Non-union

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R


3cm

Keypoints

Non-union treatment:

- The host
- Patient expectations
- Principles of treatment = individualized

Definition of non-union is an inexact science:

- Definition of time from fracture (6 months?):
    - large variation in healing time as multiple factors affect healing.
- Definition of healing: when is healing sufficient ?

Diagnosis: non-union

- Clinical: pain, swelling, (mobility)

- X-ray

  Radiographic union score in tibial fractures (*Whelan,* J Trauma 2010):

  - Reliable (*Leow,* Bone Joint Res 2016)
  - Union vs. non-union ?(*Litentra,* J Orthop Trauma 2015)

Score per cortex	Callus	Fracture Line
1	Absent	Visible
2	Present	Visible
3	Present	Invisible

Minimum score: 4

Maximum score: 12

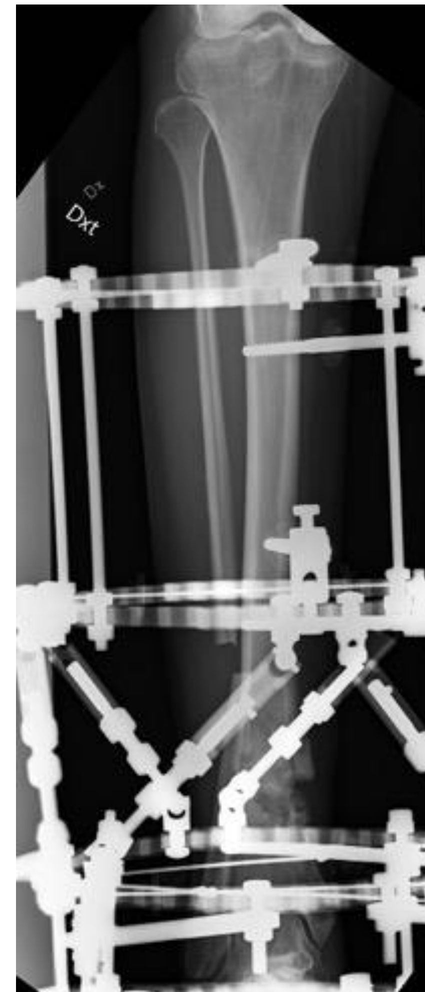
- CT (*Bhattacaryya,* JBJS Am 2006)
- 100% sensitivity
- 62% specificity:
  - risk of intervention on healed fracture

Indication for non-union surgery:

- Symptoms (pain,…) and:
    - When progress in healing will not occur without surgery
    - Earlier surgery if healing will result in significant malalignment

4 months:

- Pain
- 15 varus



Classification: Septic versus Aseptic

Infection screening

- History:
  - wound drainage
  - sinus formation
  - previous infection treatment
- Clinical evaluation
- X-ray
- CRP, (SR, blood-count)

Option

- MRI: no implants
- PET-CT
  - Sensitivity: 95%
  - Specificity: 87%
- Leucocyte scientigraphy /SPECT

Specificity dependent on time from trauma/surgery

20% of aseptic non-unions have positive intra-operative cultures (*Moghaddam et al.* Injury 2015).

Non-union scoring system (*Calori et al.* Injury 2008):

- Non-union personality: Bone, soft tissue, patient (infection, smoking).
- 15 parameters: score from 0-100

The bone

The bone		Score	Max. score
Bone quality	Good	0	3
	Moderate	1	
	Poor	2	
	Very poor	3	
Primary injury – open or closed fracture	Closed	0	5
	Open grade I	1	
	Open grade II – IIIA	3	
	Open grade IIIB and IIIC	5	
Number of previous interventions on the bone to procure healing	None	1	4
	<2	2	
	2–4	3	
	>4	4	
Invasiveness of previous interventions	Minimally invasive – closed surgery	0	3
	Internal intra-medullary nailing	1	
	Internal extra-medullary	2	
	Any osteosynthesis which indude bone grafting	3	
Adequacy of primary surgery	Inadequate stability	0	1
	Adequate stability	1	
Weber & Cech group	Hypertrophic	1	5
	Oligotrophic	3	
	Atrophic	5	
Bone alignment	Non-anatomical alignment	0	1
	Anatomical alignment	1	
Bone defect – gap	0.5–1 cm	2	5
	1–3 cm	3	
	>3 cm	5	

Non-union scoring system: *Calori et al.* Injury 2008

Soft tissues		Score	Max. score
Soft tissue status	Intact	0	6
	Minor scarring	2	
	Previous treatment of soft tissue defect	3	
	Previous free flap	4	
	Poor vascularity	5	
	Presence of skin lesion / defect	6	
The patient		**Score**	**Max. score**
ASA grade	1 or 2	0	1
	3 or 4	1	
Diabetes	No	0	2
	Yes – well controlled	1	
	Yes – poorly controlled	2	
Blood tests: FBC, ESR, CRP	FBC: WCC > 12	1	3
	ESR > 20	1	
	CRP > 20	1	
Clinical infection status	Clean	0	4
	Previously infected or suspicion of infection	1	
	Septic	4	
Drugs	Steroids	1	2
	NSAIDs	1	
Smoking	No	0	5
	Yes	5	

Validation of the Calori non-union scoring system (NUSS)

The classification should guide treatment !

- *Abumunaser and Al-Sayyad,* Orthopedics, 2011

NUSS	Treatment	
< 25	Autograft/IMN/plate	3/3
25-75	Circular fix., vascularized bone graft, free flap, BMP, bone transport	33/33
> 75	Amputation	4/4

