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Defining the Mean Angle of Diaphyseal Long Bone Non-Unions – Does Shear Prevail?

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Abstract:

Objectives:

To define the mean angle of a series of diaphyseal non-unions based on radiographic analysis.

Design:

Retrospective cohort study

Setting:

Two level-1 trauma centers

Patients:

One hundred and twenty patients presenting with non-union

Intervention:

A mean non-union angle was calculated from a series of AP and lateral X-rays using a standardised technique. The non-union angle was then estimated in a single plane by considering the greater of the two measured angles. Additional data collected included patient age, sex, non-union site, initial fracture angle and original fracture pattern.

Main Outcome Measurement:

Single plane non-union angle

Results:

The mean angles of all non-union in coronal plane was 42 degrees (SD 17 degrees) and 42 degrees in sagittal plane (SD 18 degrees) and 48 degrees (SD 15 degrees) in single plane. The single plane non-union angle in fractures which were originally multiplanar was steeper to those occurring in originally single plane fractures (p 0.002) although both were close to 45 degrees. There was no significant difference in the non-union angles on sub-group analysis of cohort location, sex or anatomic location.

Conclusions:

This study demonstrates the mean angle of diaphyseal non-unions from long bones of the lower limb approaches 45 degrees. This is noted in all types of fractures and is irrespective of anatomic location or sex. This confirms the hypothesis that shear is likely to play a role in the development of a non-union. This study provides further evidence that non-unions occur primarily due mechanical instability.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

Key words

Non-union, trauma, biomechanics, mechanical; strain; shear; fracture

Background

Diaphyseal non-unions of the lower limb are a clinically significant[1] and costly[2] problem in orthopaedics. Patients with non-union have poor quality of life, including pain, functional limitation and restriction in returning to work[3].

Whilst the process and physiology of normal fracture healing and bone remodelling is well understood [4,5], the pathophysiology of non-union is subject to much debate. Both biomechanical[6] and biological theories[7,8] have been proposed. Non-unions are observed radiographically as hypertrophic or atrophic[9], and while hypertrophic non-unions are thought to be due to mechanical factors, the cause of atrophic non-unions is less well understood. While atrophic non-unions are traditionally defined as avascular [10], they have now been shown to have recovery of vascularisation [11,12] and highly active viable cell types [7] . Other biological factors contributing to the development of a non-union include high-energy injuries causing severe damage to the bone and soft tissue at the time of injury[13], smoking[14], metabolic and endocrine abnormalities[15,16], non-steroidal anti-inflammatory drugs[17] and infection [18].

It is accepted that there is a major mechanical influence on fracture healing and thus the development of non-union and recently, the bone healing and non-union (BHN) theory [19] has been proposed suggesting that biomechanical causes of non-union predominate. Following Perren[5], BHN suggests that a persisting strain above the threshold for bone formation may be the main factor causing non-union. However for a theory to be ultimately accepted, it requires evidence to support it.

The two senior authors have long observed that non-unions tend to develop in a single plane and that this is typically oblique to the load bearing axis of the bone. This is unlikely to be in the true coronal (AP) or sagittal (Lateral) plane and thus a non-union, whilst still occurring in a single three-dimensional plane, will usually display two measurements on a pair of orthogonal radiographs. It is hypothesised non-union formation may be because of the concentration of shear strain in this plane. This study aims to provide evidence in support of this. We investigate the orientation of a large series of diaphyseal non-unions of the lower limb. We also assess whether there is any difference in the non-union angles of different sub-groups, including sex, anatomic location and fracture characteristic.

There are no known studies that have attempted to assess the mean angle of the non-union in relation to biomechanical theories. Clearly if identified as important then surgeons should plan to overcome this shear strain as part of their surgical management of non-unions. We hypothesise that if mechanical issues predominate the majority of non-unions will have a single plane and have a mean angle approaching 45 degrees to the long axis of the bone.

