Original Article

Management Modalities Of Humeral Fracture Nonunion

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DOI: 10.47750/pnr.2023.14.02.246

Abstract

Background: Humeral fractures comprise 5-8% of all fractures. Nonunion is uncommon and it was reported to be less than 10-13% of all humeral fractures. But when they do occur, they present a challenge to orthopedic surgeons and often debilitate patients. Nonunion of fractured humerus often need operative treatment. Many factors have been associated with delayed union or nonunion. Both local and systemic factors are thought to contribute to the development of nonunion. Radiological investigations focus on bone and soft tissue pathology. The most commonly used investigations are; X-ray, MRI, CT and bone scan. Before embarking on any method of treatment, one should be aware of the objectives in treating nonunion. Obviously, treatment is primarily directed at healing of the fracture. However, this is not the only objective because a functionless, deformed limb with pain and stiffness of adjacent joints and a healed nonunion will not be a satisfactory end point for most patient. Emphasis must therefore be placed on returning the limb and the patient to the fullest function possible during the frequently prolonged periods of time it takes to treat nonunion. It is the surgeon's role to identify the proper stimulus that will lead to uneventful fracture healing. In hypertrophic nonunion, the proper stimulus is stable fixation of the fracture allowing capillary ingrowth with enchondral ossification . The addition of biologic stimulus as bone graft is not necessary. However, atrophic nonunion with the restricted blood supply require the additional biologic stimulation e.g. shingling or augmentation with bone graft. Systemic as well as local fracture management must be considered in the treatment of nonunion; metabolic and nutritional factors should be optimized, patients should be encouraged to discontinue tobacco use and activity levels may require alteration. Mechanical properties of the Ilizarov device, particularly in comparisons with other external fixators have been an area of research interest. The stability provided by fixation devices is an important variable; instability can lead to ineffective bone regeneration, while an overly rigid fixation can lead to a delay of fracture consolidation. A limited degree of axial micromotion is important to promote osteogenesis and thus it is hypothesized that an optimal fixation device will provide stability while still permitting some axial micromotion. However, there are currently no data that identify what level of instability is beneficial

Keywords: Humeral Fracture Nonunion

INTRODUCTION

In 1986, an FDA panel defined nonunion as established when a minimum of 9 months has elapsed since injury and the fracture shows no visible progressive signs of healing for the last 3 months (LaVelle, 1998). Aronson and Cornell in 1999 described definitions for delayed union, nonunion and fractures at risk of nonunion. Delayed union is defined as the failure of a fractured bone to heal within an expected time course while maintaining the potential to heal. Nonunion is defined as a state in which all healing processes have ceased without any potential to heal without intervention. Fractures at risk are those commonly associated with problematic healing as those due to high energy trauma.

Incidence:

Humeral fractures comprise 5-8% of all fractures. Nonunion is uncommon and it was reported to be less than 10-13% of all humeral fractures. But when they do occur, they present a challenge to orthopedic surgeons and often debilitate patients. Nonunion of fractured humerus often need operative treatment (Volgas et al, 2004).

Causes of Nonunion:

Many factors have been associated with delayed union or nonunion. Both local and systemic factors are thought to contribute to the development of nonunion.

Causes of nonunion have been classified as either due to mechanical failures or biological failures (Smith et al, 2002):

A. Mechanical Causes:

1) Excess motion due to inadequate immobilization and gaps between fragments due to Soft tissue interposition or loss of bone substance.
2) Distraction by traction or hardware: Failure to manage fractures properly has been shown to increase the incidence of nonunion. Distraction at the fracture site and instability with failure to immobilize the fracture adequately are known to increase the incidence of nonunion (Connolly, 1985).

