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The "Orthoplastic" combined surgical approach to open tibia fractures: a multicentric prospective outcome study.

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Esame finale anno 2015

A Ilaria e Guglielmo,
i miei dolci compagni di viaggio.

SUMMARY

1. Introduction

Open fractures of the leg represent a severe injury, which requires an optimal treatment approach in order to optimize the return of limb function. The need for a combined management, shared between plastic and orthopaedic surgeons, is requisite for this aim[1,2].

This type of treatment has been recently named as “Orthoplastic” treatment[3-6] in the medical literature, which refers to a well coordinated joint approach to osteocutaneous injuries.

However the multidisciplinary approach is not the consistently practiced treatment of open tibial fractures, all over the world and many recommendations are still based on tradition[7-8].

The common rule is to treat the bone injury acutely and then refer the patient if and when the cutaneous defect appears non-healing or beyond the usually basic skills of soft tissue reconstructions belonging to an orthopaedic team. The referral may occur at any time during the evolution of the injury. Unfortunately the patient is often referred to the plastic team too late, when the high microbiological risk related to the relevant contamination is extremely hard to counteract with adequate wound excision and reconstruction, which are skills normally owned by plastic reconstructive surgeons and less frequently by orthopaedics.

To the best of our knowledge, no mention exists in the literature with regard to a multicentric comparison between units devoted to “orthoplastic” treatment and units stuck to “traditional” simply orthopaedic treatment of open tibia fractures.

Furthermore, due to the relatively low incidence of these injuries, a multicentric inclusion of these patients may help create an adequate cohort to be followed up and studied with a sufficient statistical power. The centres included in the study have different approaches to the problem, which makes the material of the study more heterogeneous and likely to produce interesting results.

1.1 Aims of the study:

To evaluate and compare the outcomes of open tibia fracture repair across three different centres in the world. Two of these units, of which one is located in the developing world (Pakistan), practice the orthoplastic approach, whereas the third unit is inevitably a simply orthopaedic centre, as plastic surgery is lacking in their hospital and far away from them. Outcome measures will be:

1) surgeon reported outcomes including

-deep infection

-flap loss

-surgical complications

-reintervention

-time for bone union

-time for soft tissue closure

-amputations

2) patient reported outcomes including

-Enneking score for lower limb function

-duration of hospital stay

2. Open tibia fractures

2.1 Definition

An open fracture is defined as a bony fracture and soft tissue laceration that are in communication with each other. Open tibia fractures are high energy osteocutaneous injuries consisting of a fracture of the leg (tibia only or tibia and fibula) and of a variable degree of damage to the overlying soft tissues, which causes exposure of the fracture focus to the outer environment and contamination. Among all open fractures, tibia is the most commonly affected because of its subcutaneous localization.

2.2 Classification of open fractures of the lower limb

Two main methods have been created to classify open tibia fractures, grading and scoring systems. Grading focuses on the limb injury only, whereas scoring also includes information about patient's general conditions.

Extremity injury scoring systems.

Mangled extremity severity score (MESS)[9-10]

This was based on the skeletal/soft tissue damage, limb ischaemia, shock and age. It was created to select those cases who would benefit from a primary amputation. A MESS score of 7 or greater was found to be predictive for amputation.

NISSSA[11]

This is an acronym standing for **n**erve injury, **i**schaemia, **s**oft tissue injury, **s**keletal injury, **s**hock and **a**ge.

Limb salvage index[12]

This is an indicator of arterial compromise in an injured limb. A limb salvage index (LSI) score of 6 or greater is an indication to limb amputation.

Extremity injury grading systems

Gustilo and Anderson[13-15]

The Gustilo and Anderson classification is the most commonly used.

In 1976, the team from Minnesota performed an audit of open fractures, in which infection was the outcome measure. The high energy injuries (grade III) with severe soft tissue damage had the highest rate of infection. These injuries were then further subclassified according to soft tissue loss and arterial injury requiring repair. The system may be subject to poor interobserver reliability, especially with inexperienced surgeons. Recently it has been pointed out that injured limbs are appropriately categorized with this system after wound excision. Another disadvantage of the Gustilo classification is the relative lack of sophistication in the description of the skeletal injury. Despite these drawbacks, this system is simple and has found widespread application.

Comprehensive systems

Byrd and Spicer[16]

This classification is based on the vascularity of the fracture and the surrounding soft tissues. In type I lesions, both the periosteal and endosteal circulation to the bone fragments are maintained and the surrounding soft tissues are relatively intact.

In type II injuries, the endosteal circulation is disrupted but the periosteal circulation is preserved through the surrounding soft tissues. In Type III injuries there are devascularized bone fragments and the wound requires flap coverage, whilst the Type IV injuries require free flap coverage.

This classification lacks sophistication and has not found widespread application.

Ganga hospital score

This method of classification[17-19] is intended to combine the best elements of the scoring systems and the grading systems based on the experience of a dedicated trauma/reconstruction team of plastic surgeons, orthopaedic, and anaesthetists. The system assigns scores for injuries to skin and fascia, bone and joints, musculotendinous units and nerves.

Added points are considered for comorbidities such as time to debridement of greater than 12 h, sewage/farmyard contamination, age over 65 years, diabetes and cardiorespiratory disease, polytrauma involving chest or abdomen, hypotension and another major injury to the same limb or compartment syndrome. A cutaneous score of 3 or greater was indication to necessity of complex soft tissue reconstruction and a score of 17 or greater was predictive of amputation.

Association of Orthopaedics (AO)[20-1]

The AO group has invented a sophisticated classification, including elements of both the scoring and grading systems. Thus, the skin, muscle/tendon, neurovascular structures and the skeleton are scored separately. Grading of the fracture appears to be the most unreliable aspect of this

classification. The accuracy of grading increases with the surgeon's experience. The AO score seems to allow a more accurate prediction of prognosis than the Gustilo grading. However, the system is complex, which limits how it can commit to memory and therefore its acceptance.

2.3 Epidemiology of open tibia and fibula fractures.

Open long bone fractures affect 11.5 per 100,000 persons per year, more frequently in males[22]. The majority of these fractures are open tibial diaphyseal fractures, of which about 60% are Gustilo type III, but open femoral diaphyseal, distal femoral and proximal tibial fractures tend to occur in the most seriously injuries. Open fractures of the lower limb are more severe than upper limb open fractures. Not only is the soft tissue damage less severe in open upper limb fractures, but there are fewer associated musculoskeletal lesions.

2.4 State of the art in the treatment of open tibia and fibula fractures.

The management of open tibial fractures and associated soft tissue loss has evolved in the last decades. In 1974 Chacha[23] showed in his study how fragmentary the participation of the various involved specialists used to be. In fact, previously, the repair of the soft tissue defect was relegated to the "delayed" stage of reconstruction, because the importance of the structures surrounding the fractured bone was not considered. High rates of leg amputation following these injuries were therefore simply accepted.

