Original Article

NON-UNION OF TIBIAL SHAFT FRACTURE: FRACTING SCORE ANALYSIS IN A RETROSPECTIVE MULTI-CENTER STUDY

D. Quarta[1*], M. Grassi[1], G. Lattanzi[1], D. Potena[2], A. D'Anca[2], A. Gigante[1]

[1]Clinical Orthopedics, Department of Clinical and Molecular Science, School of Medicine, Università Politecnica Delle Marche, Ancona, Italy;
[2] Department of Information and Engineering, Università Politecnica Delle Marche, Ancona, Italy

**Corresponding author:*
Davide Quarta, M.D.
Department of Clinical and Molecular Science,
School of Medicine,
Università Politecnica delle Marche,
Ancona, Italy
e-mail: davide.quarta18@libero.it

ABSTRACT

Delayed union, malunion and non-union are serious complications in the healing of fractures. Predicting the risk of non-union before or after surgery is challenging. We analyzed FRACTING score for each patient. The aim of this study was to find out if this score is accurate to predict this complication.

We collected tibial shaft fractures undergoing surgery from January 2016 to December 2020 in three different trauma hospitals. In a retrospective multicenter study, we considered only fractures treated with intramedullary nailing, calculating FRACTING score at the time of definitive fixation.

Of the 130 patients enrolled, 89 patients (68.4%) healed within 9 months and were classified as union, 41 patients (31.5%) healed in more than 9 months or underwent other surgical procedures and were classified as non-union. For each patient, FRACTING score was calculated, and based on the clinical outcome the score was compared in a statistical analysis.

FRACTING showed a good performance predicting the non-union risk. From our data is clear that male gender and greater age is a risk factor for non-union.

KEY WORDS: *trauma, bone, tibial fracture, nonunion, scores, prediction model.*

INTRODUCTION

Bone fracture healing is one of the most important and debated issues in olden and modern orthopedics. “Pseudarthrosis” (the Greek stem "pseudo-" means false and "arthrosis" means joint) is nowadays a less common word than “delayed union” and “non-union”, which constitute two variations of it. Although in the literature there are a lot of different definitions (1), we speak of a delayed union when the fracture healing time does not correspond with period of time expected for a specific site and type of fracture. Instead, “non-union” is the failure of a fracture to heal after twice the period of healing time (which usually takes at least 6 months after trauma).

Non-union is currently defined (according to the Food and Drugs Administration - FDA) as a fracture older than nine months that presents no signs of healing in the last three months (2). Conversely, Brinker et al. define non-union as a fracture that, in the opinion of the treating physician, has no possibility of healing without further intervention (3).

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Delayed union or non-union represents one of the most challenging complications for modern orthopedics. Among the long bone fractures, non-union rate is estimated to be between 5% and 10% (4).

However, these data could raise in the next future because of the increasing high-energy trauma and the improvement of Basic Life Support (BLS) techniques. These types of trauma often involve diaphyseal fractures of several limbs, serious muscle and tendon injuries as well as causing damage to the parenchymal organs (4, 5).

A recent population-based study from Scotland estimated the incidence of non-union at 13 per 1000 pelvis and femur fractures per year, 30 per 1000 humerus fractures per year, and approximately 55 per 1000 tibia and fibula fractures per year (6). The management of these long fractures is complex, and the risk of mal-union, delayed union and non-union remains high. That contributes to considerable patient disability, reduced quality of life, and significant treatment costs (5).

Naturally, delayed union and non-union (like fracture healing) are multi-factorial events, so their complications are not easy to predict. Many risk factors contribute to non-union. Calori et al. identified gender, age, diet, diabetes, osteoporosis, muscular mass, smoking and alcohol habits, nonsteroidal anti-inflammatory drugs (NSAIDS) use, fracture personality, type of fracture, exposure, infection, multiple fractures as parts of this multi-factorial events (7).

Nevertheless, some studies in the literature trying to foresee the risk of non-union with some different score, calculated after the surgical treatment.