Chi-squared test: $p<0.0001$; Contigency coefficient: 0.76

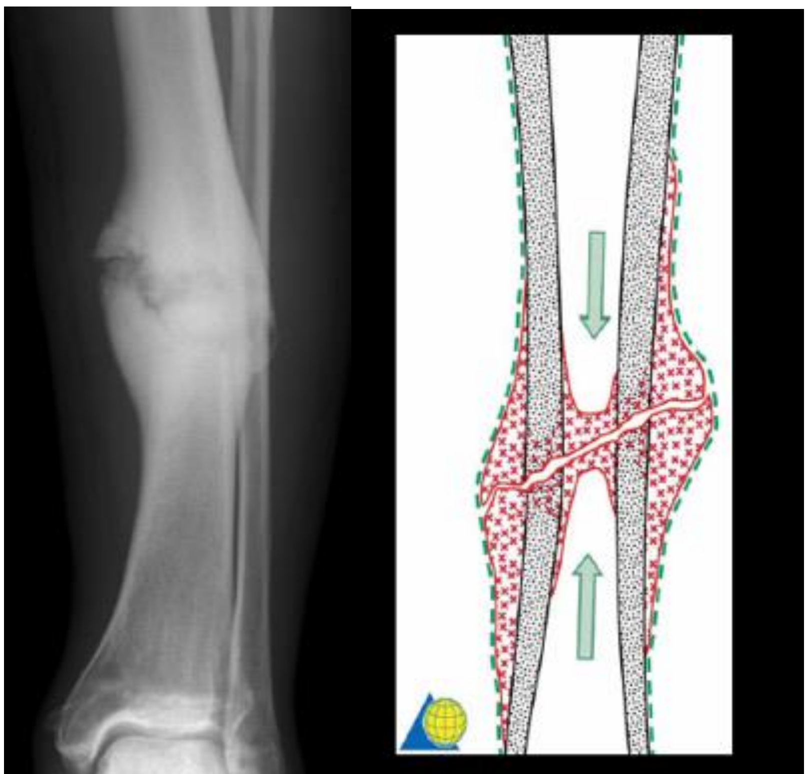
BASIC treatment principles

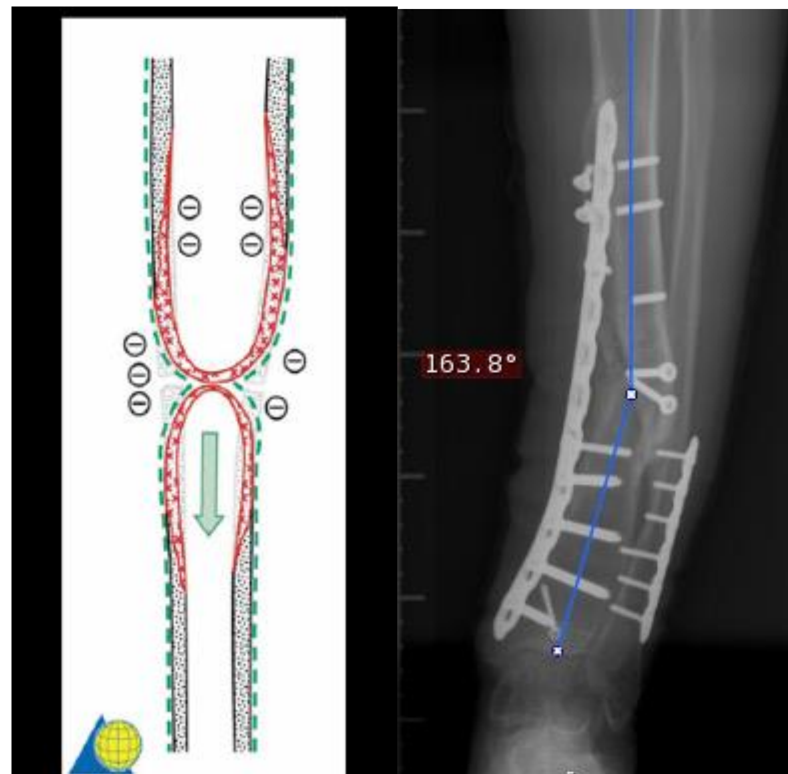
Stability:

- hypertrophic (stiff)

Biology:

- oligotrophic / atrophic (mobile)
- pseudoarthrosis (hypertrophic mobile)





■ ANNOTATION: TRAUMA

A unified theory of bone healing and nonunion

Cite this article: *Bone Joint J* 2016;98-B:884–91.

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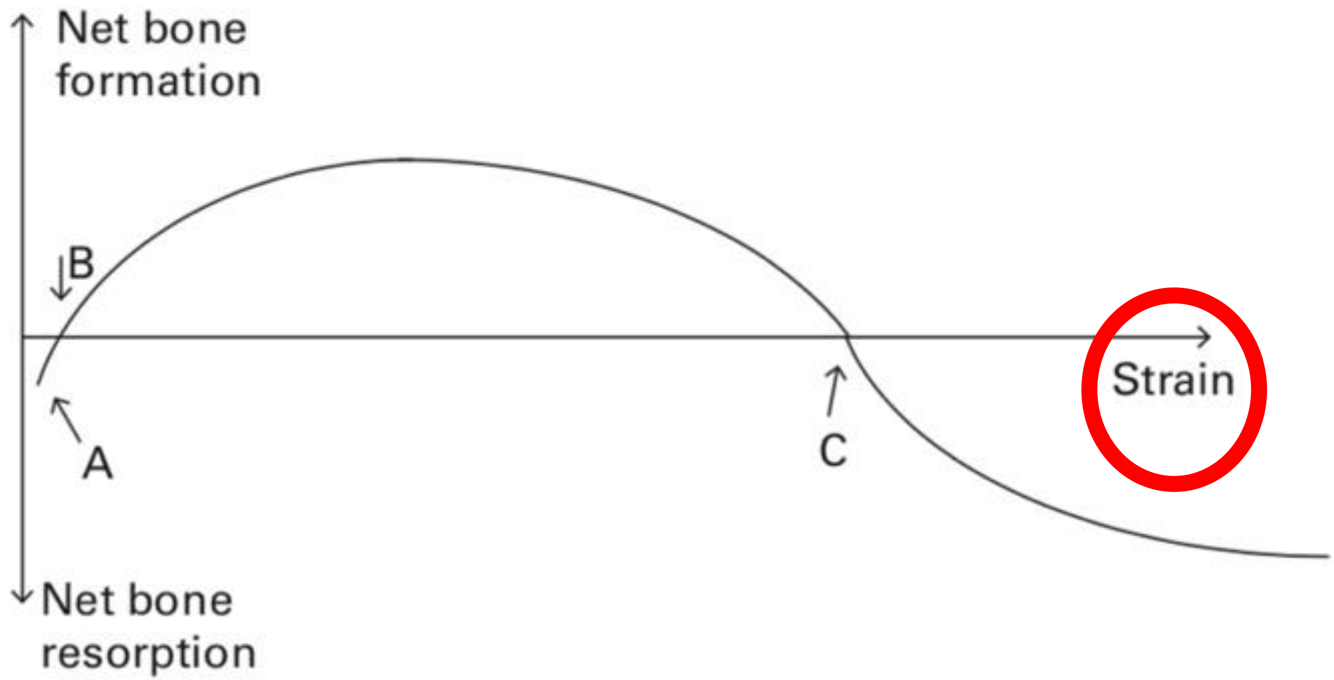
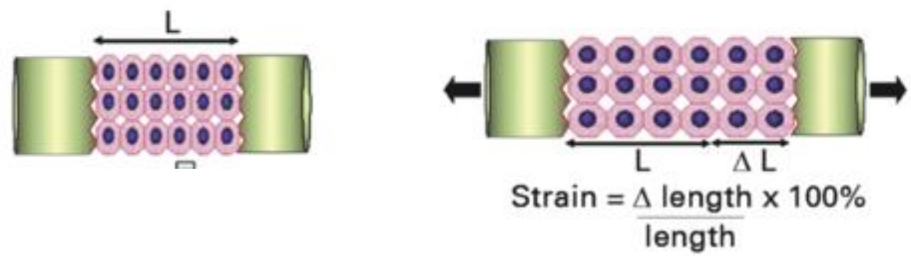
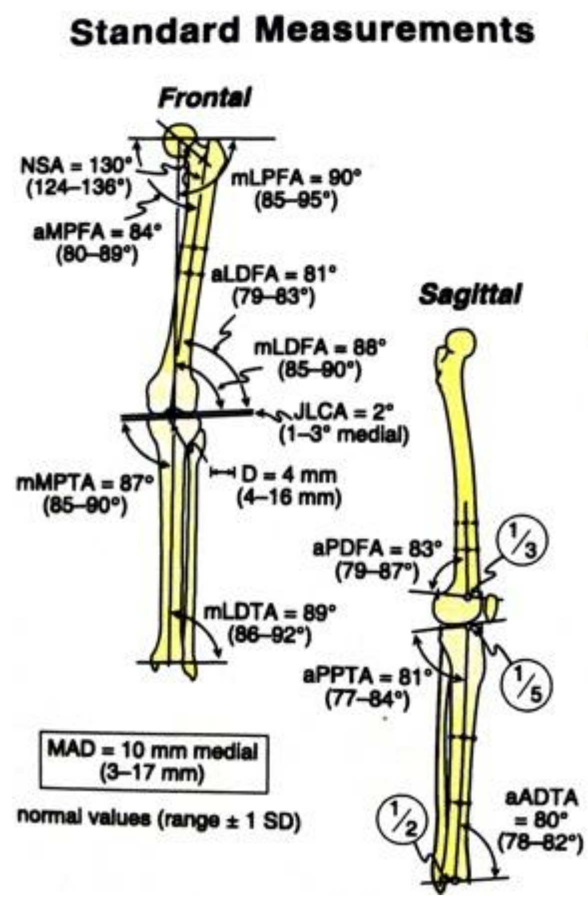




