ORIGINAL RESEARCH

The Cambridge Experience with Lower Limb Long Bone Non-union Following Fixation and the Treatment Algorithm

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Abstract

Aim: Non-unions have been traditionally classified as atrophic, oligotrophic and hypertrophic and their management was primarily dictated by that. In our Unit, we have based our treatment rationale mainly on the stability of the metalwork and the presence of symptoms rather than the radiologic appearance of the non-union or the presence of infection. The aim was to present the treatment algorithm for lower limb long bone non-union following operative fixation.

Materials and methods: All patients treated for a femoral or tibial non-union following fixation between 2014 and 2020 in our unit and with a minimum follow-up of 2 years were included. Non-union was defined as having no evidence of fracture healing in any cortices six months after the index procedure. Union was defined as bridging callus in at least three cortices visualized on at least two orthogonal radiographs. Information retrieved included demographic and fracture characteristics, presence of infection, evidence of metalwork stability and treatment. Outcome measures included union rate, time to union and complications. Data were analysed with the Statistical Program for Social Sciences (SPSS) using contingency tables and linear regression. A *p*-value of less than 0.05 was considered statistically significant.

Results: Seventy-seven consecutive patients were included in the study. Union was achieved in 91% of the cases, while union was noted in all the patients treated non-operatively. The mean time to union was 14.49 months (9.98). Complications were encountered in 20 of the patients and the most common were docking site non-union and metalwork breakage. Infection was the only factor that affected time to union in a statistically significant manner ($p = 0.006$).

Conclusion: The results of our study suggest that in cases of long bone non-union following operative fixation using signs of metalwork instability and the presence of clinical symptoms as the main indication for surgical intervention provides a satisfactory outcome. This approach prevented operative management in a large proportion of patients.

Clinical significance: This article presents an algorithmic approach that could aid clinicians in their decision-making in long-bone non-union management.

Level of evidence: Therapeutic level III.

Keywords: Circular external fixator, Femoral non-union, Non-union, Revision surgery, Tibial non-union, Watchful waiting.

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Introduction

Fracture non-union is a common complication with an estimated incidence of 18.94 non-unions per 100,000 population per annum, associated with significant physical and psychological implications and with a high socioeconomic burden.[1,2] Non-union treatment has been associated with multiple procedures and revision surgeries, high complication rates and poor functional outcomes.[3]

Traditionally, non-union have been classified as atrophic, oligotrophic and hypertrophic and their management was primarily dictated by that.[4,5] A decade ago, the "diamond concept" was introduced, emphasizing the importance of both mechanical stability and biological environment in fracture healing and providing a framework for non-union management.[6] Accordingly, various treatment options have been proposed, including circular frames, intramedullary (IMs) nails and plate fixation and several treatment algorithms have been developed.[5]

In the present study, we present our outcomes with lower limb long bone non-union management in a level I trauma center and provide a novel algorithmic approach for their treatment. The study received an approval by the Research Ethics Committee of the Cambridge University Hospitals NHS Foundation Trust. This treatment algorithm puts more emphasis on the stability of the metalwork and the presence of symptoms rather than the radiologic appearance of the non-union or the presence of infection.

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Materials and Methods

All patients treated for a femoral or tibial non-union in our department between January 2014 and December 2020 were