B. Biological Causes:

1) Loss of blood supply: Increased periosteal stripping and the resultant amount of devascularized bone vary with the fracture type and contribute substantially to delayed union or nonunion (Goulet and Templeman, 1997). A direct correlation exists between the energy absorbed by the bone and soft tissues and the complications of healing (Cierny et al, 1983). The incidence of nonunion especially infected nonunion, increases with the severity of open fractures. The presenting factors contributing to nonunion or delayed union include fracture displacements, bone loss, comminution and infection (Gershuni and Halma, 1983).
2) Infection: Infection predisposes to nonunion by creating sequesturm formed by cortical bone death, gaps by osteolytic infectious granulation tissue and motion from loosening of implants (Rpsen , 1998). Recent evidence has highlighted the adverse effect of smoking on bone healing (Raiken et al, 1998).
3) General factors: such as old age, cachexia, malnutrition, steroids, anti-inflammatory agents such as indomethacin, burns and

radiation may be contributory but are not the primary causes of nonunion (Rosen, 1998).
Classifications oF Nonunion:

Weber and Cech in 1978 classified nonunion according to their biological potential into two major groups:

1- Viable Nonunion (Figure 15):

- Elephant's Foot: Hypertrophic and rich in callus. It results from insufficient stabilization.
- Horse's Hoof: Mildly hypertrophic. It typically occurs after moderately unstable fixation with plate and screws.
- Oligotrophic Nonunion: Not hypertrophic and callus is absent. They typically occur after major displacement of a fracture, distraction of fragments or internal fixation without accurate apposition of fragments.

2- Non-Viable Nonunion (Figure 16):

- Dystrophic Nonunion: Torsion wedge with butterfly revascularizing from one side.
- Necrotic Nonunion : Comminuted or avascular fragments.
- Atrophic Nonunion: The ends of the fragments have become osteoporotic and atrophic.
- Defect Nonunion (Smith et al, 2010).

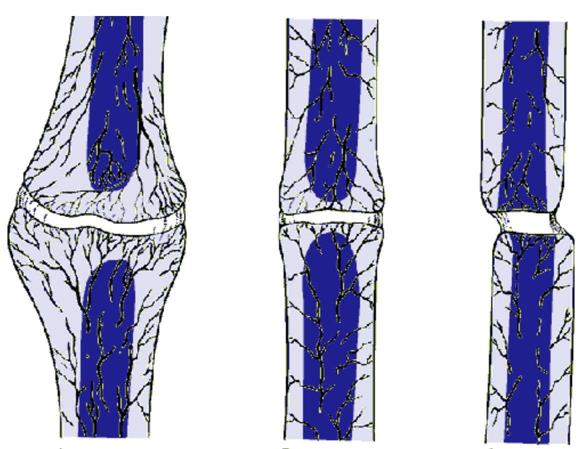

Figure (1): Classification of viable nonunion according to Weber and Cech A- Elephant's Foot B- Horse's Hoof C- Oligotrophic Nonunion (Rosen, 1998).

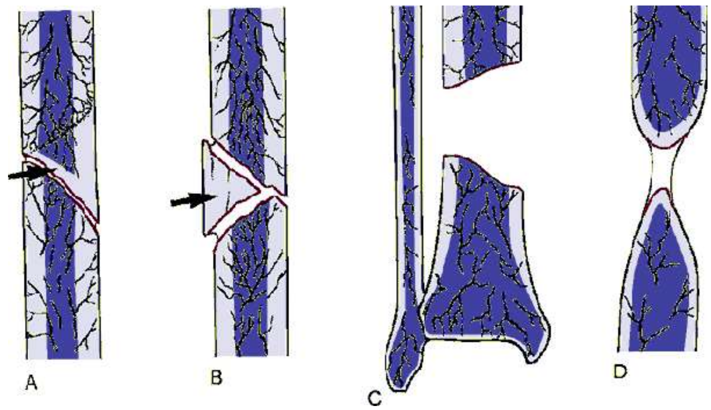

Figure (216): Classification of non-viable nonunion according to Weber and Cech A- Dystrophic B-Necrotic C-Defect D-Atrophic Nonunion (Rosen, 1998).

