lax (A1), stiff without deformity (A2-1) and stiff with fixed deformity (A2-2) (*upper row*, from *left* to *right*). Bone defect without shortening (B1), shortening without bone defect (B2), and bone defect with shortening (B3) (*lower row* from *left* to *right*)

the first 3 weeks, but not at a later time-point, may prevent fractures from uniting [33].

- Normotrophic nonunions share the characteristics of both atrophic and hypertrophic nonunions. The bone ends exhibit moderate healing potential.

Ilizarov classified nonunions into two categories: lax and stiff. Lax nonunions have radiologically apparent atrophic bone ends, they exhibit pathological movement at more than 7°, and they exhibit shortening of more than 2 cm. On the other hand, stiff nonunions feature hypertrophic bone ends, pathological movement of less than 7° and shortening of less than 2 cm [40].

Another recent classification for tibial nonunions was described by Paley and Herzenberg in terms of clinical mobility, which roughly correlates with the three categories of the Weber–Cech classification (Fig. 20.4). Although initially described only for tibial nonunions, this classification may be applied to nonunions of other bones. In this classification, there are two major types: Type A – a bone defect of less than 1 cm; and Type B – a bone defect of more than 1 cm.

A1: Lax (mobile) (Fig. 20.5)
A2: Stiff (nonmobile)
  A2-1: No deformity
  A2-2: Fixed deformity
B1: Bone defect, no shortening
B2: Shortening, no bone defect
B3: Bone defect and shortening

20.3 Evaluation

20.3.1 Clinical Evaluation

Clinical evaluation of the nonunited segment includes an inspection for gross deformity, overall alignment, venous stasis, and lymphedema. In segments with signs of local malnutrition, an arteriogram is advisable. A complete neurovascular examination must be carried out documenting the peripheric pulse status. The motor function and the sensitivity of the skin of the affected limb are checked, and an electromyography must be obtained in cases with positive results. Limb-length discrepancy should be checked via spinomalleolar measurement. In ambulatory patients, the gait pattern should be documented. The skin should be inspected for the presence, location, and healing status of previous wounds and incisions (Fig. 20.6). Pain and motion produced by the manual stress test applied to the nonunion site and any contracture at the adjacent joints should be checked and documented. Photographic documentation is also very useful for treatment planning (Fig. 20.7).

Fig. 20.5 A patient with a lax humeral nonunion

Fig. 20.6 A patient's tibia with scars from previous injury and surgery

Fig. 20.7 A patient's clinical picture showing the deformity and shortening

20.3.2 Radiologic Evaluation

True anteroposterior and lateral x-rays of the affected limb segment must first be obtained. The image should be perpendicular to the long axis of the segment. An orthoroentgenogram is useful to document and measure limb-length discrepancy and deformity (Fig. 20.8). In subtle nonunions, a computerized tomography (CT) scan will be helpful for the diagnosis (Fig. 20.9). If hardware causes the interpretation to be difficult, then plain tomography may be helpful. Bone scanning will identify increased uptake in viable nonunions but decreased uptake in nonviable nonunions. Synovial pseudarthrosis typically appears as a cold spot on bone scans. Indium-labeled leukocyte scanning may help to distinguish between infected and noninfected nonunions [7, 23]. If there is a sinus tract, a sinogram will help to determine whether it communicates with the nonunion site. A magnetic resonance imaging study is most helpful to show the presence of osteomyelitis and the status of the ligaments at adjacent joints.

Ultrasonographic evaluation of callus formation is a useful alternative technique when an abnormal healing process is encountered. It allows for the evaluation of bone formation during the first 4 weeks, during which radiograms are not appropriate for this purpose. Because the ultrasonographic exam does not involve radiation, it can be repeated often and routinely [30]. Application and interpretation of the resulting ultrasonography, however, may be challenging in the presence of metallic implants or external fixators.

Fig. 20.9 A CT scan of the femur, showing nonunion after intramedullary nailing

Fig. 20.8 Orthoroentgenogram of a patient with a femoral nonunion, causing deformity and shortening

20.3.3 Laboratory Studies

Total blood count, erythrocyte sedimentation rate, and quantitative CRP levels should be routinely monitored. These parameters may help assess the healing process of the patient. Additionally, total protein and albumin levels are checked to evaluate the nutritional status of the patient. Patients with low albumin and lymphocyte levels may need parenteral nutritional aids in addition to a high protein and high calorie diet.

20.4 Treatment

The process and outcome of bone repair is determined by the magnitude and interaction of the anabolic (bone-forming) and catabolic (bone-resorbing) responses [21]. Prior to injury, most anabolic and catabolic responses are very subtle in normal homeostatic states;

however, when a fracture occurs, there is an appropriate inflammatory response in the bone and surrounding tissues, followed by cellular recruitment and proliferation. The anabolic phase precedes and dominates the catabolic removal of unwanted tissue and bone resorption associated with subsequent remodeling. Anabolic treatments can be mechanical (e.g., distraction osteogenesis, ultrasound), biological or pharmacological (e.g., bone morphogenetic proteins, parathyroid hormone), graft based (e.g., autologous bone graft, allograft), and cell based (e.g., bone marrow or mesenchymal stem cells, platelets, gene therapy). Anticatabolic treatments are usually pharmacological, for example, the administration of bisphosphonates to inhibit resorption of osteoclasts. Mechanical stimuli may also decrease catabolism by reducing stress shielding, as with the dynamization of external fixators.

As the treatment period is long, for a successful outcome in the treatment of complex nonunions, there should be a team consisting of a surgeon, a clinical nurse, a physical therapist, a radiologist, and a microbiologist. This is of paramount importance, especially if an external fixator and its combined techniques are used. In such cases, the patient himself/herself must be included in the team because he/she will play an active role, such as overseeing care of the frame and the pin site [24].

Early referral to a tertiary center is recommended, since this may reduce the morbidity and duration of time off work for some patients [29].

20.4.1 External Fixation Modalities

Ilizarov asserted that distraction alone may be a potent stimulus, at least for nonunions of the hypertrophic type. This assertion has been confirmed in the literature [24, 38]. It is possible to achieve stable fixation with the Ilizarov frame, even in the presence of osteopenia or bone defects. Unless there is infection, exposure of the nonunion site is often not required, except for implant removal.

20.4.1.1 Monofocal Distraction

Monofocal distraction is most suitable for hypertrophic nonunions because they exhibit callus-forming capacity. If there is an angular deformity, eccentric distraction may be performed until the deformity is corrected, followed by longitudinal distraction until the desired amount of lengthening is achieved [37, 41] (Fig. 20.10).

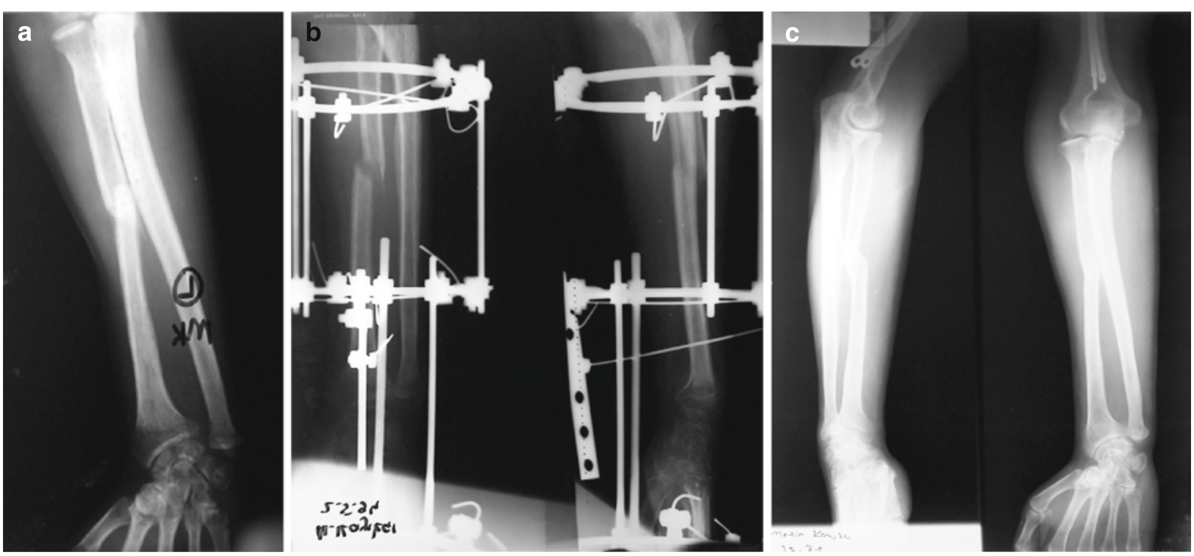


Fig. 20.10 Nonunion of the forearm with shortening (**a**). Monofocal distraction using a circular external fixator (**b**). X-rays (**c**) and clinical views (**d**, **e**) at the end of the treatment