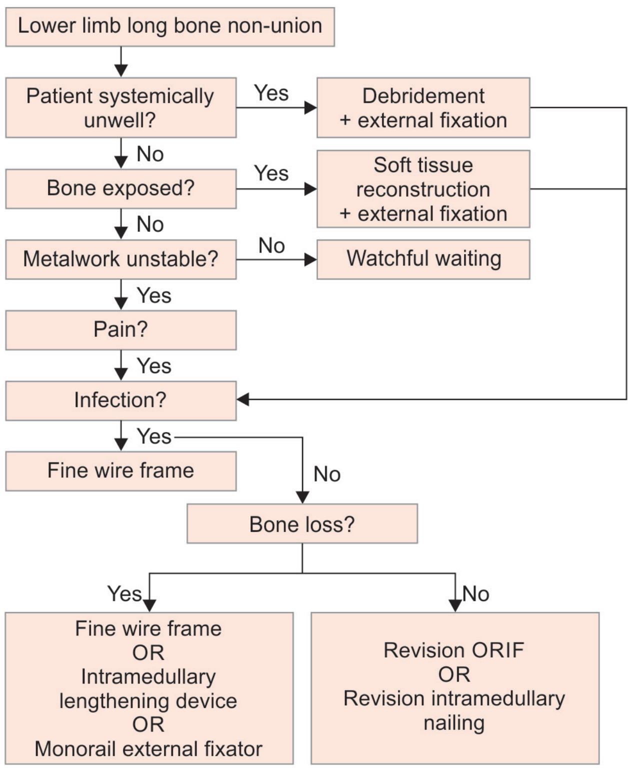


Fig. 1: The Cambridge algorithm for lower limb non-union management

reviewed {[International Classification of Diseases, 10th Revision (ICD-10) diagnosis M8415 [non-union of fracture (pseudarthrosis): Pelvic region and thigh] and M8416 [non-union of fracture [pseudarthrosis]: Lower leg]}. Non-union was defined as having no evidence of fracture healing in any cortices [anterior posterior (AP) and lateral radiographs or computed tomography (CT) scan] 6 months after the index procedure. Union was defined as bridging callus in at least three cortices visualized on at least two orthogonal radiographs. Patients with a follow-up period of less than 2 years were excluded from the study. The data were extracted from the hospital's electronic patient record (EPIC). Patient notes, outpatient letters and diagnostic imaging results were reviewed. Information retrieved from each patient included sex, age, side, smoking status, fracture location, history of an open fracture, presence of infection [and C-reactive protein (CRP) levels and pathogen isolated when infection present], evidence of metalwork instability, treatment (operative/non-operative and number and type of operations when operative treatment), outcome, time to union (if applicable) and complications. Complications were considered the following: Non-union, malunion, refracture, deformity, metalwork failure, neurovascular damage and thromboembolism. The diagnosis of infection was based on microbiological samples taken intraoperatively or the presence of a sinus. Metalwork was considered stable when there was no breakage or lucency of the implants and no displacement of the fixation.

Our treatment algorithm for non-union management is presented in (Fig. 1). The first factor taken into consideration is the presence of systemic symptoms of infection which dictates urgent debridement and application of an external fixator. In the presence of associated soft tissue loss and exposed bone, treatment includes initial management with an external fixator and soft tissue reconstruction. Next, the stability of the metalwork is evaluated.

Table 1: Patient demographic data, non-union characteristics

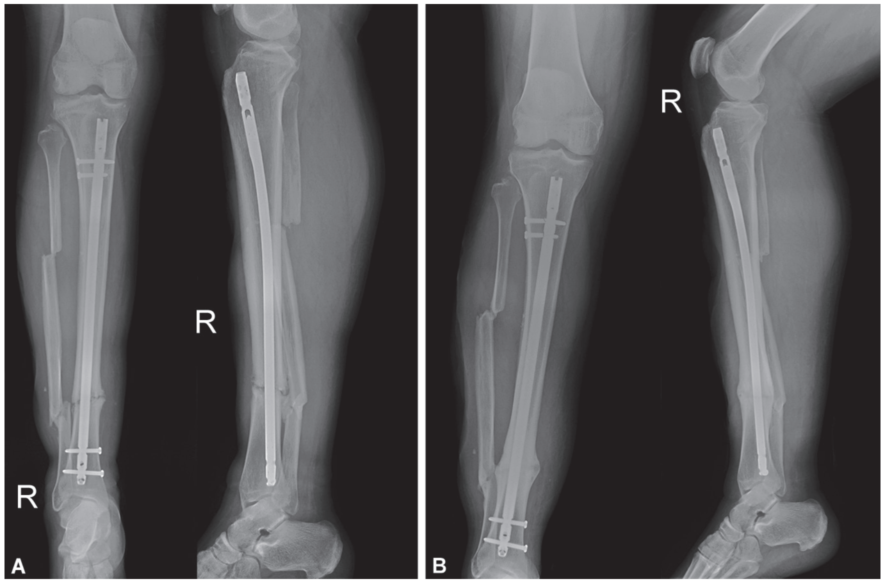
	N	*Percentage (%)*
Gender (males)	58	75.3
Side (right)	47	61
Smoking	17	22
Fracture location		
Proximal femur	5	6
Femoral shaft	18	23
Distal femur	9	12
Proximal tibia	7	9
Tibial shaft	16	21
Distal tibia	22	29
Open fracture	35	45
Infected	26	34
	Mean	*SD*
Age (years)	46.69	16.83
Time from initial injury (months)	13.57	7.57

