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Delayed union and nonunions: Epidemiology, clinical issues, and financial aspects

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ABSTRACT

Fracture healing is a critically important clinical event for fracture patients and for clinicians who take care of them. The clinical evaluation of fracture healing is based on both radiographic findings and clinical findings. Risk factors for delayed union and nonunion include patient dependent factors such as advanced age, medical comorbidities, smoking, non-steroidal anti-inflammatory use, various genetic disorders, metabolic disease and nutritional deficiency. Patient independent factors include fracture pattern, location, and displacement, severity of soft tissue injury, degree of bone loss, quality of surgical treatment and presence of infection. Established nonunions can be characterised in terms of biologic capacity, deformity, presence or absence of infection, and host status. Hypertrophic, oligotrophic and atrophic radiographic appearances allow the clinician to make inferences about the degree of fracture stability and the biologic viability of the fracture fragments while developing a treatment plan. Nonunions are difficult to treat and have a high financial impact. Indirect costs, such as productivity losses, are the key driver for the overall costs in fracture and non-union patients. Therefore, all strategies that help to reduce healing time with faster resumption of work and activities not only improve medical outcome for the patient, they also help reduce the financial burden in fracture and non-union patients.

Introduction

It has been estimated that 100,000 fractures go on to nonunion each year in the United States. [1]. The reported incidence and prevalence on nonunion vary significantly based on anatomic region and the criteria used to define nonunion. This variability reflects the overall complexity of understanding the epidemiology of nonunion. Risk factors for nonunion can be characterised as either patient dependent or patient independent. Established patient dependent risk factors include advanced age, various medical comorbidities, sex, smoking, non-steroidal anti-inflammatory use, various genetic disorders, metabolic disease and nutritional deficiency [2–5]. Patient independent factors include fracture pattern, location, and displacement, severity of soft tissue injury, degree of bone loss, quality of surgical treatment and presence or absence of infection [6].

Assessment of nonunion

Assessing a patient with a suspected nonunion involves obtaining a clinical history and physical examination, imaging studies, as well as laboratory testing. Important elements of the patient history include pain with weight bearing and subjective fracture instability. Physical examination should focus on tenderness or motion at the fracture site, deformity, status of the soft tissue envelope, signs of infection, and range of motion at joints adjacent to the fracture site. Radiographic evaluation involves orthogonal views of the involved extremity to assess the state of fracture healing as well as the presence or absence of deformity. Radiographic findings suggestive of a healing problem include persistent fracture lines, absence of bony bridging, lack of progressive healing on serial radiographs, progressive deformity

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and the presence of loose or broken implants. Computed tomography (CT) scanning can also be undertaken to assess fracture union and has been shown to be highly sensitive in the identification of unhealed fractures, but this modality is somewhat limited by low specificity [7]. Laboratory evaluation is undertaken to assess for the presence of infection as well as for metabolic and endocrine abnormalities in the setting of unexpected or unexplained nonunion [8].

An established nonunion also needs to be characterised in terms of biologic capacity, deformity, presence or absence of infection, and host status. Hypertrophic, oligotrophic and atrophic radiographic appearances allow the clinician to make inferences about the degree of fracture stability and the biologic viability of the fracture fragments while developing a treatment plan. The presence of deformity increases the complexity of the problem, mandating not only fracture healing but deformity correction as well. When infection is present, it too must be eradicated prior to, or during, nonunion management. Finally, the patient's overall ability to withstand and benefit from any proposed treatment must be considered. Although originally designed for osteomyelitis, the Cierny-Mader classification is also useful in making this assessment of patients with compromised fracture healing [9].

"Doctor, is my fracture healed yet?"

Following a traumatic injury, patients most common question is whether their fracture is healed. The answer to this question has a very important impact for the patient because it may determine whether they can weight-bear, whether they can return to work, or whether additional surgery may be required. Not knowing whether their fracture is healing normally creates uncertainty as the patient plans their future. When the possibility of additional surgery is added to this uncertainty, significant anxiety may develop in some patients.