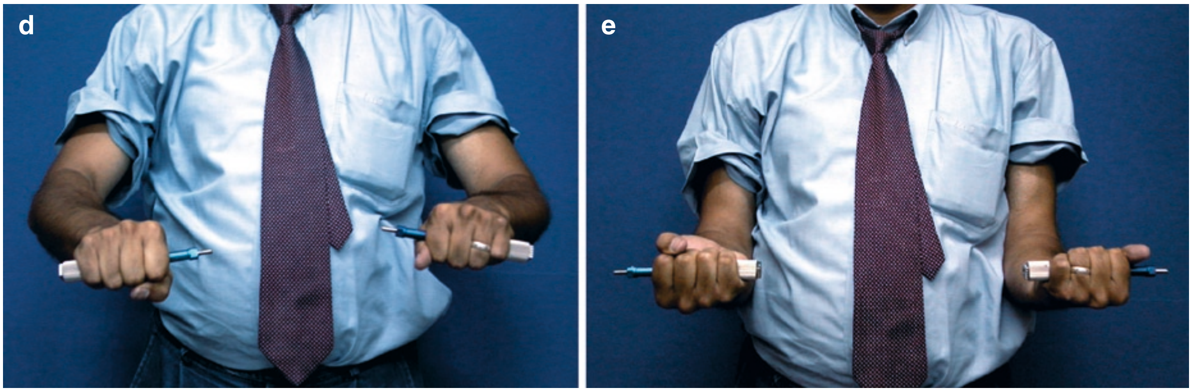


Fig. 20.10 (continued)

20.4.1.2 Consecutive Monofocal Compression Distraction

This method consists of alternating short periods of progressive distraction with periods of compression, which is also known as "callus massage" or the "accordion technique" [18, 28, 31]. Raschke et al. recommend 0.5 mm of distraction per day for 7 days, followed by 1 mm compression per day for 7 days over a 4-week period. Our preference is for distraction at a rate of 4 × 0.25 mm per day for 10 days, followed by a latency period of 10 days and compression at a rate of 2 × 0.25 mm for 20 days thereafter. These sequences may be repeated three times until bone healing is complete (Fig. 20.11).

Monofocal compression distraction using external fixators can be appropriate for the treatment of humeral shaft nonunions, especially after failed plate fixation or in cases with severe shortening [3].

20.4.1.3 Bifocal Strategy: Acute Shortening and Gradual Lengthening

In cases with bone loss, acute shortening until the gap is closed followed by gradual lengthening through another osteotomy may be performed [41]. Our experience indicates that the safe limits for acute shortening are up to 4 cm in the tibia and 6–7 cm in the femur. If additional compression is required, it must be performed gradually at a rate of 2 mm/day. During surgery, the arterial pulses of the foot, a Doppler ultrasound evaluation, capillary refill time, and oxygen saturation of the hallux help to evaluate the circulatory status of the extremity. If these parameters deteriorate, the distraction must be reversed until normal circulatory status is achieved (Figs. 20.12 and 20.13).

20.4.1.4 Computer-Assisted External Fixation (Hexapod Systems)

Hexapod external fixator systems (Smart Correction, Gotham Medical LLC, NJ, USA; Taylor Spatial Frame, Smith and Nephew Inc., Memphis, TN, USA) are modular systems that offer multiple frame options and allow for precise computer-assisted adjustment and 3D control of the frame. Circular rings are connected with six struts, which are gradually adjusted by the patient to correct the deformity, and to lengthen, compress, or distract the nonunion site. These adjustments are cumbersome and complex when classic Ilizarov type external fixators are used. The "virtual hinge" calculation, with the help of Internet-based software, guides any treatment via hexapod external fixator systems.

The first method can be used with these devices to reduce surgical time. Under this scenario, the rings are applied independently to the fragments and subsequently connected with six struts in a prespecified manner. Additionally, this technique also enables the rings to remain free for ideal placement with regard to soft tissue (Fig. 20.14).

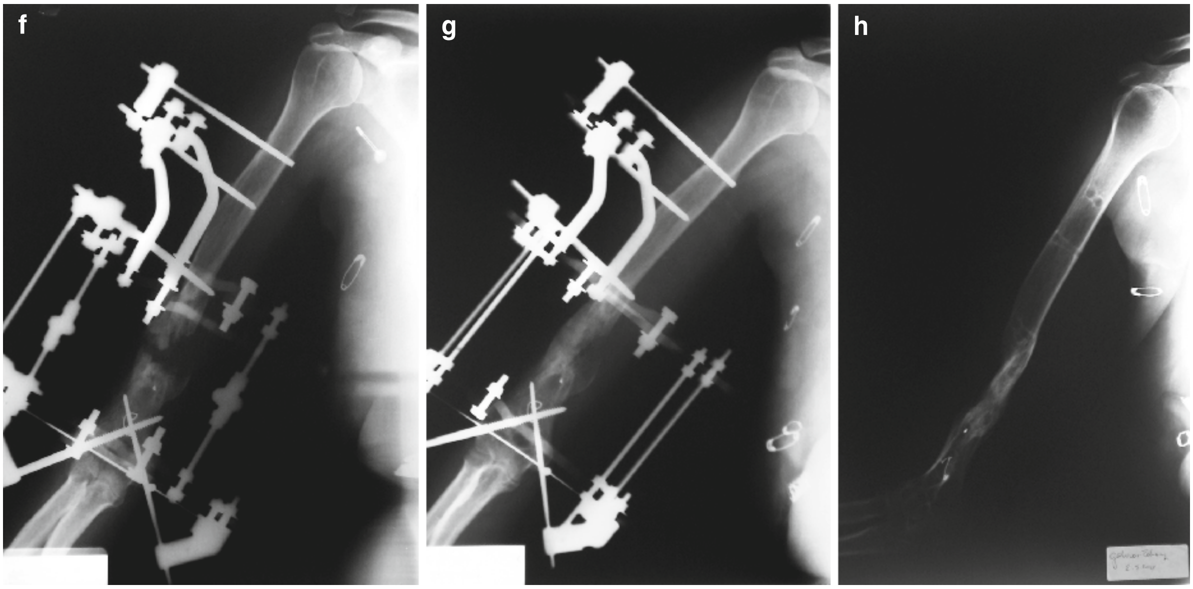
20.4.2 Internal Fixation

20.4.2.1 Plate Osteosynthesis

Plate osteosynthesis provides stability and compression, which in turn minimize the motion and reduce the gap at the nonunion site. Several types of plates can be used to treat nonunions. Metaphyseal and specifically located aseptic nonunions with excellent soft tissue envelopes are the best indications for plate fixations (Fig. 20.15).

A wave plate has been recommended by various authors, as it has a contour bent into its midportion so that it stands away from the bone at the abnormal

Fig. 20.11 A humeral nonunion. (**a**, **b**) Preoperative stress x-rays. (**c**–**e**) The deformity is corrected gradually by the use of a circular external fixator. (**f**, **g**) Consecutive monofocal compression and distraction is applied (accordion technique). (**h**) X-ray at the end of the treatment



