Current Concepts: Aseptic Nonunion of Femoral Shaft Diaphysis

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Abstract

In spite of increased understanding of biomechanics and improvements of implant design, nonunion of femoral shaft fractures continues to hinder the treatment of these injuries. Femoral nonunion presents a difficult treatment challenge for the surgeon and a formidable personal and economic hardship for the patient. In most series of femoral fractures treated with intramedullary nailing techniques, the incidence of this complication is estimated to be 1%. A higher frequency has recently been reported due to advances in trauma care leading to increased survivorship among severely injured patients and expanded indications of intramedullary nailing. Whereas the treatment of femoral shaft fractures has been extensively described in the orthopedic literature, the data regarding treatment of femoral shaft nonunions are sparse and conflicting, as most of the reported series consisted of a small number of cases. However, careful review of the existing literature does provide some answers regarding either conservative or operative management. The gold standard for femoral shaft nonunions invariably includes surgical intervention in the form of closed reamed intramedullary nailing or exchange nailing, but several alternative methods have been reported including electromagnetic fields, low-intensity ultrasound, extracorporeal shock wave therapy, external fixators and exchange or indirect plate osteosynthesis. In this paper, a comprehensive review of the current treatment modalities for aseptic midshaft femoral nonunion is presented, after a concise overview of the incidence, definition, classification and risk factors of this complication.

Key Words

Femoral fractures · Revision surgery · Osteosynthesis · Intramedullary nailing · Fracture healing

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Introduction

Repair of fractures involves a sequence of dynamic events, which ultimately restores the integrity of the bone and its biomechanical properties [1]. In some cases healing is compromised leading to delayed union or nonunion. It is estimated that 10% of the fractures, which occur annually, will require further surgical procedures because of impaired healing [2].

Modern surgical nailing techniques for femoral shaft fractures have reduced the incidence of femoral nonunion to as low as 1% [3, 4]. Recently however, it has been reported that the incidence of femoral shaft nonunion is increasing due to improved survival of more severely multiply injured patients and expansion of intramedullary nailing indications [5].

A number of techniques have been proposed for treating nonunion of the femoral shaft including electromagnetic fields [6], low-intensity ultrasound [7], extracorporeal shock wave therapy (ESWT) [8] nail dynamization alone [9], external fixators [10] and plate osteosynthesis [11, 12]. The most common treatment modality for aseptic nonunion of the femoral shaft is the insertion of a reamed locked intramedullary nail with or without the use of autogenous bone graft [13].

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Historically, excellent results have been achieved by the insertion of an unlocked intramedullary nail of the Küntscher type, for uncomplicated diaphyseal nonunions, with union rates in the region of 96–100% [14]. The indications of reamed intramedullary nailing in the treatment of femoral nonunions were extended with the introduction of locking techniques, once again with excellent union rates reported for a single nailing procedure [15, 16].

Femoral nonunion nowadays is usually seen after a previously unsuccessful nailing procedure and is usually treated by exchange nailing [17, 18]. Recently, Weresh et al. [19] reported a 47% incidence of failure for this procedure with one or more additional procedures required to achieve fracture union. This led the authors to conclude that routine exchange femoral nailing may require re-evaluation. As an alternative to exchange nailing, modern indirect plating osteosynthesis [20], augmentative Ilizarov techniques [21], autologous bone marrow transplantation [22] and intramedullary fibular allograft [23] have been recently proposed in complex femoral nonunions after previous intramedullary nailing.

Incidence of Femoral Nonunion

Current treatment of fractures of the femoral shaft appears to be relatively straightforward with a low reported risk of failure. Published results using reamed intramedullary nails have shown healing rates of 96–100% [4, 24–32]. In addition, open fractures of the femoral shaft treated with modern nailing techniques have similar high rates of union [33]. In most series of femoral fractures treated with intramedullary nailing the incidence of aseptic nonunion is estimated to be from 0.9–4%. Winquist et al. [24] reported a nonunion rate of 0.9% in 520 patients with femoral shaft fractures treated with intramedullary nailing. Similar results were reported by Brumback et al. [25–27] who noted a 2% nonunion rate. Wolinsky et al. [28] and Folleras et al. [29] stated that a union rate of 97–100% can be expected, whereas Nowotarski et al. [30] reported a 97% union rate after delayed intramedullary nailing for fractures of the shaft of the femur in multiply injured patients. Lambiris et al. [4] in a multicenter study completed in 1999 reported a nonunion rate of 0.6% in 550 femur fractures. The same author in 2003 noted only one case of pseudarthrosis over 63 combined femoral fractures treated with closed locked intramedullary nailing [31]. As a result of these and other studies [34–38], intramedullary nailing became the treatment of choice for femoral shaft fractures in adults; in contrast only a few studies have reported increased frequency of femoral nonunion because of technical faults in not specialized teaching hospitals [39] or due to improved survivorship among severely injured patients and increasing trends toward early internal fixation [5, 40–42].

Definition and Classification of Nonunion

Several textbooks have proposed definitions for delayed healing based upon time: 3–4 months for delayed union and 6–8 months for nonunion [43]. Nonunion of the femoral shaft is usually defined as a failure to achieve clinical union at 6–12 months following fixation or if there is no healing progress during the last 3 months or an implant failure is obvious [11, 17, 18, 44]. Some authors suggest earlier intervention at 4 months postoperatively [39, 45]. Einhorn [46] reported definitions for nonunion and delayed union that move beyond a simple time line describing nonunion as the "cessation of all healing processes and union has not occurred." He further defines delayed union as a continuation of healing processes, but union has not occurred in the expected time, and the outcome is uncertain.