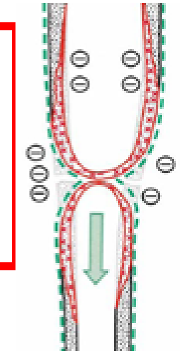
Reduction in Strain

- Reduce external load force
- Reduce inter fragmentary strain
- Correction of axis

1. Mechanical alignment
2. Rotation
3. Limb length (often shortening)



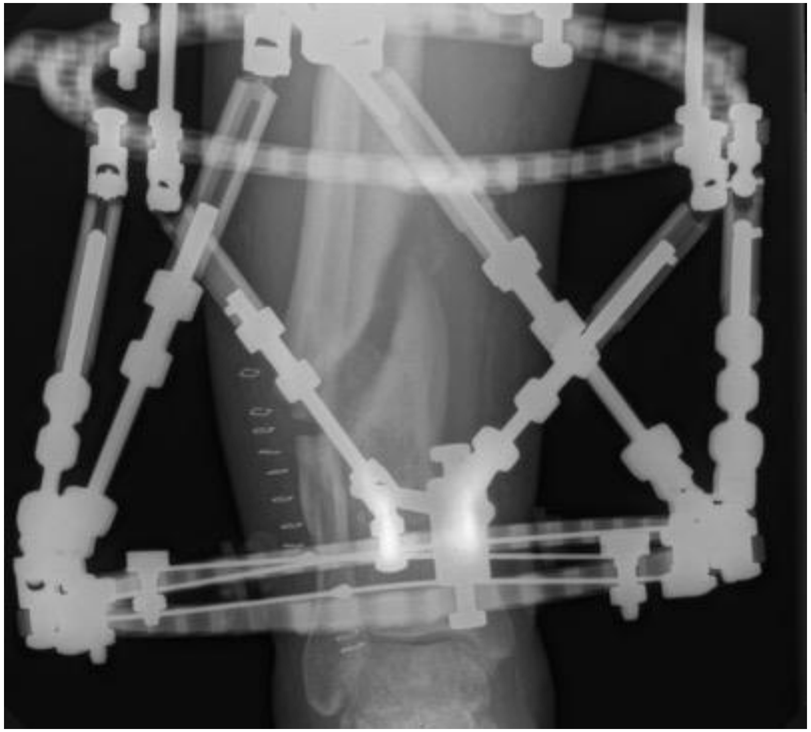
Biological stimulation



Osteo-inductive/osteogenic/(osteoconductive)

- Autograft (gold standard)
- Bone transport
- Masquelet
- BMP/BMA(C)
- Mechano-biology
- Vascularized bone graft
- Free flap (vascularity)

Mechano-biology



Mechano-biology

Management of tibial non-unions according to a novel treatment algorithm

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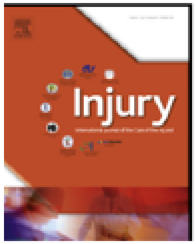
Injury. 2015;46(12):2422-7.