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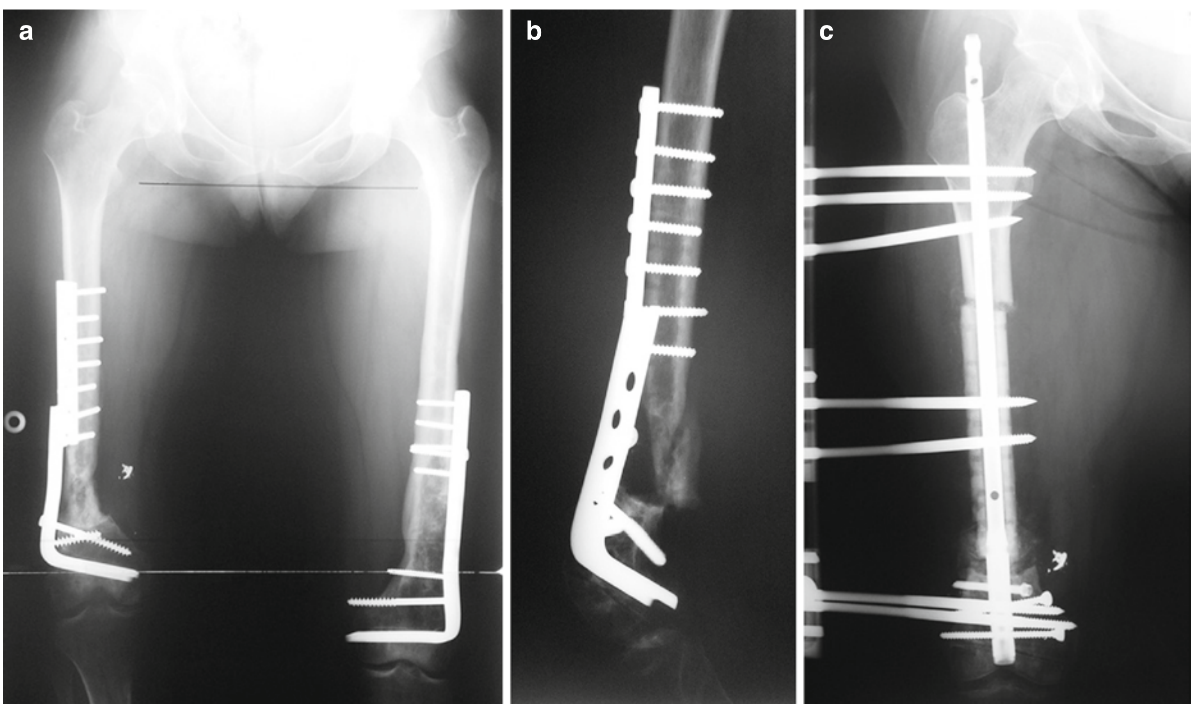

Fig. 20.12 Patient with a femoral nonunion following corrective osteotomy (**a**, **b**). As a bifocal strategy (compression distally, distraction proximally), the distal deformity is corrected acutely by fixator-assisted nailing and Poller screws, and lengthening over intramedullary nail technique is used to treat shortening (**c**, **d**). The external fixator is removed at the end of the lengthening process, and the intramedullary nail is locked proximally (**e**, **f**). Note that strut grafting was performed in the context of the lengthening site

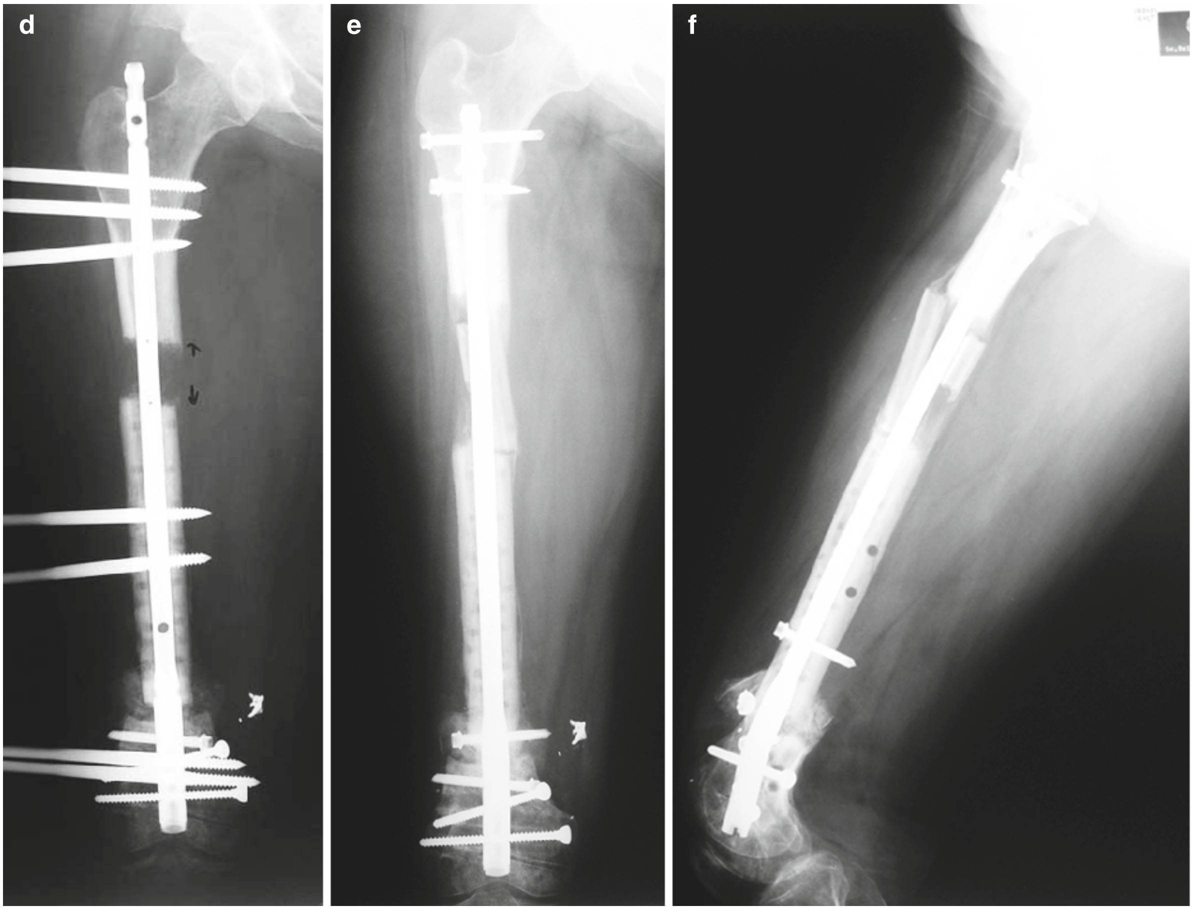

Fig. 20.12 (continued)

area, thus providing biological and mechanical advantages; the local blood supply is preserved by reducing the amount of dissection and the area of plate-bone contact, and there is more space for autogenous bone grafts on the lateral cortex [5, 35]. Wave plates can be used in the presence of a complete segmental defect, as it will not fail until the bone graft consolidates because cyclic loading is distributed over a wide area rather than at a local fulcrum (Fig. 20.16).

20.4.2.2 Exchange Nailing

Nonunion can occur following intramedullary nailing of the long bones in the lower extremities. Of note, it is more common if unreamed intramedullary nailing is used in femoral shaft fractures. Concerns about reaming include disruption of the cortical blood flow, thermal necrosis of the cortical bone, marrow immobilization due to elevated intramedullary pressure, and increased consumption of coagulation factors [20, 22, 25, 39, 43]. Despite these concerns, clinical success of reamed intramedullary nailing has been confirmed by several studies [6, 9, 14, 42, 45]. Exchange nailing is a good choice for nonunions of the long bones, which may be treated initially using an intramedullary nail (Fig. 20.17).

Exchange nailing for the treatment of a nonunion includes removal of the current intramedullary nail, reaming of the medullary canal, and placement of an intramedullary nail of a larger diameter than the removed nail. This leads to biological effects (resulting from reaming) and mechanical effects (resulting from the use of a larger-diameter nail) that promote bone healing. Exchange nailing has been shown to be successful for the treatment of both atrophic nonunions (for biological effects) and hypertrophic nonunions (for mechanical effects). Reaming of the medullary canal increases periosteal blood flow and stimulates periosteal new bone formation. Blood flow in the cortex, although initially diminished, returns to normal level or even better than normal within a few days after medullary reaming. Moreover, the products of reaming contain osteoblasts and multipotent

