Challenges and controversies in defining and classifying tibial non-unions

N Ferreira BSc, MBChB, HDip Orth(SA), FC Orth(SA), MMed(Orth)
Tumour, Sepsis and Reconstruction Unit, Department of Orthopaedics, Grey's Hospital, University of KwaZulu-Natal
LC Marais MBChB, FCS Orth(SA), MMed(Ortho)
Tumour, Sepsis and Reconstruction Unit, Department of Orthopaedics, Grey's Hospital, University of KwaZulu-Natal
C Aldous BSc, BSc(Hons), MSc, PhD
Medical Research Scientist, School of Clinical Medicine, College of Health Sciences, University of KwaZulu-Natal

Correspondence:
Dr N Ferreira
Department of Orthopaedic Surgery
Grey's Hospital
School of Clinical Medicine
University of KwaZulu-Natal
Private Bag X9001
Pietermaritzburg
3201
Email: drferreiran@gmail.com
Tel: +27 033 897 3299
Fax: +27 33 897 3409

Abstract

Tibial non-unions not only result in significant physical impairment but also serve as a source of considerable psychological and socio-economic stress for the patient. Unnecessary delays in recognising potential non-unions lead to treatment delays that further exacerbate the morbidities associated with non-unions. Current definitions are not universally accepted and are considered by some to be too esoteric for general use. The lack of clear defining criteria for non-union may result in delays in diagnosis and appropriate management. The most frequently used classification systems currently are more than 30 years old and do not take new knowledge of biology and modern treatment modalities into account.

Key words: tibia, non-union, definition, classification, healing

Introduction

Non-unions are encountered frequently with multiple factors being implicated in their development.[1-7] These include systemic compromise of the host, local condition of the involved limb, specific injury characteristics and iatrogenic factors relating to the management of the initial injury.[1,8-11]

The management of non-unions is challenging and requires more healthcare services than the initial injury.[2,12-14] Non-unions are almost universally associated with delays in diagnosis leading to significant loss of limb function due to muscle atrophy, joint contractures and disuse osteopaenia.[10,13,15-17] These associated findings significantly complicate the management that is often protracted, expensive and may even fail in 20% of cases.[2,14,18-22]

The definition and classification of non-unions should limit the potential protracted course of diagnosis and management. To date, no consensus exists regarding the definition of non-unions and none of the current classifications has proven universally useful.[2,10,13,14,23-25] Most classifications fail to take all aspects of tibial non-union development into account, and more importantly, do not aid in the decision making as to the most appropriate treatment strategy.[12,14] This may result in non-unions being managed on anecdotal evidence that could exacerbate the existing morbidity.

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The ideal definition and classification is elusive and would allow early recognition of a non-union in progress, and provide guidelines to the most effective treatment strategy.

Defining non-unions

> 'Medicine is a science of uncertainty and an art of probability.' Osler[26]

The existing definitions of non-union are more controversial than most other definitions in orthopaedics and medicine and are not universally accepted.[2,10,13,14,23-25] The majority are temporal systems that use time as the sole variable to define the presence of a non-union. The 1986 United States Food and Drug Administration (US FDA) definition, for example, defines non-unions as nine months having elapsed with no progression of union in the preceding three months.[2,27] This definition was not intended for clinical use, but was specifically devised for the testing and comparison of medical devices. It does however remain the most widely used definition of non-union in clinical practice. Other proposed temporal definitions use the absence of radiographic progression of healing between the third and sixth month after injury, six to eight months having elapsed without union, or double the expected union time as a definition for an established non-union.[2,24,25]

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The reason that temporal systems are used to define non-unions is because non-unions are regarded at the extreme end of a time scale continuum, along with normal fracture healing and delayed union. The distinction between normal fracture healing and delayed union is based on the time needed to achieve union, where delayed union occurs after the arbitrary 'expected' time for union.