An important transition from this era started with Ger[24] who described in 1977 the significance of early muscular coverage of compound tibial fractures to prevent osteomyelitis and subsequent amputation. This concept was then developed by Godina[25] with the use of microsurgical flaps. In his large series, including both upper and lower limb injuries, not all with underlying fracture, a free flap is performed within three days of the injury. This method showed an improved flap survival and also decreased deep infection rate. Subsequently many studies[26-35] tried to define the appropriate timing for soft tissue coverage and generally arrived to the common view that early closure is recommended, except for heavily contaminated wounds. However, it soon appeared very clear that whilst this early approach may be appropriate in the relatively rare centres with multiple senior microsurgical teams available 24 hours a day, it may be more realistic to manage these complex injuries in a slightly more staged fashion when free tissue tranfer is required, in order to allow senior dedicated teams in specialist centres to deal with these traumas[36]. A delay of soft tissue repair beyond 7 days in wounds temporarily treated with negative pressure foam dressings was accompanied by a relevant increase in the deep infection rate[37]. The available evidence favours

definitive reconstruction of soft tissue overlying open fractures as soon as possible, in the aim of limiting free flap failure and deep infection rates. Based on the available scientific evidence, it is difficult to be prescriptive about the precise number of days post injury that soft tissue repair should be obtained. Immediate reconstruction is best suited to the use of local flaps. More complex surgery should be undertaken electively once the patient has been thoroughly investigated and adequately prepared. This is balanced by the technical difficulties, because the perivascular soft tissues become increasingly oedematous, friable and eventually fibrotic as time elapses post injury. In addition to this, published evidence to date favours the treatment of open tibial fractures by a multidisciplinary team, including orthopaedic and plastic surgeons with appropriate experience, in order to obtain similar infection and union rates to those of closed fractures[1,2]. However this type of multidisciplinary approach is only exceptionally utilized in the clinical practice and not commonly described in the scientific literature. In many clinical settings the soft tissue reconstruction is delayed or not even performed and a wait and see management with dressings and negative pressure is adopted.

3. Material and Methods.

Three trauma centres were included in the study. These are units operating in their territories as the main specialist units for complex open lower limb fractures.

The units are:

- Orthopaedic Department, Maggiore Hospital, Bologna, Italy
- Lower Limb Reconstruction Unit, Frenchay Hospital, Bristol, United Kingdom
- Plastic Surgery Department, Jinnah Hospital, Lahore, Pakistan

A fourth unit was included, as the centre supervising the data collection and independent assessor of outcomes. This was Rizzoli Orthopaedic Institute, teaching Hospital within the University of Bologna, Italy.

All patients consecutively admitted to the participating trauma centres for an open tibial fracture with severe soft tissue damage (mainly but non only grade 3, according to Gustilo Classification) were included in the study and followed up prospectively as a single cohort of patients. Demographic data, mechanism of injury, pattern of injury, Gustilo classification, tissue cultures, timing and modality of referral to the trauma centre, timing and modality of treatment and rehabilitation, in particular details of soft tissue repair were recorded, including any bone-stimulating procedures. Identical proformas for collection of data were used in all the units participating in the study, in order to record the same data in same fashion. All proformas were filed and kept as record of the study and as documents for verification of the results obtained.

The study was completely based on patients'hospital number and study reference number, progressively increasing according to patients'inclusion in the study. Anonymity was strictly respected in all phases of data management, also by means of dedicated computers not connected to the internet. Approval from an Ethical Board was obtained.

The Outcome measures taken into account were :

- time for soft tissue closure
- duration of hospital stay (overall, with all hospitalizations included)
- number of reinterventions
- time for bone union
- time for full weight bearing
- deep infection
- functional recovery of the limb (Enneking score)
- time for bone union
- flap or skin graft loss and other complications including amputations

Two proformas were utilized to collect data and they were identical in the three units:

1) Patient enrollment proforma (from injury until discharge from hospital, Table 1).

LOCATION	PATIENT NUMBER	DATE/TIME OF INJURY
DATE OF BIRTH:	SEX:	
JOB:	HOBBIES/SPORTS:	
COMORBIDITIES:		

MECHANISM OF INYURY:	SITE OF INJURY:	MODE OF TRANSPORT:
ADMITTING HOSPITAL (TRAUMA/ NONTRAUMA CENTRE):	TRANSFER INTERVAL AND REASON OF DELAY:	INITIAL ASSESSING TEAM (ORTHOPAEDIC+- PLASTIC+- MICROBIOLOGIST):
CLASSIFICATION OF INJURY		
GUSTILO & ANDERSON	ASSOCIATION OF ORTHOPAEDICS	OTHER

FIRST OPERATION		
DATE AND TIME:	TRAUMA/NONTRAUMA CENTRE:	ELECTIVE/EMERGENCY:
TEAM:	DETAILS OF PROCEDURE:	
FIXATION		
DATE AND TIME:	TRAUMA/NONTRAUMA CENTRE:	ELECTIVE/EMERGENCY:
TEAM:	DETAILS OF PROCEDURE:	BONE-STIMULATING PROCEDURES:
SOFT TISSUE COVER		
DATE AND TIME:	TRAUMA/NONTRAUMA CENTRE:	ELECTIVE/EMERGENCY:
TEAM:	DETAILS OF PROCEDURE:	
REINTERVENTIONS		
DATE AND TIME:	TRAUMA/NONTRAUMA CENTRE:	ELECTIVE/EMERGENCY:
TEAM:	DETAILS OF PROCEDURE:	
HOSPITAL STAY		
DATE OF DISCHARGE	DURATION:	COMPLICATIONS:

Table 1: enrollment proforma for initial collection of data at patient's presentation and during first hospitalization.

2) Patient continuation proforma (follow up and rehospitalizations, Table 2) and Enneking score scheme (Table 3).

LOCATION	PATIENT NUMBER

FOLLOW UP			
NUMBER OF OUTPATIENTS CLINICS UNTIL DISCHARGE:	ENNEKING SCORE AT 3 MONTHS:	ENNEKING SCORE AT 6 MONTHS:	ENNEKING SCORE AT 12 MONTHS:
TIME UNTIL WEIGHT BEARING	PLANNED	PARTIAL	FULL
TIME UNTIL RETURN TO WORK	TIME UNTIL RETURN TO SPORTS/ HOBBIES:	PATIENT'S EVALUATION AT 12 MONTHS (QUESTIONNAIRE):	
TIME UNTIL BONE UNION	TIME UNTIL SOFT TISSUE CLOSURE	COMPLICATIONS AND MODE OF TREATMENT:	BONE-STIMULATING PROCEDURES

FURTHER REHOSPITALIZATIONS		
DATE:	CAUSE:	ELECTIVE/EMERGENCY:
TEAM:	DETAILS OF PROCEDURE:	DURATION OF HOSPITAL STAY:

Table 2: continuation proforma for follow up and further hospitalizations.