Dr Nando Ferreira

Dr Len Marais

Five pillars of non-union management

Optimisation of modifiable risk factors

Mechanical alignment

Stable fixation

Biological stimulation (mechano-biology)

Early functional rehabilitation

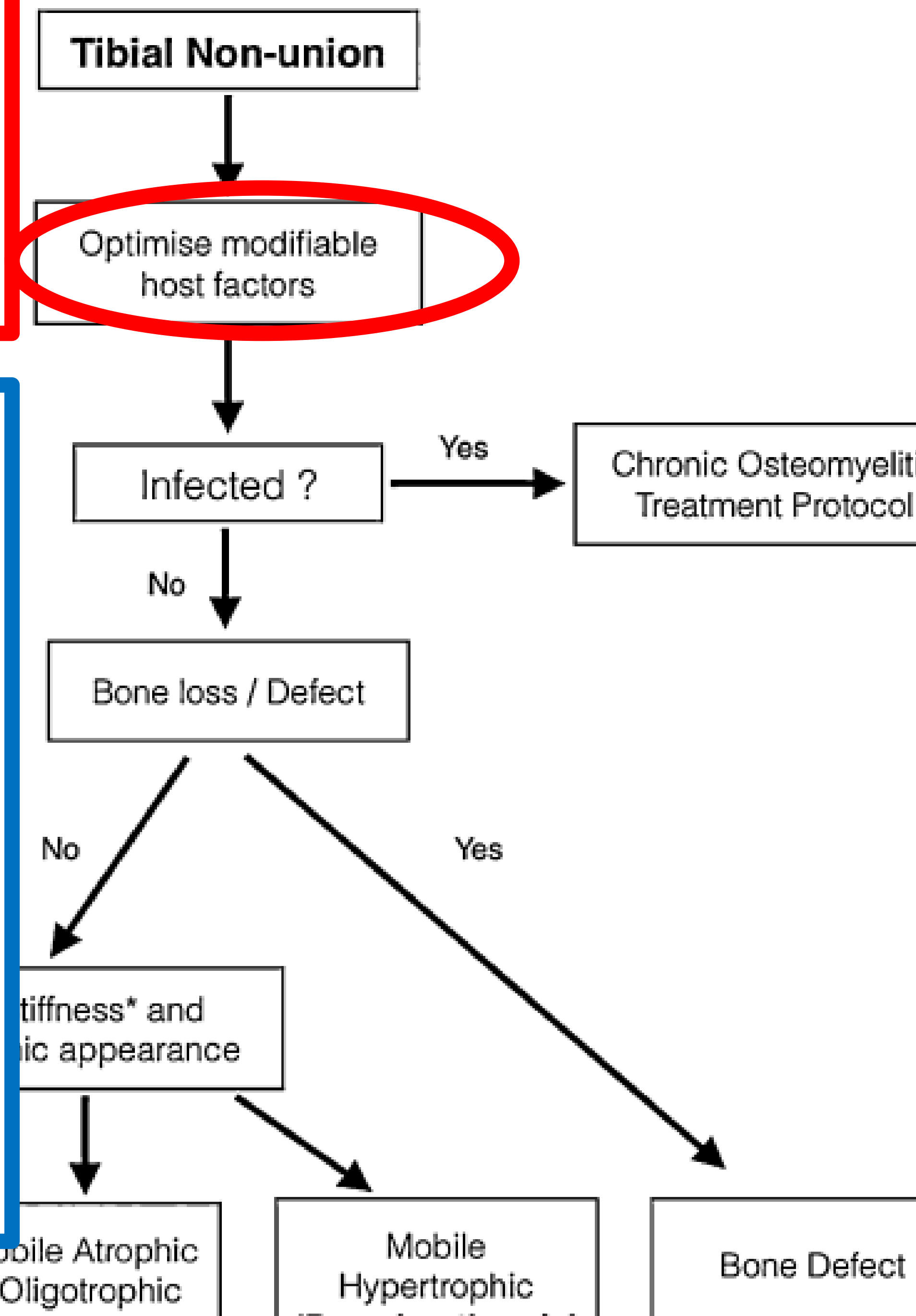
Ferreira and Malais. *Injury.* 2015

Optimise modifiable host factors:

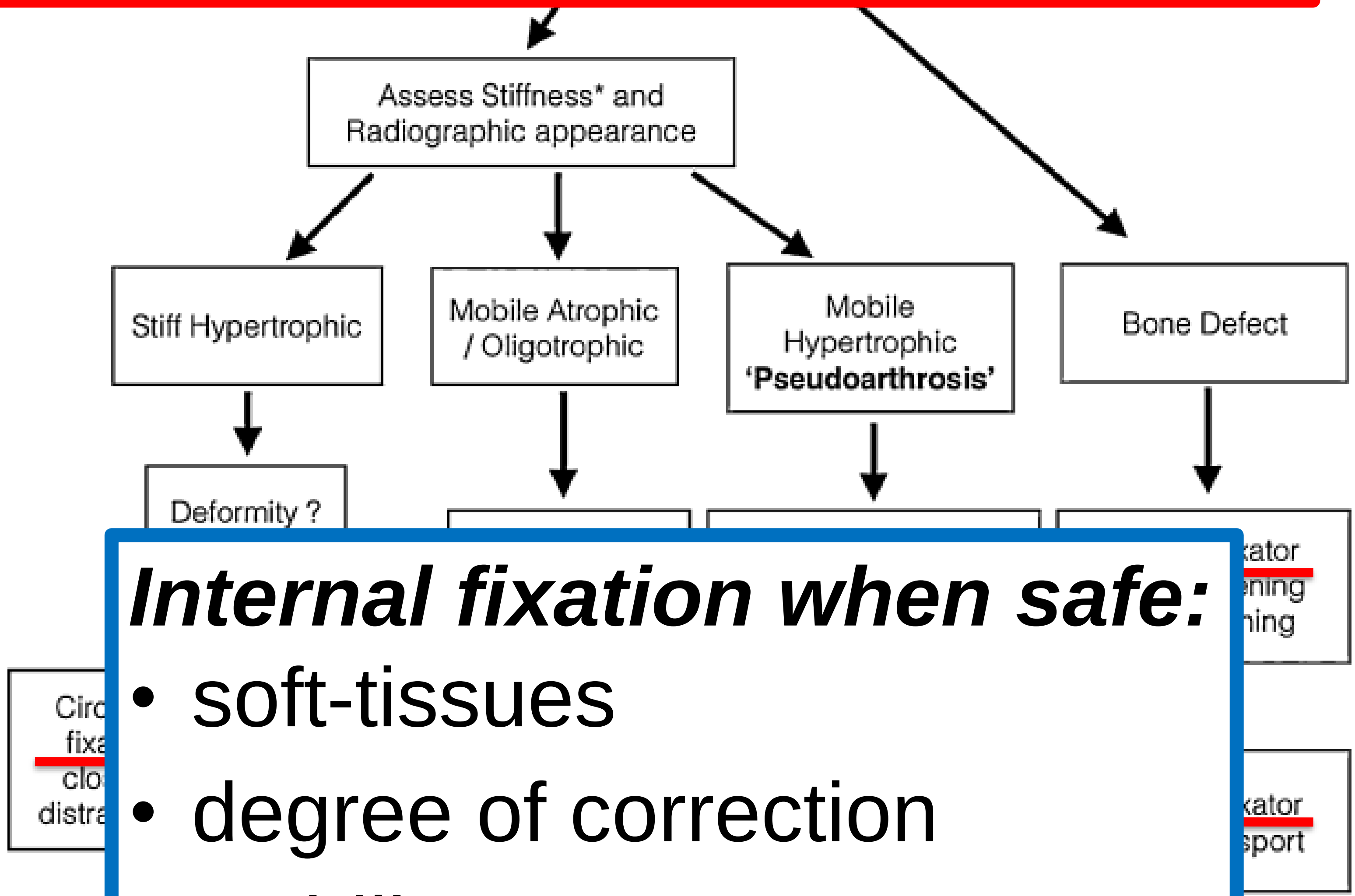
- Smoking
- Diabetic control
- antiretroviral for HIV positive