Methodology

Participants

Data consisted of two retrospective cohorts, collected from trauma reconstruction databases at two level 1 tertiary referral trauma centres – Massachusetts General Hospital, Boston, USA and St. George's University, London, UK. All consecutive patients requiring treatment for diaphyseal non-union between June 2014 and May 2018 were included. Patients were included if 18 years of age and older, presented with a diaphyseal fracture non-union in the lower limb. Patients were not included if they had an articular or purely metaphyseal non-union, or did not have a suitable radiograph for analysis. All cases where infection was diagnosed pre-operatively, either clinically such as a draining sinus or radiologically such as radionucleotide imaging, were excluded. Cases where intra-operative sampling was taken and came back positive were excluded. Routine sampling was not taken in the cases of percutaneous hardware exchange for non-union (i.e. exchange nail).

The data collected included patient age, sex, anatomic location of fracture, previous implant and fracture characteristic. Fracture characteristic of the diaphysis was defined as per the 2018 OTA/AO Fracture and Dislocation Classification Compendium[20]; transverse, oblique, spiral, wedge and multifragmentary. Single plane fractures were defined as those that were transverse, oblique or spiral. Multiplanar fractures were defined as those that were either wedge or multifragmentary. Data was collected and analysed in accordance with both centre's governance processes. A data sharing agreement was set up between institutions.

Defining the angle of non-union

Non-unions have typical radiographical characteristics that can be referenced to the anatomic axis of the bone. In order to define the non-union angle a reproducible method of radiographic analysis was developed. A best fit line is drawn between the two places where the non-union exits through the bony cortex (medially and laterally, or anteriorly and posteriorly) as seen on plain radiographs. A line is also drawn along to the anatomic axis of the bone (the longitudinal centre line of the whole diaphysis). The 'non-union angle' is defined as the angle between these two lines. This typically can be calculated in both coronal and sagittal planes from AP and lateral radiographs respectively. For this study we have assumed all AP views to be equivalent to coronal plane non-union and lateral views equivalent to sagittal plane non-union.

If the point of intersection of the non-union through the cortex was ambiguous, the angle was taken on each cortex as the point furthest away from the centre of the non-union. The non-union angle as defined by this method therefore had a range between 0 and 90 degrees.

Figure 1 shows a radiographic example of a tibial non-union with adjacent magnification of image and how measurements were made. *Figure, Supplemental Digital Content* 1 shows radiographic examples of the measurements taken from the PACS software. *Figure, Supplemental Digital Content 2,* demonstrates a schematic of how the measurement of the non-union angle was performed.

Single Plane Non-Union Estimate

A non-union angle can be measured in both the coronal and sagittal plane, but the true angle will lie obliquely between the coronal and sagittal view, in the majority of cases. From basic geometry, rotation of the view about the true non-union angle may reduce the apparent angle until it actually disappears. Similarly, the largest measurement between the coronal and the sagittal non-union measurement logically sits closest to the maximal true angle of the non-union. A ‘non-union angle single plane estimate’ was therefore calculated to take into account the three-dimensional nature of the non-union by taking the largest value of either the coronal or sagittal measurement. *Figure, Supplemental Digital Content 3,* illustrates the three-dimensional nature of a non-union

Statistical Analysis:

Multivariate analysis was performed using a generalised linear model in order to investigate the effects of the explanatory factors of sex, bone type and type of break upon the estimated single plane non-union. Sex, bone (femur versus tibia), and initial fracture pattern (multiplanar versus single plane) were entered as fixed factors. For the purpose of analysis wedge and multifragmentary were coded as multiplanar fractures, with spiral, oblique and transverse as single plane fractures. The assumptions of normality in the fitted residuals were verified. The critical level of statistical significance was 0.05 (5%). No adjustment to the critical level of significance was made due to multiple hypothesis testing. For each category of the explanatory variables, the estimated marginal means of the estimated single plane non-union angle (i.e. mean angle having been adjusted for all other variables in model) are presented. All analyses were undertaken using SPSS Version 26[21] (Chicago, Illinois, United States).

