

# Principles of NonUnion Management(Article Review)

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## Abstract

A “non-union” is a fracture of a bone induced either by trauma or surgery which fails to progress to union within a reasonable time span. Defining healing times is difficult. A diaphyseal tibial fracture, for example, may heal in 10 weeks or twelve months depending on endogenous and exogenous factors which in turn are modulated by the effects of surgery

## Introduction

### Bone Healing

For bone healing to happen, the bone needs adequate stability and blood supply. Good nutrition also plays a role in bone healing.

- **Stability.** All treatment of broken bones follows one basic rule: the broken pieces must be put back into position and prevented from moving out of place until they heal. Some fractures can be held in position with a cast. Some fractures require surgical fixation with devices like screws, plates, rods and frames.
- **Blood supply.** Blood delivers the components required for healing to the fracture site. These include oxygen, healing cells, and the body's own chemicals necessary for healing (growth factors). The blood supply to the injured bone usually comes back on its own during the healing period.
- **Nutrition.** A broken bone also needs adequate nutrition to heal. Eating a healthy and well-balanced diet that includes protein, calcium, vitamin C, and vitamin D is the best way to ensure adequate nutrition; dietary supplements that go beyond the daily requirements are not effective. (The rare exception is the severely malnourished patient with many injured organs. In this case, the doctor will discuss dietary guidelines and make recommendations for adding dietary supplements.)

### Blood Supply

.Nonunions are more likely to happen if the injured bone has a limited blood supply  
be

.expected to heal with minimal treatment expected to heal with minimal treatment  
Some

bones, such as the upper thighbone (femoral head and neck) and small wrist bone (scaphoid), have a limited blood supply. The blood supply can be destroyed when these bones are broken

Some bones, such as the shinbone (tibia), have a moderate blood supply, however, an injury can disrupt it. For example, a high-energy injury can damage the skin and muscle over the bone and destroy the external blood supply. In addition, the injury can destroy the internal blood supply found in the marrow at the center of the bone

## Epidemiology

In the U.S., 100000 fractures go onto nonunion. The rate of all fracture nonunion is between 1.9% to 10%. Variable rates of nonunion exist depending on the anatomic region. Femoral shaft nonunions are estimated to be 8% overall with the use of intramedullary nailing. Tibial shaft nonunions occur at a rate of 4.6% after intramedullary nailing. However, there are several discrepancies, as some studies have shown tibia nonunion to be as high as 10% to 12% overall. Also, soft tissue damage impacts the ability to heal. Studies of open fractures with extensive soft compromise showed nonunions to be much higher at 16%. Sex is a predictor of nonunion, showing male gender increases the risk of nonunion, and this was proposed to be because of gender-specific activity types and injury patterns. However, this needs to be taken with caution because 1 replicated in larger studies could not replicate these findings. Brown and colleagues showed nonunion rates to be similar between males and females (12% vs. 12%).

## Pathophysiology

There are several physiologic processes responsible for the nonunion of the bone.

**One**, dysfunctional blood supply decreases the ability for the fracture to heal, which in response decreases osteogenic cells.

**Second**, damage to the osteoconductive scaffold causes reduced new bone formation due to the distance needed to heal bone.

**Third**, pathological biologic processes listed above will not only decrease blood flow but also decrease new bone formation by decrease the biologic growth factors needed to heal bone.

**Fourth**, poor mechanical stability at the fracture site can lower the ability of the fracture to heal. If any of these processes are altered negatively, the probability of developing nonunion increases dramatically, and patients should be counseled as such.

## • **Biomechanics of Nonunions**

### • Important factors for consideration

-Biologic and Mechanical environment -

1- Presence or absence of infection-

2- Septic vs Aseptic-

3- Vascularity of fracture site – Stability – mechanical environment-

4-Deformity-

5-Bone involved and surrounding soft tissues-5

## **Smoking**

Decreases peripheral oxygen tension •

Dampens peripheral blood flow •

Well documented difficulties in wound healing in patients who smokes.