	5	4	3	2	1	0
Pain	None		Modest		Moderate	Severe
Function	No resriction		Social restriction		Partial restriction	Severe restriction
Emotional acceptance	Enthused		Satisfied		Accepts	Dislikes
Supports	None		Brace		1 crutch/stick	2crutch/sticks
Walking	Unlimited		Limited		Inside only	Unabel uassisted
Gait	Normal		Minor cosmetic		Major cosmetic/ minor disability	Major handicap
Skin Quality	Normal		Abnormal colour		Occ breakdown, fragile	Persistent problems
Donor Site	Unnoticed		Occassional irritation or cosmesis		Moderate resriction or cosmesis	Severely restricted or distress
Totals (40 max)						

Table 3: modified Enneking's score for assessment of functional recovery of the leg.

The outcome measures were evaluated against the several demographic and clinical features and against surgeon-controlled variables and statistical analysis was used to identify any relevant difference in terms of outcome, through statistical tests of significance.

Patients were included in the study over a period of two years (January 2012 to December 2013) and followed up for three years (January 2012 to December 2014) in order to determine a sufficient statistical power for significant results.

3.1 Initial management

Most patients were admitted to hospital and operated within 24 hours of the trauma. The widespread initial operation (common thorough all units) was a generous washout of gross contamination and the positioning of an external fixator for bone stabilization, then the general types of treatment were either a combined orthopaedic-plastic approach (orthoplastic) or a simple (orthopaedic) approach.

3.1.1 Combined "orthoplastic" approach

This type of treatment consists of a simultaneous coordinated and well organized management of both the bony and the soft tissue lesions, according to the recent guidelines agreed by the Plastic and Orthopaedic Associations of the United Kingdom[38].

The mainstays of this recommended practice are:

- an initial treatment in Accident & Emergency aimed at administration of antibiotics, tetanus vaccination/serum and analgesia, removal of the gross contamination and wound dressing
- a joint orthoplastic procedure, run during daylight lists, in which the fracture is stabilized through an external fixture by the orthopaedic surgeon, and the overlying laceration is thoroughly washed and explored by the plastic surgeon, in order to detect any contaminated and/or nonviatal tissue, which has to be excised, even at the expense of a larger resulting wound. The soft tissue defect is then covered with negative pressure treatment
- a second joint orthoplastic procedure, planned within 5-7 days of the first one, is meant to convert the external fixator into internal fixation through plate and screws or intramedullary nail and to

cover the fixed fracture with a local or microsurgical flap. The effect is therefore the conversion of an open fracture into an artificially obtained closed fracture, virtually aseptic, thanks to the early multidisciplinary approach including an extensive debridement and rapid soft tissue coverage

3.1.2 Simple orthopaedic approach

The emphasis of this surgical approach is only on the bony lesion, which is effectively stabilized with an external fixator as an emergency procedure. The soft tissue lesion is minimally debrided by the bony espert, but no attempt is made, at least initially to reconstruct the soft tissue after a thorough excision of contaminated/nonviable structures.

The main difference relating to the two types of management is about the soft tissue coverage, which is delayed in the first case and associated with a less effective debridement, and 'more' refined and rapid in the case of orthoplastic management in addition to include a more effective and generous removal of nonviable or contaminated soft tissues.

3.2 Statistical analysis

Statistical analysis was performed using StatView 5.01 for Windows (SAS Institute Inc, Cary, NC). Quantitative data were expressed as arithmetic mean plus or minus the standard error of the mean (SEM). We hypothesized that differences of the outcomes could be influenced by multiple independent variables, including sex, age, other demographic and clinical features.

The frequency distribution was calculated, and the chi square test was used to highlight differences attributable to categorical variables. The analysis of variance (ANOVA) was applied to detect the effects of multiple variables on the quantitative results. An unpaired t-test was used when only two independent variables were assigned. Differences were considered significant if the p value was less than 0.05

We hypothesized that the outcomes could be influenced by the type of surgery, i.e. the simple on combined procedures. In addition, we evaluated if the distribution of demographic and clinical features varied in patients treated with different surgical techniques.

4. Results

4.1 Demographics

The number of patients included in the recruitment period (2012-2013) is 164, of whom 44 from Bologna Unit, 98 from Bristol Unit and 22 from Lahore Unit

Initial management is exclusively orthopaedic in 53 cases (32%), combined orthopedic and plastic (orthoplastic), in 111 patients (68%).

The main age of patients is 45, with a minimum of 3 and a maximum of 96. Males were 120 (73%) and females 44 (27%).

Comorbidities were divided into major and minor, depending on the degree of compromise on bone and soft tissue healing processes. One hundred patients had no associated pathologies, in 31 there were major comorbidities, whereas 33 patients were affected by minor associated diseases. Major comorbidities were: diabetes, ischaemic heart disease, obesity, multiple sclerosis, pancreatitis, multiple deep venous thrombosis, hepatitis C, liver failure, intravenous drug abuse, atrial fibrillation with anticoagulation, hereditary spherocytosis, long standing poliomyelitis to the same leg, chronic arteriopathy, chronic obstructive pulmonary disease, venous ulcer, Parkinson's disease. Minor comorbidities were: asthma, IBS, achalasia, gallstones, epilepsy, isolated hypertension, sciatica, cannabis use, alcoholism, hypercholesterolaemia, depression, mild dementia, hyatus hernia, bipolar disease, previous trauma to legs resolved, anaemia. Most patients were nonsmokers (115), whereas 49 were smokers.

The main mechanisms of trauma are road traffic accidents (64%) and falls (29%).

Associated injuries coexisted in 76 patients and were classified as minor in 53 cases, major in 23. Major associated traumas were: open femur fracture, vascular lesion, liver lesion, bilateral compartment syndrome and contralateral degloving injury, open fractures of ulna and radius, neuropathy, splenic rupture, lesion of the posterior tibial artery, burn plus motor oil contamination, open fracture of the metatarsal bone, deep venous thrombosis, polytrauma (more than 3 anatomic regions).

Minor traumas were thoracic vertebral fracture with no involvement of the spine, talus fracture, rib fractures plus lung contusion or pneumothorax, metatarsal fracture, fracture-dislocation of the hip, closed ankle fracture, ulna and radius fractures, small splenic laceration, contralateral degloving injury, knee laceration, small liver laceration, degloving injury to hands, fracture of sternum, neck laceration, mandibular fracture, metatarsal fracture, lacerations on multiple sites, minor pelvis fracture, mild head trauma.

The ankle joint was involved in 32 cases (19%) out of 164.

There were 15 cases of 3A, 5 cases of 3C, 8 cases of grade 2 and 136 of 3B.

The most common mechanism of injury causing open tibia fractures was a road traffic accident in 109 cases (67%), a fall in 34 patients (21%), 11 injuries were caused by accidents with industrial, agricultural or gardening machines, 4 patients were kicked by a horse, one case was related to a shotgun, in one case the mechanism was unknown to the patient (unwitnessed in the garden).