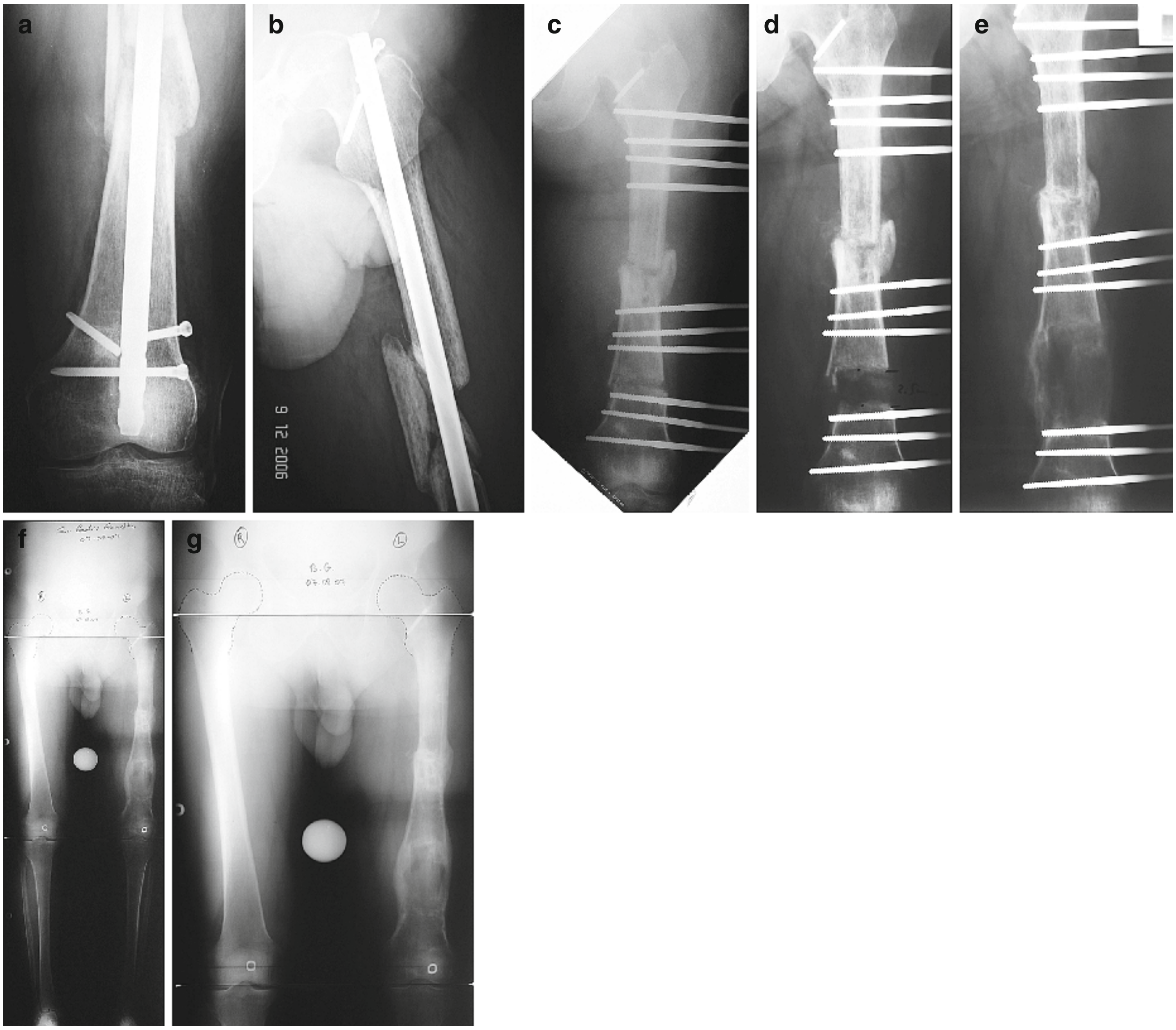

Fig. 20.13 A patient who had failed to heal following intramedullary nail for the femoral fracture (**a**, **b**). The bifocal strategy was used with a monolateral external fixator (compression proximally at the fracture site and distraction distally through an osteotomy for limb-length equalization) (**c**–**e**). X-rays at the end of the treatment, showing successful healing and equalized limb length (**f**, **g**)

stem cells. This may lead to an internal grafting effect. The use of a nail with a larger diameter guarantees greater bending rigidity and strength than the original nail. A larger-diameter nail offers higher bending rigidity (proportional to the fourth power of the radius) and strength (proportional to the third power of the radius).

The exchange nail should be at least 1 mm larger in diameter than the nail being removed, and others have recommended that it be up to 4 mm larger if the nail to be removed is substantially undersized. Canal reaming should continue until osseous tissue is apparent in the reaming flutes.

Exchange nailing is indicated if there is an aseptic nonunion in a long bone of the lower extremity (without comminution or defect) following prior intramedullary nailing [8]. The main indications for exchange nailing are as follows:

- Aseptic diaphyseal femoral nonunions
- Proximal tibial nonunions
- Tibial shaft nonunions
- Distal tibial nonunions
- Lower extremity nonunions with angular or rotational deformities

Exchange nailing is not recommended for the treatment of humeral shaft and very distal femoral nonunions.

Failure to heal the nonunion may occur even following exchange nailing. In such patients, we prefer to

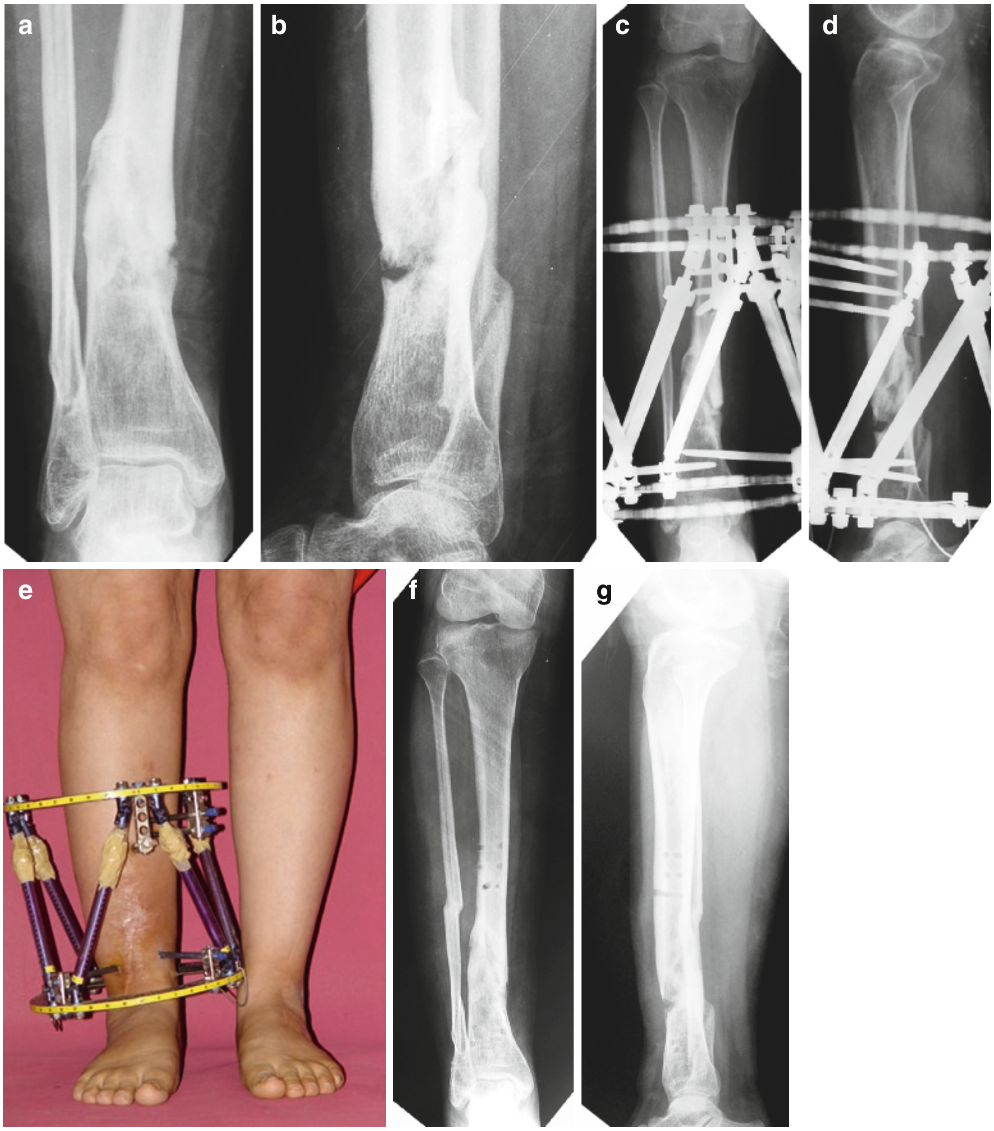

Fig. 20.14 A patient with tibial nonunion and mild deformity (**a**, **b**). A hexapod external fixator was used (**c**–**e**). X-rays at the end of the treatment (**f**, **g**)

remove the locking screws that are associated with the intramedullary nail and then to compress using a circular external fixator (Fig. 20.18).

20.4.2.3 Cage and Grafting for Defect Nonunions

The cage and grafting technique is described in Chap. 21.