Results

A total of 187 patients presented between June 2014 and May 2018. Overall, 67 patients were excluded because 13 had inadequate radiographs, 12 had an infected non-union, 41 had metaphyseal fractures, whilst one patient was under 18 years of age. After exclusions, 120 patients were included in the study with 43 from the UK and 77 from the USA.

The demographic and clinical characteristics for each cohort, and the two cohorts combined, are shown in *Table 1*. The two cohorts were similar in sex distribution, plus mean age and categorised age. The two cohorts combined consisted of 110 males (62.9%), with a mean age of 46.5 (SD 17.18) years and a majority were 41 to 60 years of age (n=72; 41.1%).

Descriptive statistics for the demographic and clinical features by initial fracture characteristic for the combined cohorts are shown in *Table, Supplementary Digital Content 4*. Non-unions were observed following conservative treatment, as well as treatment following either intramedullary nail, open reduction internal fixation and frame fixation.

Descriptive statistics for the non-union angle measured on coronal, sagittal plane and estimated single plane are shown in *Table 2* for each cohort, and the two cohorts combined. The overall mean non-union angle was 42 degrees on in both coronal and sagittal planes, with a mean of 48 degrees for the single plane estimate.

Non-Unions

A histogram of the estimated single plane non-unions is shown in *Figure 2*. The corresponding normal distribution is shown, with the overall mean (47.9 degrees) indicated. All non-unions occurred in a single plane, irrespective of whether the original fracture was single or multiplanar.

Multivariate Analysis

The results of the multivariate analysis using a generalised linear model in order to investigate the effects of the explanatory factors of sex, bone type and type of break upon the estimated single plane non-union are shown in *Table 3*. Following adjustment for confounding, the multiplanar fractures, compared to the single plane fractures, had a statistically significant steeper single plane non-union angle (54.1 versus 45.1 degrees; *P*=0.002). There were no statistically significant differences between the cohorts (*P*=0.854), sexes (*P*=0.554) or bones (*P*=0.827).

Discussion

We present the largest reported multicentre analysis of the radiographic orientation of diaphyseal long bone non unions. As far as the authors are aware, this is the first study to try to establish the geometry of non-unions based off radiographs. This study demonstrates that non-union angles appear centered around 45 degrees from the anatomic axis of the bone. The finding of 45 degrees supports a biomechanical theory of non-union given that shear is the plane where strain is highest in response to any given load.

There was no significant difference in the mean non-union angles observed between the two international cohorts. There was no difference noted in the sub-groups of sex and bone type. This provides further evidence that a biomechanical model is dominant over biological variations from geography and sex. While the femur and tibia are subject to different biomechanical loading regimes, these do not appear to significantly affect where the plane of non-union forms.

Perren's strain theory [5] dictates that strain determines the nature of cellular differentiation and the resulting tissue that forms in a fracture gap. Strain is defined as a change in length of a material at a given mechanical load and fracture healing requires a low strain environment to occur. Perren suggested that lamellar bone typically requires less than 2% strain to form, while woven bone could tolerate strain up to 10%. If the strain is higher than this then granulation tissue will form instead of bone. Subsequent studies have confirmed similar mechanical factors that affect the tissue formed following fracture [22] [23]. Biomechanical theories in non-union suggest that following a fracture, bone healing will typically transition through different types of tissue that become gradually stiffer. As the overall construct becomes stiffer the strain environment is reduced enough to allow eventual bony union.

Shear strain refers to a plane of strain that occurs perpendicular to the axis of the bone. As with other types of strain, it occurs due to stress being applied over a structure, where stress is defined as the force per unit area (N/m2). Shear strain is related to shear stress according to the stiffness or Young's modulus of the material. Different magnitudes of shear occur throughout different planes with reference to the anatomical axis of the bone. For any given load, the maximal strain occurs at 45 degrees to the application of that load [24]. Therefore, strain at a plane at 45 degrees to the long axis of the bone - in shear.

The study shows a peaked distribution curve rather than a single angle at which all non-unions occur. This implies that shear is part of the problem, but not the sole driver. Variation in non-union angle may occur due to biomechanical and biological reasons. High strain environments can exist outside of the shear plane which could give higher or lower non-union angles. The plane of the primary fracture must clearly have an influence, as will biological factors, which can cause a non-union in any plane. Given the peak of the curve exists around 45 degrees, this study lends evidence that non-unions have a variety of causes, but biomechanical models dominate.