In general, there is no universally accepted or validated approach to evaluate the progression of fracture healing in lower extremity fractures [47, 48]. Determination of fracture union in lower extremity fractures is almost always based upon serial clinical and radiographic assessments. Pain on weight bearing is an important clinical measure among several reported approaches to assess fracture healing [17, 18, 24]. Patients often describe an increase in pain in the preceding months and an inability to continue with physical therapy or resume basic activities such as prolonged walking. Pain is usually increased with activity and accompanied by limb swelling. Radiographic parameters used in the assessment of fracture healing have included cortical continuity, loss of fracture line on serial radiographs, and callus size [17–19, 24, 49]. These parameters had also combined by Hammer et al. [50] and Lane & Sandhu [51] in certain scales for more accurate accessing of fracture healing. Bhandari et al. [52] reported a lack of consensus in the assessment of fracture healing among orthopedic surgeons which led to varying definitions of nonunion and malunion that can influence the decision to intervene in an effort to promote fracture healing. Serial plain tomographies and volumetric computed tomography [53] are reliable tools to detect early changes in normal bone healing and may serve as useful addition to subjective image analysis in monitoring fracture healing in clinical trials.

Nonunions are classically categorized as hypertrophic, normotrophic (oligotrophic), or atrophic [43]. Hypertrophic nonunions present radiographically with abundant callus and persistent radiolucent line at the fracture site whereas normotrophic nonunion has minimal callus but relatively normal bone ends with no resorption. Atrophic nonunions are characterized by the absence of callus, resorption of the bone ends and a significant fracture gap. As these distinctions describe the biology at the fracture site they considered important in the clinical determination of treatment although some authors did not pay any attention to the radiographic appearance of nonunion, after intramedullary nailing in particular [39].

Nonunions without callus (atrophic) have impaired biology, which most often results from severe open fractures, infection or systemic disease. Biologic improvement is mandatory to achieve healing of an atrophic nonunion. Bellabarba et al. [20] used autologous bone grafting in all atrophic femoral nonunions after intramedullary nailing, treated with indirect reduction and plating and in 8 out of 11 oligotrophic nonunions. The criteria he used to graft the oligotrophic nonunions were the presence of a significant bony defect or unfavorable bony architecture. In contrast, hypertrophic nonunions appear in a relatively healthy biologic environment. Blood supply is sufficient and abundant new bone formation occurs. Union is not achieved because of the lack of mechanical stability. Therefore, the objective is to provide improved stability while simultaneously preserving biology [54].

Factors Predisposing to Nonunion

Although the exact causes of delayed union and nonunion are unknown, both systemic and local factors are thought to contribute to its development. Systemic factors include the patient's metabolic and nutritional status, general health, and activity level. Recently, the use of tobacco has been implicated in the development of nonunions [55]. Nicotine has been shown experimentally to affect union rate and fracture callus strength [56]. The detrimental effect of smoking on bone healing should be reviewed in all patients with nonunions.

According to Boyd et al. [57] the following local factors should be taken under consideration for nonunion of long bones: (1) open fractures, (2) infection, (3) segmental fractures, with impaired blood supply, usually to the middle fragment, (4) comminuted fractures due to severe trauma, (5) insecurely fixed osteosynthesis, (6) insufficient time of immobilization, (7) ill-advised open reduction, and (8) distraction either by traction or by a plate and screws.

Furthermore, Beredjiklian et al. [42] reported several factors that have a statistical significant effect ($p < 0.05$) on nonunion healing: (1) advanced patient age, number of prior surgical procedures and duration of nonunion, (2) presence of osteomyelitis or synovial pseudarthrosis, (3) initial treatment with flexible intramedullary devices or compression plating, (4) poor bone stock, (5) malalignment in the anteroposterior plane of more than 10° and/or malalignment in the lateral plane of more than 20°. Synovial pseudarthrosis is thought to result from gross motion at the fracture site due to inadequate immobilization. The authors believed that poor fixation results in metaplasia of the lining tissue at the fracture site consisting of fibroblasts and histiocytes, a novel tissue comparable to that present in synovial joints. Given the poor healing rates in these cases, it is clear that this environment is not conductive to fracture healing. The authors state also that the mode of initial treatment of the femoral shaft fracture did not significantly impact the result of nonunion treatment. However, statistically significant differences in healing rates were found between different treatment modalities for established nonunions.

Giannoudis et al. [58] assessed 32 patients with nonunion of a fracture of the diaphysis of the femur and compared them with 67 patients whose fracture had united. The authors found no relationship between the rate of union and the type of implant, mode of locking, reaming, distraction or smoking. There were fewer cases of nonunion in more comminuted fractures (type C) and in patients who were able to bear weight earlier. There was only a marked association between nonunion and the use of NSAIDs after injury and delayed healing was noted in patients who took NSAIDs and whose fractures had united.

In contrast, another report by Yokoyama et al. [59] showed that only AO fractures of type C and the existence of multiskeletal trauma in lower extremity (double lesions, floating knee, bilateral fractures) were significantly ($p < 0.05$) related to nonunion among several variables such as age, gender, smoking history, severity of soft tissue injury, and polytrauma patients. They also reported that static intramedullary nailing did not inhibit the process of fracture healing and there were no differences in healing time between the reamed and unreamed groups.

Intramedullary reaming and the mode of interlocking (static or dynamic) have been extensively discussed in the literature as risk factors to the development of femoral nonunion and need further analysis.

In general, the use of unreamed intramedullary nailing has been implicated to higher rates of nonunion. Most published investigations have noted fewer nonunions associated with reamed nailing than with nailing without reaming [26, 60–62]. Despite this clinical success, several concerns have persisted about the biological consequences of reaming; for example, disruption of cortical blood flow, thermal necrosis of the cortical bone, marrow embolization triggering the development of ARDS, increased consumption of coagulation factors and the concern of an increased risk of infection in open fractures [63–65]. Conical, low-spinning reamers, who are advanced slowly into the medullary canal, seem to cause less thermal damage to the inner cortex. Recent studies have yielded contradictory results as to whether small diameter nails without reaming give improved results, especially with regard to rates of fracture healing [66, 67].