Professor Ilizarov preferred to classify nonunion based on the clinical behavior and the resistance encountered with physical manipulation of the fracture fragments into:

1. Stiff Nonunion: demonstrates less than 7 degrees of motion in any one direction of manipulation. In practice, it is more reliable to assess the motion restricted to a single plane of motion. So, stiff

nonunion demonstrates less than 15 degrees of motion in any plane of manipulation.

2. Lax Nonunion: demonstrates some resistance to manipulation, but greater than 15 degrees of motion in any plane of manipulation.
3. Flail Nonunion: demonstrates little or no resistance to manipulation, and corresponds to synovial pseudoarthrosis (Testsworth, 2001).

Paley et al in 1989 and Catagni in 1991 presented another more detailed classification that also takes deformity, bone defects and infection into consideration:

Type A: Aseptic Nonunion: without bone loss or with less than 1cm of bone loss.

Type A1: Mobile nonunion.

Type A2.1: Stiff nonunion without deformity. Type A2.2: Stiff nonunion with deformity.

Type B: Aseptic Nonunion: with greater than 1cm bone loss.

- Type B1: Bony defect and no shortening.
- Type B2: Bony defect and shortening.

Type C: Infected Nonunion.

AO Classification: On the basis of AO classification, infected nonunion was classified as; (1) Non-draining quiescent which is non-draining without local or general signs of infection in the last 3 months, (2) Non- draining active which is non-draining but with local or general signs of infection in the last 3 months and (3) Draining nonunion with sinuses discharging pus (Muller et al, 1991).

Radiographic Assessment:

Radiological investigations focus on bone and soft tissue pathology. The most commonly used investigations are; X-ray, MRI, CT and bone scan.

- Plain X-Ray (PXR):

Plain radiography is the standard imaging modality used in assessment and follow up of nonunion. The standard anteroposterior and lateral views that should include the joint above and joint below is mandatory. These views give important information about the site and configuration of nonunion, the biological condition of nonunion (hypertrophic or atrophic), the presence of bone defect and its amount, the presence of sequestrum, the presence of implants or foreign bodies, and the presence of associated deformity.

- Computed Tomography (CT):

CT is excellent in delineating the extent and the pattern of bone involvement. It's most useful in the detection of gas in soft tissue infections, identification of sequestra in cases of chronic osteomyelitis and it is particularly useful in the evaluation of intramedullary ostietis (Paley, 1991).

- Magnetic Resonance Imaging (MRI):

MRI is excellent in differentiating between bone and soft tissue infection, an important point to know before pre-operative biopsy (Motsitsi, 2008). It has a reported sensitivity of 88-100% and a specificity of 75-100% in the detection of osteomyelitis. The positive predictive values for MRI and Tc-99m Scintigraphy are comparable (85%

and 83%) (Paley, 1990), However, MRI can provide biplanar images of the infected site and is superior to Scintigraphy and CT for depicting the marrow cavities of long bones and adjacent soft tissues. The use of gadolinium enhancement can aid in identifying sinus tracts and distinguishing cellulites from abscess. Like Scintigraphy, MRI is limited by a lack of specificity, the signal patterns seen with fractures, bone infarction, tumors, post-surgical changes, bone contusions and sympathetic edema are similar (Paley, 1991).

- Bone Scan:

Radionuclide scintigraphy is a very useful diagnostic tool and can be performed with various algorithms. Technetium-99m is the principal radioisotope employed in most bone scans. Reported sensitivities of bone scintigraphy for the detection of osteomyelitis vary considerably from 32% to 100%. Reported specificities have ranged from 0% to 100%. 99Tc-MDP scan is commonly used in the investigations of infections. The sensitivity is 100% and the specificity is 0% (Nijhof et al, 1997).

Laboratory Investigations:

These investigations are an integral part of the patient's work up and they are commonly overlooked. They are cheep easily available and can be very informative. They are useful in diagnosis of infection and monitoring the response during treatment, although they can be equivocal or negative particularly in subclinical infection.