All non-unions occurred in a single plane, irrespective of whether the original fracture was single or multiplanar. By definition, multiplanar fractures will have multiple initial fracture planes. If a multiplanar fracture fails to heal, clinical experience illustrates that it commonly heals down to one residual plane which forms the non-union. In these cases, the initial fracture environment strain is shared amongst all the fracture planes. Since the fracture planes heal at different rates, the strain will end up being concentrated on one fracture plane. In clinical practice, and in the experience of the senior authors, the resultant non-union tends to be in the oblique plane. This approximates 45 degrees to the axis of the bone where we hypothesise the strain is concentrated and too high. If initially single-plane fractures go to non-union, the non-union has to occur in a similar plane to that of the initial fracture. If this plane is oblique perhaps this increases the chance of non-union by the same mechanism as above.

Multiplanar fractures have an interesting role to play in the formation of non-unions. While we have noted that the mean angle was still close to 45 degrees, it is unclear why the mean angle of multiplanar fractures is greater than single-plane fractures. We suggest that given the variety of fracture planes available in a zone of comminution, it is likely that the one most susceptible to excess strain may form the non-union. Multiplanar fractures may occur in the context of higher energy injuries and these co-existing soft tissue injuries may affect the biological and strain environment as well.

This study does have some limitations. While the method of radiographic analysis was standardised in terms of method, it has not been validated. However, it used a validated line for the anatomical axis, and a standard parameter that was easy to assess parameter – where it crossed the cortex. Further research is required to assess intra-observer reliability.

The imaging itself was not standardised. While an experienced radiographer is likely to be consistent in reproducing an AP or Lateral image, it is accepted that the images are not all exactly AP or lateral. With reference to this study AP and lateral and indeed coronal and sagittal are arbitrary constructs. In reality the non-union plane is 3 dimensional. The single plane angle, using the greater of the two measurements, is only an estimate and provides a best guess of the plane of the non-union. Further studies could evaluate the nature of the non-union through cross sectional imaging.

The study only included adult diaphyseal, lower limb fractures. The upper limb and metaphyseal areas could be subject to different forces, paediatric bone has different biomechanical properties, and as such the results cannot be generalised to all non-unions. Further research is required in these areas.

This study only investigated non-unions. Broader research could aim to incorporate a control group of diaphyseal fractures that go to heal. This could also include calculating the relative risk of non-union for multiplanar and single plane fractures. The fact that the single plane non-unions had a mean closest to 45 degrees is perhaps indicative that it is these initial fracture types (ie those closest to 45 degrees) are a risk factor for developing a non-union.

This study has observed the macroscopic architecture of a non-union over the whole of the diaphysis. Given strain environments occur down to a microscopic level, the exact morphology of a non-union could be made up of many individual fracture angles. Closer, microscopic analysis of non-unions may show a saw-tooth type pattern made up of 45 degree angles that, when aggregated, appear to run transversely. This could provide further reason for variability.

Implications:

If we understand the biomechanical nature of a non-union even better, then we can employ surgical strategies to address the problem with more confidence. To reduce strain surgeons should seek to make stiffer constructs. An example of this is application of interfragmentary screws over oblique fractures in conjunction with intramedullary nailing. This can provide better compression, reduced strain and could be used as a method of treating non-unions or potentially in the initial treatment of fractures.

Conclusions

This study demonstrates the mean angle of diaphyseal non-unions of the long bones of the lower limb approach 45 degrees. This is noted in all types of fractures and is irrespective of sex or anatomic location. This confirms the hypothesis that shear is likely to play a role in the development of a non-union. It provides further evidence that non-unions occur primarily due mechanical instability. Further research is required to reference non-unions compared to fractures that go on to heal and to evaluate the three-dimensional nature of non-unions.