Giannoudis et al. [68], Krettek et al. [69], and Kropfl et al. [70] demonstrated good results using a femoral nailing technique without reaming. Hammacher et al. [67] did not find the same results in a study of 129 acute femoral fractures treated with undreamed nailing in eight different centers. Five percent of the patients had a nonunion, 2.9% had a delayed union, and 6.6% needed secondary intervention to achieve union. In a retrospective study, Clatworthy et al. [71] compared 23 patients who had nailing without reaming with 22 who had nailing after reaming. More than 9 months were necessary to union for 57% of the fractures treated without reaming and only for 18% of those that had reaming. In a prospective, randomized study, Tornetta & Tiburzi [72] analyzed the results of 89 fractures that had nailing without reaming and 83 that had nailing with reaming. The mean time to union was 80 days for the reaming group and 109 days for the group without reaming. They noted that the difference was most disparate in fractures of the distal third of the femur. Finally, in a prospective, multicenter, randomized clinical trial contacted by the Canadian Orthopaedic Trauma Society [73], in 107 femoral shaft fractures treated without reaming and 121 fractures treated with reaming, the rate of nonunion was significantly higher in the group treated without reaming.

Reaming disrupts the circulation of the inner two-thirds of the cortex but has a sixfold increase in periosteal blood flow and allows the insertion of a larger nail, which improves its mechanical purchase and provides greater stability [74]. The reaming products are thought to have osteoinductive properties also [75]. Several investigators have described an intensive new-bone formation around the reaming effluent seen both on histological sections and on plain radiographs [76]. The improved biomechanics associated with complete filling of the canal and the osteoinductive properties of the reaming may be responsible for the higher rate of union observed in patients who received reaming. The stimulatory effect of reaming on bone formation (higher number of bone nodules) has recently been reported by Bhandari & Schemitsch [77] in an experimental study in rats. Antibodies to insulin growth factors I and II, and indomethacin reversed the stimulatory effect of reaming on bone nodule formation, suggesting their role in modulating the course of fracture healing following intramedullary reaming. Kouzelis et al. [78] investigated recently in our Department the composition of reaming products in correlation to reaming drill diameter; limited reaming, 1 mm less than the inner shaft diameter at the level of isthmus, provides better quality of viable bone graft and is less traumatic procedure for the inner cortex of medullary canal without any consequences to union achievement.

On the other hand, the use of static or dynamized locking in the progress of femoral fractures healing remains controversial. Investigations based on animal models have shown that although dynamization might have beneficial effect on the quality of early bone healing, static interlocking did not decrease the rate of bony union [79]. Similar results were reported by Takahashi et al. [80] in a random, prospective trial between static and dynamized (mean time after 3 months) femoral fractures as well as by Yokoyama et al. [59]. The authors concluded that although dynamization seems favorable to promote callus formation, static locking does not inhibit fracture healing. Moreover, it is important to remember that dynamization carries the risk of implant failure and significant shortening, as pointed by Wu [9].

Treatment Options for Femoral Nonunion

Conservative Therapy

Noninvasive strategies for femoral nonunion include ultrasound, ESWT and electromagnetic fields but their effectiveness is not well documented. Noninvasive strategies offer limited morbidity but a decreased chance of healing compared with surgical techniques. Additionally, cases of hardware failure and infection necessitate surgical intervention.

Low-intensity Ultrasound

Low-intensity ultrasound has demonstrated a positive effect on the bone healing process through high frequency, acoustic pressure waves that cause low-level micro-mechanical pressure on the bone tissue. Animal studies, using ultra-sound stimulation for bone healing, have shown increased callus tissue and acceleration of bone healing [81–82]. The stimulation mechanism of low-intensity ultrasound is thought to derive from electrical potentials (piezoelectricity) rather than its thermal effect [83]. Prospective, randomized, double-blinded and placebo-controlled studies in humans have demonstrated a 40% acceleration of time to clinical and radiologic healing in both fresh tibial diaphysis fractures [84] and distal radial metaphysis [85]. None such trial had been made especially for femoral nonunions; isolated cases of femoral nonunions treated with low-intensity ultrasound have been shown a 70–80% union rate with no serious side effects [86].

Extracorporeal Shock Wave Therapy

The effect of extracorporeal shock wave therapy on the bone is still poorly understood. The investigations by Delius et al. [87] revealed an indirect influence on the bone involving cavitation. The main theory describes an osteoinduction of osteogenesis by creating microfractures, with an impairment of fibroblasts and induction of angiogenesis and osteoblast formation with consecutive acceleration of bone healing [88, 89]. Birnbaum et al. [90] reported in 2002 a meta-analysis of ten publications analyzing the outcome of 635 patients with nonunions of different locations that underwent ESWT. Atrophic nonunions seem to have less predictable outcome in comparison with hypertrophic nonunions. Most investigations showed a consolidation of the nonunion during 3 months, so that in the case of treatment failure, operative treatment in the form of a re-osteosynthesis would only be delayed for this period of time. Again none report dealing especially with the use of ESWT in femoral nonunions has ever been published. Schaden et al. [91] reported successful outcome in 11/12 femoral nonunions among 115 patients with various types and locations of nonunions treated with ESWT. Rompe et al. [92] reported 66% union rate in 9 femoral nonunions and 80% consolidation of 15 nonunited femur osteotomies, whereas Wang et al. [93] in a prospective study of 72 nonunions of long bones (41 femurs) reported a healing rate of 40% at 3 months, 60.9% at 6 months, and 80% at 12 months. The success rate was 67.6% in patients with hypertrophic nonunions and only 27.3% in patients with atrophic nonunions. Furthermore, multicenter studies are necessary to define the indications and specifications of ESWT in the treatment of nonunions. A standardization of the dosage (energies and impulse rates) for the treatment of nonunions is indispensable prior to classifying ESWT as evidence-based medicine.