20.4.3 Combination Techniques

The latest medical advances offer not only a shortened treatment time but also guarantee increased patient comfort. Combined techniques that utilize external fixators and internal fixation modalities (intramedullary nails, plates) combine the advantages of both techniques, with a decrease in external fixation time of almost 50%. By decreasing the external fixation time, patient comfort increases and the rate of external fixator-related complications decreases,

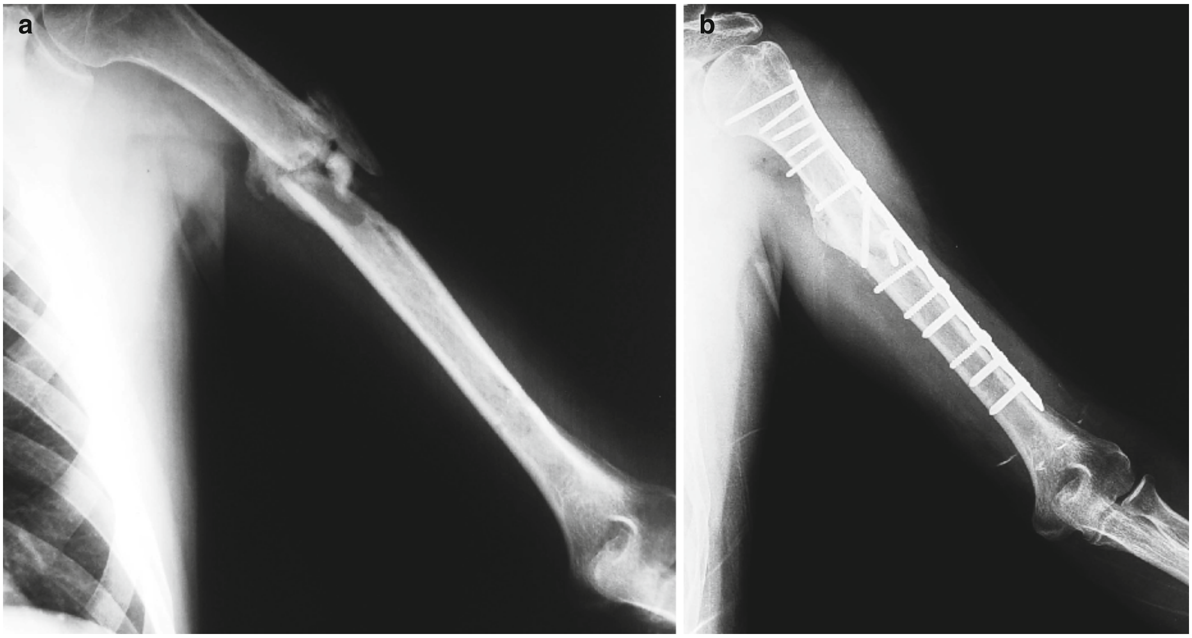

Fig. 20.15 A humeral fracture that failed to heal after conservative management (**a**). Plate fixation was performed (**b**)

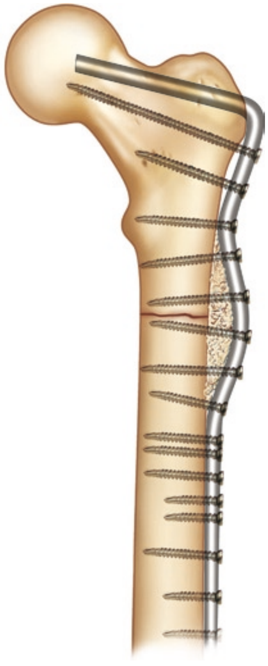

Fig. 20.16 Wave plate. Note that grafting was possible under the wave plate to the nonunion site

including pin track infections and joint contractures. The internal fixation hardware left in place after removal of the external fixator guarantees stability, inhibiting refracture or the recurrence of deformity, and enabling accelerated rehabilitation. Many combination techniques are described in the literature. Fixator-assisted acute femoral or tibial deformity corrections and consecutive lengthening over nails allow surgeons to address the deformity together with the limb-length discrepancy. This technique may also be applied in the case of a nonunion associated with a deformity – this is known as the monofocal compression-distraction technique combined with deformity correction. Combined techniques are satisfactorily used for nonunions with defects and/or infections [4, 19, 41].

20.4.3.1 Bone Transport

Bone transport is used for defect nonunions. Three methods exist: internal bone transport, external bone transport, and bone transport over nail (BTON) (Figs. 20.19–20.21). Bone transport with the use of an external fixator is known to be a reliable solution that leads to successful outcomes. The time spent in an external fixator (the external fixation time) depends on the length of distraction required and does carry a risk of complication. When the distraction phase is complete, the consolidation phase (which often lasts more than twice as long as the distraction time) becomes difficult for the patient to tolerate. Removal of the external fixator before satisfactory consolidation is associated with fracture, deformity, and shortening

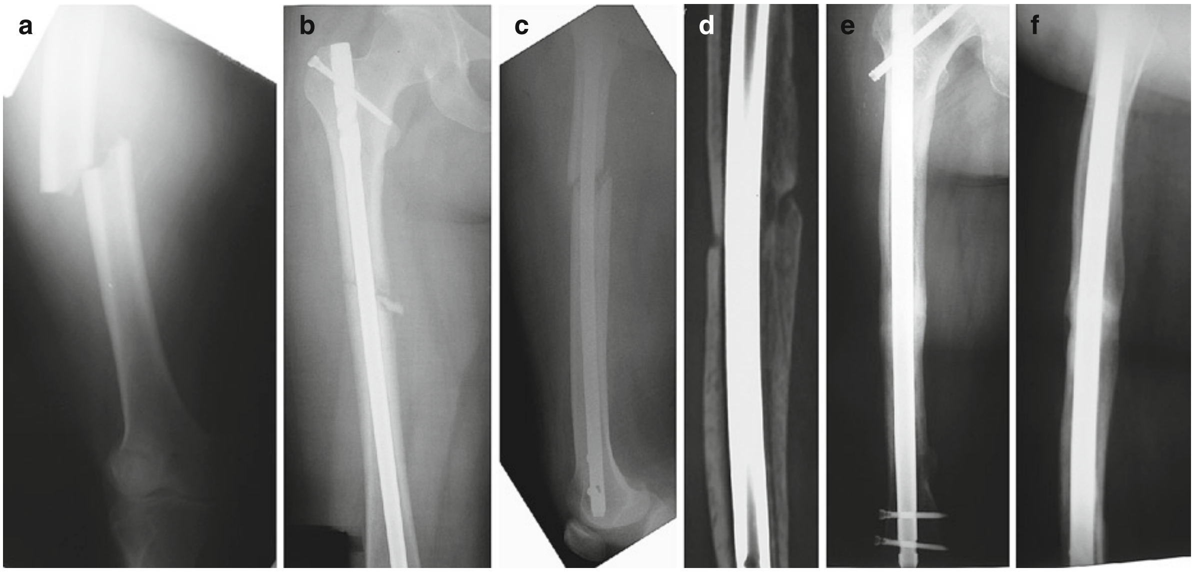

Fig. 20.17 A femoral shaft fracture (**a**) was initially treated with intramedullary nailing (**b**, **c**). CT suggested nonunion after 7 months (**d**). Exchange nailing resulted in union of the femur (**e**, **f**)

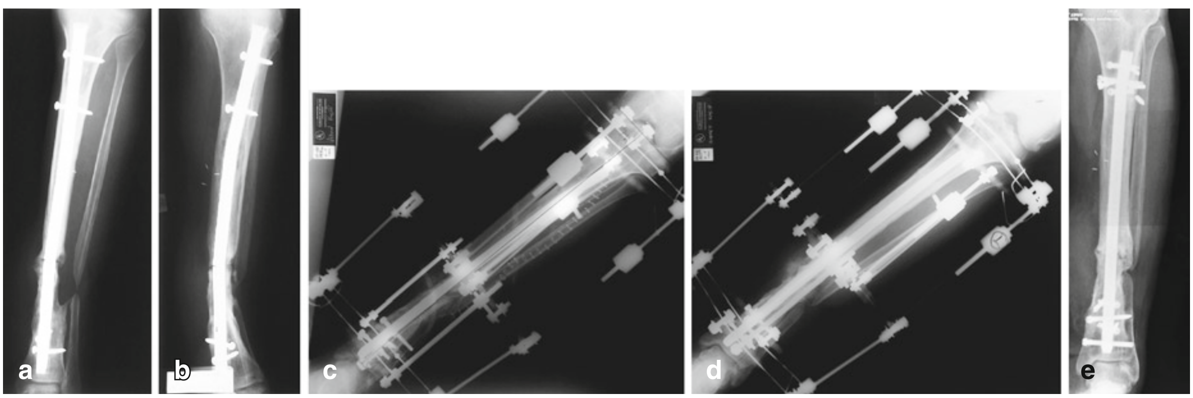

Fig. 20.18 A patient who had failed exchange nailing for tibial fracture nonunion (**a**, **b**). Subsequently, the nail was broken due to nonunion. Monofocal compression over the nail was used by a circular external fixator (**c**, **d**), and a tibial union was achieved (**e**)

through the distracted callus [27]. Older frames often required repeated adjustments to prevent misalignment of the docking site. The usage of the intramedullary nail in addition to the external fixator served to help avoid misalignment of the docking site, leading to significant decreases in external fixation time together with better maintenance of anatomical length and alignment [32].