## **Diabetes**

(Neuropathic Fractures)

:Best studied in ankle and pilon fractures •

– Complicated diabetics – those with end organ disease •

neuropathy, PVD, renal dysfunction

Increased rates of infection and soft tissue complications –

Increased rates of nonunion, time to union significantly longer –

Prolonged NWB required –

Inability to control response to trauma can result in •

hyperemia, osteopenia, and osteoclastic bone resorption

Charcot arthropathy –

## **Malnutrition**

Adequate protein and energy is required for •

wound healing

Majority of organic phase of bone is protein •

:Screening test •

serum albumin –

total lymphocyte count –

Albumin less than 3.5 and lymphocytes less •

than 1,500 cells/ml is significant

## ***Causes***

Nonunions happen when the bone lacks adequate stability, blood flow, or both. They also are more likely if the bone breaks from a high-energy injury, such as from a car wreck, because severe injuries often impair blood supply to the broken bone.

***The reasons for nonunion are;*** •

*1-avascular necrosis (the blood supply was interrupted by the fracture*

*2-the two ends are not apposed (that is, they are not next to each other* •

*3-infection (particularly osteomyelitis* •

*4-the fracture is not fixed (that is, the two ends are still mobile* •

*5- soft-tissue imposition (there is muscle or ligament covering the broken ends and preventing them from touching each other*

## ***Risk Factors***

- **A- Related to the person:**
- 1. Age: Common in old age
- 2. Nutritional status : poor
- 3. Habits : Nicotine and alcohol consumption

- 4. Metabolic disturbance : Hyperparathyroidism
- 5. can be found in those with NF1
- 6. Genetic predisposition[3]
- **B- Causes related to fracture:**
- 1. Related to the fracture site
- 2. Soft tissue interposition
- 3. Bone loss at the fracture
- 4. Infection
- 5. Loss of blood supply
- 6. Damage of surrounding muscles
- **C- Related to treatment**
- 1. Inadequate reduction
- 2. Insufficient immobilization
- 3. Improperly applied fixation devices

## **Classification of Nonunion of Bone Into Four Categories[7]:**

- **1-Hypertrophic Nonunion[7]**
- • Shown by radiographically abundant callus formation
- • Importantly, there is no bridging bone, and the ends are not united
- • This finding implies there is adequate blood supply and biology (with the formation of callus), but inadequate stability
- **2-Atrophic Nonunion**
- • Evidenced by radiographically absent callus, which indicates poor biology (from one or several of causes above) and a lack of blood supply (see above).
- • Inadequate fixation
- **3-Oligotrophic**
- • Is a balance and combination of atrophic and hypertrophic in that there is incomplete callus formation
- • Inadequate reduction
- **4-Septic Nonunion**
- • Reduces blood flow from organisms consuming the nutrition to healthy bone
- • Decreases the new bone formation

## **Symptoms**

Patients with nonunions usually feel pain at the site of the break long after the initial pain of the fracture disappears. This pain may last months, or even years. It may be constant, or it may occur only when the broken arm or leg is used.

## **Patient Evaluation – Medical**

### **History**

- Diabetes, endocrinopathies, vit D, etc
- Physiologic age – co-morbidities

- Heart disease, COPD, kidney/liver disease
- Nutrition
- Smoking
- Medications
- Ambulatory/functional status now and prior to original injury

## **Patient Evaluation – Physical**

### **Exam**

- Appearance of limb
  - Color, skin quality, prior incisions, skin grafts
  - Erythema or drainage
- Range of motion of all joints
- Pain – location and contributing factors
- Strength, ability to bear weight
- Vascular status and sensation
- Deformity
  - Clinically = Length, alignment, AND rotation

## **Patient Evaluation – Imaging**

### **1-Tomography**

- CT and MRI have replace linear tomography
- Consider Digital Tomography if available

## **2-Radionuclide Scanning – Infected Nonunion?**

- Technetium - 99 diphosphonate
  - Detects repairable process in bone ( not specific)
- Gallium - 67 citrate
  - Accumulates at site of inflammation (not specific)
- Sequential technetium or gallium scintigraphy
  - Only 50-60% accuracy in subclinical osteomyelitis

Nonunion?