Pulsed Electromagnetic Fields

Clinical studies demonstrating the efficacy of pulsed electromagnetic fields (PEMF) have been conducted by Bassett et al. [94] for the treatment of 127 tibial diaphyseal delayed unions or nonunions; using PEMF for 10 h/day; a 87% healing rate was achieved in a mean time of 5.2 months. A multicenter, prospective, follow-up study conducted by Heckman et al. [95] showed a success rate of 64% in a series of 149 patients who received PEMF treatment. Several double-blinded, clinical studies on recalcitrant fracture repair have been reported [96, 97] but the efficacy of this method in femoral nonunions has not been exclusively investigated. The mechanism by which PEMF promote skeletal repair yet is not understood. It seems that PEMF stimulate chondrogenesis and subsequent endochondral ossification resulting to an increase of cartilage mass, providing a greater surface to serve as a scaffold for bone formation. Additionally, human nonunion cells in cultures respond to PEMF at signals similar to those used clinically in the treatment of persistent nonunions, resulting in changes in their morphologic features and an increase in TGF-β1 production [98]. Moreover, cells from atrophic nonunions responded to PEMF more slowly than did cells from hypertrophic nonunions [98]. All these results suggest that immature fibrous cells present at a nonunion might be influenced to undergo differentiation when PEMF stimulation is applied. More studies are needed to prove the enhancement of nonunion healing under PEMF stimulation in the future.

Surgical Treatment

Surgical intervention remains the primary treatment for femoral nonunion as was defined in 1982 by Watson-Jones [99]:

> In a number of cases, more than one operation may be needed before union is achieved; and in some cases there will be failure, ending in amputation. But one thing is certain, no established nonunion will unite with conservative treatment alone; all require operation and all will need some form of bone-grafting before union is achieved.

Although this definition is old and does not take under consideration the modern conservative treatment options for nonunion, it is still in value. The accepted standard therapy today for femoral nonunion includes some kind of surgical intervention, in the form of simple nail dynamization, exchange nailing (or nailing after plating or external fixation), exchange plate osteosynthesis after nail removal or plate augmentation with the nail in situ, Ilizarov augmentation and fibular allograft, or bone marrow transplantation with the possibility of additional autogenous or synthetic bone grafting in all these cases.

Nail Dynamization

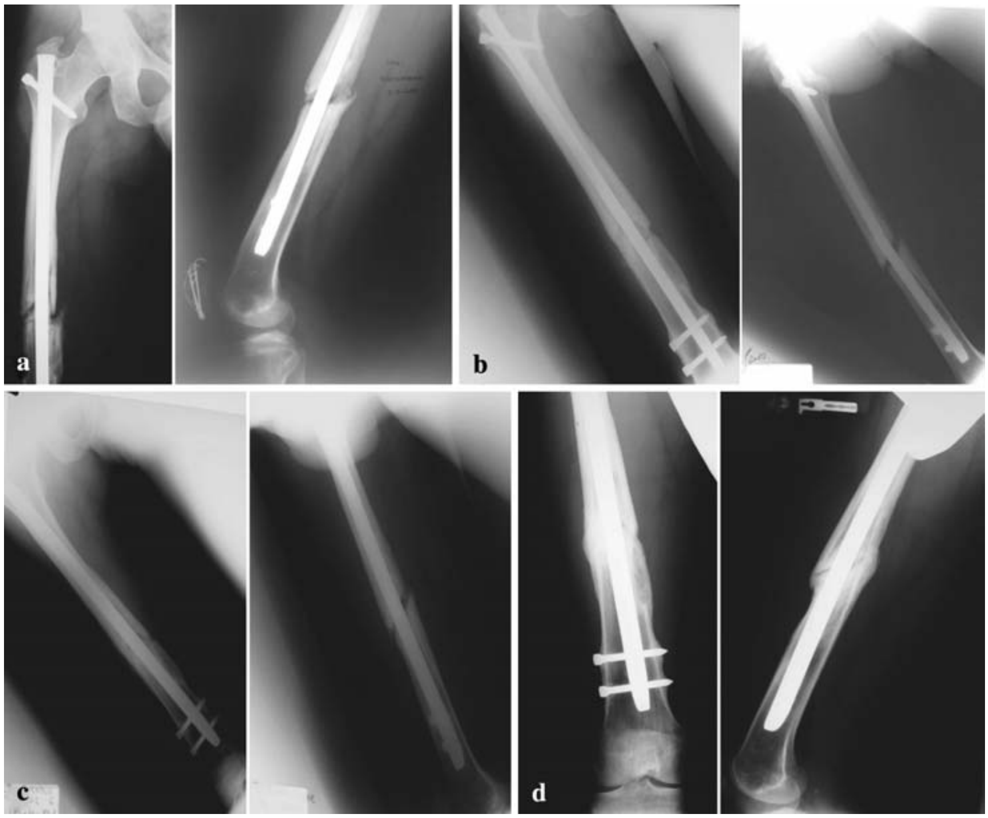
Dynamization of a static interlocking nail with or without the use of autogenous bone grafting offers a theoretically sound and minimally invasive treatment option. Patients suitable for this technique are those without unacceptable angulatory deformity or limb shortening. Its effectiveness in femoral nonunions is less predictable than in tibial nonunions, with low union rates reported, as well as a significant risk of femoral shortening, angulation, hardware failure, rotational deformity, and conversion of a hypertrophic to atrophic nonunion [39, 54, 100, 101]. Wu [9] reported a 58% union rate after dynamization, performed 6 months on average after the initial procedure. More than 2 cm of femoral shortening was noted in 21% of these patients. The author concluded that dynamization alone provides only a 50% chance of bone union and, if this eventually took place, it generally occurred about 5 months after the procedure. During this period the patient must be regularly followed for any evidence of femoral shortening. Basumallick & Bandopadhyay [102] in a prospective randomized comparative study found that although dynamization after open interlocking nailing significantly shortens the mean time to union, it does not significantly affect the union rate of femoral shaft fractures. Pihlajamäki et al. [39] dynamized 19/34 femoral nonunions using cancellous bone graft in two of them and achieved a solid union in 13 cases. They considered this method in selected cases with primary static interlocking nailing, in which distraction at the fracture site was the main problem. In conclusion, dynamization should be reserved for axially stable fractures without significant angular deformity, particularly if statically locked has been applied to distraction.