Complete blood count (CBC), C-reactive protein (CRP) and erythrocytes sedimentation rate (ESR) are the usual tests requested in infections. The white blood cell (WBC) count may be high, normal or borderline; depending on the activity of infection. All these parameters
may be normal in subclinical infection. The ESR and CRP are helpful in monitoring progress during treatment (Motsitsi, 2008).

Treatment of Nonunion:

Before embarking on any method of treatment, one should be aware of the objectives in treating nonunion. Obviously, treatment is primarily directed at healing of the fracture. However, this is not the only objective because a functionless, deformed limb with pain and stiffness of adjacent joints and a healed nonunion will not be a satisfactory end point for most patient. Emphasis must therefore be placed on returning the limb and the patient to the fullest function possible during the frequently prolonged periods of time it takes to treat nonunion (Rosen, 1998).

Treatment must be designed to correct axial or rotational malalignment, equalize limb lengths, prevent infection or treat established infection and allow function restoration of the limb (Wiss and Stetson, 1996).

It is the surgeon's role to identify the proper stimulus that will lead to uneventful fracture healing. In hypertrophic nonunion, the proper stimulus is stable fixation of the fracture allowing capillary ingrowth with enchondral ossification . The addition of biologic stimulus as bone graft is not necessary. However, atrophic nonunion with the restricted blood supply require the additional biologic stimulation e.g. shingling or augmentation with bone graft (Wiss and Stetson , 1996).

Systemic as well as local fracture management must be considered in the treatment of nonunion; metabolic and nutritional factors should be optimized, patients should be encouraged to discontinue tobacco use and activity levels may require alteration (LaVelle, 2003). A wide variety of

methods are used in the management of humeral nonunion. A brief overview of different methods is provided here:

A. Non-Surgical Methods:

1- Functional Casts or Braces:

Although disability may be extended, the costs are minimal and the risks appear relatively low. If the fracture fails to unite, alternative methods are possible (Wiss and Stetson, 1996).

2- Electrical Stimulation:

Electrical stimulation has been proposed as a non-operative alternative treatment for established nonunion. Considerable laboratory and clinical evidence has been accumulated to suggest that electrical stimulation enhances fracture healing (Lavine and Grodzinsky, 1987).

Three forms of electrical stimulation has been used clinically; constant direct current stimulation with the use of percutaneous or implanted electrodes (invasive), magnetic field (non-invasive) or capacitive coupling (noninvasive) (Einhorn, 1995).

Although much has been written concerning the effects of electrical stimulation, little is known of the scientific basis for the observed results (Cavallo and Einhorn, 1998). The application of electrical stimulation for fracture healing is still controversial largely due to the lack of well- controlled clinical trials (Aaron, 1996). The technique requires excellent patient compliance, expensive and generally requires immobilization. The major drawback is the inability to address the associated problems of angulation, malrotation and limb shortening (Wiss and Stetson, 1996). It is seldom effective in synovial pseudoarthrosis or when there are gaps or necrotic ends of more than 1cm (Rosen, 1998).

3- Ultrasound Stimulation:

Low intensity ultrasound has been shown to stimulate bone healing of fresh fractures in experimental animals. Xavier and Duart in 1987 presented the first clinical applications for ultrasound stimulation in treatment of nonunions. Schaden et al in 2002 presented the use of Extracorporeal Shock Wave Therapy (ESWT) in treating nonunited fractures and reported a 74% rate of bony union within 6 months of shock wave treatment.

B. Surgical Methods:

(1) Soft Tissue Coverage in Nonunion:

Successful management of nonunions depends on viable soft tissue coverage as well as on skeletal stability.

(2) Bone Grafts and other Biological Methods:

Many methods of bone grafting for bone defects have been described. These include non-vascularized fibular graft, autogenous bone graft, allograft and synthetic bone graft (LaVelle, 1998).

