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COMPARISON OF THE VALUES OF EFT (External Fixation Time) IN THE TREATMENT OF LOWER LEG OPEN FRACTURES AND NON-UNIONS WITH THE METHOD OF COMPRESSION-DISTRACTION OSTEOSYNTHESIS BY ILIZAROV

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Abstract

Open tibial fractures rank among the most common injuries to long bones, with an annual incidence of 3.4 per 100,000. Complications such as non-unions may arise in 2-10% of these injuries. The Ilizarov method offers a universal opportunity for definitive treatment in both conditions.

This retrospective unicentric cohort study aims to assess the value of External Fixation Time (EFT) in patients with open tibial fractures and non-unions treated with compression-distraction osteosynthesis by Ilizarov, followed by a comparative analysis.

We evaluated 30 patients treated between 2014 and 2019 for open fractures or non-union of the tibia. The average ages for the two groups were 46 and 50 years, respectively. The latter group had an average of 1.6 prior surgical treatments, with approximately 14 months elapsed since the injury. All subjects examined achieved bone healing. The average EFT values were 160 and 210 days for the treatment of open fractures and non-unions, respectively. There is a statistically significant difference in the EFT values between both groups. 97% of the patients demonstrated satisfactory radiographic results based on the ASAMI scoring system.

Treatment with compression-distraction osteosynthesis by Ilizarov proved effective for both open fractures and non-unions of the lower leg. A statistically significant difference exists between the two groups in terms of EFT values representing the duration of treatment.

Keywords: open fractures, non-unions, Ilizarov, EFT.

Introduction

Fractures of the tibia are among the most frequent long bone fractures with according to some data incidence of 11.5 over 100000 population and with 40% of open fractures being in lower extremities. [1] Other research claim that 0.2% of all injuries are open tibial fractures [2] or that incidence of these open tibial fractures is 3.4 over 100000 population per year. [3]

Average age of the patients who suffer from these injuries is 43.3 years but with bimodal distribution in young men and older women. High energy trauma like motor vehicle accident or high height fall is the main reason for these fractures with over 50% of all of them. [4, 5]

In a prospective observational study of 416 patients from 41 trauma center who were surgically treated for diaphyseal tibial fractures in 13% there was delayed union or non-union. In open fractures with skin wound bigger than 5cm the probability for these complication was 5.7 times higher compared to closed fractures. [6, 7] Usually the open fractures are the ones prone to complications like infections, delayed or non-unions and with all that are burdens not only for the individuals but for the whole healthcare system.

Historically, the definitions of delayed union or non-union of bones were contingent on the time elapsed since the injury. However, presently, the precise timing of the injury has diminished in significance. Bone healing is now recognized as a dynamic and progressive process, warranting

intervention when radiological findings reveal an absence of progression in the bone healing process within 3 to 5 months from the time of injury.[8]

The term "delayed healing" is applied to fractures that do not heal within the anticipated timeframe. In cases of delayed healing, the healing process is slower, but there is still a possibility of eventual healing without the need for additional treatment. Fractures of the tibia are categorized as delayed healing fractures when there is insufficient bridging callus even after 16 weeks from the time of injury. In contrast, non-union or pseudoarthrosis is diagnosed in fractures where healing is not achievable without supplementary treatment, whether surgical or conservative. This determination is typically made within the period of 6 to 9 months.

Tibial non-unions are estimated as a complication of 2-10% of all tibial fractures. Zura et al. analyzed over 12000 tibial fractures and documented 7.37% of non-unions. [9]

The incidence is increased in high energy trauma and open fractures. The development of non-union is usually influenced from type and extension of the injury, the extent of bone comminution and bone loss, the soft tissue injury, the presence of compartment syndrome or infection etc. [10]

In one observational study that included over 200 patients with tibial fractures Fong et al. concluded that non-union is developed when there is less than 25% of cortical continuity. [11] The biggest risk is noticed when the open wound is at the place of bone defect. Smoking is also an additional risk for delayed or non-union. [12] There is a discussion whether NSAIL could inhibit bone healing but definite negative effect is not stated in human studies. [13]

In any case fast and thorough treatment is needed in lower leg injuries because iatrogenic injury of the soft tissue envelope, distraction at the site of fracture, inadequate immobilization and absence of the stabilization effect of the intact fibula are factors that could contribute to non-union development.

