Approach to Femoral Shaft Nonunions: Diagnosis and Management

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VIDEO 1

ABSTRACT

Despite the high union rate of femoral shaft fractures treated with intramedullary nailing (90% to 100%), the annual incidence of femoral shaft nonunion ranges from 2% to 6%. Although less common than tibial nonunions, femoral shaft nonunions remain a clinical problem in orthopaedic surgery. Proper treatment begins with appropriate diagnosis, workup, and identification of risk factors followed by a multidisciplinary approach to treatment. This article provides current evidence-based guidance for providers on the diagnosis and management of femoral shaft nonunions.

Diagnosis

Definition

To date, there is no unified definition of a nonunion other than what has been stated by the US Food and Drug Administration, which states that a nonunion is a fracture that has not healed by 9 months and shows no progressive radiographic healing for 3 months.[1,2] In general, it is agreed on that a nonunion is a fracture that has minimal potential to heal without additional intervention. Healing should be based on radiographic findings, such as bridging callus and disappearance of fracture lucency, and clinical findings, such as decreasing fracture pain and increasing function. Understanding the desired mode of healing is necessary to assess healing potential. Most often femoral shaft fractures are treated with an intramedullary nail and thus expected to undergo secondary healing with callus formation and visible fracture lines for a longer period of time, but if treated with a goal of primary healing, one should not anticipate bridging callus formation.

History

A thorough medical and surgical history is essential in the diagnosis of femoral shaft nonunions. This can identify both patient-specific and injury-specific risk factors of nonunion (Supplementary Table 1, http://links.lww.com/JAAOS/B354). A full understanding of the original injury and subsequent management may further elucidate risk factors. A thorough social history should be performed to understand quality of life, ambulatory status, activity level, and treatment goals to allow for shared decision making in the treatment plan.

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Clinical Examination

Clinical examination is a critical component of a nonunion diagnosis, especially when imaging is equivocal. A thorough clinical examination should include assessment of gait and asymmetry which may be secondary to malalignment, leg length discrepancy, and/or pain. Prolonged use of an ambulatory assistive device or pain medications may raise suspicion for symptomatic nonunion. Gross fracture mobility may indicate the fracture is not yet clinically healed, but this finding may only be evident in long bones treated nonsurgically compared with a femoral shaft treated with an intramedullary implant or plate as it is unlikely to show evidence of motion at the fracture site unless the implant has catastrophically failed. Any pain to palpation of the fracture site may raise suspicion for nonunion, but unlike the tibia which is more superficial in nature, this may be harder to elicit in the femur. Patients may describe referred pain patterns including groin and knee pain.

Assessment of soft tissues should be performed to identify wound breakdown, sinus tracts, drainage, or surrounding erythema that may raise suspicion for an infected nonunion. A thorough neurovascular examination may help to identify undiagnosed vascular disease and poor healing potential. This should include assessment for neuropathy, skin integrity, hair distribution, and pulses. Neuropathy may affect wound healing potential and ability to assess pain associated with nonunion. If there is concern for vascular dysfunction, ankle-brachial indices or transcutaneous peripheral oxygen levels can be obtained. Identification of vascular dysfunction that may be amenable to vascular intervention and improve healing potential should be performed before proceeding with nonunion repair.

Imaging

Despite recent advances in advanced imaging techniques, orthogonal radiographs remain the benchmark for the diagnosis of nonunions when combined with history and examination. When analyzing serial orthogonal radiographs, it is often subjective to determine whether there has been interval healing. To date, the most validated and reliable scoring system to identify radiographic nonunion is the modified Radiographic Union Scale for Tibia score. Graf et al[3] identified a sensitivity and specificity of 94% and 92%, respectively, using the modified Radiographic Union Scale for Tibia score on femoral radiographs. Furthermore, close assessment for implant failure is essential because implant failure is a common indicator of nonunion as the implant has "lost the race" between bone healing and implant failure (Figure 1).

In cases where serial radiographs are equivocal, the next best step is to obtain a CT scan of the affected femur. CT has shown greater sensitivity (100%) but poor specificity (62%) compared with serial radiographs.[4] CT has not shown to have better interobserver reliability than conventional radiographs.[5] There is no current consensus on a recommendation for CT scanning to diagnose nonunion, but the authors recommend CT to confirm nonunion when serial radiographs are equivocal.