Exchange Nailing

Exchange nailing appears to be an effective treatment for aseptic nonunion of long bones following a primary nailing procedure; improving the mechanical stability by exchanging to a somewhat larger nail should allow weight bearing and loading of the fracture and this should stimulate healing [103]. Reaming also causes a marked increase in periosteal blood flow, which should stimulate the formation of periosteal new bone [104]. Finally, the reaming products are osteoinductive, especially when limited reaming is applied [78]. After primary nailing, these products are extruded through the fracture site, but at exchange nailing the fibrous tissue will tend to confine the reaming products to the medullary canal [103]. Probably, the increase in periosteal blood supply following reaming is the most important stimulus to healing of the nonunion [74, 75, 104].

Actually, when a patient presents with a femoral shaft nonunion, he often asks "will the fracture be healed the second time?" Having been told initially that acute femoral fractures almost always heal after intramedullary nailing, he is concerned that a repetition of the same operation might not lead to healing. The question for the surgeon becomes whether to perform bone grafting at the time of exchange nailing. Since some controversy exists regarding the effectiveness of closed exchange nailing, the surgeon must weight the potential risks of graft harvesting and incision at the nonunion site versus the potential need for further procedures. With the current expansion of graft alternatives and percutaneous delivery systems, the morbidity of adjunctive grafting is decreasing.

Several authors recommend removal of the present intramedullary nail, reaming of the intramedullary canal, and insertion of a larger diameter nail (Figure 1). Webb et al. [3] reported on 44 femoral nonunions treated with closed, reamed noninterlocking intramedullary nailing. The union rate was 96% after one operation and 100% after additional procedures. Furlong et al. [17] achieved 96% (24/25) union rate also after a single procedure in a mean period of 29.75 weeks. He noted earlier but not statistical important union in patients who received additional bone grafting. Wu & Chen [105] treated 36 femoral nonunions characterized from less than 1 cm shortening, no bony defect and a simple radiolucent line on plain radiographs. The union rate was 91.6% after an average period of 4 months. Hak et al. [45] reported 78.3% union rate in 23 patients after exchange nailing. The five nonunions that not healed were of atrophic type in smoking patients. Finkemeier & Chapman [13] reported 39 patients who had a 74% union rate after closed intramedullary nailing for femoral nonunion; 97% healed after two or more procedures. Pihlajamäki et al. [39] performed exchange nailing in 11/34 patients



Figures 1a to 1d. a) Atrophic nonunion after intramedullary nailing of a midshaft fracture of the femur (6 months postoperative). b) No signs of healing and nail breakage 20 months postoperative. c) Exchange nailing (1 month postoperative). d) Solid union with excellent functional outcome 3 years postoperative.

with femoral nonunion (in three autogenous bone grafting was used) with excellent results (90% union rate). Only one patient underwent repeat exchange nailing and secondary dynamization that led finally to union. Despite the need of further operations in all these series, the final outcome was very good indicating that exchange nailing remains the procedure of choice for femoral nonunion after intramedullary nailing. In contrast, Weresh et al. [19] found that only 53% (10/19) femoral nonunions healed with reamed exchange intramedullary nailing. Additional procedures were required in 47% of their patients. The eight of nine nonunited patients underwent more than two additional operations to achieve union. The author concluded that one of the reasons of failure might be the expanded indications of intramedullary nailing, which include nowadays high energy fractures with increased comminution and application closer to the proximal and distal ends of the femur. Similar fair results were recently reported by Banaszkiewicz et al. [18]; the union rate of 19 aseptic nonunions was only 58% after exchange nailing in a mean period of 9 months. The nonunion did not heal in five patients, two developed septic nonunion and one patient required dynamization of the exchanged nail. Although healing was eventually achieved in 18 nonunions (95%), 11 of the patients underwent some kind of surgery, including 4 repeated exchange nailings. The authors state that exchange intramedullary nailing in the treatment of femoral nonunion needs to be re-evaluated.