Additional:

- Anaemia
- Malnutrition
- Endochrine/metabolic:
  - Vitamine D
  - Hypothyoidism
- Medications
  - NSAIDs, steroids, methotrexate, biological anti-rheumatoid



Circular fixator: 122/122 non-unions !

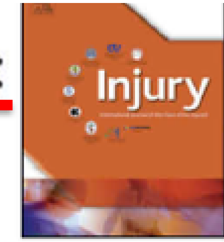


Internal fixation when safe:

- soft-tissues
- degree of correction
- stability

Injury, Int. J. Care Injured 46S4 (2015) S39–S50

Treatment of atrophic tibia non-unions according to 'diamond concept': Results of one- and two-step treatment



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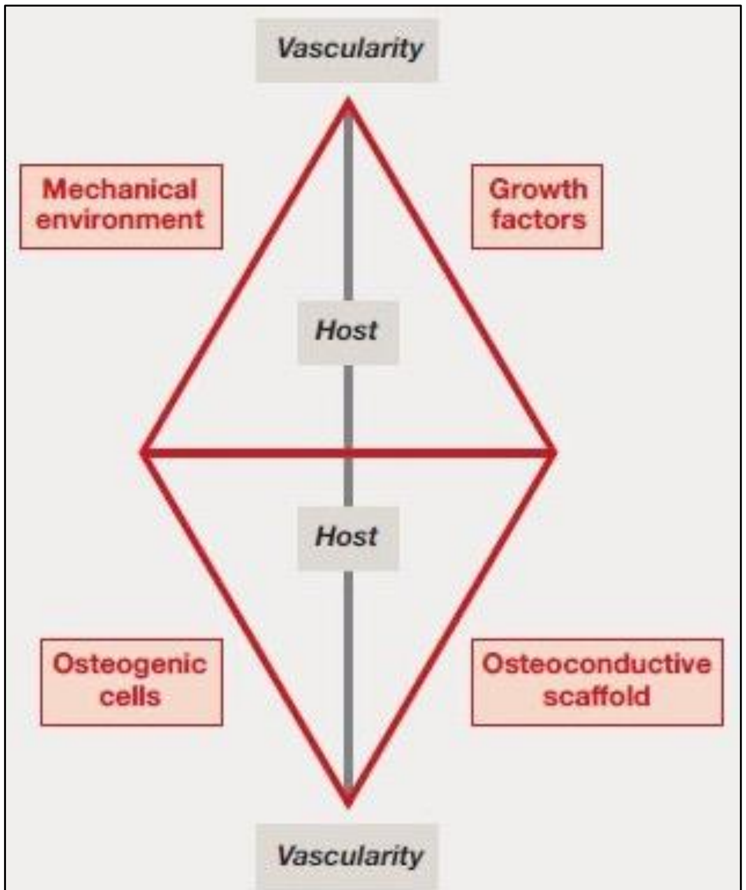
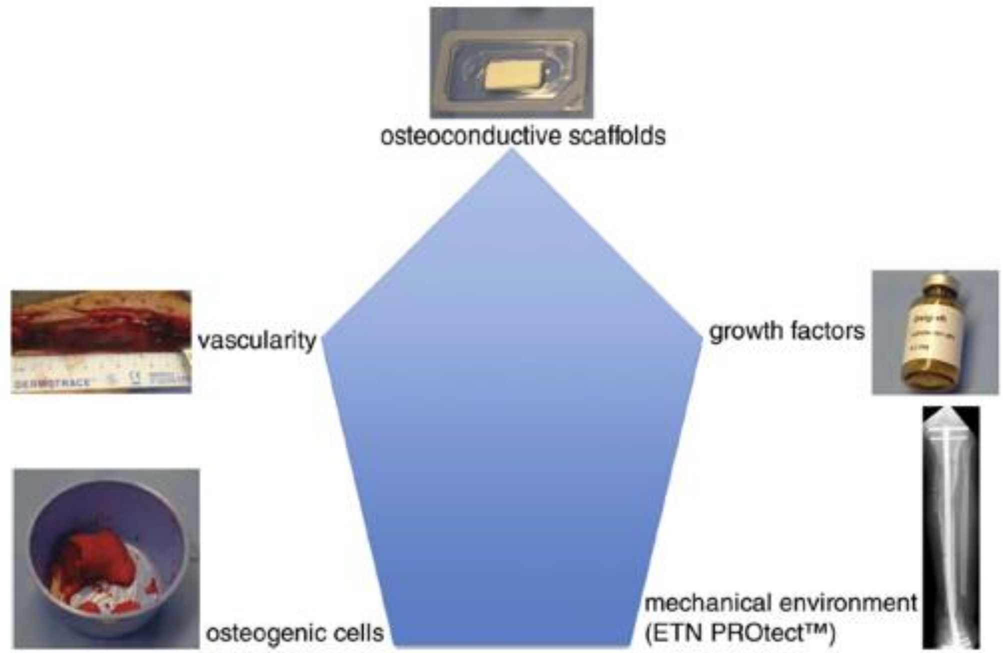
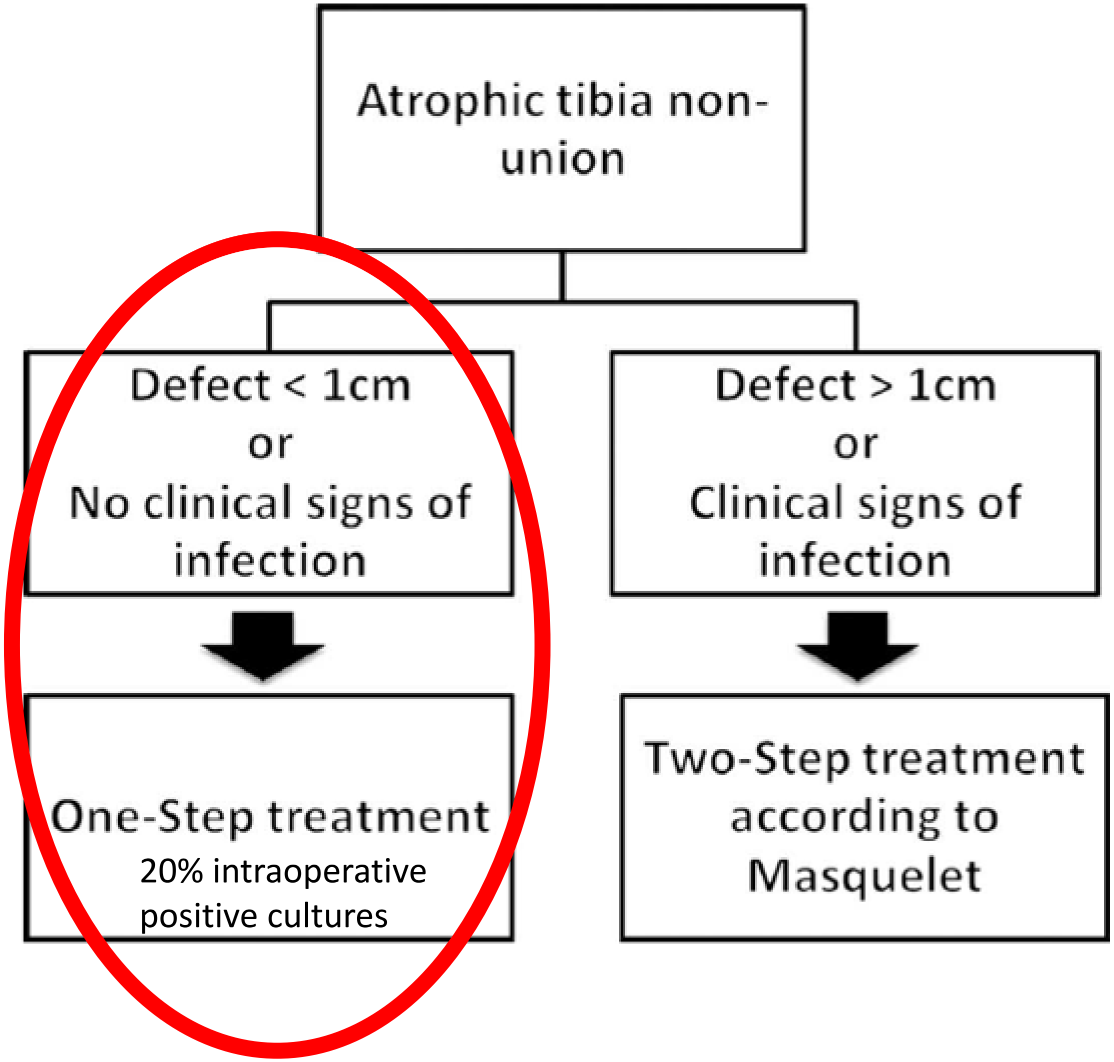