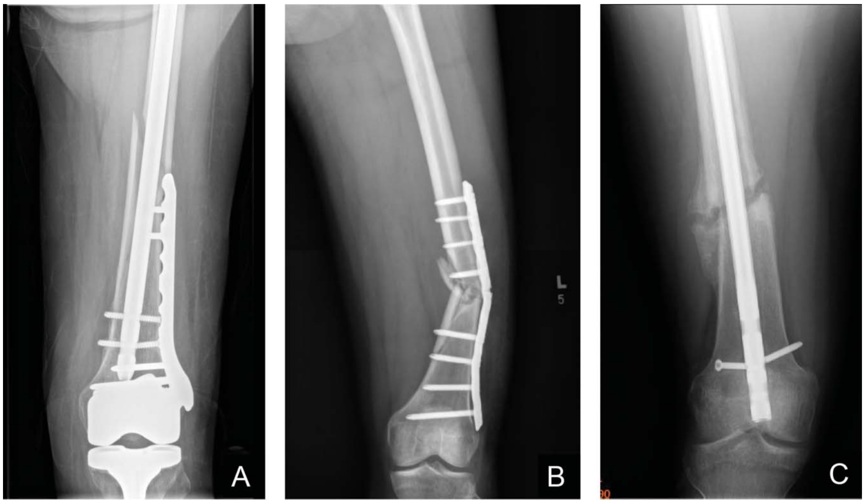
MRI has limited utility in nonunion workup. MRI has not been shown to predict nonunion but is more useful when assessing the extent of infected nonunions though artifact scatter from implants may obscure the interpretation of the imaging.[6] Along these lines, nuclear imaging including positron emission tomography (PET) and tagged white blood cell (WBC) scans can help diagnose infected nonunions when other imaging is equivocal.[7] These scans may help determine the extent of infection, but in general this should be an intraoperative decision based on bone viability (punctate bleeding) to determine how much bone should be removed during resection. Even if the bone of concern is infected, if it has adequate blood supply then it has the potential for infection eradication through local and systemic antibiotics. These scans come at a higher cost and often limited availability and efficacy.

Classification

The original classification of nonunions was described by Weber and Oldrich.[8] Nonunions are either viable or nonviable. Viable nonunions are vascular and are based on the amount of radiographic callus: hypertrophic (robust callus) and oligotrophic (poor callus). Hypertrophic nonunions have adequate biology but lack mechanical stability, whereas oligotrophic nonunions have inadequate biology as well as mechanical instability. Nonviable nonunions often lack adequate biology with or without mechanical instability. These nonunions can be aseptic or septic. Correctly classifying a femoral shaft nonunion is critical to appropriate management (Figure 2).

Hypertrophic nonunions have robust callus formation secondary to continued motion from mechanical instability, but the strain is too great to generate adequate bridging callus. Oligotrophic nonunions produce less callus because of inadequate biology and lack

Figure 1



Radiographs showing femoral shaft nonunion resulting in implant failure which may be less obvious (**A**) or more obvious (**B**). Femoral shaft nonunion that underwent auto-dynamization of a retrograde nail to promote osseous union (**C**).

bridging bone because of mechanical instability. Atrophic aseptic nonunions lack biology to heal and often show evidence of resorption or sclerosis at the fracture ends. Septic nonunions lack biology because of underlying infection but may or may not show evidence of callus formation.

Workup

After identifying and classifying the nonunion, understanding the cause of the nonunion will allow for optimal treatment (Video 1).

Mechanical Instability

Mechanical instability is important in all nonunion types. Instability can be secondary to inadequate or improper implants, fracture gapping, malalignment, or delayed union where the implant "lost the race" (Figure 1).

The most common implant choice for femoral shaft fractures is an intramedullary nail. Unlike nonunion data for the tibial shaft, healing rates for femoral shaft fractures are markedly improved with intramedullary reaming.[1] There is controversial evidence regarding nail diameter and risk of nonunion. Millar et al found that a nail diameter to canal ratio less than 70% is predictive of hypertrophic nonunion (OR 11.4, $P < 0.001$), whereas Serrano et al found no difference in union rate based on nail fit and recommended a 10-mm nail for treatment of femoral shaft fractures.[9,10] The presence of residual fracture gap of greater than 3 mm (averaged on AP and lateral radiographs) or total of 6 mm (AP + lateral radiographs) has been shown to lead to mechanical instability and thus higher risk of nonunion.[11] Fracture malreduction leading to mechanical axis malalignment increases mechanical instability and risk of nonunion. Full length hip-to-ankle standing films may be beneficial to assess for any malalignment that may contribute to mechanical instability. When performed, these images should be obtained with a balanced pelvis and with patellas facing forward to provide the most accurate assessment of alignment.