These scores aim to quantify non-union high-risk patients (8-10). We analyzed only FRACTING score, in order to find out if this score is accurate to predict the risk of non-union in tibial shaft fracture. The aim of this study was to evaluate in a group of patients, the risk of non-union after the surgical treatment of tibial fracture.

MATERIAL AND METHODS

We retrospectively reviewed all consecutive cases of tibial shaft fractures undergoing intramedullary nailing surgery from January 2016 to December 2020. We collected data from three different hospitals: Azienda Ospedaliera Universitaria delle Marche (via Conca 71, Ancona (AN), 60126, Italy), Ospedale Carlo Urbani Jesi (via Aldo Moro 52, Jesi (AN), 60035, Italy) and Azienda Ospedali Riuniti Marche Nord, Pesaro (piazzale Cinelli Carlo 1, Pesaro (PU), 61121, Italy).

All patients gave their informed consent at the enrolment and were included in a retrospective observational database. Both pre- and post-operative data, including sex, age, type of surgical procedure, and others more were collected from the hospital database and patient medical records. Declaration of Helsinki and Guidelines for Good Clinical Practice were applied.

We included open and closed tibial no-articular fractures (42-A-B and C, 43-A) according to AO/OTA classification (11) in patients older than 18 years. We excluded patients that reported articular fractures, periprosthetic fractures, open fractures IIIC according to Gustilo et al. classification (12) as well as patients with active neoplasia, doubt of pathological fracture and genetic disorders with bone involvement (i.e. Paget, Osteogenesis imperfecta). Pregnant women and patients younger than 18 years were excluded. Patients who underwent amputation or who died because of complications related to the trauma were also excluded from the study. We excluded the polytrauma patients according to the definitions reported in the literature (13, 14).

To obtain a homogeneous sample we had to value only the tibial fractures treated by intramedullary nailing. The patients underwent clinical examination and bi-projective X-Rays to assess the type of fracture. Tibia FRACTure prediction healING days (FRACTING) score was applied after the definitive fixation.

This score can be used both to predict fracture healing time-span, both to identify prolonged healing risk patients immediately after surgical treatment. FRACTING score was validated in a prospective, multicenter, observational study (9). FRACTING score parameters include age, malnutrition, smoking status, diabetes, use of NSAIDs, fracture exposure grade, location (diaphysis, metaphysis or epiphysis), synthesis device (nail, plate, external fixator, angular stability plate), instability, misalignment (>5°), bone graft use, type of fracture, loss of bone substance, bone diastasis (> 2mm), surgery duration (> 2 hours), cast and blood loss before and after treatment (Hb<10g/dl). The values of the score ranged from 3 to 18.

FRACTING score is able to predict fracture healing time in five-time intervals: ≤3, 4, 5, 6, and >6 months from trauma. All the patients underwent follow-up for at least 12 months. We collected patients' data about age, gender, type of fracture, surgery approach and pseudoarthrosis scores (Table I).

Table I. *Example of pre-release data collection.*

PATIENT	AGE AT THE SURGERY	SIDE	GENDER	TYPE OF FRACTURE (AO/OTA)	FRACTING SCORE	UNION	NON-UNION	FOLLOW-UP (months)
1	22	RIGHT	M	4.2C	9		X	18
2	28	LEFT	M	4.2A	6	X		12
3	82	RIGHT	M	4.2A	6		X	12

We used FDA definitions of non-union (2). The end-point of fracture healing was radiological and usually clinical: the patient can handle full weight-bearing without pain. The most common clinical features used for the definition of non-union were pain over fracture site, pain during weight bearing and mobility at fracture site.

By the way, all the fractures underwent to reoperation were considered non-union as well, according to Brinker definition (3).

All the fractures were nailed within 21 days at most from the injury (range 1-21 days). 14 patients with open fractures, soft tissue wide injuries, or life-threatening polytrauma were treated according to the damage control orthopaedics (DCO) principles and received a temporary external fixation.