Alternatively, minimal invasive plate osteosynthesis (MIPO) may be used to confer similar advantages [1, 2]. Bone transport may also be accomplished through the use of fully implantable intramedullary lengthening devices, such as internal lengthening nails (ISKDs). Cole reported a technique through which he achieved healing of the nonunion first, and then performed lengthening with an ISKD to address limb-length discrepancy [11].

For defects of 5–12 cm, we prefer the BTON technique. The contraindications of the BTON technique are vascular disease, diabetes mellitus, and active infection. Bone defects larger than 12 cm and tobacco abuse are relative contraindications.

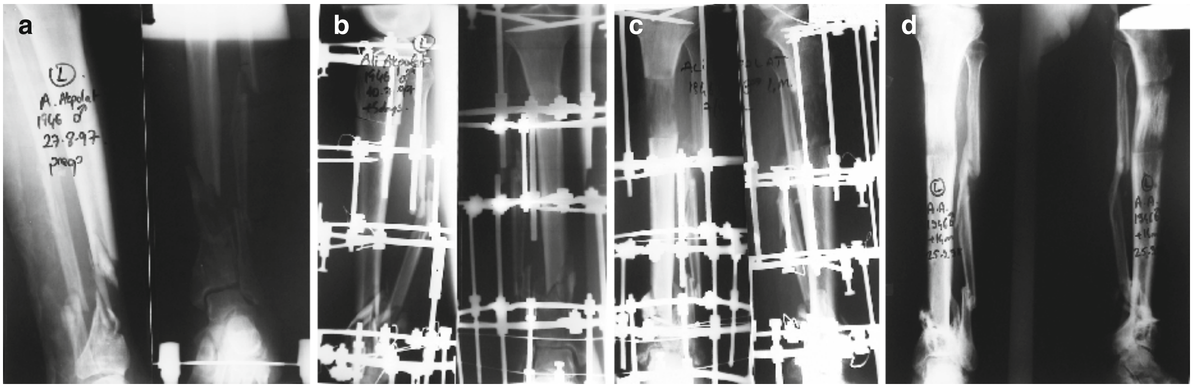

Fig. 20.19 A patient with a distal tibial fracture likely to develop nonunion (**a**). External bone transport through a proximal osteotomy was performed using a circular external fixator (**b**, **c**). X-rays at the end of the treatment (**d**)

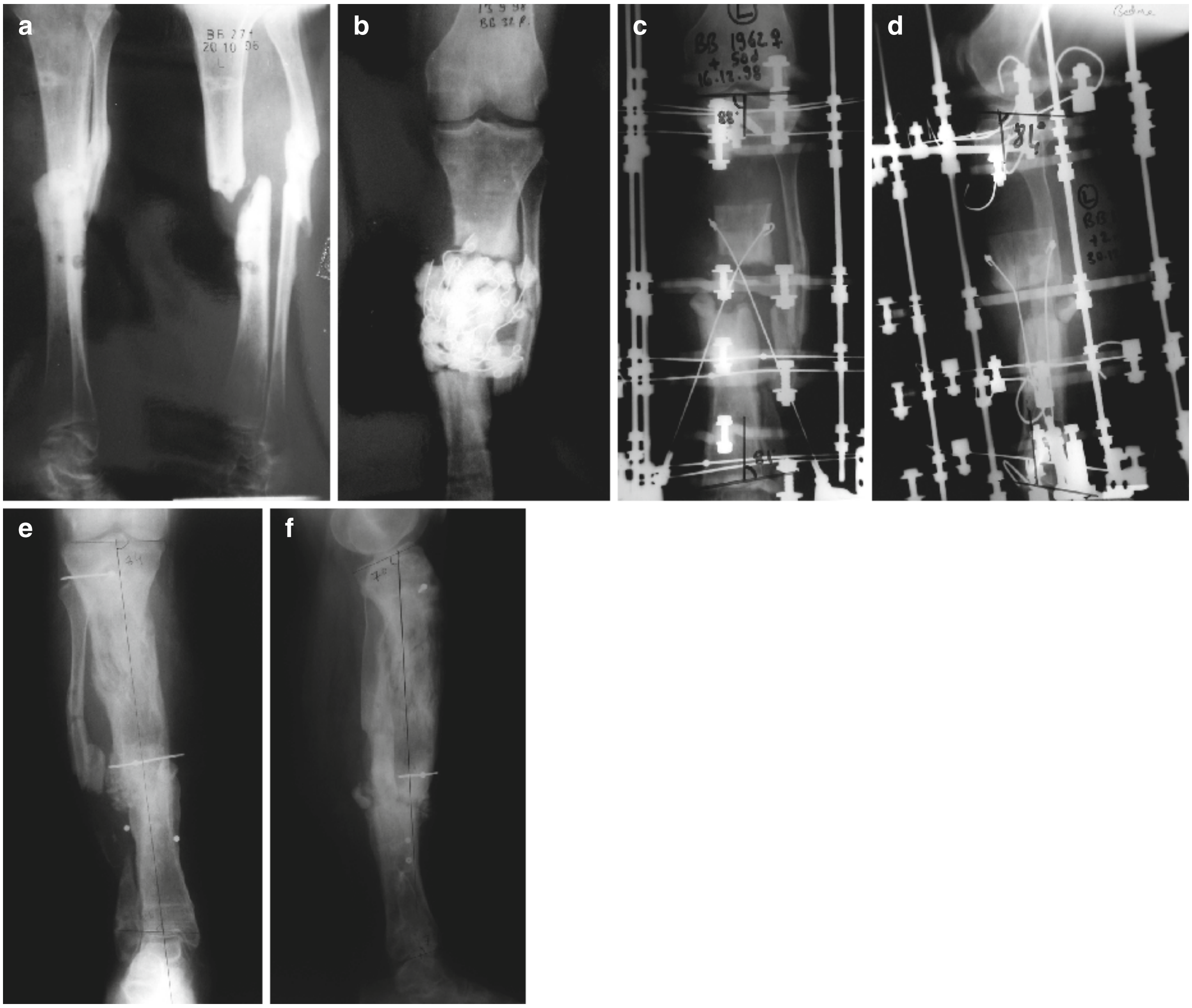

Fig. 20.20 A patient with an infected tibial nonunion (**a**). The non-vital infected portion of the tibia was removed, and antibiotic incremented bone cement was used as a spacer (**b**). Internal bone transport was used (**c**, **d**). X-rays at the end of the treatment (**e**, **f**)