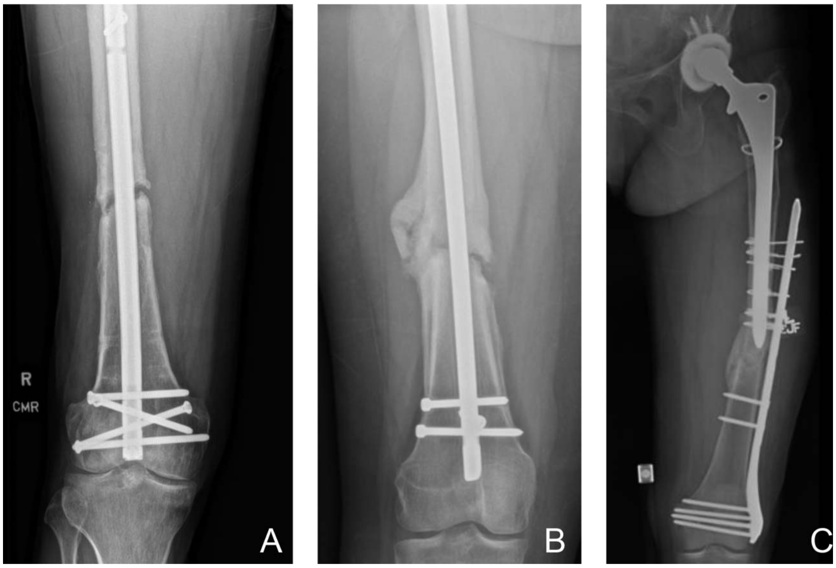
Femoral shafts with ipsilateral concomitant femoral neck fractures are thought to be at higher risk for nonunion because of the high-energy mechanism with likely greater disruption of biology and the segmental nature of the injury and thus an increased risk of instability. The topic of single versus dual implant construct for combined femoral neck and shaft injuries remains controversial with no current evidence suggesting a higher nonunion rate in one construct over the other.

Biology

In atrophic nonunions, poor biology is the primary cause of nonunion. Poor biology can be secondary to the injury itself causing notable soft tissue damage and periosteal stripping. Open fractures are at markedly higher risk of femoral nonunion (OR 1.8).[12] Fractures that require open reduction are at risk of disruption of biology, but with proper soft tissue handling biology can be preserved.

Certain patient-specific modifiable and nonmodifiable risk factors may contribute to poor biology and poor healing potential. These include diabetes (OR 2.73), tobacco use (OR 2.32), obesity (OR 1.90), age > 60 years (OR 2.60), nonsteroidal anti-inflammatory

Figure 2



Radiographs showing examples of a nonviable atrophic nonunion (**A**), viable nonunion with poor callus (oligotrophic) (**B**) and a viable vascular nonunion with robust callus (hypertrophic) (**C**).

drug use (OR 1.84), and male sex (OR 1.26).[13,14] Nonsteroidal anti-inflammatory drugs have shown to contribute to nonunion in retrospective studies but are routinely used to reduce opiate usage. Metabolic and endocrine abnormalities including vitamin D, calcium, thyroid hormone, parathyroid hormone, magnesium, phosphorus, alkaline phosphatase, and testosterone have shown to be associated with nonunion. The following laboratory panel can be considered in nonunion workup: thyroid stimulating hormone (TSH), parathyroid hormone (PTH), vitamin D, albumin/prealbumin, hemoglobin A1c (for diabetics), and testosterone (for men).[15] Metabolic abnormalities should be identified and corrected in parallel with nonunion repair, but in some cases medical treatment alone may lead to union. Brinker et al[15] evaluated 31 patients with nonunion and newly diagnosed metabolic and endocrine abnormalities. Twenty-five percent of patients went on to union with medical treatment alone at an average of 7.6 months from their initial visit with an endocrinologist. Most these patients had vitamin D deficiency and were treated with calcium 500 mg with vitamin D 800 international units (IU) three times a day. Furthermore, providing resources for tobacco-cessation programs is recommended to help improve nonunion repair outcomes. The decision to proceed with nonunion repair based on preoperative nicotine levels should be part of the patient-centered decision-making process. This emphasizes the importance of multidisciplinary care in nonunion patients.