In terms of referral to the specialist centre, 148 patients (90%) were referred within one week of injury, whereas in 16 cases (10%) the referral was delayed by at least one week.

In 67 cases (41%) the patient was admitted to a peripheral district hospital before being transferred to the trauma centre. This mainly occurred in Bristol, where the specialist centre functions as a main regional referral unit.

The distribution of demographic and clinical features was explored and found to be variable in patients treated with different surgical techniques (table 4).

However most features were homegeneously distributed in the combined group versus the simple group.

The only significant distribution differences between combined and simple study arms were:

- Transfer delay beyond 1 week: 13% in the combined versus 4% in the simple group
- Major associated injuries: 8% in the combined arm versus 28% in the simple arm
- Frequency of Gustilo 3B (more severe) fractures: 79% versus 63% in the combined and simple groups respectively

The age of patients in the combined group was younger and this result was at the limit of statistically significance.

INDEPENDENT VARIABLE	COMBINED TREATMENT GROUP	SIMPLE TREATMENT GROUP	p-value
Sex Male Female	 75% 25%	 69% 31%	0,357
Age	43±22	49±21	0,0641 (age younger in the combined group, borderline for statistical significance)
Comorbidities Major Minor Nil	 22% 16% 62%	 17% 24% 59%	0,443
Smoking Yes No	 33% 67%	 29% 71%	0,621
Transfer delay Beyond 1 week Within 1 week	 13% 87%	 4% 96%	**0,048** (transferred beyond 1 week significantly more numerous in the combined versus the simple group)
Associated injuries Major Minor Nil	 8% 34% 58%	 28% 28% 44%	**0,0038** (major injuries significantly more frequent numerous in the simple verus the combined group)
Ankle joint involvement Joint No Joint	 22% 78%	 17% 83%	0,471
Gustilo Classification 3C 3B 3A Less than 3	 5% 79% 11% 6%	 6% 63% 28% 4%	**0,031** (3B high grade injuries more frequent in the combined versus the simple group)

Table 4: distribution of demographic and clinical features in the combined versus the simple arm of the study. A non-significant variability between the groups was found, except for transfer delay, associated injuries and frequency of Gustilo high grades (3B).

4.2 Time for soft tissue closure

The skin coverage of the soft tissues is obtained mainly with a reconstructive plastic surgery in 101 cases (62%), the negative pressure therapy until healing of wounds in 43 patients (28%) or by direct suture or dressings in 20 cases (12%). The average time required for the healing of soft tissue is 10 weeks with a maximum of 245 and a minimum of 1 .

As shown in Figure 1, by comparing the two treatments, the mean time for soft tissue closure is 2 weeks with a multidisciplinary approach compared to 25 weeks in case of purely orthopedic treatment (p-value <0.0001).

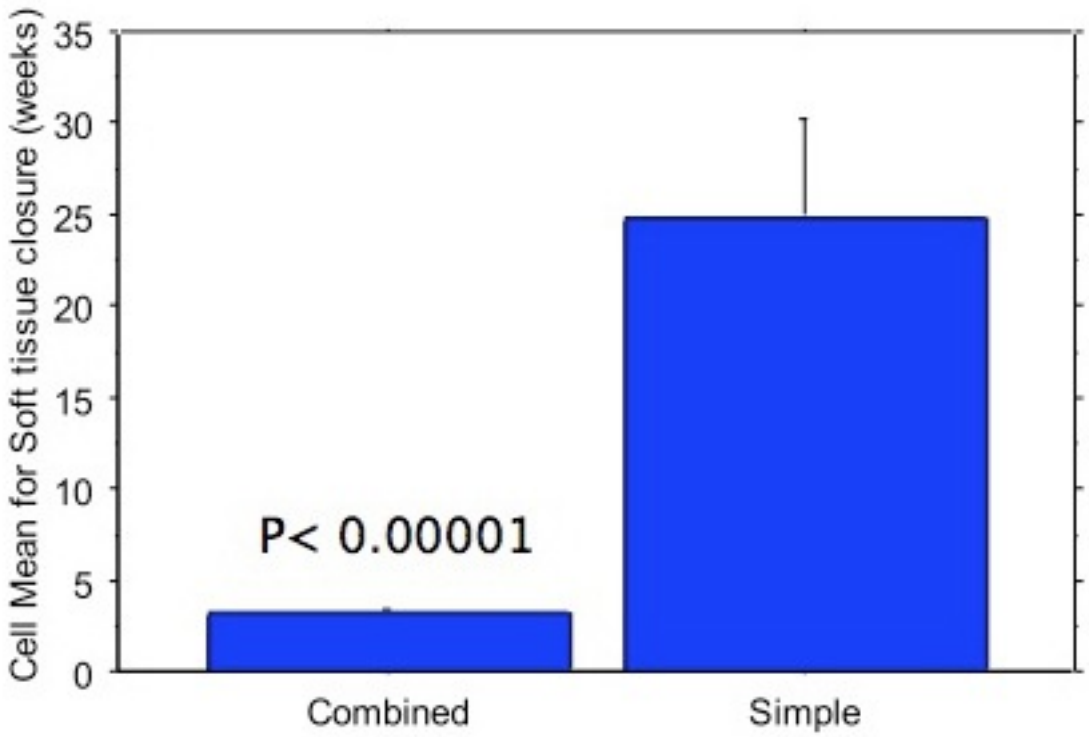

Figure 1: mean time (weeks) for soft tissue closure in case of orthoplastic combined treatment or simple orthopaedic treatment. Combined treatment allows a faster closure of the wounds compared to simple orthopaedic one (2 versus 25 weeks) and the result is statistically significant (p-value<0.00001).

4.3 Duration of Hospital Stay

The average length of hospital stay is 33 days, with a minimum of 2 and a maximum of 241.

Patients treated in a center with an orthoplastic combined team (Bristol and Pakistan) spent an average of 33 fewer days in hospital, compared to patients who underwent simple orthopaedic pathway (22 days on average versus 55, p-value <0.0001).