Other Information:

No funding was received for this study

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Characteristic	Total Sample (n=120)	Cohort XX1 (n=77)	Cohort XX2 (n=43)
Sex			
Male	76 (63%)	48 (62%)	28 (65%)
Female	44 (37%)	29 (38%)	15 (35%)
Age (years)			
Mean (SD)	46 (17)	45 (17)	46 (17)
Median (LQ : UQ)	45 (30 :57)	44 (33 :57)	47 (29 : 57)
Minimum: Maximum	19 : 82	19 : 81	23 : 82
Categorised Age			
≤ 40 Years	46 (38%)	28 (36%)	18 (42%)
41 to 60 Years	49 (41%)	34 (44%)	15 (35%)
≥ 60 Years	25 (21%)	15 (19%)	10 (23%)
Bone			
Femur	62 (52%)	39 (51%)	23 (53%)
Tibia	48 (48%)	38 (49%)	20 (47%)
Previous Implant			
Plate	20 (17%)	8 (10%)	12 (28%)
Nail	73 (61%)	54 (70%)	19 (44%)
Frame	7 (6%)	0	7 (16%)
None	7 (6%)	4 (5%)	3 (7%)
Other	13 (11%)	11 (14%)	2 (5%)
Initial fracture pattern			
Single Plane	*54 (45%)*	*33 (43%)*	*21 (49%)*
Transverse (<30 degrees)	23 (19%)	16 (21%)	7 (16%)
Oblique (>30 degrees)	23 (19%)	15 (19%)	8 (19%)
Spiral	8 (7%)	2 (3%)	6 (14%)
Multiplanar	*64 (55%)*	*44 (57%)*	*20 (47%)*
Wedge	26 (22%)	24 (31%)	2 (5%)
Multifragmentary	38 (33%)	20 (26%)	18 (42%)

Table 1. Descriptive statistics for the demographic and clinical features for the two cohorts combined, plus each cohort separately. Figures are frequencies and percentages (unless otherwise stated). Percentages are within the cohorts combined, and within each cohort. Two patients did not have their initial fracture characteristic recorded.

Characteristic	Total Sample (n=120)	Cohort XX1 (n=77)	Cohort XX2 (n=43)
Non-Union Angle AP (degrees)			
Mean (SD)	42 (17)	43 (16)	40 (18)
Median (LQ : UQ)	42 (31 : 55)	43 (32: 55)	41 (26 : 57)
Minimum: Maximum	4 : 74	10 : 74	4 : 71
Non-Union Angle Lateral (degrees)			
Mean (SD)	42 (18)	42 (18)	42 (19)
Median (LQ : UQ)	45 (28 : 56)	45 (28 : 55)	44 (26 : 57)
Minimum: Maximum	0 : 78	0 : 71	4 : 78
Non-Union Angle Single Plane Estimate (degrees)			
Mean (SD)	48 (15)	48 (13)	47 (18)
Median (LQ : UQ)	49 (38 : 60)	49 (41 : 59)	48 (33 : 62)
Minimum: Maximum	10 : 78	21 : 74	10 : 78

Table 2. Descriptive statistics for the outcome measure of the non-union angle measured on the AP and lateral views and single plane estimate.

Explanatory Factor	**Model Estimates**	***P*-value**
Cohort MGH SGH	 n=77, mean=49.9 (SE 1.99) n=41, mean=49.3 (SE 2.49)	 *P*=0.854
Sex Male Female	 n=74, mean=48.7 (SE 2.29) n=44, mean=50.5 (SE 2.36)	 *P*=0.554
Bone Femur Tibia	 n=61, mean=49.3 (SE 2.05) n=57, mean=49.9 (SE 2.42)	 *P*=0.827
Fracture Type Multiplanar Single Plane	 n=64, mean=54.1 (SE 2.33) n=54, mean=45.1 (SE 2.18)	 *P*=0.002

Table 3. Results of multivariate analysis using generalised linear model in order to investigate the effects of the explanatory factors upon the estimated single plane non-union angle. The means shown are the least squares means of the estimated single plane non-union angle i.e. those after having adjusted for all other factors in the model.