Basic treatment protocols of these injuries include treating of the soft tissue injury, minimizing the risk of infection, stabilizing and repair of the skeletal injury and functional restitution of the injured extremity. [14, 15, 16, 17] Treatment of these conditions is still a field of orthopedics where there could be expected improvement of the standardized treatment modalities. [18]

There are different ways of treating the skeletal trauma of the lower leg including intramedullary fixation, plating, external fixator etc. The non-unions as one of the most treatment challenging complications following the open tibial fractures are still clinical and economical burden not just for the patient but also for the society. Despite the need for evidence based protocols for treatment in literature there are still not unified agreements even for the definition of the condition itself. From that point of view we can see that the treatment is still and most frequently base on individual approach.

The principle of compression-distraction osteosynthesis with Ilizarov frame is a concept that respects the biomechanical characteristics of the bone and in the same time enables activation of the bone healing potential in these injuries. [19, 20, 21]

Biomechanical surrounding could be the main reason for developing delayed or non-unions as complications of tibial fractures. Therefore to enhance the optimal biological surrounding for bone healing this method of compression - distraction osteosynthesis by Ilizarov acquires all the principles for that. [22, 23] Those are the mechanical principles: rigid fixation, possibility for fracture reduction in three dimensions simultaneously, possibility for early mobilization and weight bearing and biological principles: preservation of the osteogenic tissues (periost, endost and bone marrow), enabling and preservation of the circulation locally. All these principles are aiding the reparative osteogenesis with activation of bone healing potential trough consolidation of the bone and shortened treatment timing. Two illustrative cases are presented in the text showing intraoperative and postoperative x-rays of two patients, first one with bilateral open tibial fractures – picture 1, and second one with tibial non-union – picture 2.

Additional advantage of the Ilizarov circular external fixator (frame) is the ability to manipulate the biomechanical rigidity of the apparatus depending of the bone fragments, the possibility for correction of the frame based on individual approach and radiological progress of the healing, the unique option to study the process of bone and soft tissue healing and regeneration as an basic and also clinical research. The universality of the frame practically offers endless possibilities.

On the other hand as in any method there are also some disadvantages: learning curve, the need for frequent monitoring of the patient, the risk for local inflammation around the wires, the risk for development of contractures in the need for fixation of adjacent joints, aesthetic inconvenience from its

dimensions and at last the need of full consent and collaboration with the patient during the treatment. During the whole treatment and afterwards the role of physical therapy and rehabilitation should be accented to preserve the muscle tonus and ROM in adjacent joints.

During one study of open tibial fractures type III by Gustillo in patients older than 75 years of age Steel and al. concluded that the functional results were not satisfying in this group suggesting that these patients could benefit from bigger accent on intensive rehabilitation. [24]

Material and methods

In the research we included patients with open tibial fractures and non-unions treated with the method of compression – distraction osteosynthesis by Ilizarov in the Specialized hospital for orthopedics and traumatology "Sv. Erazmo" – Ohrid during the period from 2014 – 2019. In both of the groups (open fractures vs non-unions) 15 patients are included retrospectively which fulfilled the inclusion criteria: age 18 or over, condition with open tibial fracture or non-union, surgical treatment of the condition with the suggested method, possibility for postoperative monitoring and evaluation of the patient 3-6 months after removing the apparatus. All the patients were preoperatively evaluated for the possible risk of the treatment and anesthesia and signed consent for anesthesia and surgical treatment by themselves. In the group with open fractures the time from injury till present treatment is calculated in days – Table 1. In the other group of patients with non-unions the time in months from injury to present treatment is calculated and also the number of previous treatments – Table 2.

Picture 1. Treatment of patient with bilateral open tibial fractures (type 3 by Gustillo-Anderson classification)

In the group with open fractures the ratio women/men was 0.25 (w:m=3:12) with average age of 46 years (ranking 18 to 83 years). In the group with non-unions the ratio women/men was 0.36 (w:m=4:11) with average age of 50 years (ranking from 34 to 67 years). In average there were 14 months from the initial injury in these patients with approximately 1.6 previous surgical treatments per patient.