Autogenous cancellous bone graft remains the golden standard in grafting material. Its osteoconductive (matrix) and osteoinductive (protein) properties, as well as osteoprogenitor cells, make it an ideal substance for grafting (LaVelle, 2003).

The disadvantages of autogenous bone grafting include the limited quantity of bone available for harvest and significant donor site morbidity. Pain at the donor site has been reported to occur in as many as 25% of patients (Summers and Eisenstein, 1989). Morbidity including infection, increased operative time and blood loss has been reported in 8.6% of cases (Younger and Chapman, 1989). In addition, grafting alone provides little opportunity for deformity correction, bone graft incorporation can be slaw and supplemental immobilization is usually necessary (Wiss and Stetson, 1996).

Non-vascularized cortical grafts are often chosen for the initial support they provide in bridging large defects. However, we must be aware that cortical grafts rapidly loose their structural strength as integration develops (Aronson and Cornell, 1999). It is estimated that cortical grafts are at 50% strength at 6 months (Aaron, 1996).

Free vascularized autogenous bone graft may be useful for treating nonunion with segmental defect. First successfully reported by Talyor and associates in 1978, the technique involves the isolation and transfer of a bone segment, most commonly the fibula. It has the advantages of one stage procedure, has a fast union rate and has the potential for graft hypertrophy. However, the procedure is long and demanding, necessitates a vascular sacrifice, may lead to graft fracture and creates a doner bone defect that may result in instability of the foot with restricted motion of the of the ankle and big toe. There is no role for this technique in infected nonunions until the infection is completely under control, adequate soft tissue coverage has been obtained and drainage has been eliminated with the patient free of all antibiotics. It may be considered for defects greater than 6 cm (Goulet and Templeman, 1997).

Percutaneous bone marrow injection has been used in treating delayed union and nonunion. Connoly et al in 1991 and Grag et al in 1993 have shown, both in vitro and in vivo, that healing of nonunion can be successfully stimulated by injecting autologous bone marrow into the nonunion sites. It is important to remember that marrow injection is not a substitute for adequate fracture stabilization (Wiss and Stetson, 1996).

Allografts can be used when the source of fresh autogenous bone is either inadequate or inaccessible. There are several forms of allograft bone. The most currently used allograft material consists of freeze-dried allograft ships (Aaron, 1996). Allografts can generate an intense immune response that interferes with graft incorporation. In addition, any form of allograft is inferior to autograft due to decreased osteogenic and osteoinductive capacities. Also, allograft readily transmits retrovirus infection in spite of routine processing and removal of bone marrow (Aronson, 1999).

Tissue Engineering of Bone:

Three general approaches have been applied to the art of tissue engineering of bone:

1. Matrix Based Therapies (Osteoconductive Substitutes):

They simply introduce structural implants to replace the missing bone to provide a substrate for cellular attachment, proliferation and differentiation. These methods use calcium-based ceramics (composed of hydroxyapatite, tricalcium phosphate or both), calcium-collagen composite grafts, bioactive glasses and synthetic polymers (Hollinger et al, 1996).

The first graft substitute approved by FDA was Interpore which is predominately hydroxyaptite biomatrix. Another recently approved material is Collagraft which is a mixture of hydroxyapatite, tricalcium phosphate and fibrillar collagen (Einhorn, 1995). Cermaics avoid problems with donor site morbidity but they are very brittle. Particulate ceramics can be mixed with bone marrow or with limited volume of cancellous autograft to add an osteoinductive effect (LaVelle, 2003).

2. Factor Based Therapies (Osteoinaductive Methods):

Using growth and differentiation molecules that provide osteoinductive stimuli e.g purified or rhBMPs (recombinant human Bone Morphogenic Protein) (Bruder and Fox, 1999). Friedlander et al in 2002 used rhOP ‘‘recombinant human osteogenic protein-1”, also known as BMP-7, implanted with type I collagen carrier in treating tibial nonunions and found it to be comparable to fresh cancellous bone autograft.