If metalwork is considered unstable and the non-union is painful, this is then treated operatively. Otherwise, patients are managed conservatively with watchful waiting. Following this, if the non-union is infected but without any systemic symptoms, then a circular external fixator is applied. The preoperative diagnosis of infection was based on clinical appearance (presence or not of a sinus), CRP levels and magnetic resonance imaging (MRI) findings. Each case was discussed in a multidisciplinary meeting consisting of a consultant musculoskeletal radiologist, an infectious disease consultant, an orthopaedic and a plastic surgeon and a microbiologist. If there is no evidence of infection and no bone loss then a revision open reduction and internal fixation ORIF or a revision IM nailing with poller screws is attempted. Finally, when there is bone loss of at least 2 cm, resulting in limb length inequality, the patient is treated with a circular external fixator or an IM lengthening device.

Data were entered into an Excel sheet and were analysed using Statistical Program for Social Sciences (SPSS) software, version 21.0 (IBM Corporation, Armonk, NY). Categorical variables were expressed as frequencies. Continuous variables were given as mean [standard deviation (SD)]. Categorical variables were compared using contingency tables. Linear regression was used when the dependent variable was continuous. A *p*-value of less than 0.05 was considered to be statistically significant.

Results

The demographic data of the patients and the characteristics of the non-unions are summarized in Table 1. Seventy-seven cases were included in the study, sixty-seven of them were treated operatively while the rest were managed conservatively ($n = 10$). The mean follow-up period was 41.41 months (10.06). Patients managed with operative treatment had from 1 to 6 surgeries (mean, 1.37). The operative method for non-union treatment included revision ORIF, revision IM nailing with poller screws, circular external fixator [Taylor spatial frame (TSF) with or without a corticotomy and bone transport], application of lengthening IM devices (Precise/Fitbone nail) and application of monorail external fixators. Union was achieved in 91% of the cases ($n = 70$). The lowest



Figs 2A and B: Anteroposterior and lateral X-rays of a non-union managed with non-operative treatment. (A) X-rays of a tibial non-union with stable metalwork and the 46-year-old patient denied any pain or discomfort; (B) The X-rays after 12 months of watchful waiting showed a consolidation of the fracture

Table 2: Union rate, the mean time to union and the complications encountered per treatment method

Treatment method	*Number of patients (n)*	*Union rate (%)*	*Time to union (months) [mean (SD)]*	*Complications*
Revision IM nail + poller screws	20	90	11.82 (8.31)	Metalwork breakage ($n = 3$) Malunion ($n = 1$)
Revision ORIF	7	100	11.29 (7.67)	Metalwork breakage (n=1)
TSF	32	93.8	13.67 (7.41)	Docking site non-union ($n = 3$) Malunion ($n = 1$) TSF loosening ($n = 2$) Refracture ($n = 2$) Equinus deformity ($n = 2$)
Lengthening IM nail	5	60	35 (22.11)	Mechanical failure ($n = 1$) Healed corticotomy ($n = 1$)
Monorail Ex-fix	3	100	29.33 (13.32)	Metalwork breakage ($n = 1$) Docking site non-union ($n = 1$)
Conservative treatment	10	100	13.10 (6.14)	Metalwork breakage ($n = 2$) Malunion ($n = 2$)