## **3-Labeled Leukocyte Scan – Infected Nonunion?**

- Good with acute osteomyelitis, but less effective in diagnosing chronic or subacute bone infections
- Sensitivity 83-86%, specificity 84-86%
- Technique is superior to technetium and gallium to identify infection

## **4-MRI – Infected Nonunion?**

- Abnormal marrow with increased signal on T2 and low signal on T1
- Can identify and follow sinus tracts and sequestrum
- Mason study- diagnostic sensitivity of

100%, specificity 63%, accuracy 93%

## Treatment

Nonsurgical and surgical treatments for nonunions have advantages and disadvantages. More than one alternative may be appropriate.

### Nonsurgical Treatment

Some nonunions can be treated nonsurgically. The most common nonsurgical treatment is a bone stimulator. This small device delivers ultrasonic or pulsed electromagnetic waves that stimulate healing. The patient places the stimulator on the skin over the nonunion from 20 minutes to several hours daily. This treatment must be used every day to be effective.

#### Nonoperative

- Electrical stimulation
- Ultrasound
- Extracorporeal shock wave therapy

#### 1-Electrical Stimulation

- Applied mechanical stress on bone generates electrical potentials
  - Compression = electronegative potentials = bone formation
  - Tension = electropositive potentials = bone resorption
- Basic science suggests e-stim upregulates TGF- $\beta$  and BMP's suggesting osteoinduction

#### 2-Ultrasound

- Piezoelectric transducer generates an acoustic pressure wave
- Some evidence to show faster healing in fresh fractures
- Evidence is moderate to poor in quality with conflicting results
- SR/MA suggests there may be improvement in healing but not function

#### 3-Extracorporeal Shock Wave Therapy

Single impulse acoustic wave with a high •  
amplitude and short wavelength  
Microtrauma induced in bone thought to •  
stimulate neovascularization and cell  
differentiation

## Surgical Treatment

Surgery is needed when nonsurgical methods fail. You may also need a second surgery if the first surgery failed. Surgical options include bone graft or bone graft substitute, internal fixation, and/or external fixation

**Bone Graft.** During this procedure, bone from another part of the body at the •  
fracture site to "jump start" the healing process. A bone graft provides a scaffold on which



new bone may grow. Bone grafts also provide fresh bone cells and the naturally occurring chemicals the body needs for bone healing

During the procedure, a surgeon makes an incision and removes (harvests) pieces of bone from different areas on the patient. These are then transplanted to the nonunion site. The rim of the pelvis or "iliac crest" is most often used for harvesting bone. Although harvesting the bone may be painful, the amount of bone removed usually does not cause functional, structural, or cosmetic problem

Allograft (cadaver bone graft). An allograft (cadaver) bone graft avoids harvesting bone from the patient, and therefore, decreases the pain involved with treating the nonunion. Like a traditional bone graft, it provides scaffolding for the patient's bone to heal across the area of the nonunion. As time goes on, the patient's bone replaces the cadaver bone. Although there is a theoretical risk of infection, the cadaver bone graft is processed and sterilized to minimize this risk

**Bone graft substitutes and/or osteobiologics.** As with allografts, bone graft substitutes avoid the bone harvesting procedure and related pain. Although bone graft substitutes do not provide the fresh bone cells needed for normal healing, they do provide a scaffold chemicals needed for growth

Depending on the type of nonunion, any of the above materials, or a combination of materials, may be used to fix the nonunion

Bone grafts (or bone graft substitutes) alone provide no stability to the fracture site. Unless the nonunion is inherently stable, you may also need more surgical procedures (internal or external fixation) to improve stability

**Internal Fixation.** Internal fixation stabilizes a nonunion. The surgeon attaches metal plates and screws to the outside of the bone or places a nail (rod) in the inside canal of the bone

If a nonunion occurs after internal fixation surgery, another internal fixation surgery may be needed to increase stability. The surgeon may use a more rigid device, such as a larger rod (nail) or a longer plate. Removing a previously inserted nail and inserting a larger one (exchange nailing) increases stability and stimulates healing within the bone. Internal fixation can be combined with bone grafting to help stability and stimulate healing

**External fixation.** External fixation stabilizes the injured bone, as well. The surgeon attaches a rigid frame to the outside of the injured arm or leg. The frame is attached to the bone with wires or pins. External fixation may be used to increase the stability of the fracture site if instability helped cause the nonunion. External fixation can treat nonunions in a patient who also has bone loss and/or infection.