Atrophic tibial non-union: diamond concept

- 49 aseptic tibial non-unions without defect
- 97% follow-up
- NUSS (Calori): 38+/-12
- Treatment:
  - Plate: 65%
  - IMN: 26%
  - Ext. fix. 0%
  - Screws: 2%
- Union: 41/49
- Amputation: 2/49



Moghaddam et al. *Injury.* 2015

Mobile, oligotrophic, non-union

Mobile, oligtrophic, non-union

- Removal of ext. fixation and prox. screws

- 4 weeks in a cast

- Debridement, reaming, gentafleece, IMN, autograft

Majority of patients:

Goal is to achieve fracture union

1. Reduction in symptoms: (pain, swelling)
2. Improvement in function

Minority of patients:

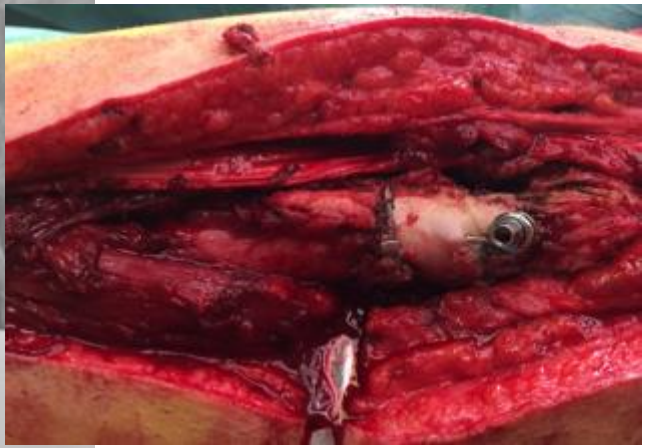
- Amputation
- ”Stable”/”pain-reduced” non-union

Mechanical solution ?

Biological solution ?

Both?

Mechanical Axis Correction *AND* Bone Grafting *AND* Shortening



Summary: ASEPTIC non-union

- Are you sure it is aseptic ?
- Read the patient and the non-union
- Broad armementarium of treatments availaible
- Treatment principles:
  - Five pillars
  - Diamond concept

Thank You

Trauma

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www.efortopenreviews.org

EFORT open reviews

Nonunion – consensus from the 4th annual meeting of the Danish Orthopaedic Trauma Society

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Michael Brix[1]
Mats Bue[3]
Anna Ekman[4]
Nando Ferreira[5]
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Søren Kold[7]
Andrew Taylor[8]
Peter Toft Tengberg[9]
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Bone graft

Need of graft depends on treatment strategy:

- Significant bone defect
- Biology (atrophic non-union)

Seldom alone

Autograft is gold standard

When is bone grafting needed ?