Conversion to definitive surgery was performed as soon as soft tissue conditions allowed and when the patient overcame the immunodeficiency period after trauma (15). All nailing procedures were performed prior to antibiotic prophylaxis and with the patient in the supine position on a fracture table with fluoroscopic-guided imaging. The surgical technique was performed both by infra-patellar and supra-patellar incision according to the type of fracture and the surgeon's preference.

Tibial shaft was both reamed and unreamed, and a guide wire was used for all procedures. All nails were of the same brand and type, with different length and diameter. All the nails were locked with at least 2 proximal and 2 distal locking screws. In both tibial and fibular fractures, fibular was never fixed. There were no intraoperative complications. Patients were weight-bearing as tolerated postoperatively.

Participating surgeons did not offer stimulation modalities to promote bone growth (such as ultrasound and electrical stimulation) during the follow-up.

RESULTS

A total of 174 patients with tibial shaft extra-articular fractures surgically treated were assessed for eligibility, 17 did not satisfy the inclusion criteria, 11 did not accept to be enrolled, and 16 were lost during follow-up. Finally, 130 patients with tibial shaft fractures were entered into the database and completed the follow-up (Fig. 1).

Overall, 23 patients (17.6%) had open fractures; 9 patients (6.9%) occurred loss of bone tissue. 109 patients (90.8% of fractures), sustained both bone fractures (tibia and fibula). According to AO classification, 64 (49.3%) of fractures were type 4.2A, 31 (23.8%) were type 4.2B, 17 (13.07%) were typed 4.2C, and 8 (6.6%) were 4.3A type.

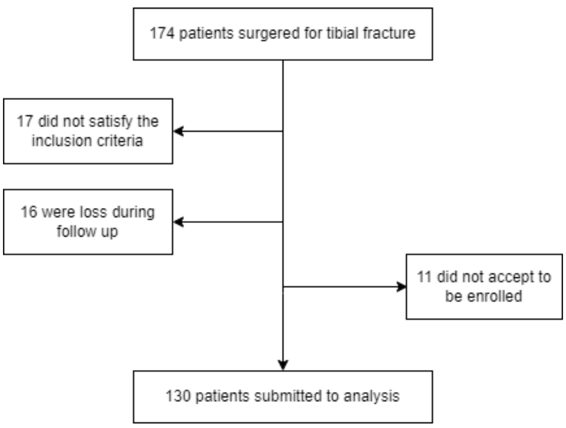

Fig. 1. *Case selection flow chart.*

Among the 130 patients with tibial shaft fractures, 89 (68%) healed within 9 months and were classified as Union, 41 fractures (31.5%) healed in more than 9 months or underwent other surgical intervention and were classified as Non-union.

The second surgery intervention included: nail dynamization, bone grafting, re-nailing, compression plating, and external fixation. Among the non-union group, male patients have a mean age of 45, with FRACTING score avg. 7.8 ± 1.8. Females patients, non-union group, instead have a mean age of 52, with FRACTING avg. 7.7 ± 2.1. Remember that the score is directly proportional to the risk of non-union.

Therefore, the higher the score, the lower the chances of healing the fracture. Scores owned their decision rule which depends on the threshold value. The cutoff value for FRACTING score was ≥ 8, as suggested by the authors.

Statistical analysis

The descriptive analysis is computed on following samples: the total size is first divided into gender (Female = 47; Male = 83); subsequently, each gender sample is divided into NON UNION and UNION.

Results for each sample size, as minimum and maximum value, median, IQR (interquartile range) and mean, are summed up in Table II.