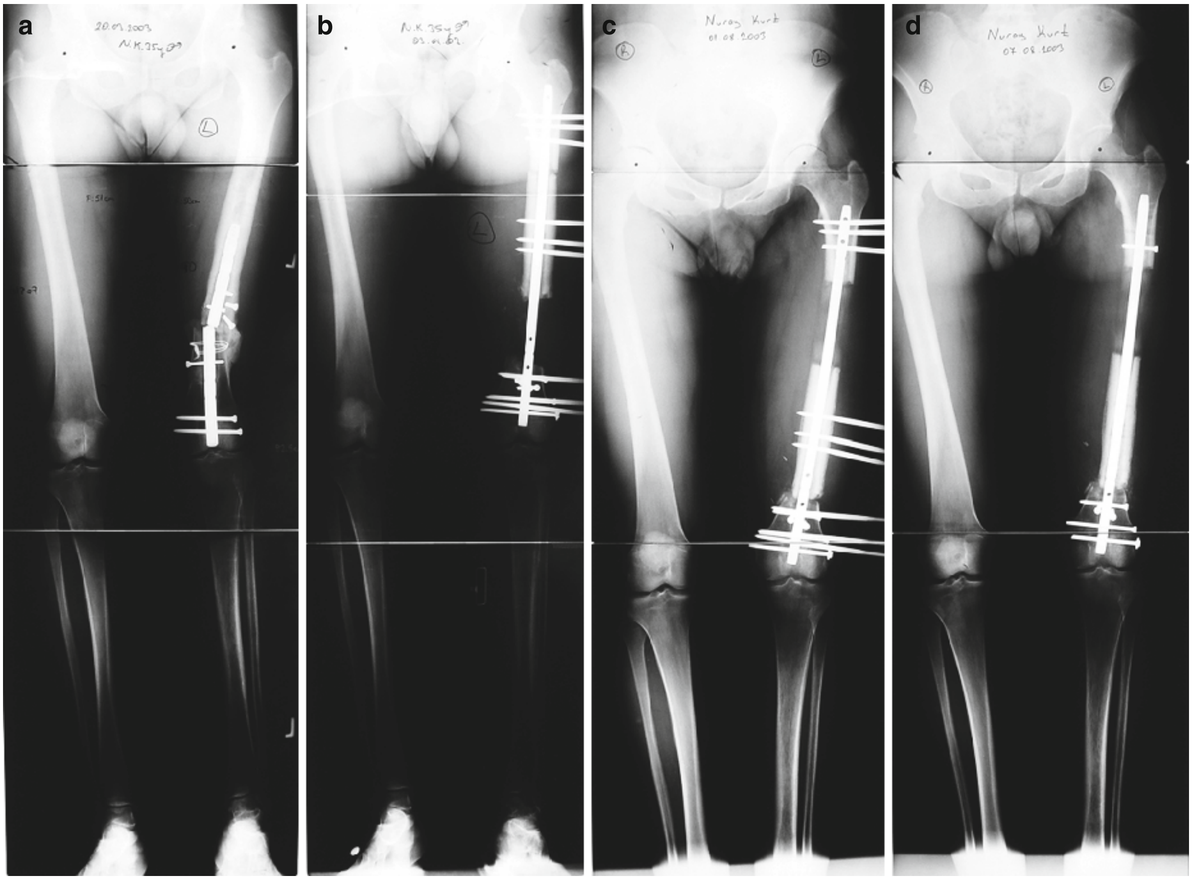

Fig. 20.21 A patient with a femoral nonunion. We note the shortening deformity and a broken nail (**a**). Bone transport over nail was used to treat the shortening deformity and the nonunion (**b**, **c**). Orthoroentgenogram at the end of the treatment (**d**)

20.4.4 Biologic Stimulation

20.4.4.1 Central Bone Grafting for Tibial Nonunions

Central bone grafting is an operative technique that uses a lateral approach, anterior to the fibula and the interosseous membrane, whereby a central compartment is created for autologous cancellous bone graft placement, thereby achieving a tibiofibular synostosis. The central bone mass and the fibula consolidate into a tubular bone that is sufficiently strong for weight bearing. This technique is a relatively simple and safe method for the treatment of tibial nonunions compared to posterolateral bone grafting, bone transport, rib or free vascular fibula grafts [34, 36]. It heals faster, requires fewer operations, and achieves similar rates of union in comparison to traditional posterolateral bone grafting. Central bone grafting may be used for bone defects of up to 5 cm, without previous infection, or in patients with previous infection exhibiting a defect of up to 2 cm after debridement.

20.4.4.2 Electrical Stimulation

The use of electrical energy for the treatment of nonunions started in the 1950s. It was pioneered by Yasuda, who demonstrated new bone formation around the cathode in a rabbit femur. Today, three devices are approved for use with humans [12, 13]:

1. Direct current stimulator supplied by Zimmer (Warsaw, IN, USA)
2. Inductive coupling system from Electro-Biology, Inc. (Fairfield, NJ, USA)
3. Direct current stimulation using a completely implantable system supplied by Telectronics Proprietary Ltd. (Milwaukee, WI, USA)

20.4.4.3 Partial Fibulectomy

The application of a partial fibulectomy is controversial for the treatment of tibial nonunions. It has been routinely recommended on the basis that the intact fibula may hold an ununited tibia in distraction (Fig. 20.22).

20.4.4.4 Bone Marrow Injection

Bone marrow contains osteoprogenitor cells that are key elements in the process of bone formation and fracture healing. Autogenic bone marrow grafting is a useful technique in the treatment of delayed unions and nonunions [15, 17]. We prefer the percutaneous technique to expedite the operative procedure and eliminate wound-healing difficulties. Using specific needles for iliac punctures, a bone marrow volume of 50 ml is aspirated under fluoroscopic control and immediately injected into the nonunion site (Fig. 20.23). Because of the short interval between aspiration and

Fig. 20.22 A patient with a tibial nonunion (**a**). Partial fibulectomy and elastic intramedullary nailing resulted in tibial union (**b**)

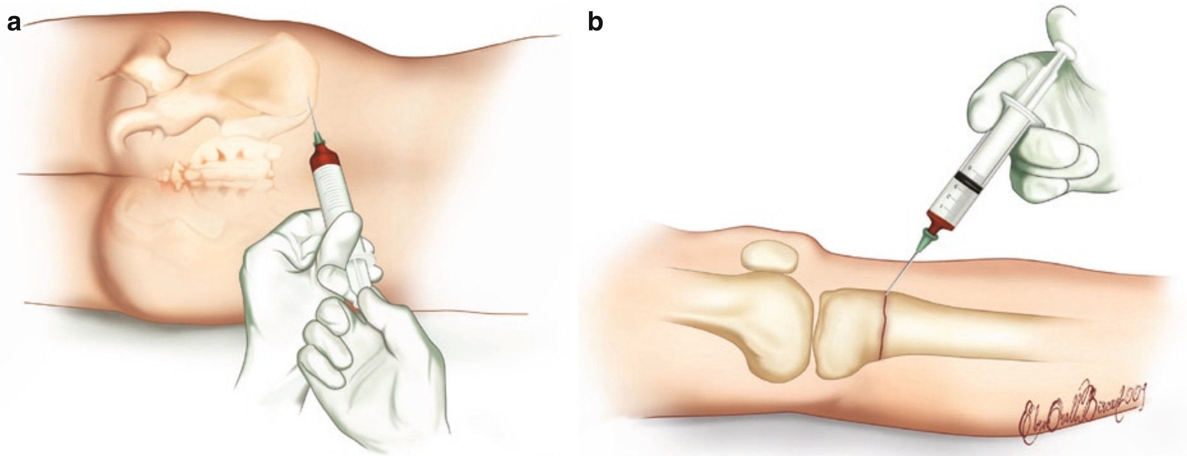

Fig. 20.23 Bone marrow was taken percutaneously from the posterior iliac crest (**a**) and immediately injected into the nonunion site (**b**)

injection, an anticoagulant (e.g., heparin) is not needed. Heparin usage is associated with potential impairment of bone healing. Repeat injections may be performed when no healing is observed on follow-up x-rays. Perioperative complications are uncommon, but heterotopic bone formation may occur following bone marrow injection [15]. A bone matrix may enhance the effectiveness of bone marrow injections.

20.5 Future

Bone tissue engineering offers significant potential in the management of refractory nonunions. There are only a few reports of its successful use in the literature and translation into clinical practice remains limited at this time. Recent advances in stem cell therapy, cell biology, and biomaterials science are promising, and some bone morphogenetic proteins and growth factors are commercially available; however, further studies are needed to promote clinical application.