In all patients at least two standard x-rays were performed in AP and LL view of the lower leg preoperatively, as a complete laboratory blood analysis, and in those with skin defect or open wound swab from the wound was taken for microbiological analysis. Surgical treatment was performed in spinal anesthesia. The usual way of performing the osteosynthesis with the Ilizarov frame was with 4 segmental rings with 3,2,2,3 wires respectively. During the surgery there were additional radiological investigations for assessment of the fracture fragments and the wires of the fixator. During the surgery an antibiotic therapy was administered and continued for 7 days in patients without osteomyelitis or in the next 6 weeks in the patients with osteomyelitis. Postoperatively thromboprophylaxis was administered with low molecular heparin for the next 1 month in all patients. In all the patients starting

from the second postoperative day a physical therapy and walking with minimal to partial weight bearing was initiated with crutches or walker.

Table 1. Patients with open tibial fractures treated with the method of compression – distraction osteosynthesis by Ilizarov

	Age	Days till treatment	Gender	Previous treatments	EFT in days	ASAMI radiographic score
1	18	17	F	0	97	4
2	61	0	M	0	153	3
3	39	9	M	0	228	4
4	50	0	M	0	155	3
5	32	12	M	0	145	4
6	41	0	M	0	145	4
7	61	7	F	0	219	4
8	27	5	M	0	257	4
9	83	2	F	0	129	3
10	34	5	M	0	208	3
11	77	0	M	0	68	3
12	65	10	M	0	76	4
13	43	8	M	1	179	4
14	44	0	M	0	198	4
15	22	0	M	0	148	4

Hospitalization usually lasted in average 9 days, and after that in all the patients regular outpatient check-up were performed for sterile dressing of the frame on every 1-2 weeks. Additionally regular radiological investigations with 2 standard x-rays were performed on every 4-6 weeks in order to evaluate bone healing process. On individual assessment if needed additional manipulations of the apparatus were performed (usually compression at the site of fracture/non-union) as an additional stimulus to the bone healing potential. Consolidation of the fracture/ non-union is confirmed when there is no radiolucent line or when the defect is filled with new bone formation on minimum 3 of 4 cortices at the standard AP and LL radiological projections. Additionally this radiological assessment is confirmed with clinical testing of the functional stability at the site of fracture/non-union with loosening the rods locally.

After that one more surgical procedure for removing the external fixator is scheduled in short term anesthesia and plaster immobilization of the lower leg is put in the next 2-3 weeks with allowed weight bearing through the immobilization.

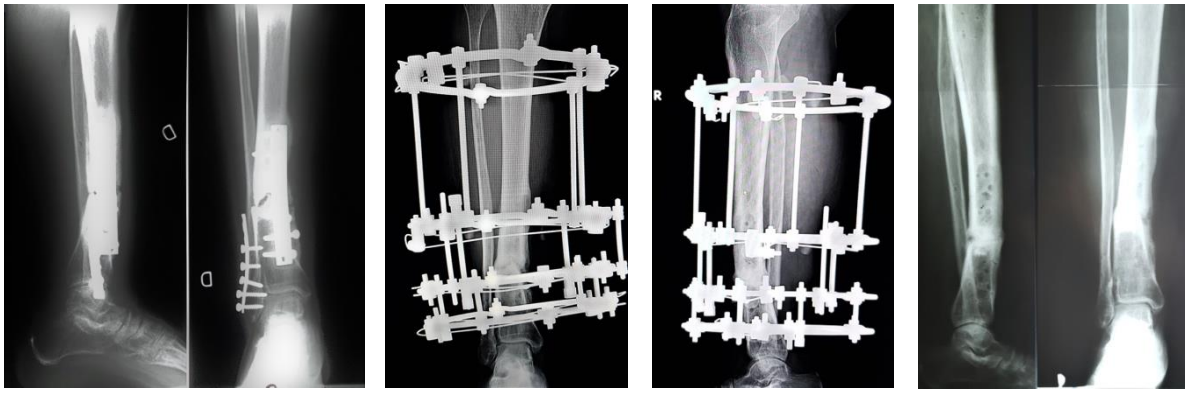
Results

All the patients were evaluated postoperatively after removing the Ilizarov frame and External Fixation Time (EFT) was calculated – the whole period from the surgery when the frame was implanted till the extraction of the frame. The patients were also evaluated according to the ASAMI (Association for studying and implementation of the Method of Ilizarov) scoring system for radiological (bone) results in 4 categories: excellent, good, fair and poor results.