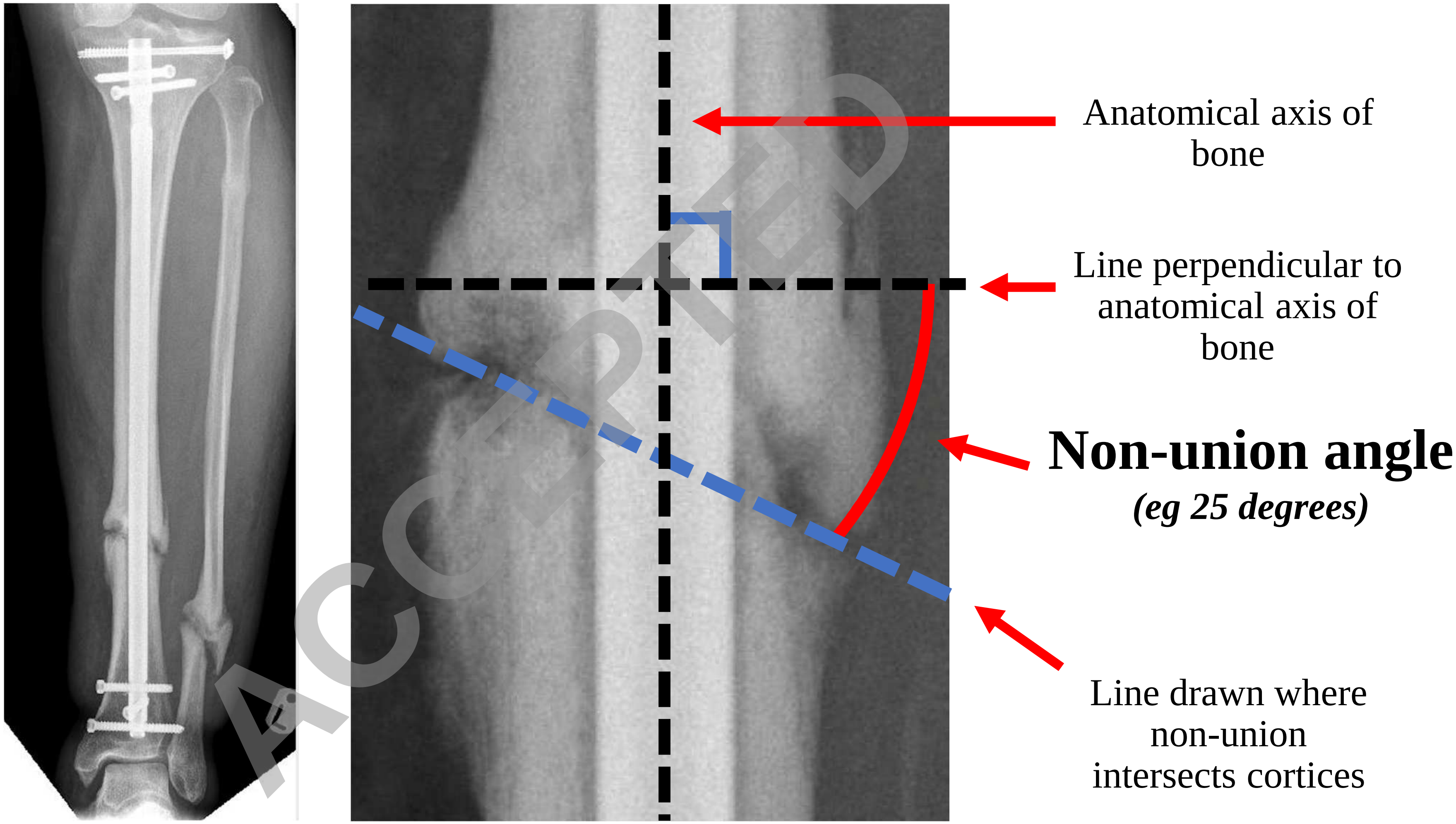

Figure 1: Radiographic example of tibial non-union with adjacent magnification of image demonstrating methodology used to measure *non-union angle*