References

1. Apivatthakakul, T., Arpornchayanon, O.: Minimally invasive plate osteosynthesis (MIPO) combined with distraction osteogenesis in the treatment of bone defects. A new technique of bone transport: a report of two cases. Injury **33**, 460–465 (2002)
2. Apivatthakakul, T., Sananpanich, K.: The locking compression plate as an external fixator for bone transport in the treatment of a large distal tibial defect: a case report. Injury **38**, 1318–1325 (2007)
3. Atalar, A.C., Kocaoglu, M., Demirhan, M., et al.: Comparison of three different treatment modalities in the management of humeral shaft nonunions (plates, unilateral and circular external fixators). J. Orthop. Trauma **22**, 248–257 (2008)
4. Bilen, F.E., Kocaoglu, M., Eralp, L., et al.: Fixator-assisted nailing and consecutive lengthening over an intramedullary nail for the correction of tibial deformity. J. Bone Joint Surg. Br. **92-B**, 146–152 (2010)
5. Blatter, G., Gasser, B., Weber, B.G.: Die Wellenplatte. AO Bulletin. Version 29 (1989)
6. Braten, M., Terjesen, T., Rossvoll, I.: Femoral shaft fractures treated by intramedullary nailing. A follow-up study focusing on problems related to the method. Injury **26**, 379–383 (1995)
7. Brighton, C.T., Esterhai Jr., J.L., Katz, M., et al.: Synovial pseudoarthrosis: a clinical, roentgenographic-scintigraphic, and pathologic study. J. Trauma **27**, 463–470 (1987)
8. Brinker, M.R., O'Connor, D.P., et al.: Exchange nailing of ununited fractures. J. Bone Joint Surg. Am. **89-A**, 177–188 (2007)
9. Brumback, R.J., Reilly, J.P., Poka, A., et al.: Intramedullary nailing of femoral shaft fractures. Part I: decision-making errors with interlocking fixation. J. Bone Joint Surg. Am. **70-A**, 1441–1452 (1988)
10. Burd, T.A., Hughes, M.S., Anglen, J.O.: Heterotopic ossification prophylaxis with indomethacin increases the risk of long-bone nonunion. J. Bone Joint Surg. Br. **85-B**, 700–705 (2003)
11. Cole, J.D.: Internal lengthening nail: intramedullary skeletal kinetic distractor. In: Rozbruch, S.R., Ilizarov, S. (eds.) Limb Lengthening and Reconstruction Surgery, pp. 639–652. Informa, New York (2007)
12. Esterhai Jr., J.L., Brighton, C.T., Heppenstall, R.B., et al.: Detection of synovial pseudarthrosis by 99mTc scintigraphy: application to treatment of traumatic nonunion with constant direct current. Clin. Orthop. Relat. Res. **161**, 15–23 (1981)
13. Esterhai Jr., J.L., Brighton, C.T., Heppenstall, R.B., et al.: Nonunion of the humerus. Clinical, roentgenographic, scintigraphic, and response characteristics to treatment with constant direct current stimulation of osteogenesis. Clin. Orthop. Relat. Res. **211**, 228 (1981)
14. Grover, J., Wiss, D.A.: A prospective study of fractures of the femoral shaft treated with a static, intramedullary, interlocking nail comparing one versus two distal screws. Orthop. Clin. North Am. **26**, 139–146 (1995)
15. Healey, J.H., Zimmerman, P.A., McDonnell, J.M., et al.: Percutaneous bone marrow grafting of delayed union and nonunion in cancer patients. Clin. Orthop. Relat. Res. **256**, 280–285 (1990)
16. Helfet, D.L., Jupiter, J.B., Gasser, S.: Indirect reduction and tendion-band plating of tibial non-union with deformity. J. Bone Joint Surg. Am. **74-A**, 1286–1297 (1992)
17. Hernigou, P., Poignard, A., Manicom, O., et al.: The use of percutaneous autologous bone marrow transplantation in nonunion and avascular necrosis of bone. J. Bone Joint Surg. Br. **87-B**, 896–902 (2005)
18. Ilizarov, G.A.: Pseudoarthrosis and defects of long tubular bones. In: Ilizarov, G.A. (ed.) Transosseous Osteosynthesis: Theoretical and Clinical Aspects of Regeneration and Growth of Tissue, pp. 454–508. Springer, Berlin (1992)
19. Kocaoglu, M., Eralp, L., Bilen, F.E., et al.: Fixator-assisted acute femoral deformity correction and consecutive lengthening over an intramedullary nail. J. Bone Joint Surg. Am. **91-A**, 152–259 (2009)
20. Leunig, M., Hertel, R.: Thermal necrosis after tibial reaming for intramedullary nail fixation. A report of three cases. J. Bone Joint Surg. Br. **78-B**, 584–587 (1996)
21. Little, D.G., Ramachandran, M., Schindeler, A.: The anabolic and catabolic responses in bone repair. J. Bone Joint Surg. Br. **89-B**, 425–433 (2007)
22. Malik, M.H.A., Harwood, P., Diggle, P., et al.: Factors affecting rates of infection and nonunion in intramedullary nailing. J. Bone Joint Surg. Br. **86-B**, 556–560 (2004)
23. Marsh, J.L., Buckwalter, J.A., Evarts, C.M.: Delayed union, nonunion, malunion, and avascular necrosis. In: Epps Jr., C.H. (ed.) Complications in Orthopaedic Surgery, 3rd edn, pp. 183–200. J.B. Lippincott, Philadelphia (1994)

24. Marsh, D.R., Shah, S., Elliot, J., et al.: The Ilizarov method in nonunion, malunion and infection of fractures. J. Bone Joint Surg. Br. **79-B**, 273–279 (1997)
25. Martin, R., Leighton, R.K., Petrie, D., et al.: Effect of proximal and distal venting during intramedullary nailing. Clin. Orthop. Relat. Res. **332**, 80–89 (1996)
26. Milgram, J.W.: Nonunion and pseudarthrosis of fracture healing. A histopathologic study of 95 human specimens. Clin. Orthop. Relat. Res. **268**, 203–213 (1991)
27. Paley, D., Chaudrey, M., Pirone, A.M., et al.: Treatment of malunions and nonunions of the femur and tibia by detailed preoperative planning and Ilizarov techniques. Orthop. Clin. North Am. **21**, 667–691 (1990)
28. Patel, V.R., Menon, D.K., Pool, R.D., et al.: Nonunion of the humerus after failure of surgical treatment. J. Bone Joint Surg. Br. **82-B**, 977–983 (2000)
29. Patil, S., Montgomery, R.: Management of complex tibial and femoral nonunionusing the Ilizarov technique, and its cost implications. J. Bone Joint Surg. Br. **88-B**, 928–932 (2006)
30. Pedrotti, L., Bertani, B., Mora, R.: Assessment of fracture healing. In: Mora, R. (ed.) Nonunion of the Long Bones. Springer, Italia (2006)
31. Raschke, M.J., Mann, J.W., Oedekoven, G., et al.: Segmental transport after reamed intramedullary nailing: preliminary report of a 'monorail' system. Clin. Orthop. Relat. Res. **282**, 233–240 (1992)
32. Raschke, M., Khodadadyan, C., Matino, P., et al.: Nonunion of the humerus following intramedullary nailing treated by Ilizarov hybrid fixation. J. Orthop. Trauma **12**(2), 138–141 (1998)
33. Reed, A.A.C., Joyner, J.C., Isefuku, S., et al.: Vascularity in a new model of atrophic nonunion. J. Bone Joint Surg. Br. **85-B**, 604–610 (2003)
34. Rijnberg, W.J., van Linge, B.: Central grafting for persistent nonunion of the tibia: a lateral approach to the tibia, creating a central compartment. J. Bone Joint Surg. Br. **75-B**, 926–931 (1993)
35. Ring, D., Jupiter, J.B., Sanders, R.A., et al.: Complex nonunion of fractures of the femoral shaft treated by wave-plate osteosynthesis. J. Bone Joint Surg. Br. **79-B**, 289–294 (1997)
36. Ryzewicz, M., Morgan, S.J., Linford, E., et al.: Central bone grafting for nonunion of fractures of the tibia. J. Bone Joint Surg. Br. **91-B**, 522–529 (2009)
37. Saleh, M., Rees, A.: Bifocal surgery for deformity and bone loss after lower-limb fractures. Comparison of bone-transport and compression-distraction methods. J. Bone Joint Surg. Br. **77**, 429–434 (1995)
38. Saleh, M., Royston, S.: Management of nonunion of fractures by distraction with correction of angulation and shortening. J. Bone Joint Surg. Br. **78-B**, 105–109 (1996)
39. Schemitsch, E.H., Kowalski, M.J., Swiontowski, M.F., et al.: Comparison of the effect of reamed and unreamed locked intramedullary nailing on blood flow in the callus and strength of union following fracture of the sheep tibia. J. Orthop. Res. **13**, 382–389 (1995)
40. Schwartsman, V., Choi, S.H., Schwartsman, R.: Tibial nonunions. Treatment tactics with the Ilizarov method. Orthop. Clin. North Am. **21**(4), 639–653 (1990)
41. Sen, C., Eralp, L., Gunes, T., et al.: An alternative method for the treatment of nonunion of the tibia with bone loss. J. Bone Joint Surg. Br. **88-B**, 783–789 (2006)
42. The Canadian Orthopaedic Trauma Society: Nonunion following intramedullary nailing of the femur with and without reaming. Results of a multicenter randomized clinical trial. J. Bone Joint Surg. Br. **85**, 2093–2096 (2003)
43. Trueta, J., Cavadias, A.X.: Vascular changes caused by the Kuntscher type of nailing. An experimental study in rabbit. J. Bone Joint Surg. Br. **37**, 492–505 (1955)
44. Weber, B.G., Cech, O.: Pseudoarthrosis: Pathology, Biomechanics, Therapy, Results. Hans Huber Medical, Berne, Switzerland (1976)
45. Winquist, R.A., Hansen Jr., S.T., Clawson, D.K.: Closed intramedullary nailing of femoral fractures. A report of five hundred and twenty cases. J. Bone Joint Surg. Am. **66**, 529–539 (1984)
46. Wiss, D.A., Stetson, W.B.: Tibial nonunion: treatment alternatives. J. Am. Acad. Orthop. Surg. **4**, 249–257 (1996)