Radiological results are based on 4 criteria: acquiring bone healing, presence of infection postoperatively, axial bone deformity less/more than 7 degrees and leg length inequality less/more than 2.5 cm.

Average EFT value in the group with open fractures is 160 days (ranking from 68 till 257 days), and in the group with non-unions is 210 days (with values ranking from 116 to 331 days). We used Student t-test to evaluate the statistically significant difference of the calculated values between the two groups. The calculated value of $p=0.0342$ with previously determined values of $p<0.05$ as statistically significant difference means that there is statistically significant difference between the EFT values of the two given groups.

In the group with patients treated for tibial non-union in 6 of them there was infection present or fistula with secretion at the level of non-union. When we used Student t-test to evaluate if there is statistically significant difference in EFT in the patients with tibial-non union but divided in subgroups with or without infection we gained $p=0.5683$ with previously stated values of $p<0.05$ as statistically significant difference. That means that there is no statistically significant difference in the values of EFT between these two subgroups. Also there is no statistically significant difference between the two main groups when taking into account the age of the patients in both groups.



Picture 2. Treatment of patient with infected non-union of tibia comparatively before and after treatment with compression – distraction osteosynthesis with Ilizarov method

When performing the Pearson correlation test for defining the possible correlation of numeric variables we didn't get significant correlation between the values of EFT and the number of previous surgical treatments. The same result we got when investigating the correlation of the values of EFT with the patient age – meaning there is no statistically significant correlation between these two parameters.

According to the postoperative results from the scoring by the ASAMI scoring system in all the patients bone healing was achieved. All the patients within the group with open fractures according to the radiological (bone) results have excellent or good result (67% of them excellent and 33% of them good result).

When evaluating the patients treated with tibial non-union according to the radiological (bone) results by the ASAMI scoring system in all of them bone healing was also achieved. In this group in 93% (14 patients) there is satisfying result (from which 36% excellent and 64% good radiological result). In 7% of the group (1 patient) there was fair radiological result because of persistent shortening of the lower extremity more than 2.5 cm compared to contra lateral side and also persistence of small fistula with occasional secretion despite achieving bone healing of the non-union.

Table 2. Patients treated because of non-union of tibia with suggested method

	Age	Months from injury	Infection	Gender	Previous surgeries	Additional conditions	EFT in days	ASAMI bone score
1	35	24	Yes	F	1		154	3
2	53	8	No	M	1	Peroneal palsy	172	4
3	44	12	Yes	M	2		116	4
4	56	14	No	M	2		125	3
5	49	19	Yes	M	1		215	3
6	41	19	Yes	M	7		204	3
7	53	12	No	M	0	Femur fracture	288	3
8	53	8	No	F	0		331	4
9	34	3	Yes	M	1		229	3
10	54	12	No	M	1	Ankle arthrodhesis	125	4
11	62	4	No	M	2		265	3
12	67	13	No	F	2	Ankle arthrodhesis	221	4
13	50	9	Yes	M	2		266	3
14	51	31	No	M	3		165	2
15	50	23	No	F	0	Chronic renal insuf	272	3

We used Mann-Witney U test for evaluating if there is statistically significant difference between the two groups according to the ordinal values from the ASAMI scoring system. We got values for $p=0.0505$ with previously stated values of $p<0.05$ as statistically significant difference. The evaluated result means that there is no statistically significant difference in the evaluated radiological (bone) results according to ASAMI scoring system between the group with open fractures and the group with non-unions treated with the method by Ilizarov.

Discussion

In the past, the Ilizarov compression-distraction osteogenesis method was extensively employed for treating and reconstructing posttraumatic complications in lower extremities. This

technique provides clinicians with a crucial tool for addressing a variety of challenging cases, including long bone reduction defects in the lower leg, infected non-unions involving both bone and soft tissue defects, pronounced angular and rotational deformities, joint contractures, and the stabilization of open fractures with substantial compromise to the soft tissue envelope. [25]

Main advantages of this method are: minimally invasive approach with decreased risk for infection, the possibility to address besides the bone deformity also a soft tissue defect, adjacent joint contractures and at the same time allowing early postoperative weight bearing in order to minimize the risk for developing sympathetic algodstrophic changes of the lower leg. On the other hand there are some disadvantages like the length of the treatment, the need for regular monitoring of the patients etc. That's why it is important to communicate with the patient the real prognosis for the treatment before the surgery. [26]