Table II. *Descriptive statistics for scores and AGE on outcome of NON-UNION and GENDER.*

	Female (N=47)		Male (N=83)		Total
	Non Union (N=7)	Union (N=40)	Non Union (N=34)	Union (N=49)	
Age					
Min / Max	32 / 84	18 / 86	19 / 82	18 / 87	18 / 87
Med [IQR]	52 [43;55.5]	54 [42.2;62]	45 [28.2;57.8]	45.0 [27;60]	46.5 [34;60]
Mean ± St. Dev.	52.1 ± 16.4	52.5 ± 17.5	44.6 ± 17.9	44.5 ± 20.0	47.4 ± 18.7
Fracting					
Min / Max	5.0 / 10	1.0 / 10.0	5.0 / 10.0	2.0 / 9.0	1.0 / 10.0
Med [IQR]	8.0 [6.0;9.5]	5.0 [3.0;7.0]	8.0 [6.0;9.0]	4.0 [3.0;7.0]	6.0 [4.0;8.0]
Mean ± St. Dev.	7.7 ± 2.1	5.2 ± 2.3	7.8 ± 1.8	5.1 ± 2.2	6.0 ± 2.4

As described, a non-union score assumes an integer value calculated as the sum of risk factors, clinical parameters, and/or demographic variables observed. From Table III, it turned out that the increasing age does not affect the percentage of non-union patients.

Table III. *Percentage proportion of patients grouped by age ranges.*

Age	Non Union	Union	Total
18 - 45	21 (34%)	41 (66%)	62 (48%)
46 - 60	13 (35%)	24 (65%)	37 (28%)
> 60	7 (23%)	24 (77%)	31 (24%)

By applying the decision rule of FRACTING score to the patients, which depends by cutoff value, the prediction is computed and results are listed as confusion matrix (Table IV, V), Then, the score performances were evaluated in order to compare the reliability of decision rule.

Table IV. *FRACTING - Confusion matrix.*

	Union	Non Union	Total
Predicted Union	77	15	92
Predicted Non Union	12	26	38
Total	89	41	130

Table V. *Score evaluation performance metrics results.*

Score	Sensitivity	Specificity	PPV	NPV	F-measure
FRACTING	63.41%	86.52%	68.42%	83.70%	67.00%

In Fig. 2, it is shown the distribution of scores values for non-union and union patients, grouped into three groups where the last group has values equal and greater than the cutoff.

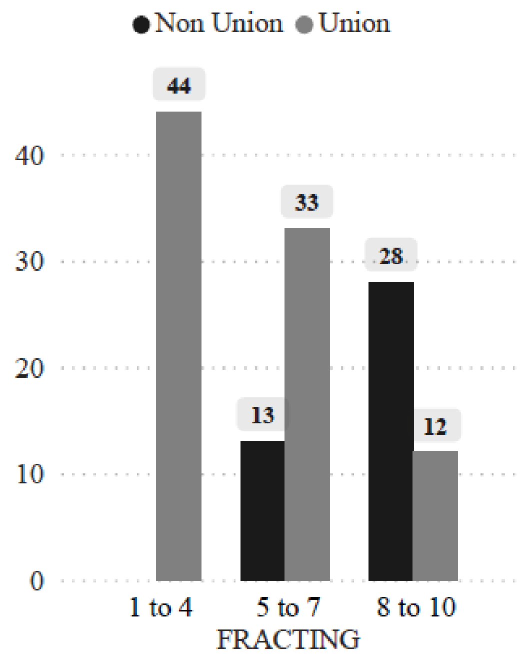

Fig. 2. *Histograms of score distribution.*

Considering the presence of class imbalance ratio (16) equal to 41,07% which determines a greater ease of predicting union patients, we have calculated Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and F-measure.

DISCUSSION

Malunion or non-union of long bones are one of the most challenging complications for the orthopaedic surgeons. This condition involves residual pain, lameness, use of aids for walking and the inability to lead a normal lifestyle, thus causing a great impact on the quality of life (17). Moreover, the healing time of tibial fractures are very variable for each person and may be affected by many factors.

Among the long bones fracture, a comprehensive review of studies reported non-union rates of 0–12% in femoral fractures, 0–33% in humeral fractures, and 1–80% in tibial fractures (18). It is often necessary a second surgery to obtain healing. Reoperations included bone grafts, implant exchanges or removal for hardware failure. In case of infected non-union: irrigation, débridement and soft tissue coverage procedures.

Numerous clinical factors were documented as having a prognostic value for delayed bone healing or non-union of tibial shaft fractures. For this reason, there are some different non-union scores (19).