Infection

Infection should be considered a potential cause in any nonunion. Most often, infected nonunions are atrophic in nature, but this is not mutually exclusive.[16] Workup for nonunion should be performed preoperatively, intraoperatively, and postoperatively. Preoperatively, it is recommended to obtain inflammatory laboratory test results including complete blood count (CBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), although sensitivity and specificity of these laboratory tests are poor with a WBC positive predictive value (PPV) of 0.20, ESR PPV of 0.23 and CRP PPV of 0.27.[17] Advanced imaging including MRI, PET, and tagged WBC scans can help assess for infected nonunions when imaging and clinical examination is equivocal.

Management

Nonsurgical Management

Nonsurgical management of femoral shaft nonunions includes electrical stimulation, extracorporeal shock wave therapy, and low-intensity pulsed ultrasonography. In general, evidence supporting the reliable success of these modalities is lacking, but poor surgical candidates may benefit from these options.[18]

Septic Nonunions

Septic nonunions are commonly treated with a two-staged approach including removal of implants, deep tissue cultures, and antibiotic spacer/nail placement for 6 weeks of antibiotic treatment followed by definitive nonunion repair. At minimum, a two-stage approach is recommended for patients with soft-tissue compromise (draining sinus, wound dehiscence, wound breakdown) and/or purulence at the nonunion site. Patients with elevated inflammatory laboratory test results but no soft tissue compromise and no purulence at the nonunion site may have success with a single-stage procedure. Hackl et al[19] retrospectively reviewed 58 patients who underwent single-stage diaphyseal femoral nonunion repair without clinical signs of infection, of which 25 (43%) were found to have positive occult infection. Although all patients went on to osseous union, patients with occult infection were found to require more revision surgeries to achieve union and had poorer clinical outcomes.

The two-stage approach should consist of preoperative inflammatory laboratory test results for diagnosis and trending purposes. Implants should be removed in their entirety, when feasible. A soft-tissue friendly approach to the nonunion site should be performed followed by thorough débridement including débridement of the medullary canal. The sinus tract, if present, should be thoroughly excised. Bone should be assessed for viability via irritation of the bone ends with a burr, curet, rongeur, etc. In general, bleeding bone has the potential to clear local infection, whereas necrotic avascular bone does not. At least five deep tissue cultures should be obtained from different areas of the nonunion with separate clean instruments to avoid contamination. Recent studies suggest obtaining at least five deep tissue cultures to decrease the risk of missing clinically relevant microorganisms and optimizing postoperative antibiotic coverage.[20] Cultures should be sent for aerobic, anaerobic, fungal, and mycobacterial investigation and incubated for at least 14 days to capture any slow-growing organisms. Implant sonication may be a helpful adjunct especially in indolent low-grade infections but should not replace standard tissue cultures. Furthermore, cultures should be sent from tissue obtained from intramedullary reamings because it has been found to grow different bacteria in 15% of cultures compared with cultures obtained from the débridement site.[21]

Once débridement is complete, there are multiple options for temporary stabilization. Infection thrives on instability; therefore, improving stability even for temporary stabilization will increase success of clearing the infection.[22] Most commonly, an antibiotic intramedullary implant is used. An antibiotic-coated interlocking intramedullary nail is advantageous because it provides notable stability and weight-bearing with success rates up to 85% when used as definitive treatment, but comes with the risk of possible cement delamination if nail removal is desired.[23] To decrease the risk of cement delamination, it is recommended to over-ream the canal by at least 2 mm greater than the diameter of the antibiotic coated nail and to use Simplex with tobramycin cement because of its mechanical properties.[24] As an alternative, an Ilizarov threaded rod can be manufactured into an antibiotic nail with a decreased risk of cement delamination but comes with decreased mechanical stability and load-bearing. Examples of antibiotic coated nails are depicted in Figure 3. Other options include femur spanning external fixation or plate fixation which is less desirable in the femur. In cases where a bone defect is present following débridement, bone grafting after creation of a pseudomembrane (ie, the Masquelet technique) over an intramedullary nail has been found to be superior to Masquelet with a plate or Masquelet alone.[25] In contrast to the tibia, massive bone defects in the femur can be successful with Masquelet but are often limited by bone graft availability. Successful union starts to wane with larger defects when using the Masquelet technique, whereas bone transport has demonstrated more reliable union rates in more massive defects.[26]

After the initial stage, patients should be placed on systemic antibiotics. The benchmark after infected nonunions was a 6-week course of IV antibiotics which require a peripherally inserted central catheter (PICC) line and home health care; although, recent data suggest that IV inpatient antibiotics followed by an oral antibiotic 6-week course is noninferior.[27] After an adequate course of antibiotics, patients then return to the operating room for removal of temporary implants (when necessary) and placement of definitive fixation and/or grafting.