Besides that there is also a psychosocial burden of the patient including pain, stress, as well as prolonged treatment time that can restrict the patient everyday activities. [27]

When discussing the prognosis of tibial non-union treatment in the literature, there is a notable scarcity of data regarding the functional outcomes post-treatment. Simply achieving bone healing does not automatically ensure the full functional restoration of the extremity. It's not uncommon for properly treated patients with satisfactory clinical results to experience residual pain, weakness, and functional limitations.This underscores the importance, during treatment, of consistently emphasizing the necessity for extended rehabilitation and an exercise program. This approach is crucial for sustaining the mobility of adjacent joints and addressing any lingering issues related to pain, weakness, or functional constraints.

Usage of additional therapeutic modalities is still controversial part of the treatment of the non-unions like electrostimulation, ultrasound, different synthetic osteoconductive materials or osteoinductive bone growth factors like BMP. [28]

One Meta analysis which reviewed 138 studies concluded that the bone healing is achieved 2 months earlier when ultrasound therapy was used. [29]

During the treatment we face different complications among which most frequent is local soft tissue inflammation around the wires which is considered as minor complication and usually is treated with frequent sterile local dressings and antibiotic therapy administered orally. In this study in 60% of the subjects we registered this complication and almost all of them were treated successfully. Only in one patient (3% of all subjects) there was a need for removing the wire and local curettage.

It was performed in local anesthesia without long term effect to the result that was achieved by the treatment. Most of the complications that are registered during the treatment of the non-unions are prolonging the time needed for bone healing and that is why our approach to the problem should be extremely carefully. Probably the biggest worry is not to develop infected from aseptic non-union. [30] In a study performed by Wu in 1994 in 13% of the patients treated for tibial non-union an infection developed independently from the type of the treatment (plating or intramedular fixation). [31]

This study has several limitations that should be acknowledged. Firstly, it is a retrospective unicentric study with a relatively small number of subjects, raising concerns about the potential for generalization and introducing bias to the results. The limited number of subjects also constrains the scope of statistical evaluation. Additionally, the study lacks the ability to provide a long-term assessment of patients and their functional outcomes. However, there are plans to address this limitation through continued research, incorporating patient questionnaires for comprehensive functional evaluations. Furthermore, only half of the subjects have available functional results one year after the removal of the apparatus. Despite these limitations, we contend that this small patient series is valuable as it provides additional support for considering the Ilizarov compression-distraction osteosynthesis method as a reliable approach for achieving bone healing and correcting bone deformities in challenging reconstructive cases. It is crucial to note that while the method may yield excellent bone results, especially in challenging bone conditions, favourable functional outcomes are not guaranteed unless the patient maintains good neurovascular status. The functional result is predetermined from the condition of the muscles, nerves, circulation, adjacent joints, and in less degree from the bone itself. [32] In addition by defining the preoperative and postoperative protocols with special accent of the rehabilitation, the patients are given opportunity for reaching satisfactory functional results. Although in the open fractures the prompt and early treatment is very important, the incidence of non-unions is more in correlation with the fracture characteristics then with the type of the treatment. [33] In one

study by Tanner and al. is concluded that the diabetes has negative effect on the results from the treatment of the tibial non-unions, and at the same time the age over 60 by itself is not contributing the same way. [34]

The current statistically significant difference in External Fixation Time (EFT) values between the two groups cannot be elucidated by the performed statistical evaluations. This discrepancy is not correlated with the age of the patients, the time elapsed from injury to treatment, or the number of prior surgical treatments. To ascertain the reasons for this significant difference in EFT values, an additional analysis is imperative. This analysis should incorporate data on the type of fracture, the size of the skin wound at the fracture site, and factors associated with the patient's general health status, such as diabetes, smoking, anemia, and other relevant variables.

Conclusion

The application of the compression-distraction osteosynthesis method by Ilizarov proves to be effective in treating both open tibial fractures and tibial non-unions. The assessment of the treatment reveals a high overall percentage of bone healing, accompanied by a substantial proportion of excellent and good radiological (bone) results. A statistically significant difference in External Fixation Time (EFT) values is observed when comparing the two groups, indicating a significantly longer time required for bone healing in the tibial non-union group. Despite the variables evaluated in this research, the primary reason for this outcome remains undetermined. Therefore, we recommend an extension of the current research to further investigate and identify the underlying factors contributing to this result.