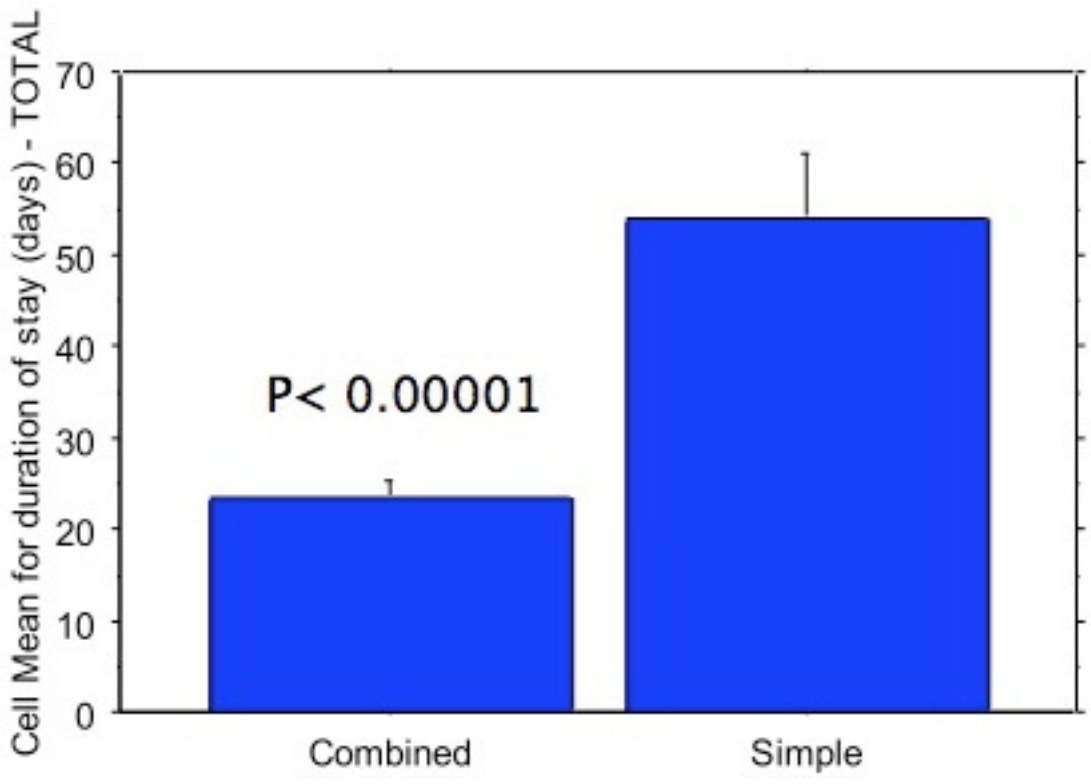

Figure 2: mean duration of hospital stay (days) in case of orthoplastic combined treatment or simple orthopaedic treatment. Combined treatment allows a shorter hospital stay compared to simple orthopaedic one (22 versus 55 days) and the result is statistically significant (p-value<0.00001).

4.4 Number of additional operations

The predicted number of surgical procedures for patients with open tibia fractures is two, irrespective to the type of approach, combined orthoplastic or traditional simple orthopaedic only.

In case of orthoplastic treatment the minimum set of procedures includes the initial debridement and stabilization through external fixator, followed by the “fix and flap” procedure. In the simple approach, the external fixation positioning is the first operation, followed by the conversion to ORIF or removal of external fixation at completion of bone union. Any additional operation on top of this minimum set was recorded for each study patient.

The mean number of additional operations was 0.8, with a minimum of 0 and a maximum of 5. Patients from the orthoplastic arm of the study had just 0.6 additional operations compared to 1.2 in the other arm of the study (100% more) and the result is statistically significant, as shown in Figure 3.

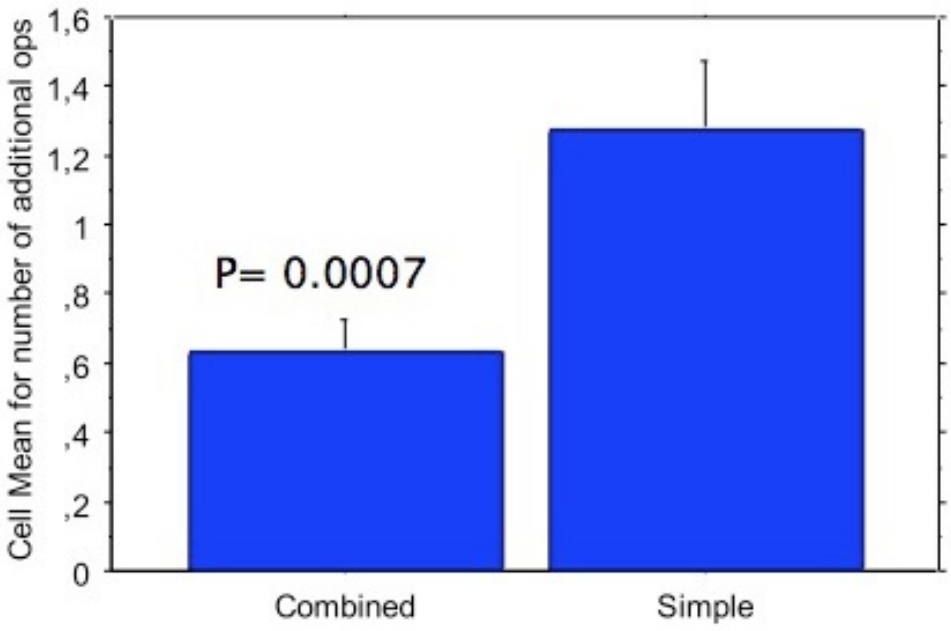

Figure 3: number of additional operations, on top of the basic predicted couple of bone stabilization plus fix and flap/ conversion to ORIF or removal of external fixator, depending on the type of treatment.

Combined treatment allows a lower number of additional operations compared to simple treatment (0.6 versus 1.2) and the result is statistically significant (p-value 0.0007).

4.5 Time for bone union

The time required for consolidation of the fracture was calculated when radiology showed a complete or subcomplete disappearance of the fracture line. The mean time was 6.9 months, with a minimum of 1 and a maximum of 16. By splitting results based on type of approach, 6 months were necessary on average for patients treated with the combined approach, 8.5 in case of simple orthopaedic treatment (Figure 4). This result is statistically significant (p-value: 0.0003).