When non-union is seen in this frame of reference, one can understand why a time variable for the diagnosis of non-union is enforced on the definition. This approach is based on the assumption that all non-unions go through a delayed union phase. Although this might be true for some fractures, where the treating surgeon is unsure of the healing potential, there are definite fracture scenarios where union without surgical intervention is unlikely. Examples would include fractures with segmental bone loss, minimal bone contact, fractures with extensive circumferential soft tissue loss and operatively managed fracture with a fixed gap.

One obvious problem with these stipulative definitions is the erroneous implication that fractures will heal over similar time frames. Multiple factors affect normal fracture union and therefore a large variation in healing time can be expected.[23] Between individuals, for example, several host factors can affect the time to union. These include the age of the patient, where fractures in children can generally be expected to heal twice as fast as in adults.[5] Other host factors affecting union include smoking, malnutrition, HIV infection and pre-existing pathological bone conditions.[6,28-31] Even in the same individual, a wide variation in fracture healing times is considered normal. Upper extremity fractures generally heal faster than lower extremity fractures. Injuries with severe bony and soft tissue damage may take longer to heal, and treatment strategy, aiming for either primary, direct bone healing or secondary bone healing with callus formation also influence the healing time.[6,29,32-34] An average time to union for each anatomical site, fracture configuration and method of treatment, at any given age should therefore be researched. Tibial fractures in adults, for instance, may heal from anywhere between 10 and 25 weeks, depending on the fracture severity and method of treatment.[35]

A further drawback to temporal definitions is the inevitable delay in diagnosis and treatment they cause. It is during this period where most of the morbidity associated with non-unions arises. Prolonged periods of inability to work contribute to financial hardship, which combined with chronic pain and narcotic dependency, places significant psychological stress on patients and their families.[13,20] It is also during this period that most of the muscle atrophy, joint contracture, osteopaenia and complex regional pain syndrome associated with non-unions develop.[18] Fractures treated with internal fixation also frequently lose the race between union and implant failure during this period, resulting in broken metalware or bone destruction that contribute to the surgical difficulties associated with treating non-unions. This time, waiting for a definition to be fulfilled, could be better spent achieving union and supporting functional rehabilitation.

Megas defined non-union as a cessation of all reparative processes of healing without bone union, while Marsh more specifically emphasised the cessation of both the periosteal and endosteal healing responses without bridging.[25,36] These definitions are empiricist explanations of non-unions rather than true definitions. They are teleological and descriptive in nature, and of limited value in clinical practice.

Many authors have suggested more pragmatic, working definitions. Harwood *et al*. defined non-union as symptomatic fractures with no apparent potential to heal without intervention.[2] Jones *et al*. and Brinker *et al*. defined non-union as the point normal biological healing ceases and will not continue without intervention,[9,37] while Wiss *et al*. suggested that the designation of a non-union be made once the surgeon believes the fracture has little or no potential to heal.[27] Although these definitions are not limited by temporal restrictions and more directed toward clinical use, they are however dependent on surgeon experience to predict fracture healing. This drawback often contributes to delays in diagnosis and treatment, particularly when these patients are managed by junior orthopaedic surgeons without the benefit of experience to identify potential non-unions in progress.

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The ideal definition

The ideal non-union definition should not limit or prevent appropriate and timely intervention. The time parameter, however, should not completely be neglected from a comprehensive definition. Some fractures develop non-unions without any obvious predisposition and these non-unions also need to be addressed in the definition.

We suggest the following definitions:

- *Non unus potentia* (potential non-union): any fracture that when taking host factors, injury severity and management into account, has little potential to heal without further intervention.
- *Non unus certus* (established non-union): any fracture that shows no clinical or radiological union in a reasonable time, for that specific injury, host and management strategy.

The rationale for this distinction is the early identification of potential non-unions. Early identification, referral and treatment of these patients might achieve union with simple interventions without the need for complex, expensive surgeries – a saving that is not only monetary in terms of the healthcare system and the patient's personal finances, but also a saving in terms of morbidity, limb integrity and social dependency of the individual patient.