IM, intramedullary; ORIF, open reduction and internal fixation

union rate was found in patients treated with lengthening IM nails (60%). Interestingly, the union was noted in all patients treated non-operatively (Fig. 2). In the remaining 7 cases, the union was not achieved within the minimum of 2 years of follow-up ($n = 6$), or the treatment failed and resulted in amputation of the involved limb ($n = 1$). The average time to union was 14.49 months (9.98). Complications were encountered in 20 of the patients and included docking site non-union, metalwork breakage, malunion, refracture, healing of the corticotomy, loosening of the TSF, equinus deformity of the foot after bone transport of the tibia and failure of a Precice nail to lengthen. The union rate, the mean time to union and the complications encountered per treatment method are summarised in Table 2. Treatment failures are presented in Table 3. No correlation was found between age [$R^2 = 0.01$, $F(1, 68) = 0.49$, $p = 0.452$], sex [$R^2 = 0.01$, $F(1, 68) = 0.57$, $p = 0.451$), smoking status ($R^2 = 0.01$,$F(1, 67) = 0.61$, $p = 0.436$) and previous open fracture ($R^2 = 0.02$, $F(2, 67) = 0.8$, $p = 0.452$) and time to union. Infected non-unions took a statistically significant longer time to heal ($R^2 = 0.11$, $F(1, 68) =8.17$, $p = 0.006$).

Regarding the infected non-unions, the most common pathogen isolated was *Staphylococcus aureus* and other *Staphylococci* species, *Enterobacter cloacae* and *Streptococci* species. In 11.5% of the infected non-union intraoperative cultures were negative. The microorganisms isolated from the infected non-unions are presented in (Fig. 3). The CRP levels remained normal in 15.8% of the cases. In the cases where CRP levels were elevated, they returned to normal in only 18.8%, even if there were no clinical signs of infection.

Discussion

In the present algorithmic approach, the presence of infection is not the only factor that determines the course of treatment.

Table 3: Treatment failures

Case	*Location*	*Infection*	*Treatment*	*Course of treatment*	*Latest state*
1	Femoral shaft	No	IM nail + poller screws	Delayed healing, Watchful waiting	Radiological healing* Patient asymptomatic
2	Femoral shaft	No	IM nail + poller screws	Breakage of locking screws: Revision IM nail IM nail + monorail fixation ORIF of docking site IM nailing of docking site	Radiological healing* Patient asymptomatic
3	Distal tibia	Yes	TSF	Repeated washouts, inability for wound closure	Amputation, stump wound healed, prosthesis fitted
4	Distal tibia	No	TSF	Docking site non-union, treatment with IM nailing	Radiological healing* Patient asymptomatic
5	Distal tibia	No	TSF	Docking site non-union, treatment with IM nailing	Radiological healing* Patient asymptomatic
6	Distal femur	No	Lengthening IM nail	Mechanical failure of the magnetic nail, revision with a motorised lengthening nail	Radiological healing Patient asymptomatic
*7	Femoral shaft	No	Lengthening IM nail	Delayed healing corticotomy, watchful waiting	Radiological healing* Patient asymptomatic

*Radiological healing is defined as evidence of callus formation on anteroposterior and lateral X-rays that does not meet the criteria for union as defined in the article