Principles of Nonunion Management: State of the Art

Aaron Nauth, MD, MSc, FRCSC, Mark Lee, MD,† Michael J. Gardner, MD,‡ Mark R. Brinker, MD,§ Stephen J. Warner, MD,§ Paul Tornetta III, MD,|| and Philipp Leucht, MD¶*

Summary: A substantial proportion of fractures can present with nonunion, and the management of nonunion continues to present a challenge for orthopaedic surgeons. A variety of biological, mechanical, patient, and injury factors can contribute to the occurrence of nonunion, and often the cause of nonunion may be multifactorial. Successful management often requires assessment and treatment of more than one of these factors. This article reviews common factors that may contribute to nonunion including infection, impaired biology, and metabolic disorders. In addition, new and evolving strategies for diagnosing the cause and effectively treating nonunion including the diagnosis of infection, metabolic workup, bone grafting, cell-based therapies, and biological adjuvants are reviewed and discussed.

Key Words: nonunion, fracture healing, infection,
graft, metabolic causes of nonunion

(*J Orthop Trauma* 2018;32:S52–S57)

INTRODUCTION

Most operatively and nonoperatively ma
heal, but a considerable number fail to unite.
fractures with nonunion continue to prese
challenge for orthopaedic surgeons. Causes
to the formation of nonunion include biologic
patient, and injury factors, and frequently
nonunion may be multifactorial. Successfu
can often require that multiple factors are addressed concurrently. Common difficulties encountered in the treatment of nonunions include managing infection, addressing impaired biology, and assessing patients for metabolic disorders, which compromise their healing capacity. Successful management of nonunions requires a systematic approach to identifying and addressing these issues, in addition to addressing the mechanical environment.

MANAGING INFECTION IN THE SETTING OF NONUNION

Infection is an important consideration in the workup and treatment of a patient with nonunion. When assessing for infection, consideration should be given to risk factors of infection, including patient factors such as conditions of immune compromise, malnutrition, or smoking status and

reported that the use of simple blood tests (WBC count, erythrocyte sedimentation rate, and C-reactive protein) provided the best predictors of infection, particularly when the results of those 3 tests were used in combination. Their recommendation was that these simple blood tests alone be used for the preoperative assessment of infection.

Intraoperative cultures are the gold standard for the diagnosis of infection and should be obtained from any patient undergoing revision surgery for nonunion. Olszewski et al reported a multicenter series of a large cohort of patients undergoing revision surgery for nonunion who had a negative workup for infection (no clinical signs of infection and negative blood work) but were considered at risk because of the presence of risk factors.[1] Four-hundred and fifty-three at-risk patients had intraoperative cultures sent at the time of revision surgery and 91 patients (20%) had a "surprise" positive culture. The majority (>90%) were treated with culture-specific antibiotics, whereas a small percentage (9%) of results were regarded as contaminants. Most cultures grew coagulase-negative staphylococci. Overall, the results demonstrated that those patients who had a "surprise" positive culture had lower union rates (73% vs. 96%), a higher chance of

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M. Lee is a consultant for DePuy Synthes and receives research support from DePuy Synthes. P. Tornetta has intellectual property rights from Smith & Nephew and publications with Wolters Kluwer. The remaining authors report no conflict of interest.
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BONE GRAFTING: WHAT IS THE IDEAL TYPE?

The mainstay of surgical treatment for nonunions with impaired biology (atrophic nonunion) is autologous bone grafting. Three attributes are essential for successful graft-

When is bone grafting needed ?

■ ANNOTATION: TRAUMA

A unified theory of bone healing and nonunion

BHN THEORY

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This article presents a unified clinical theory that links established facts about the physiology of bone and homeostasis, with those involved in the healing of fractures and the development of nonunion. The key to this theory is the concept that the tissue that forms in and around a fracture should be considered a specific functional entity. This 'bone-healing unit' produces a physiological response to its biological and mechanical environment, which leads to the normal healing of bone. This tissue responds to mechanical forces and functions according to Wolff's law, Perren's strain theory and Frost's concept of the "mechanostat". In response to the local mechanical environment, the bone-healing unit normally changes with time, producing different tissues that can tolerate various levels of strain. The normal result is the formation of bone that bridges the fracture – healing by callus. Nonunion occurs when the bone-healing unit fails either due to mechanical or biological problems or a combination of both. In clinical practice, the majority of nonunions are due to mechanical problems with instability, resulting in too much strain at the fracture site. In most nonunions, there is an intact bone-healing unit. We suggest that this maintains its biological potential to ... theory predicts the healin... morphological characteris... nonunions will heal if the... the need for biological ad...

Cite this article: *Bone Joi...*

If the reader believes that ... advance with level 1 evide... randomised controlled tria... stop reading now. This ar... fied theory that links esta... the physiology of bone ... with those involved in the ... and the development of nonunion.[3,4] This theory was generated by clinicians, for clinicians, after observing the behaviour of bone following a fracture and its treatment. We believe that this theory enhances our clinical thinking by providing a concept to help understand the ways in which a fracture heals, how we influence it as surgeons and how nonunions can be treated.

Theories are a core part of the advancement of science. Although theories represent potential explanations,[5] they are not final answers but derived from experience and incomplete evidence. They are guesses – bold conjectures[6] that encourage thought and experimentation in order to stimulate the generation of further evidence. We have called this the bone healing and nonunion theory (BHN) and present it to

This 'bone-healing unit' produces a physiological response to its biological and mechanical environment which leads to the normal healing of bone. Developing after a bone is fractured, the bone-healing unit is active until healing is complete or has failed (nonunion). This tissue responds to mechanical forces and functions according to Wolff's law,[1] Perren's strain theory[3,4] and Frost's concept of the "mechanostat".[2] Wolff's law of 1892[1] describes the physiological response of normal bone to its mechanical environment during growth and remodelling. Perren's theory of 1978[3] deals with the physiological response of broken bone to this environment and Frost described bone homeostasis as a "mechanostat" responding to variations in the mechanical environment. The key to understanding these concepts is the

...teum when introducing bone graft may simply achieve a similar end. The authors of this paper primarily use mechanical techniques in the surgery of a nonunion and reserve the use of biological adjuncts, including bone graft, to cases where there is significant bone loss.

When is bone grafting needed ?