Classification

Classifications in orthopaedics are useful in that they assist in diagnosis, guide treatment, indicate prognosis, and/or assist with research. Very few classifications can do all of these things and often only help with one aspect of management. Although debatable, for the average treating surgeon a classification that prescribes treatment strategy is often the most useful.

The Judet and Judet classification, modified by Weber and Cech in 1976, classified non-unions according to the vascularity of the bone ends.[38,39] The distinction between avascular and hypervascular non-unions was made and a biological cause for non-union development was underlined.[39] The diagnosis was based on strontium-85 uptake at the fracture site to delineate the viability of the bone ends. Bone scintigraphy examinations are not widely used to diagnose non-unions today and are especially difficult to perform in the resource-restricted environment of the developing world. The amount of fracture callus visible on normal radiographs is therefore currently used as a surrogate marker for fracture site vascularity, giving rise to the current terms of atrophic and hypertrophic non-unions.[11,25] Although important, the radiographic appearance of a non-union should not be the only consideration when contemplating the ideal treatment strategy.

Non-union in an avascular setting is explained by insufficient osteogenic potential to affect healing, while hypervascular non-unions are attributed to inadequate stability to allow normal fracture union.[25] Many orthopaedic surgeons use this classification as the basis of non-union management, providing stability for hypervascular (hypertrophic) non-unions, and adding biology in the form of bone-graft for avascular (atrophic) non-unions. Although widely used, not all researchers subscribe to this aetiogenesis of non-union formation in the avascular setting,[40,41] as illustrated by the research of Sun *et al*. who hypothesised the existence of temporally quiescent mesenchymal cells in avascular bone ends.[4] This could explain why certain 'avascular' non-unions may unite in the ideal biomechanical environment without the addition of bone-graft.[42]

A further drawback to the classification proposed by Weber and Cech is the fact that bone loss, limb length discrepancy, angular deformities, rigidity of the non-union's site, previous fixation used or adequacy of fixation is not considered.[39] Each Weber and Cech group, therefore, has multiple potential treatment strategies, depending on these variables. The time required before the described bone end changes are seen on X-ray is also problematic and may lead to delays in diagnosis and management of patients who could benefit from earlier intervention.

The Ilizarov classification attempts to facilitate the selection of the appropriate surgery for a non-union. This system is based on the non-union morphology being stiff or lax, and whether stiff non-unions have any concomitant angular deformities.[43] This classification does not take the whole clinical scenario into account. Host factors, limb length discrepancy and bone loss are not considered, and non-union with internal fixation in situ is not addressed.

The Paley classification specifically addresses tibial non-union.[44,45] It considers bone loss, fracture site mobility, angular deformities and overall tibial length. Although this classification is an excellent advance on other existing classifications with regard to the mechanical attributes of a non-union, it again fails to address non-union biology and host optimisation.

An attempt to address some of these shortcomings was made by Wu *et al*. who developed their protocol to more clearly classify non-unions.[11] A novel addition to this classification was the incorporation of non-unions with internal fixation in situ. These non-unions were designated as either avascular or hypervascular depending on whether the fixation was stable or unstable. Another important aspect in non-union management was also raised, namely the possibility of these non-unions potentially being infected. The active exclusion of infection was emphasised. Management of each group was suggested, being either open bone-graft and intramedullary nailing, bone grafting alone, or bone grafting and implant exchange. The Wu classification successfully addressed the management of non-unions with failed internal fixation, but did not incorporate bone alignment or host optimisation. Automatically designating non-unions with stable fixation as avascular is also not necessarily biologically accurate as fractures fixed in distraction are not always avascular but may develop non-unions due to the healing process not being able to cross the fracture gap.