References

1. Court-Brown CM, Rimmer S, Prakash U, McQueen MM. The epidemiology of open long bone fractures. Injury. 1998 Sep;29(7):529-34. doi: 10.1016/s0020-1383(98)00125-9. PMID: 10193496.
2. Behrens F, Searls K. External fixation of the tibia. Basic concepts and prospective evaluation. J Bone Joint Surg Br. 1986 Mar. 68 (2):246-54. [Medline].
3. Court-Brown CM, Bugler KE, Clement ND, Duckworth AD, McQueen MM. The epidemiology of open fractures in adults. A 15-year review. Injury 2012;43:891-7. [PubMed] [Google Scholar]
4. Larsen P, Elsoe R, Hansen SH, et al. Incidence and epidemiology of tibial shaft fractures. Injury 2015;46:746-50. [PubMed] [Google Scholar]
5. Jenkins PJ, Keating JF, Simpson AH. Fractures of the tibial shaft. Surgery 2010;28:489-93. [Google Scholar]
6. Audigé L, Griffin D, Bhandari M, Kellam J, Rüedi TP. "Path analysis of factors for delayed healing and nonunion in 416 operatively treated tibial shaft fractures." Clin Orthop Relat Res. 2005 Sep.438:221-32.
7. Will RE, Fleming ME, Lafferty PM, Fletcher JW, Cole PA. "Low complication rate associated with raising mature flap for tibial nonunion reconstruction." Journal of Trauma.2011 Dec. 71(6):1709-14.
8. Wiss DA, Stetson WB. Tibial Nonunion: Treatment Alternatives. J Am Acad Orthop Surg. 1996 Oct. 4 (5):249-257. [QxMD MEDLINE Link].
9. Zura R, Watson JT, Einhorn T, Mehta S, Della Rocca GJ, Xiong Z, et al. An inception cohort analysis to predict nonunion in tibia and 17 other fracture locations. Injury. 2017 Jun. 48 (6):1194-1203. [QxMD MEDLINE Link]. [Full Text].
10. McQueen MM, Christie J, Court-Brown CM. Acute compartment syndrome in tibial diaphyseal fractures. J Bone Joint Surg Br. 1996 Jan. 78 (1):95-8. [QxMD MEDLINE Link]
11. Fong K, Truong V, Foote CJ, Petrisor B, Williams D, Ristevski B, et al. Predictors of nonunion and reoperation in patients with fractures of the tibia: an observational study. BMC Musculoskelet Disord. 2013 Mar 22. 14:103. [QxMD MEDLINE Link]. [Full Text].
12. Schmitz MA, Finnegan M, Natarajan R, Champine J. Effect of smoking on tibial shaft fracture healing. Clin Orthop Relat Res. 1999 Aug. 184-200. [QxMD MEDLINE Link].