The FRACTING score was born to predict the time of healing of tibial fractures with parameters analyzed in a retrospective study, called ARRCO (Algoritmo Rischio Ritardo Consolidazione Ossea), and later validated in the prospective, multicenter observational study, called FRACTING (20).

This is certainly the score with more parameters considered, different for each type of surgery and internal fixation. Moreover, it considers clinical, patient-related, fracture-relates surgical, and peri-surgical parameters. Bhandari et al in an observational study had identified that a set of three simple prognostic variables (open fracture, transverse fracture, and postoperative fracture gap) that can assist surgeons in predicting reoperation following operative treatment of tibial shaft fractures (21).

By the way, the presence of a large fracture gap and lack of cortical continuity after reduction is maybe the best single variable associated with delayed healing and non-union (19).

The topography of the fracture affects the fracture healing, according to the vascular anatomy and the different blood supply of the shaft. Santolini et al. divided the femur and tibial shaft into three zones, defined as zones of high, moderate, and poor vascularization (22). They argued that the tibial shaft vascularization is divisible into sections of thirds.

The upper third has a high degree of vascularization, the middle third has a moderate degree of vascularization, and the lower third has a poor degree of vascularization. Among the three scores, only the FRACTING score kept into account the localization of the fracture. Deep or superficial infections are significantly associated with tibial non-union (23, 24). FRACTING did not count infection, but other authors proposed a non-union prediction score at six weeks after surgery that included infection (25).From our results emerged that the male gender is a non-union risk factor.

Also the literature shows that male gender is a risk factor (4), maybe because males are more likely to suffer high-energy trauma for the type of sporting activity (26, 27). Smoking habit is associated with non-union in several studies (28, 29).

By the way, FRACTING score present smoking in own aims. Some drugs can involve fracture healing: not only NSAIDs (30, 31) and corticosteroid (32, 33), but also anticoagulant (34) and anticonvulsant (35). Indeed, FRACTING consider NSAID use as a conditioning factor.

The diagnostic accuracy demonstrated greater accuracy by FRACTING in low score values, this, could be explained not only for a wider range score but also because in our patient cohort, we consider only nail fixation, which potentially keeps a low score (FRACTING score assigned 3 points for external fixation and 2 point for plate and screw versus just 1 point for nailing).

The limitations of our study included the retrospective and the multicentric nature. When a multicenter study is conducted, especially in the surgical field, it is easy to have bias related to the surgeon's experience, surgical technique, postoperative treatment, and definition of healing. For example, there is no consensus about use of skeletal traction while waiting for surgery and allowing full or partial weight bearing after the surgery (36), and the score did not keep that in consideration.

Radiographic healing of the fracture was determined by the investigator based on his experience, clinical well-being and evidence of 3 out of 4 welded cortices. Moreover, there has been no utilization of any objective radiographic scoring to ensure fracture healing. In the broad panorama of leg fractures surgery, there are some additional variables that make standardization of population impossible.

These variables are: intramedullary canal reaming or not (37), fibular osteotomy vs fibular fixation vs no touch fibular fracture focus (38), the use of a Poller screw, and the time of wound closure. The use of local prophylactic antibiotic (39), like Antibiotic-Coated Nail (40) in open fractures could be a solution to prevent septic non-union.

Therefore, any intra-operative or post-operative treatments (like biophysical stimulation with pulsed electromagnetic fields), that promotes bone healing should be used (41).

CONCLUSIONS

Our multicenter study analized the predictive value of FRACTING score. From our data is clear that male gender and greater age is a risk factor for non-union. FRACTING score showed good reliability from statistical analysis. For this reason, we recommend the use of this predictive score in clinical practice, because it can change the surgeon's operative approach and the choice of adjuvant therapy (ultrasound, pulsed electromagnetic fields, coated nails, or application of growth factor).

In the future would be interesting to make a comparison of the scores cited by the recent literature, in order to find out which is more suitable to predict delayed union or nonunion.

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