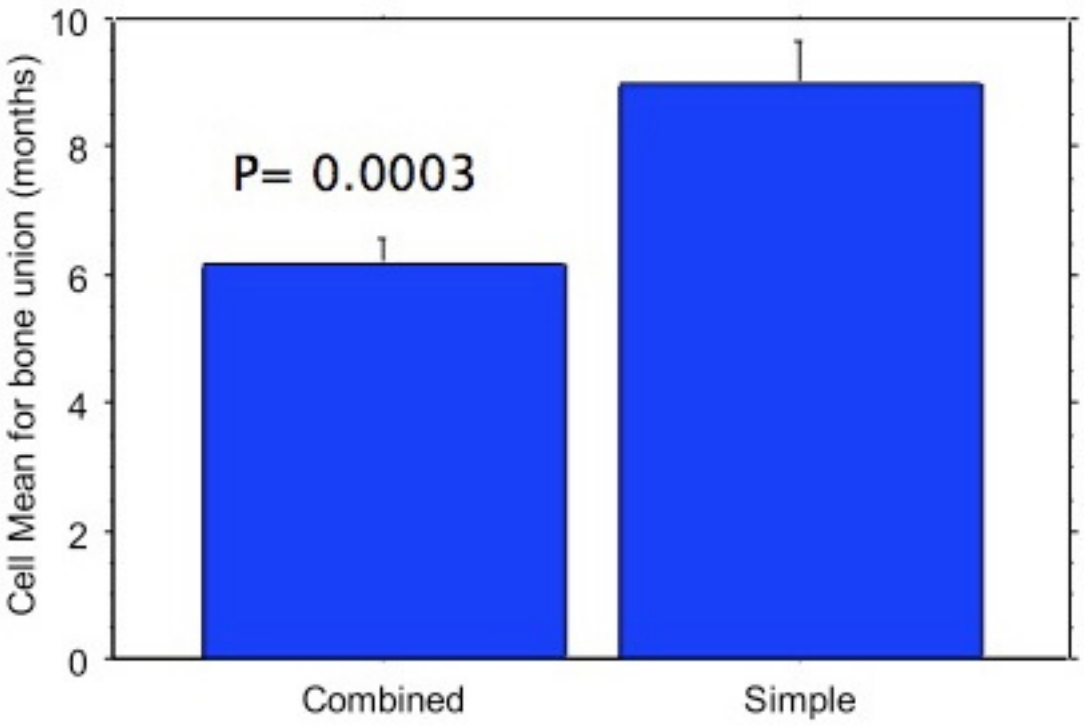

Figure 4: mean time for bone union (months) in case of orthoplastic combined treatment or simple orthopaedic treatment. Combined treatment allows a faster bone union compared to simple orthopaedic one (6 versus 8.5 months) and the result is statistically significant (p-value 0.0003).

A delayed union was diagnosed when the time for fracture consolidation was not within 6 months of the injury date. When union had not occurred by the end of the study period (decmber 2014), a nonunion was diagnosed.

The relative risk (RR) of developing a nonunion is 1.4 times higher if the trauma is dealt with by the orthopedic team only, without a rapid and coordinated program of reconstruction of the loss of skin substance.

A somewhat surprising result is that a better management of the soft tissues also affects the timing of bone healing.

The greater rapidity of bone union in case of combined approach is even more evident with higher the grade injuries, being the most statistically significant difference with regard to 3B fractures (6 months with combined versus 10 with simple, p=0.0002).

4.6 Time for full weight bearing

The time for full weight bearing is calculated as the period of time elapsed between the injury and the moment in which the patient is allowed and capable of fully loading the injured leg (i.e. 50% of their body weight is through the injured leg). The mean time for full weight bearing was within a minimum of 1 month and a maximum of 22 months. Again a statistically significant difference was noticed between the two groups, as the mean value was 4 months in the orthoplastic arm compared to 7 in the orthopaedic arm (Figure 5).

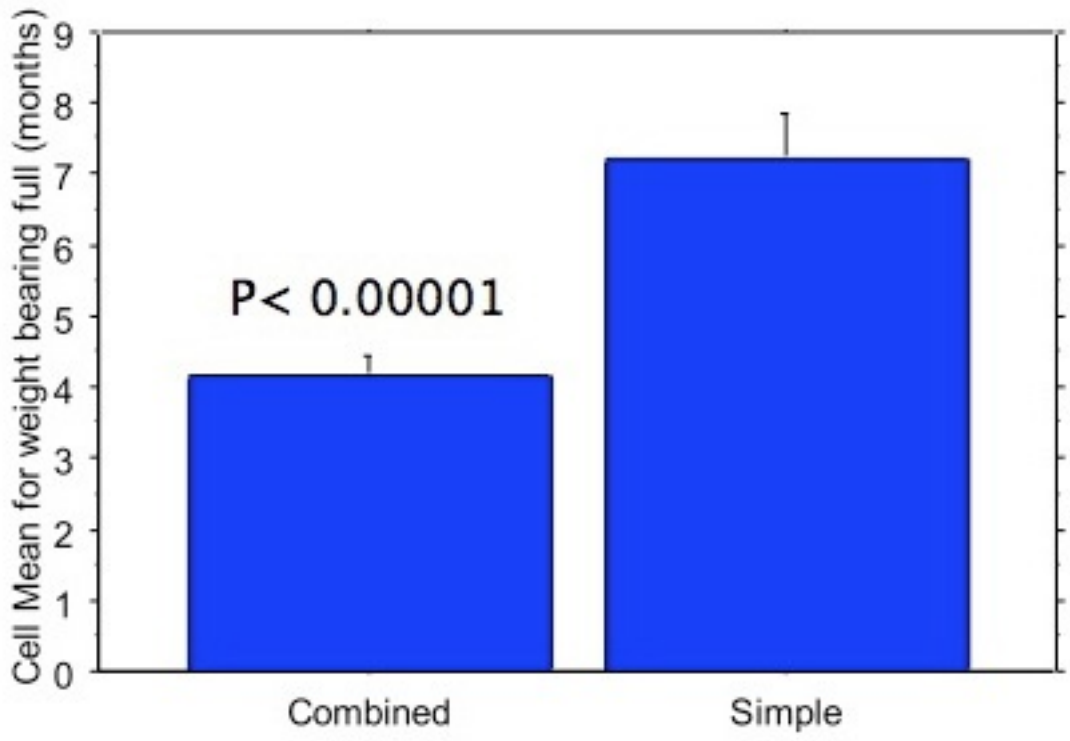

Figure 5: mean time for patient's full weight bearing on the injured leg (months) in case of orthoplastic combined treatment or simple orthopaedic treatment. Combined treatment versus simple orthopaedic allows a faster full weight-bearing (4 months versus 7) and the result is statistically significant (p-value<0.00001).

4.7 Functional recovery of the limb

The mean value of Enneking's score is 14.7 at 3 months, with a minimum of 0 and a maximum of 37, 21.3 at 6 months (range 0-38) and 25.2 at 12 months (range 0-38).

Figure 6 illustrates the progression of functional recovery at 3, 6 and 12 months in terms of Enneking scores (6 parameters evaluated from 0 to 5 with best score: 40). These data consistently increase in case of orthoplastic approach (The score in case of combined treatment is in fact on average higher by 11, 10, and 9, at 3, 6 and 12 months, respectively, p-value <0.0001).