13. Fader L, Whitaker J, Lopez M, Vivace B, Parra M, Carlson J, et al. Tibia fractures and NSAIDs. Does it make a difference? A multicenter retrospective study. Injury. 2018 Dec. 49 (12):2290-2294. [QxMD MEDLINE Link].
14. Okike K, Bhattacharyya T. Trends in the management of open fractures. A critical analysis. J Bone Joint Surg [Am] 2006;88-A:2739-48. [PubMed] [Google Scholar]
15. Zalavras CG, Patzakis MJ. Open fractures: evaluation and management. J Am Acad Orthop Surg 2003;11:212-9. [PubMed] [Google Scholar]
16. Pape H-C, Webb LX. History of open wound and fracture treatment. J Orthop Trauma 2008;22(suppl):S133-4. [PubMed] [Google Scholar]
17. Chen AT, Vallier HA. Noncontiguous and open fractures of the lower extremity: Epidemiology, complications, and unplanned procedures. Injury 2016;47:742-7. [PubMed] [Google Scholar]
18. O'Toole, Robert V. MD*; Gary, Joshua L. MD†; Reider, Lisa PhD‡; Bosse, Michael J. MD§; Gordon, Wade T. MD‖; Hutson, James MD¶; Quinnan, Stephen M. MD¶; Castillo, Renan C. PhD‡; Scharfstein, Daniel O. ScD**; MacKenzie, Ellen J. PhD‡; METRC A Prospective Randomized Trial to Assess Fixation Strategies for Severe Open Tibia Fractures: Modern Ring External Fixators Versus Internal Fixation (FIXIT Study), Journal of Orthopaedic Trauma: April 2017 - Volume 31 - Issue - p S10-S17 doi: 10.1097/BOT.0000000000000804
19. Ilizarov, Gavril A. Transosseous Osteosynthesis: Theoretical and Clinical Aspects of the Regeneration and Growth of Tissue, Springer Science & Business Media, 2012
20. Limb Lengthening and Reconstruction Surgery Case Atlas, Springer International Publishing, Editors: Rozbruch, S. Robert, Hamdy, Reggie (Eds.) Copyright: 2015
21. Gubin AV, Borzunov DY, Marchenkova LO, Malkova TA, Smirnova IL. Contribution of G.A. Ilizarov to bone reconstruction: historical achievements and state of the art. Strategies Trauma Limb Reconstr. 2016;11(3):145-152. doi:10.1007/s11751-016-0261-7
22. Compton, Jocelyn & Fragomen, Austin & Rozbruch, S Robert. (2015). Skeletal Repair in Distraction Osteogenesis: Mechanisms and Enhancements. JBJS Reviews. 3. e2-e2. 10.2106/JBJS.RVW.N.00107.
23. Goldstein RY, Jordan CJ, McLaurin TM, Grant A. The evolution of the Ilizarov technique: part 2: the principles of distraction osteosynthesis. Bull Hosp Jt Dis (2013). 2013;71(1):96-103.
24. Steele J, Pedersen JB, Jay S, Lohn J, Nielsen D, Vesely M, et al. Gustilo-Anderson type III tibial fractures have poor functional outcomes in patients over 75 years. J Clin Orthop Trauma. 2020 Feb. 11 (Suppl 1):S71-S75. [Medline].
25. Schottel PC, Muthusamy S, Rozbruch SR. "Distal tibial periarticular nonunions: ankle salvage with bone transport." J Orthop Trauma.2014 Jun;28(6):e146-52
26. Reed LK, Mormino MA. Distal tibia nonunions. Foot Ankle Clin. 2008 Dec. 13 (4):725-35. [QxMD MEDLINE Link].
27. Paley D, Maar DC. "Ilizarov bone transport treatment for tibial defects." J Orthop Trauma. 2000 Feb;14(2):76-85.
28. Valdes MA, Thakur NA, Namdari S, Ciombor DM, Palumbo M. Recombinant bone morphogenic protein-2 in orthopaedic surgery: a review. Arch Orthop Trauma Surg. 2009 Dec. 129 (12):1651-7. [QxMD MEDLINE Link].
29. Busse JW, Bhandari M, Kulkarni AV, Tunks E. The effect of low-intensity pulsed ultrasound therapy on time to fracture healing: a meta-analysis. CMAJ. 2002 Feb 19. 166 (4):437-41. [QxMD MEDLINE Link].
30. Hak DJ. Management of aseptic tibial nonunion. J Am Acad Orthop Surg. 2011 Sep. 19 (9):563-73. [QxMD MEDLINE Link].
31. Wu CC, Shih CH. Comparison of dynamic compression plating and reamed intramedullary nailing in the treatment of aseptic tibial shaft nonunions. Contemp Orthop. 1994 Jan. 28 (1):28-33. [QxMD MEDLINE Link].
32. Paley D, Catagni MA, Argnani F, Villa A, Benedetti GB, Cattaneo R. "Ilizarov treatment of tibial nonunions with bone loss." Clin Orthop Relat Res.1989 Apr;(241):146-65.
33. Dailey HL, Wu KA, Wu PS, McQueen MM, Court-Brown CM. Tibial Fracture Nonunion and Time to Healing After Reamed Intramedullary Nailing: Risk Factors Based on a Single-Center

Review of 1003 Patients. J Orthop Trauma. 2018 Jul. 32 (7):e263-e269. [QxMD MEDLINE Link].

34. Tanner M, Vlachopoulos W, Findeisen S, Miska M, Ober J, Hagelskamp S, et al. Does Age Influence the Outcome of Lower Limb Non-Union Treatment? A Matched Pair Analysis. J Clin Med. 2019 Aug 22. 8 (9):[QxMD MEDLINE Link]. [Full Text].