3. Cell Based Therapies:

Cells with osteogenic potential are transferred directly to the site requiring augmentation. This may be done through implantation of unfractioned fresh bone marrow (Bone Marrow Injection), purified culture-expanded MSCs (Mesenchymal Stem Cells), differentiated osteoblasts and cells that have been genetically modified to express a rhBMP. The latter three have been shown to enhance rate and extent of bone regeneration in animal models (Bruder and Fox, 1999).

(3) Skeletal Stabilization:

❖ Compression Plating Fixation:

Compression plating fixation has the advantages of high union rate and good functional recovery. But for humeral fractures or nonunion, it is recommended that long and broad steel plates of 4.5 mm in thickness should be used by Arbeitsgemeinscheft for Osteosyntheses Fragen/Association for the Study of International Fixation (AO/ ASIF) group. For nonunions with osteoporosis, 10 or 11 hole plates with 5 or more screws proximal and distal to the nonunion are recommended (Rosen H, 1990). Even though locking compression plates and screws may fix the bone with osteoporosis and have been reported in treating humeral nonunion with osteoporosis, this still requires a very long skin

incision and extensive soft tissue stripping that may interfere with fracture healing (Brumback, 1996). It also has the risk of radial nerve injury. The incidence of radial nerve palsy after compression plating is approximately 10% (Bajaj SK et al, 2004).

- Intramedullary Nailing:

Intramedullary nailing preserve the blood supply better and requires less soft tissue stripping, also allows homogeneous elastic stress distribution over the bone tissue and the nail and provides good fracture stabilization. However, problems of limited range of motion of the shoulder joint due to abutment of a protruding nail against the acromion, smooth IM rods not controlling rotational stresses and lack of axial compression are shortcomings of IM rods (Su JC, 2010).

- External Fixation:

It is the preferred method in cases of previous infection with the risk of reactivation of quiescent sepsis following grade II and grade III open fractures (Goulet and Templeman, 1997). Unilateral fixators have the advantages of simplicity and the ability to achieve limited axial deformity correction. It allows stabilization of the nonunion and debridement as necessary and facilitates soft tissue reconstruction once infection is under control. With some fixators, segmental bone transport can be employed when indicated (Wiss and Stetson, 1996).

However, unilateral fixators do not permit immediate load bearing and they leave large holes in the bone once the pins are removed. Moreover, corticalization of the regenerate after bone transport is slower than observed with circular fixators. Unilateral fixators do not provide enough support in patients with osteoporosis (Hardy et al, 1991). Also, they are significantly limited in their ability to adjust for rotational and transnational deformities (Paley et al, 1990).

The principles of treatment of infected nonunion are:

1. Eradication of infection: by means of surgical debrirtment combined with antibiotics. Radical and frequent debridement is necessary to eliminate infection.This is done by excising all dead soft tissues, dead bone and foreign bodies (Rosen, 1998).

The use of antibiotics can often control an infection within the limits of a vascular area, but they can not be expected to sterilize an avascular area (LaVelle, 1998). Chronic osteomyelitis occurring after trauma can be polymicrobial, but Staphylococcus aureus still remains an important pathogen. Coagulase-negative staphylococcus (Staph. epidermidis) is a major pathogen in the presence of a prosthetic joint or other foreign material. Gram negative organisms have played an increasing role in the last decade (Cunha et al 1997).

Polymethylmethacrylate antibiotic (PMMA) beads also can be used to treat infected nonunion. Heat-stable antibiotics such as tobramycin, and gentamycin can be used locally to achieve 200 times the antibiotic concentration achieved with intravenous administration (LaVelle, 1998). PMMA beads can also serve as spacers for further bone grafting procedures (Johnson, 2000).

2. Soft tissue reconstruction: split skin grafts may be sufficient. In more complex situation, local flaps, fasciocutaneous flaps or free vascularized flaps are needed (Johnson, 2000).

Skeletal reconstruction: External fixation is the standard method of stabilization in infected nonunion (Johnson, 2000)

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