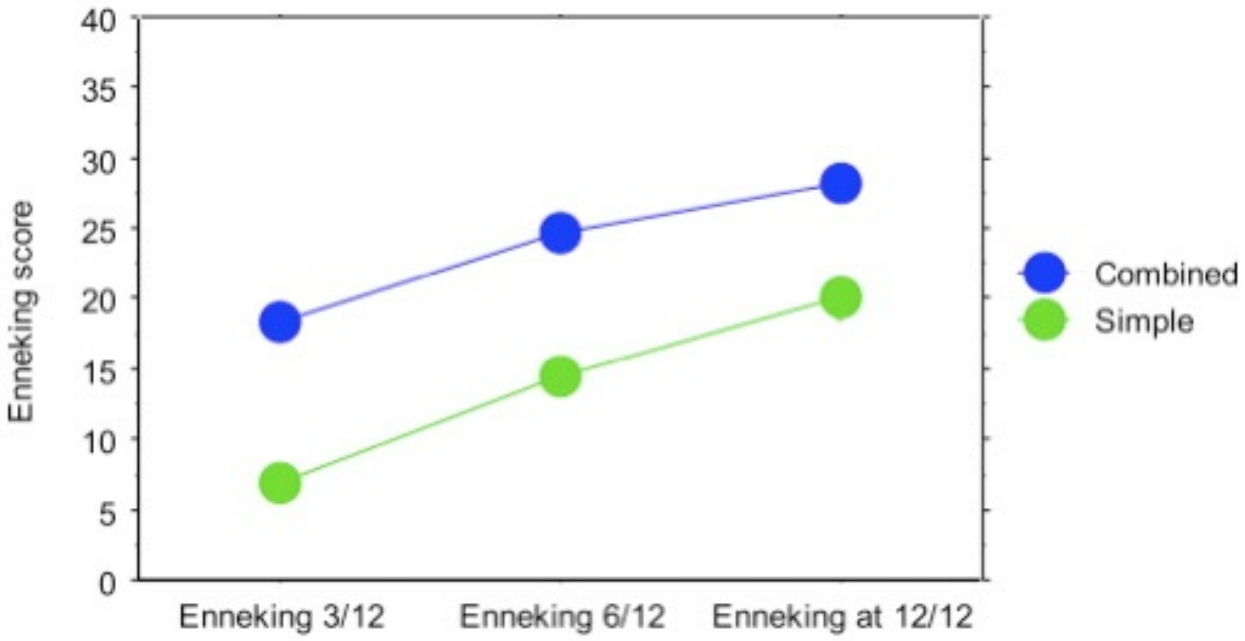

Figure 6: Enneking's scores at 3, 6 and 12 months post-injury, in case of purely orthopaedic or orthoplastic combined treatment. Combined treatment versus simple orthopaedic achieves a better and faster return of function and this is time-consistent during the whole period of study follow-up. The result is statistically significant (p-value<0.0001).

If data on functional recovery of the limb are split unit by unit, the highest score is obtained by patients treated in orthoplastic units (Frenchay Hospital first, followed by Jinnah Hospital), whereas the simply orthopaedic approach once again showed to be weaker in relation to the overall return of function, as shown by Figure 7.

Below knee amputation occurred in 4 cases of which 3 in the combined study arm and one in the simple arm and these patients were excluded from the functional assessment through Enneking's scores.

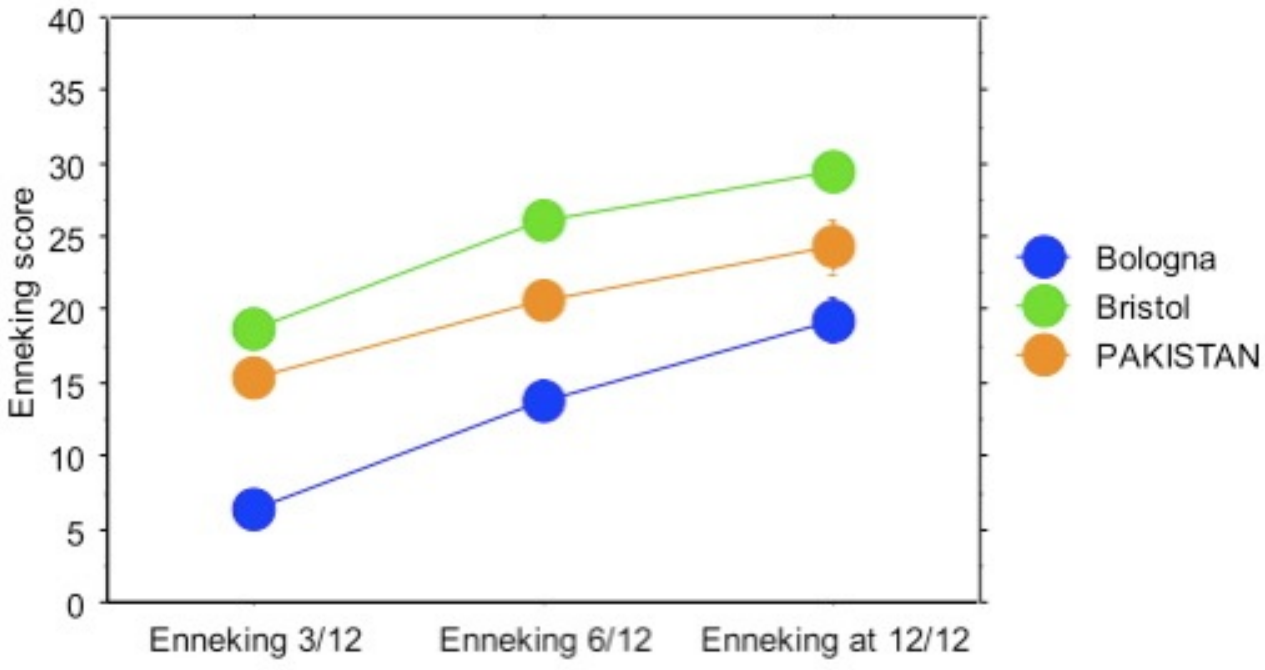

Figure 7: Enneking's scores at 3, 6 and 12 months post-injury. Data are split based on the study centre. Bologna Trauma Centre only applies a purely orthopaedic treatment. Centres accomplishing the orthoplastic approach achieve a better and faster return of function post open tibia fractures, and this is time-consistent during the whole period of study follow-up. The mean Enneking at 12 months in Bristol is 29, in Lahore 24 and in Bologna 19. All three comparisons between the included centers show an advantage of the orthoplastic unit (p-value<0.05). Bristol achieves superior outcomes compared to Lahore, probably due to the better hygienic, rehabilitative and organizational conditions of care.