The surgical technique for exchange nailing in the case of a well aligned femur, with none/or minimal bone loss and radiographic presence of callus, includes the removal of the present nail and screws, followed by antegrade reaming without opening of nonunion site (Figure 2). The ''autograft'' effect of reaming is likely to be less important by some authors [17] as the still intact fibrous nonunion will prevent access of the graft to the periosteal area and allows only a minor degree of endosteal autografting. Care has to be taken in the exchange nailing technique not to produce overthermal effect with excessive reaming, which can lead to intramedullary osteomyelitis. An attempt is made to insert a nail that is 2–3 mm larger than the preexisting

Figures 2a to 2d. a) A 28-year-old patient who was referred to our hospital 7 weeks after a poorly placed intramedullary nail. b) No signs of healing and screw breakage 13 weeks postoperatively. c) Good progress of healing 6 months postoperatively after exchange nailing. d) Solid union 1 year after the second operation.

nail [13, 18, 105]. The femur is reamed 1 mm larger than the diameter of the nail to be used. A sample of the reaming products should always be cultured. If the femur has a deformity that is not reduced by closed means, or bone loss is seen on preoperative radiographs, the nonunion site is opened through a standard lateral approach to the femur and any existing hardware is removed. Soft tissue stripping is minimized to preserve the blood supply to the bone. If necessary, deformities are corrected by osteotomizing the femur through the nonunion. Fibrous tissue is debrided from the nonunion site, the medullary canal is reopened and iliac crest autograft is usually used with or without additional graft substitutes such as demineralized bone matrix (DBM) or bone morphogenic proteins (BMP). In cases where previous large diameter nail placement precludes a significant increase in the exchange nail size, a more aggressive graft placement is performed, including petaling of the cortex both anterior and laterally. The femur then is nailed as described above.

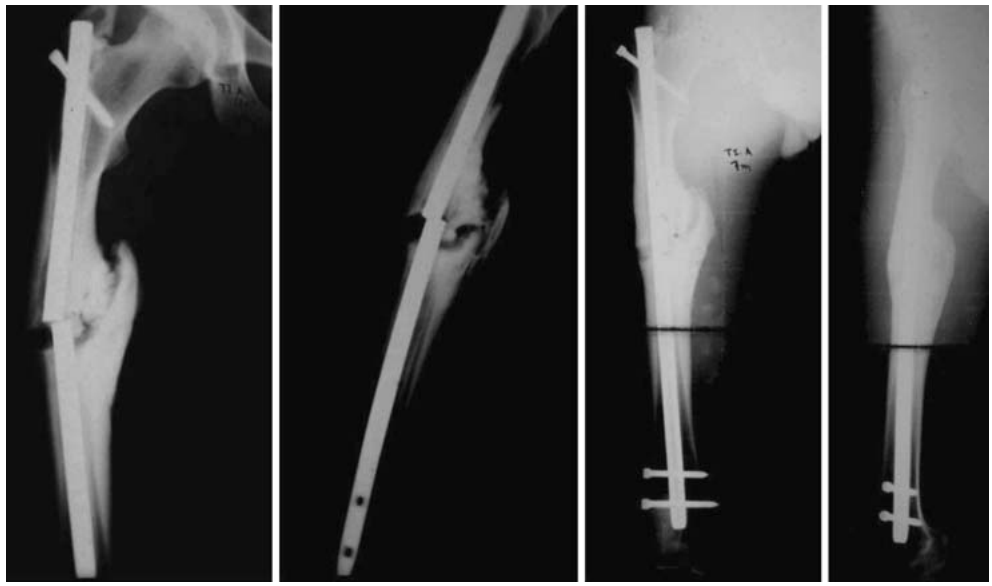


Figure 3. Hypertrophic nonunion and nail breakage 6 months postoperative. Exchange reamed nailing with static interlocking led to solid union 7 months postoperatively. The nail was removed with the open technique.

Several authors recommend checking for residual motion at the nonunion site when the open technique is used. If there is any visible motion, a small fragment 4- to 6-hole plate [13] or one or two stables [105] are applied in compression to the posterolateral side of the femur to eliminate any existing motion.

In cases of broken nails, a closed or an open extraction technique can be used (Figure 3). Clinically, the reported incidence of nail failure is between 1.7% and 5.6% [106]. Despite the fact that an intramedullary nail may be broken after fracture union [107], it often fails before the fracture has healed. Therefore, if further treatment does not proceed, instability will prevent union at the fracture site. The closed technique requires an image intensifier and specially designed hook extractors to fit different types of locked nails. If the closed technique fails, an open technique is required [108, 109]. Plating and grafting can also be used to salvage a broken femoral nail, [110] allowing the surgeon to avoid a technically difficult and often complicated nail extraction.

Intramedullary Nailing After Plating

A wide range of complications can be expected when plates are used to treat femoral shaft fractures, and the reported nonunion rate is between 8% and 19% [111, 112]. Factors favoring fracture healing are small gap, adequate stability, and sufficient nutrition supply. Additionally, extensive soft-tissue dissection to reduce bony fragments and a large open wound to insert a plate of sufficient length will seriously impair local vascularity. Additionally, loss of medial cortical abutment in a comminuted fracture will greatly reduce the fixation stability of plates. However, once a plate has been inserted and a nonunion occurs, the most reasonable choice is conversion to an intramedullary nail. Wu et al. [44] reported 100% healing in 21 patients with femoral nonunions after plating. Via the lateral approach, the lesion site is exposed as gently as possible and the inserted plate is removed first. This requires exploration of the local site initially, which would again impair the local vascularity. Therefore, gentle dissection and keeping the wound as small as possible are imperative. To maintain local stability, the nonunion site requires no debridement. The use of rigid guide wires with sharp ends could facilitate the opening of the obliterated marrow cavity if sclerosing bone blocks the insertion of the flexible guide wire. After the local wound is closed with or without drain insertion, the marrow cavity is reamed as widely as possible and the intramedullary nail is inserted. When broken screws are present, a lateral window may be required for screw removal and subsequent nail placement [113].

Plate Fixation and Plate Augmentation After Intramedullary Nailing

In contrast to intramedullary nailing, late plate fixation for femoral nonunions has received little attention in the recent literature. Several subsequent reports, however, have described a prohibitively high complication rate, including infection, high intraoperative blood loss, and higher nonunion rates than with exchange nailing [100, 114, 115].