Depends on treatment strategy:

- Masquelet (always)
- Bone transport (often at docking site)
- Significant bone loss? Graft or shortening ?
- Biology needed: Mechano-biology or graft or both ?
- Seldom only grafting

Autograft is gold standard

Osteogenesis

- Bone formation by viable cells
  - Bone marrow, bone autograft

Osteoinduction

- Bone formation at extraskeletal site by mitogenesis of undifferentiated perivascular mesenchymal cells, leading to the formation of osteoprogenitor cells and osteoblasts
  - Autograft, bone marrow, demineralized bone matrix, BMP's, platelet rich plasma, autologous growth factors

Osteoconduction

- Enhanced bone formation due to a favorable structural environment, where the osteoconductive material serves as a passive scaffold onto which bone is formed.
  - Autograft, allograft, bone substitutes (demineralized bone matrix, NRS cement, trabecular metal, tricalcium phosphate)

Which autograft ?

Iliac Crest Bone Graft versus RIA

The Reamer–Irrigator–Aspirator as a Device for Harvesting Bone Graft Compared With Iliac Crest Bone Graft: Union Rates and Complications

John Dawson, MD, Dirk Kiner, MD,† Warren Gardner II, MD,† Rachel Swafford, MPH,† and Peter J. Nowotarski, MD†*

Objectives: This study was performed to compare patient outcomes after Reamer–Irrigator–Aspirator (RIA)-harvested bone grafting with the current gold standard, either anterior or posterior iliac crest bone graft (ICBG).

Design: Prospective randomized controlled trial.

Setting: Multicenter study at 3 geographically separate Level 1 trauma centers.

Patients/Participants: One hundred thirty-three patients with nonunion or posttraumatic segmental bone defect requiring operative intervention.

Intervention: Patients were prospectively randomized to receive ICBG or RIA autograft. Supplemental internal fixation was performed per surgeon preference.

Main Outcome Measurements: Operative data included amount of graft, time of harvest, and associated surgical costs. The Short Musculoskeletal Functional Assessment and the Visual Analog Scale were used to document baseline and postoperative function and pain. Clinical and radiographic union was the defined end point; patients considered to have failed treatment if they either developed an infection requiring operative treatment or had a persistent nonunion of the grafted extremity.

Results: One hundred thirteen of the 133 enrolled patients were followed until union and included in the final analysis. Intraoperative data showed anterior ICBG to yield 20.7 ± 12.8 (5–60) cm^3 of autograft with an average harvest time of 33.2 ± 16.2 minutes, posterior ICBG yielded 36.1 ± 21.3 (20–100) cm^3 of autograft in 40.6 ± 11.2 minutes, and RIA yielded 37.7 ± 12.9 (5–90) cm^3 in 29.4 ± 15.1 minutes. Anterior ICBG produced significantly less bone graft than either RIA or posterior ICBG ($P < 0.001$). The RIA harvest was completed in significantly less operative time compared with posterior ICBG ($P = 0.005$). At $738, the RIA setup was considerably more expensive than the ~$100 cost of a bone graft tray; however, when compared with posterior ICBG, the longer operative time required for a posterior harvest came at an additional incremental cost of $990–1880, making RIA the less expensive option. Patients were followed for an average of 56.9 ± 42.1 (11–250) weeks. Forty-nine of 57 patients (86.0%) who received ICBG united in an average of 22.5 ± 13.2 weeks; 46 of 56 patients (82.1%) who received RIA healed in an average of 25.8 ± 17.0 weeks. Union rates and time to union were comparable between the 2 procedures. There was no difference in complications requiring reoperation for persistent nonunion or infection at the grafted site, nor there was any difference in donor-site complications. Postoperative follow-up showed that RIA patients had significantly lower donor-site pain scores throughout follow-up.

Conclusions: When compared with autograft obtained from the iliac crest, autograft harvested using the RIA technique achieves similar union rates with significantly less donor-site pain. RIA also yields a greater volume of graft compared with anterior ICBG and has a shorter harvest time compared with posterior ICBG. For larger volume harvests, cost analysis favors using RIA.

Key Words: Reamer–Irrigator–Aspirator, ICG, iliac crest bone graft, nonunion, bone defect

Level of Evidence: Therapeutic Level I. See Instructions for Authors for a complete description of levels of evidence.

(*J Orthop Trauma* 2014;28:584–590)

INTRODUCTION

Although most fractures heal uneventfully, nonunions remain a relatively common problem. Iliac crest bone graft (ICBG), both anterior and posterior, has long been the gold standard source of autograft used in the treatment of nonunions, being osteoinductive, osteoconductive, and providing appropriate cellular elements. However, ICBG has considerable donor-site morbidity,[1–7] and it is, for this reason, alternative autograft options are sought.

Recently, the Reamer–Irrigator–Aspirator (RIA; Synthes, West Chester, PA) has emerged as a potential source of autograft.[8–12] Although using the RIA for autograft harvest is not a new technique, it has only become a more commonplace source of autograft during the last decade, demonstrating success when used for recalcitrant nonunions.[10,13–17]

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Autograft: ICBG versus RIA

TABLE 2. Comparison of Healing Rates in Patients Between ICBG and RIA

	ICBG (n = 57)	%	RIA (n = 56)	%	*P*
Healed	49	86.0	46	82.1	0.616
Nonunion	4	7.0	5	8.9	1.000
Infected	4	7.0	5	8.9	1.000

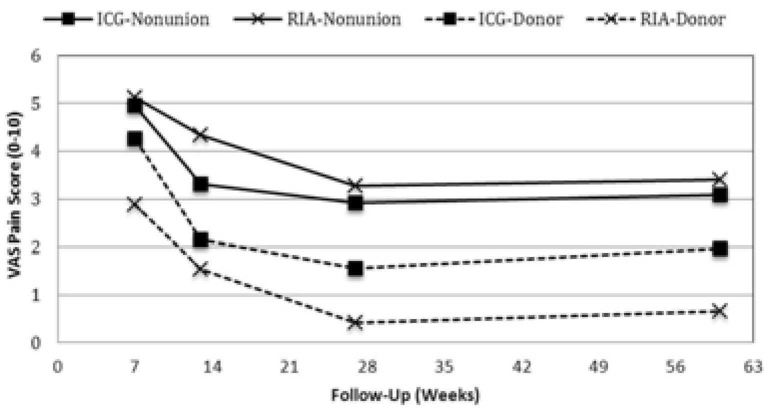

FIGURE 1. Comparison of follow-up VAS pain scores for ICG and RIA: nonunion and donor sites.

Similar union rates.

RIA: less donor site pain.

RIA: greater volume compared

with anterior ICBG

RIA: iatrogenic fracture ?

Take home message

Need of graft depends on treatment strategy:

- Significant bone defect
- Biology (atrophic non-union)

Seldom alone

Autograft is gold standard