5. Clinical cases

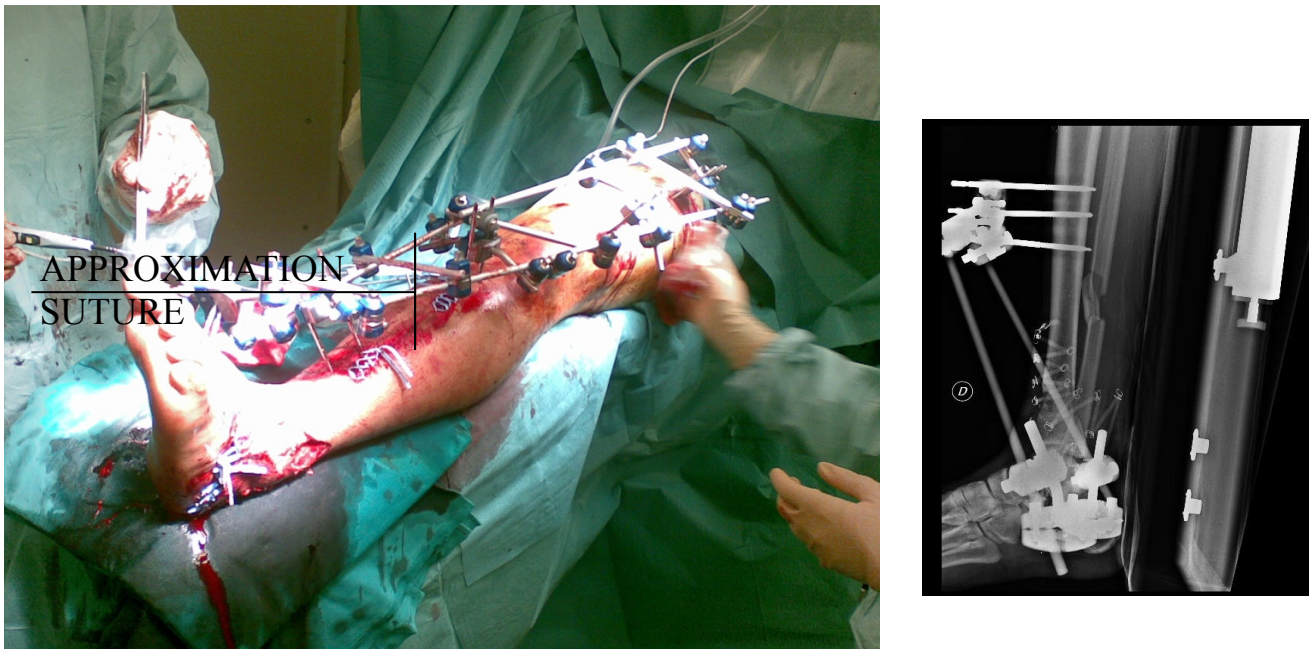

Figure 8: simple orthopaedic treatment of a 3B injury. Skin approximation is obtained with extremely tractioned skin edges through vessel loops (approximation suture). Duration of hospital stay: 192 days.

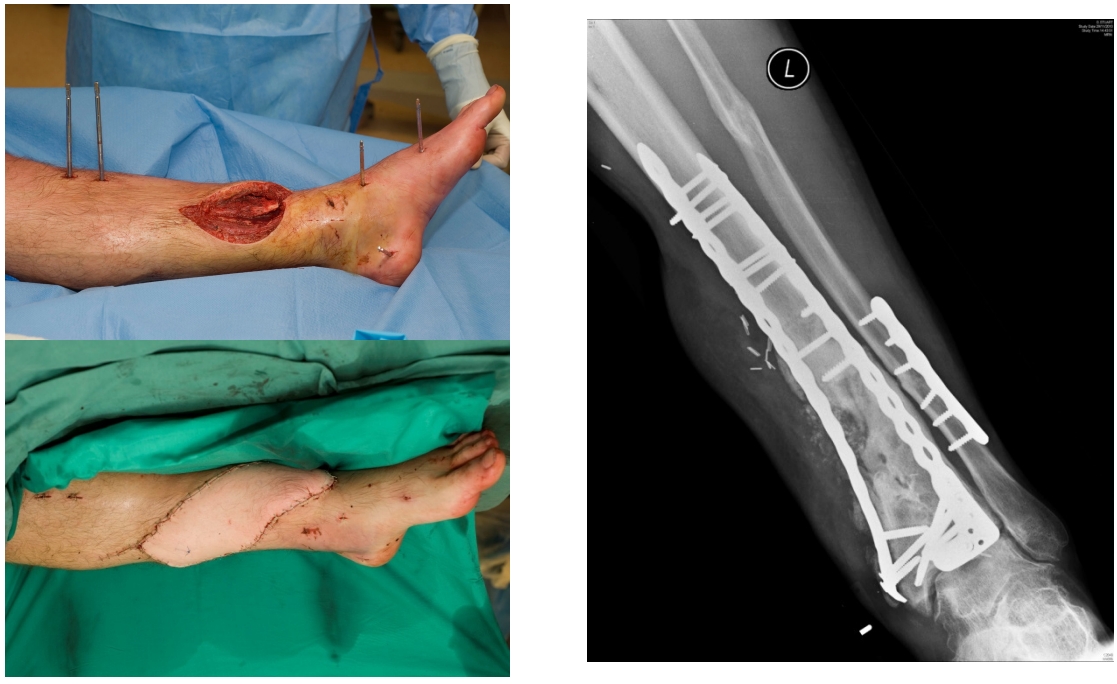

Figure 9: orthoplastic treatment of similar injury with the "fix and flap" philosophy, in an equally healthy, young patient. **Duration of hospital stay: 9 days, versus 192.**

6. Discussion

The orthoplastic approach in the treatment of open tibia fractures appears to improve clinical outcomes, in particular for patients sufferinng from high grade injuries (3B and 3C), based on the statistically significant results shown.

By comparing the three included centres, the orthoplastic approach allows a significant improvement of all outcome measures considered versus the simply orthopaedic care. Results are proven to be improved by the orthoplastic treatment even in a health care system of a country in the developing world compared to industrialized countries where the treatment of open fractures is lacking in terms of well managed, coordinated and rapid soft tissue reconstruction.

The demographic and clinical features of study patients proved to be homogeneously distributed in the two study arms with the exception of some features:

- Age appears to be lower in the combined group but this result is at the limit of statistically significance
- Transfer delay to the specialist trauma centre beyond one week is significantly more frequent in the combined group and this represents a less favourable starting point in the combined study arm, which nevertheless shows better results
- Major associated injuries occur significantly more frequently in the simple group and this can be interpreted as a reasonable prioritizing of surgical treatments, anticipating surgical procedures for life-threatening or more severe injuries (Life before limbs).
- High grade injuries (3B and 3C) are more frequently assigned to the combined group, as the higher the injury grade, the higher the advantages achieved through an orthoplastic approach.

In keeping with the results of this study, an earlier soft tissue closure, even in low degree injuries[36,37], allows an improved outcome of open tibia fractures and the biological rationale is the

recreation of an intact skin barrier which represents the fundamental, initial, mechanically-efficient arm of the immune system.

Some medical literature[38-45] has been recently published on the topic of open tibia fractures and lower limb reconstruction.

The general impression is that the combined approach to these severe injuries is the best option for both the benefit of the patient and the cost-efficiency purpose, in a period of limited and decreasing resources for insurance-based or National Health System-based organizations of care.

The apparently more costly initial surgical management with the combined treatment allows a reduction of several future costs, compared to the simple approach.

First of all hospitalization, but also outreach nurses or similar services for tissue viability and wound dressing, rehabilitation, medicaments, general assistance etc. are all huge costs that are compensated and indeed, greatly reduced by an initial well coordinated and multidisciplinary orthoplastic management.

7. Conclusion

Orthoplastic surgery of open tibia fractures results in:

1) Shorter duration of hospital stay

2) Improved functional recovery of the limb

3) Lower rate of reintervention

4) More rapid bone union and soft tissue closure

5) Lower rate of deep infection and osteomyelitis

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