The Calori Non-union Scoring System (NUSS) has recently been developed[14] and validated[12] to assist surgeons with the complex analysis of non-union surgery. It uses the 'Diamond Concept' where multiple elements are considered in non-union management, including the cellular environment, the growth factors, the bone matrix and the mechanical stability (*Table I*). Each individual factor is scored and then added to give a final score that guides treatment.

Table I: Calori Non-Union Scoring System[14]

The bone		Score	Max. score
Bone quality	Good Moderate Poor Very poor	0 1 2 3	3
Primary injury – open or closed fracture	Closed Open grade I Open grade II – IIIA Open grade IIIB and IIIC	0 1 3 5	5
Number of previous interventions on the bone to procure healing	None <2 2–4 >4	1 2 3 4	4
Invasiveness of previous interventions	Minimally invasive – closed surgery Internal intra-medullary nailing Internal extra-medullary Any osteosynthesis which include bone grafting	0 1 2 3	3
Adequacy of primary surgery	Inadequate stability Adequate stability	0 1	1
Weber & Cech group	Hypertrophic Oligotrophic Atrophic	1 3 5	5
Bone alignment	Non-anatomical alignment Anatomical alignment	0 1	1
Bone defect – gap	0.5–1 cm 1–3 cm >3 cm	2 3 5	5
Soft tissues		**Score**	**Max. score**
Soft tissue status	Intact Minor scarring Previous treatment of soft tissue defect Previous free flap Poor vascularity Presence of skin lesion / defect	0 2 3 4 5 6	6
The patient		**Score**	**Max. score**
ASA grade	1 or 2 3 or 4	0 1	1
Diabetes	No Yes – well controlled Yes – poorly controlled	0 1 2	2
Blood tests: FBC, ESR, CRP	FBC: WCC > 12 ESR > 20 CRP > 20	1 1 1	3
Clinical infection status	Clean Previously infected or suspicion of infection Septic	0 1 4	4
Drugs	Steroids NSAIDs	1 1	2
Smoking	No Yes	0 5	5

This score is an excellent starting point to improve non-union management. It does however need to be improved in terms of factors taken into account. HIV infection and genetic predisposition has been implicated in non-union development but is omitted from the NUSS system.[3,7,46,47] The weight that each factor carries towards the final score is crucial in order to guide appropriate treatment and should be devised through regression analysis. With the current NUSS score, the authors weighted each factors according to the opinions and experience of the senior authors who have tertiary referral non-union practices. Another area that needs to be addressed is the treatment strategy that the final score proposes. The present score only proposes, in broad terms, where and how these patients should be treated.

HIV infection and genetic predisposition has been implicated in non-union development but is omitted from the NUSS system

The suggested treatments include 'standard treatment', 'specialised care' and 'specialised care and specialised treatment'. This provides an indication for junior orthopaedic surgeons of which patients to refer, but does not provide specific treatment guidelines as to what 'specialised treatments' should be offered.

The different approaches and focal points of these classification systems complicate treatment strategy decisions and research into non-union management.[14] Formulating standardised treatment strategies or protocols on existing classification systems is challenging, and might not take all aspects of non-union development and management into account.

The ideal classification

EF Schumacher said that any intelligent fool can makes things bigger, more complex, but it takes a touch of genius and a lot of courage to move in the opposite direction.[48] Unfortunately, we are at a point where classifications and scoring systems for non-unions are becoming more complicated. As more variables are identified that contribute to the development and negatively impact the management of non-unions, more factors are built into classifications and scoring systems. As effective treatment will depend on addressing the host, biological and mechanical factors; all of these need to be incorporated into an encompassing classification system.

Conclusion

Non-union management is resource intensive and technically demanding. Inadequate definitions and suboptimal classification systems often exacerbate the existing morbidities associated with non-unions and may even cause delays in diagnosis and treatment. In order to improve non-union management, definitions that allow the early identification of potential non-unions and a classification system that incorporates all factors identified in non-union development is required.

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