Cove et al. [11] has recently described the effectiveness of plate fixation in a heterogeneous population that included infected and noninfected femoral nonunions after various forms of acute fracture treatment. Union was achieved in 33/44 femoral nonunions (13 infected) after a single procedure. Another eight nonunions healed after additional procedures. The authors also cited the advantages of plating techniques over nailing: (a) in cases in which intercalary defects exceed 5 cm, wherein an extensive volume of cancellous autograft is required, they found plating (often in a wave configuration) to permit the placement of a larger volume of graft, and can easily be combined with a vascularized fibula transfer when the latter is part of the reconstruction, (b) in septic cases, except for the theoretical concern about spreading infection with the use of an intramedullary implant, the need of extensive debridement obviates, according to the authors, the value of a closed nailing technique and potentially requires a second approach for nail placement, and (c) in misaligned cases, plating allowed simultaneous correction of the malalignment and creation of a mechanically favorable tension band construct.

Bellabarba et al. [20] followed 23 patients with nonunion after intramedullary nailing. Using indirect plating techniques (with the DCP or the AO 95° condylar blade plate) and selective autologous cancellous bone grafting the authors reported 91% union rate (21/23) without further intervention at an average of 12 weeks. The two other patients who suffered from early hardware failure were healed after repeating plating. Double plating was used in one of these failed cases. The authors concluded that this method is particularly valuable in the presence of deformity.

An additional use of plate fixation has been recently described by Johnson & Urist [116]. A composite inductive allograft consisting of an allogenic, autolysed, antigen-free cortical bone carrier, lyophilized with partially purified human bone morphogenetic protein, was implanted in 30 consecutive femoral reconstructions for nonunions, 24 of them with significant shortening. Lengthening defects greater than 2 cm were supplemented with intercalary autogenic bone graft. Twenty-four femurs healed at an average of 6 months. The use of growth factors to achieve fracture union may gain popularity, as their clinical effectiveness becomes more clearly understood.

Ring et al. [12] reported 42 complex nonunions of the femoral shaft treated by wave-plate osteosynthesis at five different medical centers. Eight of these nonunions were after intramedullary nailing. Union was achieved in 41 patients after 6 months on average, although three patients required a second bone grafting application. The wave-plate osteosynthesis which first suggested by Blatter et al. [117] has a contour bent into its midportion so that it stands away from the bone at the abnormal area. It is claimed to have both biological and mechanical advantages. Its use preserves the local blood supply by reducing the need for operative dissection and the area of plate–bone contact and also allows autogenous bone grafts on the lateral cortex to share the axial compressive loads with the plate more effectively. In general, in the presence of medial or segmental bony defects, a conventional plate is subjected to a local concentration of bending forces, which may induce failure; the contouring of a plate into a waveform enhances its mechanical role. The bends in the plate could have an adverse effect by increasing the moment arm, but an intact or reconstituted lateral cortex will support the compressive forces on the femur and allow the plate to function as a lateral tension band [118].

Matelic et al. [119] treated seven patients with persistent femoral nonunions using a standard lateral plate in combination with an endosteal plate and primary iliac crest bone grafting. The patients had undergone one to eight (mean 3.9) previous surgical attempts to achieve union. All fractures had healed with an average time to union of 19.2 weeks. The technique of endosteal plating is technically demanding and lasts up to 6 h and is performed only in selected cases.

Finally, Ueng et al. [120] reported 100% union in 17 cases of femoral diaphysis nonunion, which have been treated initially with intramedullary nailing using augmentative plate fixation without nail removal. Additional bone grafting was used in seven patients. The technique of augmentative plate fixation includes exposure of the fracture site, subperiosteal decortication of the fracture ends and application of a dynamic compression plate to the lateral surface of the femur with at least two screws (obtaining four cortices) above and below the fracture. In the hypertrophic type of nonunion, the bone was flattened with osteotomes to receive the plate. Because of the intramedullary nail presence, screws had to be placed either in an anteromedial or a posteromedial direction and usually this could be accomplished without too much difficulty according to the authors. They also recommend avoiding removal of the dense fibrous tissue from the nonunion site.

Intramedullary Nailing After External Fixation

Limited data have been published regarding the use of external fixation for femur fractures. In adults, external

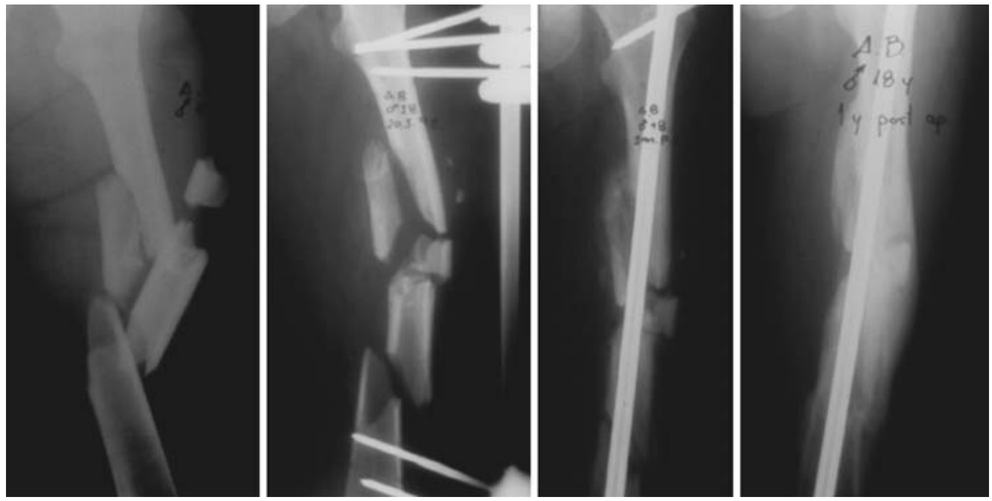


Figure 4. Segmental open (grade II) femoral fracture in a poli-trauma patient who had been stabilized initially with external fixation. Early conversion to static intramedullary nailing (30 days later) led to solid union 1 year postoperatively.