Use of crutches or a walker to maintain non-weightbearing restrictions commonly leads to shoulder and wrist pain, along with exacerbation of any underlying shoulder or wrist pathology. Crutch or walker use may not even be feasible for obese patients or patients with limited upper extremity strength, restricting them to a wheelchair. Prolonged wheelchair use may compromise patients overall fitness and cardiac reserve, prolonging their future rehabilitation and recovery.

When is a fracture healed? Clinical perspective

The clinical evaluation of fracture healing is based on both radiographic findings and clinical findings. Plain radiographic findings that are used to define fracture union include the presence of bridging callus, the number of bridged cortices, and the disappearance of fracture lines. Depending on the fracture site, orientation, and the presence or absence of fixation it can be difficult to clearly evaluate these factors. Fractures that are rigidly fixed with interfragmentary compression may not show any visible evidence of callus. In these cases, it is easier to accurately identify failure of fracture healing, since this may be associated with hardware loosening or hardware failure. While plain radiographs are most commonly used to serially evaluate fracture healing, computed tomography may be used if nonunion is suspected [10].

Several clinical factors are thought to correlate with fracture healing. In a review of fracture healing trials, absence of pain or tenderness at the fracture site during weight-bearing was the most commonly used clinical criteria, while absence of pain or tenderness on palpation or examination was the second most common clinical criteria [11]. Ability to bear weight, walk, and perform activities of daily living are also commonly used clinical criteria. However, some patients with stable internal fixation may not display abnormal clinical findings despite an absence of fracture union. Associated injuries may also confound the ability to use clinical criteria in the assessment of fracture healing.

Do we need a better assessment of fracture healing?

The answer to whether we need a better assessment of fracture healing is an unqualified yes. Fracture healing is a complex, dynamic process with both mechanical and biological components. There is tremendous variability in the characteristics of the patient, the fracture and the treatment all of which impact the time to healing and the chances of a successful repair. Although the end point is dichotomous (healed or not healed) the path to that endpoint may be long and varied, and predicting the final result at an early time point when clinical decisions are required is difficult and not reliable. Current technology allows many disease states to be quantitatively measured, but fracture healing is assessed subjectively, and frankly this assessment is not very good. Better assessment of the early phases of fracture healing would help clinicians better manage patients and to quantitatively assess fracture repair for clinical research.

In current practice fracture healing is judged clinically and radiographically. Clinically assessing the patient is important and provides clues to progress towards fracture healing. A clinician assesses whether pain is improving, whether weight bearing is progressing and whether local reaction at the fracture site is decreasing. However these are at best subjective and usually not definitive. Motion at the fracture site present months after injury is a clear clinical sign of failure of repair, but not all nonunions have gross motion and in the presence of hardware this clinical sign is of limited value.

Imaging is the cornerstone of fracture healing assessment. Serial radiographs, assessed for callus and cortical bridging, provide important information and are the most frequently used assessment of fracture healing. However difficult cases require prolonged observation with multiple sets of images to be certain of progress or failure to progress towards union. It is not uncommon for clinicians to find themselves asking: is there callus? Is it bridging? Is it mechanically sound? Will it become mechanically sound? Can I see it? Is there hardware in the way? Is it progressing? Can I judge it? CT scans add additional information and in current practice are frequently used. But CT is expensive, leads to large doses of radiation and has not been assessed as an early predictor of subsequent union. It provides more three dimensional detail than radiographs but is still an imperfect surrogate to judge how mechanically sound the repair has become.

So our assessments are not very good but they are widely used and accepted in clinics around the world. Why is it important to look critically at the ability to assess fracture healing and why do clinicians need better tools to measure fracture repair? It is because better assessment will improve patient care and will result in better clinical research that will further improve patient care.

Providing clinician's tools to better assess fracture healing in the clinic would directly benefit patient care in many ways. Here are a few examples of the clinical problems that are poorly assessed with current methods. In the early weeks after injury clinicians predict the mechanical strength of the fracture and the fracture fixation construct and prescribe levels of patient function based on these predictions. Initially this judgement is made based on the construct achieved surgically. However after a few weeks has elapsed the progress of the repair process should increasingly contribute to the strength of the fracture and its ability to resist mechanical forces. Patient weight bearing and function need to progress or continue to be restricted based on how the clinician