Aseptic Nonunions

Hypertrophic Nonunions

Hypertrophic nonunions require an increase in mechanical stability and do not generally require increased biology. There is minimal literature supporting the standardized use of additional autograft or graft substitutes, other than that from intramedullary reaming. Mechanical stability can be improved in a multitude of ways. Procedures with improved success rates come with increased surgical complexity. Having a thorough discussion with the patient in terms of surgical success and surgical complexity is important.

Figure 3

Radiographs showing fabricated temporary antibiotic nail using threaded Ilizarov rod for septic nonunion (**A** and **B**). Fabricated definitive antibiotic nail using standard interlocking nail for septic nonunion (**C** and **D**).

Nail dynamization includes converting a construct from being static to dynamic, which is often performed by removing a static interlocking screw proximal or distal to the fracture site. Nail dynamization has shown a 58% success rate in the femoral shaft but allows for a minimally invasive, outpatient procedure.[28] Nail dynamization should be reserved for hypertrophic nonunions with length stable fractures (transverse, noncomminuted, fracture gap <5 mm). This is less often used in atrophic and oligotrophic nonunions because of the need to increase biology at the nonunion site. Closed exchange nailing has shown a success rate ranging from 72% to 100% in the femoral shaft allowing for increased periosteal blood flow through the reaming process.[15] It is recommended to ream at least 2 mm greater than the previously reamed diameter and placement of a nail 1-4 mm greater in diameter. This concept is important to keep in mind at the index procedure, as the largest standard nail diameter is 15 mm. If concerned about bone stock for interlocking options, one can use different interlocking screw orientations, different implant type to allow for different interlocking options, can switch from antegrade to retrograde nail or vice-versa, or can use newer interlocking screws which lock into the implant themselves for increased angular stability when bone quality is poor. Plate augmentation at the nonunion site allows for further increase in mechanical stability allowing for a notable amount of localized compression as the expense of additional surgical exposure. Plates can be used to provide additional local compression using a compression plate or can be contoured into a wave plate to trap local bone graft from reaming if needed. Current literature suggests higher union rates with compression plate augmentation versus exchange nailing, but these data are not specific to hypertrophic nonunions.[29] Continuous compression in the treatment of nonunions using external fixation has been well described, but definitive treatment in external fixation in the femur is less desired compared with other long bones. Recent data suggest that intramedullary sustained compression may be beneficial in the setting of nonunion. Fragomen et al[30] presented a case series on the use of the intramedullary lengthening nail for the treatment femoral and tibial nonunions and found a 93% union rate. Future studies are required to further support this technique.

Atrophic and Oligotrophic Nonunions

Aseptic atrophic and oligotrophic nonunions require both an increase in biology and often improvement in mechanical stability and/or alignment. Similar techniques are used to improve mechanical stability in atrophic and oligotrophic nonunions because they are for

Figure 4

Radiographs showing nonunion repair of a oligotrophic nonunion using exchange nailing (**A**). Nonunion repair of atrophic nonunion with compression plate augmentation (**B**). Nonunion repair of hypertrophic nonunion with wave plate augmentation (**C**).

hypertrophic nonunions of the femoral shaft including exchange nailing and plate augmentation (Figure 4). Because access to the nonunion is often necessary to débride and place bone graft, supplemental plate fixation is often performed because the exposure has already been performed.

Nonunion débridement may be necessary because of fibrous tissue at the nonunion site; this includes débridement back to healthy bleeding edges (Paprika sign) and intramedullary débridement. Even if infection is not suspected, intraoperative cultures should still be obtained to rule out occult infection. An occult infection in itself does not necessarily change the surgical plan, but may indicate if a postoperative antibiotic course is necessary.[19] If feasible, intraoperative frozen section can be obtained to evaluate for occult infection. These results may alter planned postoperative antibiotic regimen while waiting for culture results.[31] Intraoperative frozen sections have shown sensitivity and specificity of 88% and 96%, respectively, in the diagnosis of occult infection.[31] It is important to first expose the nonunion before proceeding with graft harvest in case there is gross infection at the nonunion site which may alter the surgical plan and obviate the need for graft harvest. Note that when debriding a femoral shaft nonunion, be mindful of length, alignment, and rotation that may be altered. One can take preoperative contralateral films to assess length, alignment, and rotation or can place a temporary unilateral external fixator to maintain length, alignment, and rotation before nonunion débridement.