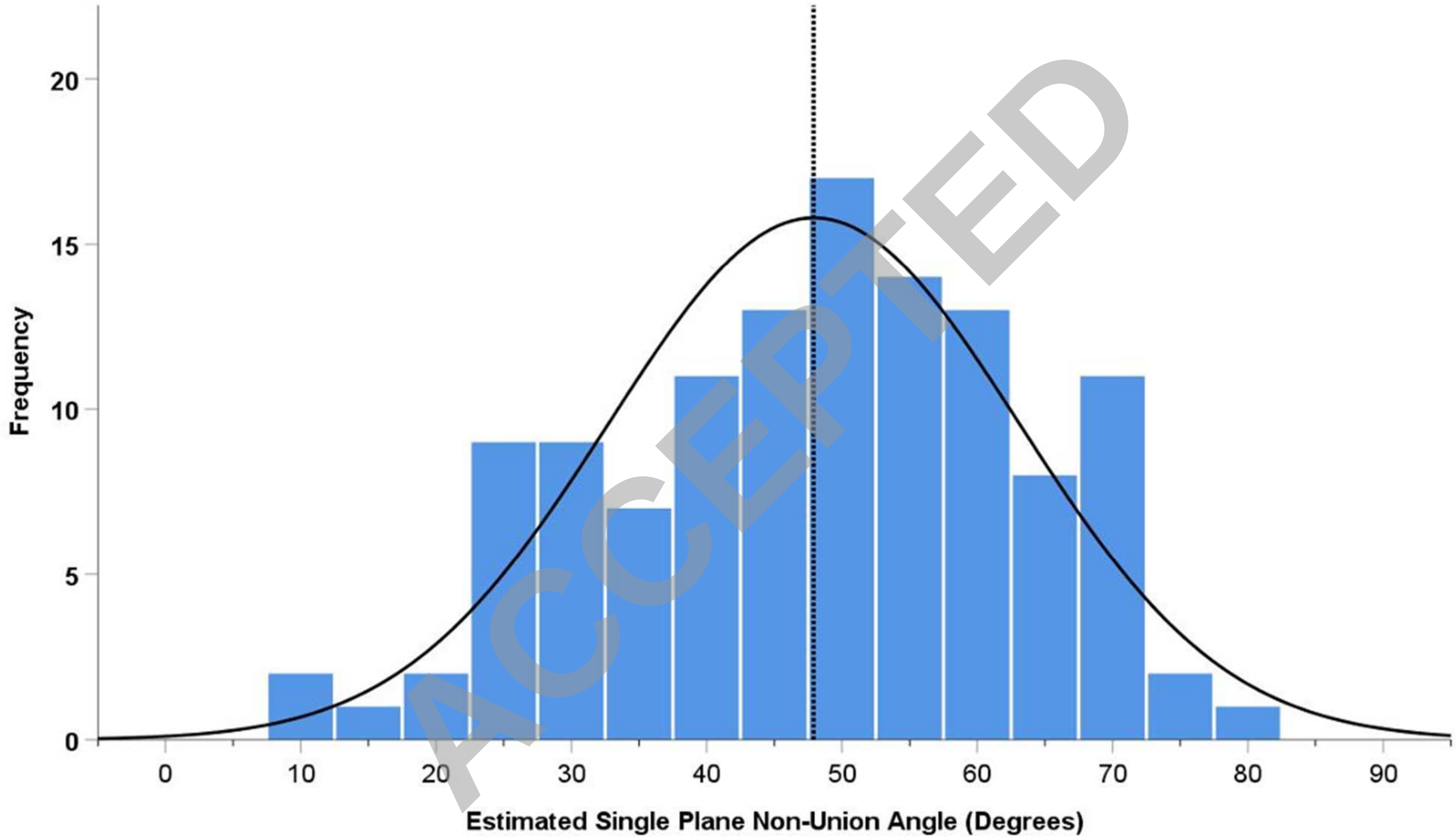

Figure 2: Histogram of the estimated single plane non-union angles