fixation has been shown to have a high rate of complications; nonunion and deep pin track infection approach 20% whereas knee stiffness should be expected in approximately 45% of the patients [121–124]. However, in these series external fixation was used only for complex and/or open femoral shaft fractures. Several authors propose planned early conversion from external fixation to intramedullary nailing for multiply injured patients that are too critically ill to tolerate the surgical stress involved with an intramedullary nailing procedure [125, 126] (Figure 4). Nowotarski et al. [127] reported on 54 multiple injured patients with 59 femoral diaphyseal fractures and achieved a 97% union rate with this procedure within 6 months. The infection rate was only 1.7%. A one-stage conversion from external fixation to intramedullary nailing, after debridement of soft tissue pin tracks and curettage of the bone holes, was applied to 55 fractures; the other 4 fractures were associated with draining pin sites and skeletal traction to allow pin-site healing was used for an average of 10 days before the nailing procedure. External fixation as a ''temporizing device'' to achieve fracture stability during early resuscitation in multiple injured patients with femur fractures was also used by Scalea et al. [128]. Secondary intramedullary nailing was applied in 35 patients initially treated with external fixation; the average time to conversion was 4.8 days. One patient had a hardware failure and another one developed acute osteomyelitis.

Our conversion protocol from external femoral fixation to intramedullary nailing includes removal of the fixation device, culture samples from the pin tracks, and temporary stabilization of the extremity with casting or skeletal traction. If the cultures are negative an intramedullary nailing procedure is followed after 1–2 weeks. If the cultures are positive the procedure is delayed for 4–6 weeks and the patient receives the appropriate antibiotic therapy.

Augmentative Ilizarov Techniques Over Nailing

Treatment options are limited for patients with femoral nonunions who had failed one or more previous exchange nailings or other interventions. Menon et al. [129] used compression with external fixation over an intramedullary nail to successfully treat two patients with nonunions of the femur, three patients with nonunions of the tibia, and four patients with nonunions of the humerus. Three of the nonunions (one femur, one tibia, one humerus) had failed exchange nailing before undergoing the external fixation technique. All patients reported decreased pain and improved function at an average follow-up of 19 months.

Recently, Brinker & Connor [21] reported five patients with femoral nonunions that had undergone an average of five (2–8) previous operations, including a mean of two repeated exchange nailings. All nonunions healed without a need for further surgery. The external fixator was removed at an average of 133 days, followed by static locking of the intramedullary nail.

Other Treatment Options for Femoral Nonunion

Significant nonunited femoral defects can also be treated with vascularized fibular grafting. Reported results vary with 75–85% healing rates [11, 23, 130]. Complications include donor site morbidity, graft fracture, and nonunion of the graft-host junction. Patients are non-weight bearing for an extended period, which can be a significant functional problem, particularly following a protracted period of prior failed treatment. However, these patients are often facing above-knee amputation and vascularized-fibular grafting offers a proven alternative.

Percutaneous autologous bone marrow transplantation has been reported by Matsuda et al. [22] to result in 80% healing in a series of seven femoral nonunions following intramedullary fixation. However, the majority of the series were hypertrophic nonunions. Healing was not achieved in atrophic or infected nonunions.

Personal Experience

During the last decade, 38 patients (25 males; 13 females; aging 21–69 years) with aseptic nonunion of the femoral diaphysis were managed in our Department, using the Grosse–Kempf nail. Initial operation was external fixation in 13 patients, internal fixation with plates and screws in 12 and intramedullary nailing in 13. Closed intramedullary nailing was applied to 25 patients and open intramedullary nailing to 13 (12 because of hard material removal) within a period of 8th to 36th months after the initial procedure. All nails were placed after reaming 1 mm over the selected nail diameter and there were 17 distally locked, 9 proximally locked, 9 statically locked and 3 unlocked (fracture at the isthmus). Additional cancellous bone grafting was applied to six patients. Dynamization was performed at 6 weeks in three patients. Partial weight bearing was allowed to all patients as earlier as possible followed by full weight bearing at 4–6 weeks postoperatively. Follow-up period ranged from 12 months to 9 years. All fractures were eventually united in an average period of 4–8 months. Repeated exchange nailings were necessary in six patients (two procedures in five patients and three procedures in one patient). Breakage of the screws was noted in three patients but it was uneventful, resulting to faster union. Shortening up to 0.5–4.0 cm was measured in four patients, > 10° varus malunion in two and none case with marked malrotation. Deep infection occurred in one case; further reaming and insertion of a larger diameter nail with continuous irrigation lead to nonunion healing. Functional recovery of the patients was excellent despite the prolonged time of rehabilitation.

Conclusion

Failure of femoral shaft fixation covers a spectrum of biologic, mechanical, and technical problems. A careful diagnostic approach is required in all cases, no matter how clear the diagnosis may appear on X-ray examination. A high index of suspicion for infection must be maintained to avoid inadvertent placement of hardware and bone graft into an infected environment. Reamed static or dynamic femoral nailing with or without bone grafting can resolve the majority of aseptic nonunions. The treating surgeon must be able to handle the possibility that even such a tried and true treatment may fail and that alternative methods may be required. Familiarity with biologic plating, bridging external fixation, distraction osteogenesis, vascularized fibular transposition, and a variety of grafting techniques improves the possibility that failed femoral fixation can be salvaged.

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