Currently, there are different strategies to augment the bone-regeneration process, however, there is no standardised clinical treatment guideline yet .

## Surgical treatment options include:

**1-Debridement:** radical surgical removal of necrotic or infected soft tissue and bone [tissue is deemed essential for the healing process

**2-Immobilization of the fracture with internal or external fixation.** Metal plates, pins, screws, and rods, that are screwed or driven into a bone, are used to stabilize the broken bone fragments

**3-Bone grafting.** Filling of the bone defect resulting from debridement must be

performed. Autologous bone graft is the "gold standard" treatment and possesses osteogenic, osteoinductive, and osteoconductive properties, although only a limited sample [can be taken and there is a high risk of side effects.][6

•4-Bone graft substitutes. Inorganic bone substitutes may be used to complement or replace autologous bone grafting. The advantage is that there is no morbidity on sampling and their availability is not restricted. S53P4 bioactive glass has shown good results as a promising bone graft substitute in treatment of nonunions, due to its osteostimulative, osteoconductive and antimicrobial properties

## Complications

- 1-Nerve injury - e.g., the radial nerve in the humeral shaft fractures- •
- 2-Persistence of nonunion •
- 3-Eventual need for amputation •
- 4-Infection with further damage to surrounding anatomy •
- 5- BMP-2 can cause osteolysis, heterotopic bone formation, retrograde ejaculation in spine surgery, and wound complications

## Prognosis

Nonoperative treatments of nonunion can be quite effective. Ultrasound union rates can be as high as 70% to 93%.The usual course of nonoperative treatment with ultrasound is the placement of ultrasound therapy within three months after the last surgical procedure.

[There are better union rates when ultrasound is applied less than six months from surgery  
The surgical treatment of nonunions has high union rates. Nail dynamization with an 83% union rate . Exchange nailing in humeral shaft fractures has shown a 95.6% union rate  
Infected nonunion, however, portends a poor prognosis with most studies showing low union rates after surgical treatment. The prognosis of nonunion if treated depends on many factors including the age and general health of the patient, the time since the original injury, the number of previous surgeries, smoking history, the patient's ability to cooperate with the treatment. In the region of 80% of nonunions heal after the first operation. The success rate with subsequent surgeries is less.].

## Prevention of nonunion

- .1-Controll of diabetes mellitus-
- .2-using good aseptic technique to avoid infection and give prophylactic antibiotics
- 3-With the improvement of quality of life, the negative impact of obesity has gradually .become a hot issue of concern. Obesity can lead to vitamin D deficiency
- 4-The use of NSAIDs was also associated with fracture nonunion. Some experiments have - .proved that NSAIDs can temporarily inhibit the process of fracture union
- .5-Stop smoking because it decreases blood supply and affects bone healing-
- 6-Good fracture reduction-
- 7-Good fracture stability-
- 8-Protect fracture vascularity-
- 9-The tools currently available to determine union including various imaging modalities, biomechanical testing methods, and laboratory and clinical assessment
- 10-Open reduction had a higher rate of fracture nonunion than closed reduction. In surgery, although open reduction can bring good fracture repair, but closed reduction can .better protect blood supply and soft tissue
- 11-Nonunion rate of conservative treatment was the highest one compared with that of surgical treatment
- 12-IMN(itramedullaray nail) can achieve better healing effect in the treatment of tibial

fractures, comparing to ORIF and external fixation .MIPPO (minimally invasive percutaneous plate osteosynthesis) can maximize the protection of soft tissue and bone marrow around the fracture site. so it had the lowest nonunion rate of all fixation modes.

## Conclusion

There are many possible approaches for patients who develop a non-union. One of the best .methods of treatment is prevention.

Howev,

if a non-union does occur, there are multiple conservative and surgical options available.

Early diagnosis is very important to allow for the initiation of conservative treatment methods. Clinical, radiographic and advanced imaging are available to help in early diagnosis. Patient selection and preparation for surgery are very important to limit risk .factors and optimize the possibility of fusion.

Good surgical technique to provide a stable construct and maintaining immobility are keys, not only of prevention, but also of surgical treatment of a non-union. External products are often indicated to aid in the basic principles of bone healing and one can often mix these products with bone marrow to provide an even higher probability of success.

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