Autograft remains the benchmark for biologic augmentation.[32] Cancellous autograft is most commonly used (Supplementary Table 2, http://links.lww.com/JAAOS/B355). Local autograft is often deposited during reaming for exchange nailing or one can collect reamings of the ipsilateral femur using Reamer-Irrigator-Aspirator (RIA; Synthes). The average autograft volume from using RIA is approximately 30 to 90 mL per long bone. If more is needed, one can obtain RIA reamings from the ipsilateral tibia or contralateral femur. Potential complications from using RIA include blood loss and fracture. Other common sources of cancellous autograft for the femoral shaft include iliac crest (anterior or posterior) and proximal tibia metaphysis at the expense of donor site morbidity (Supplementary Table 2, http://links.lww.com/JAAOS/B355).

Bone marrow aspirate (BMA) can also easily be taken from the iliac crest, in a less invasive manner than iliac crest bone graft. A Jamshidi needle is used and is inserted into the iliac crest at the anterior superior iliac spine. One can usually obtain up to 150 mL of aspirate, but BMA lacks osteoconductive properties and therefore is often combined with cancellous allograft for volume and structural support. Masquelet recommends a ratio of autograft to allograft of 3:1, but the optimal ratio remains unknown.[33] Other less commonly used autografts include cortical autograft such as tricortical iliac crest graft and vascularized grafts such as a free fibula which can be used as an onlay or in a single/double-barrel technique. To further increase biology, an osteoperiosteal decortication should be performed at the site of atrophic or oligotrophic nonunions. This involves elevating an osteoperiosteal flap circumferentially around the nonunion site. This technique has shown excellent outcomes with union rates up to 97%.[34]

In the recent decade, bone graft substitutes have become more and more abundant with varying levels of evidence and associated costs, but with the benefit of no donor site (Supplementary Table 2, http://links.lww.com/JAAOS/B355). Osteoconductive grafts alone generally have worse outcomes in atrophic and oligotrophic diaphyseal nonunions, but when combined with osteogenic or osteoinductive graft, success increases. Allograft bone chips are often used in combination with RIA reamings or BMA to increase volume. Demineralized bone matrix provides both osteoinductive and osteoconductive properties but comes at a higher cost with little structural support. Synthetic grafts and biocomposites come in a multitude of forms and at an even greater cost with the goal of combining multiple graft properties, but high-level evidence supporting one synthetic over another is lacking. Bone morphogenic proteins—2 has been shown to have higher union rates, reduced time to union, and earlier weight-bearing over bone morphogenic protein-7 in long bone nonunions.[35]

Postoperative Protocol

In most cases, immediate postoperative weight-bearing after femoral shaft nonunion repair is recommended assuming adequate mechanical stability is obtained. In special circumstances, weight-bearing may be restricted for several weeks often for soft-tissue rest. The same monitoring protocol should be used to assess nonunion repair healing as with index fracture healing, looking for serial radiographic progress and improvement in preoperative symptoms (painless weight-bearing). Recalcitrant nonunions are less common in the femur compared with the tibia (16% vs. 27%), but are still a concern, thus follow-up should be no less than 1 year or until radiographic union is achieved.[36] Recalcitrant nonunions should raise suspicion for undiagnosed metabolic or endocrine abnormalities or occult infection. Symptomatic recalcitrant nonunions often require more complex and invasive nonunion repair including vascularized bone graft, nonunion resection followed by bone transport, or amputation.

Outcomes

Femoral shaft nonunions are less common and detrimental than tibial nonunions but still have a negative effect on quality of life. With proper identification and appropriate surgical management, success rates of femoral shaft nonunion repair can reach up to 100% with a rate of recalcitrant nonunion up to 16%.[36] Patients should expect a notable improvement in functional status 1 year after successful nonunion repair.[37] The average time to return to work is around 8 to 9 months.[38] Predictors of poor functional outcome after nonunion repair include tobacco use, worker's compensation insurance, radiographic bone loss, and short musculoskeletal function assessment (SMFA) score using the validated PRoFiT-NU score, which can help provide prognostic aid for surgeons and patients.[39]

Summary

Femoral shaft fractures in general have excellent healing rates when treated with intramedullary nail, yet primary and recalcitrant nonunions remain a clinical problem, thus as a specialty we still have much to learn regarding this topic. The ability to properly identify and classify a nonunion is essential to allow for successful treatment. With advances in implant design, surgical techniques, and bone graft substitutes, the treatment of nonunions continues to evolve but a fundamental understanding of nonunion principles should dictate management.

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