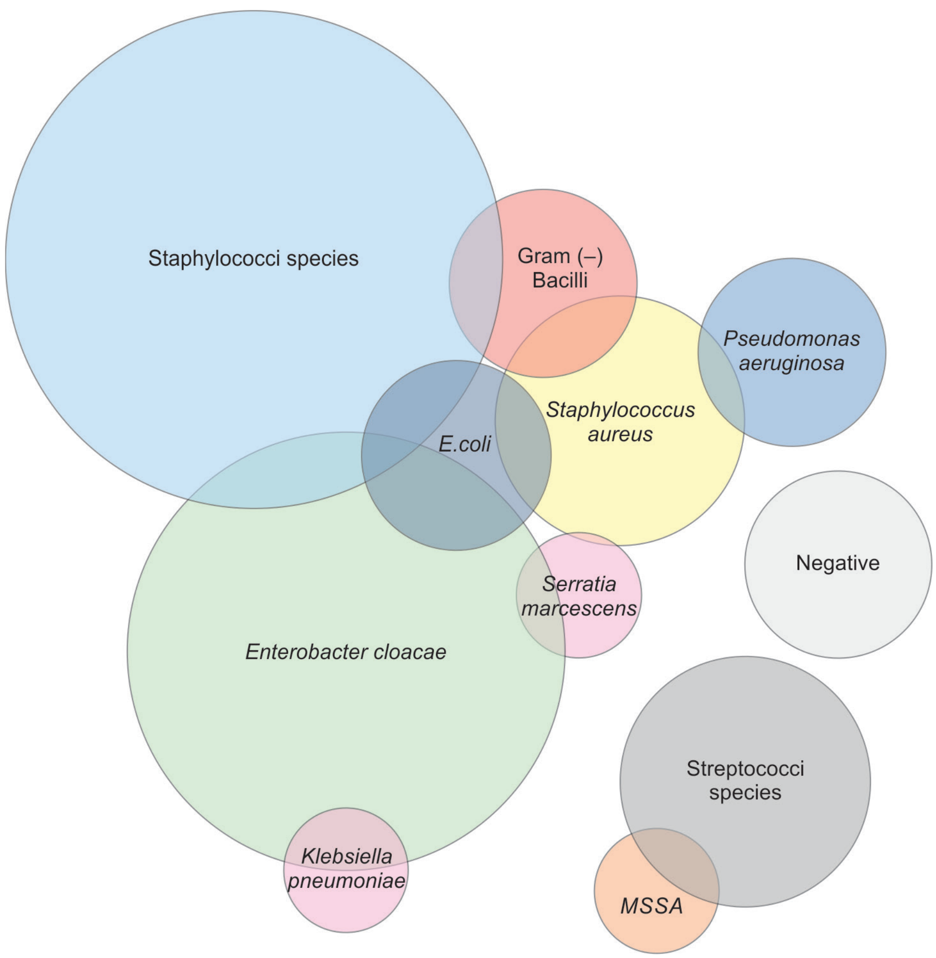


Fig. 3: Venn diagram indicating the isolated pathogens from the infected non-unions. Pathogens that were isolated only once are not presented in the diagram

Apparently, the presence of symptoms of sepsis dictates an urgent treatment with debridement of the infected non-union, irrigation and stabilization with an external fixator. Accordingly, a non-union accompanied by extensive soft tissue loss and exposed bone requires input from plastic surgery and coverage with a flap or a skin graft. In the absence of those two parameters, if the metalwork is stable and the patient does not complain of pain, even if the non-union is infected, a strategy of watchful waiting may be beneficial for the patient. The results of the present study indicate that this approach led to the union in all non-operatively cases and within a reasonable time.

In our study, the union was achieved in 91% of the cases. Seven cases were categorized as failed treatment. One case was an infected tibial non-union of an open fracture that was managed with a TSF. Unfortunately, because of ongoing wound complications despite repeated washouts and plastic surgery input, an amputation was required. Two more patients with tibial fractures in the TSF group were categorized as failures due to docking site non-union that was managed with IM nailing. Two patients with femoral shaft non-unions in the revision IM nailing group failed. One of them failed due to breakage of the locking screws that resulted in instability of the construct. This was followed by multiple operations and currently, the patient is asymptomatic with radiographic findings of union. There were no complications in the other patient but unfortunately, the radiological union has not been achieved yet. The patient has no pain and the metalwork is stable, therefore he is managed with watchful waiting.

All treatment methods resulted in high union rates of more than 90% with the exception of lengthening IM nailing. Lengthening IM devices resulted in union in three out of five patients (60%). This was a result of mechanical failure of the device in one of the cases and delayed healing of the corticotomy in another. The mechanical failure was encountered in a magnetic nail that is no longer used in our Unit. Similar reports were reported in the published literature.[7] The number of patients treated with a lengthening IM nailing in our study is small and therefore this outcome should be interpreted with caution.

We used a linear regression model to detect possible correlations between patient and non-union characteristics and union rate and time to union. Surprisingly, the presence of infection was the only parameter that negatively affected time to union in a statistically significant manner. We were not able to establish any correlation between the smoking status or a history of open fracture and time to union and this may be a result of the size of our sample.

Andrzejowski and Giannoudis reported a 98% success rate in the management of long bone non-union by employing the “diamond concept.”[8,9] Haubruck et al. reported a union rate of 48–97% in lower limb non-unions treated operatively and with the use of bone morphogenetic proteins (BMPs).[10] Moghaddam et al. achieved an 80–84% union rate in tibial non-unions with the Masquelet procedure.[11] Ollivier et al. had a 90% success rate in the management of recalcitrant tibial non-unions with operative treatment and bone grafting.[12] Our management does not include biologic augmentation, such as autografts, allografts or other osteoinductive factors. The union rate in our study was 91%. In seven cases, union has not been achieved; however, in six of them, there were radiological signs of callus formation. To the best of our knowledge, conservative management has not been attempted in any of the published studies. Operative treatment has not only economic implications but is also associated with psychological consequences and an impact on the quality of life of the patients. In the present study, we show that operative treatment can be avoided in a large proportion of patients with lower limb non-union following fixation.

In the clinical setting, bone infections are usually treated as soon as the clinical manifestations occur, making it impossible to evaluate long-term outcomes of bone healing in the presence of infection. In general, bone infection is associated with an impaired healing response. However, *in vitro* and animal studies have indicated that although infection delays callus formation and alters callus strength, fracture healing does occur in the presence of infection.[12,13] Croes et al. in a rabbit tibia model of periprosthetic infection, showed that paradoxically, inflammatory reaction caused by bacterial antigens stimulates bone formation. The authors noticed a twofold higher bone volume in the infected tibiae compared to the uninfected controls.[14,15] In our approach, even in the presence of infection, if metalwork is stable and there are no associated symptoms, the non-union is managed conservatively.

The present study has to be seen in light of certain limitations. This is a retrospective study and the data were extracted from patient charts and hospital records. Due to the retrospective nature of the study, there was no randomization and operative treatment was based on surgeon’s preference which might introduce selection bias. Non-union treatment often needs to be personalized to the patient given not only the unique non-union scenario but also the patient social situation, coping ability and functional goals. Also, no restriction was placed on the fixation device used or outcome subdivisions for different types of non-unions. This increases the heterogeneity of the data and relevant conclusions should be interpreted with caution. Future prospective, randomized studies and with longer follow-up periods are required to validate the results of the present study.

Conclusion

The results of our study suggest that in cases of long bone non-union following operative fixation using signs of metalwork instability and the presence of clinical symptoms as the main indication for surgical intervention provides a satisfactory outcome. By following this approach, we achieved a 91% union rate and the union was noted within a reasonable time.

This indicates that operative management can be avoided in a large proportion of patients with long bone lower limb non-union following fixation.

Clinical Significance

This article presents an algorithmic approach that could aid clinicians in their decision-making in non-union management. Although every non-union has unique characteristics and often requires an individualized approach, we provide a framework for long bone non-union treatment following operative fixation.

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