

Tibial Bone Loss: How to Treat without Circular Fixation?

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Abstract

Segmental tibial bone defects (STBD) represent a dilemma for the trauma surgeon; these defects could result from trauma, after debridement for infection, or after tumor resection. We aimed in this review to shed some light on the various reconstruction options without the need to use a circular fixator. Reconstruction options rely on various factors related to the patient, the surgeon, and the nature of the defect (location and size). Various reconstruction techniques include simple bone grafting (autograft or allografts), bone transport [distraction osteogenesis (DO)], induced membrane technique, and vascularized fibular graft. Fixation could be performed using either internal or external fixators; the latter could be a circular or a unilateral frame. Although circular frames (Ilizarov) fixators reported good results, they are still considered cumbersome, need special attention, carry pin tract infection risk, and could not be tolerated by patients. Hence, various other options were introduced, such as bone transport over an intramedullary nail (IMN), rail monolateral external fixator, and tibialisation of the ipsilateral fibula.

Keywords: Tibia; Bone Loss; Reconstruction; Ilizarov Technique

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Background

The tibia integrity regarding the length and alignment is crucial for basic daily activities such as gait, knee, and ankle function; this makes the presence of segmental tibial bone defects (STBD) a significant source of functional disability (1). Trauma surgeons could face the problem of tibial defects after various clinical situations such as open fractures, high-energy trauma, tumor resection, and debridement for infection (2-5).

The main aims of managing these defects are to achieve stable bony union with a proper alignment in all planes and offer an excellent soft tissue coverage and accepted leg length discrepancy (LLD), all of which should enable the patient to return to his normal daily activities in the shortest time possible (2, 6).

When dealing with an STBD, it is not merely a bony problem; instead, the trauma surgeon should consider the patient's general condition, comorbidities, the local soft tissue status, and the possible suboptimal vascularity (1).

Various management strategies were proposed, such as acute shortening, autogenous iliac bone graft, vascularized fibula transfers, bone transport, and the Masquelet technique (2). Each of them has its indications, advantages, and disadvantages, and the choice of the best option depends on many factors, mainly the etiology of the defect, the defect size, the surgeon's preference and expertise, and the patient's general condition (5, 6). There are no clear guidelines regarding the reconstruction techniques or fixation method (7).

A circular external fixator (the Ilizarov technique) using transosseous tensioned wires was commonly used as a fixation tool with various STBD reconstruction options with acceptable results (7); however, it carries the risk of local anatomy distortion, transfixing the soft tissues, endangering the neurovascular bundle, and longer external fixator period, and usually is poorly tolerated by

the patients (8, 9).

Some authors introduced other fixation methods to overcome the previously mentioned drawbacks of circular frames (6, 10). Therefore, this review aims to discuss various options for STBD management rather than the circular external fixation strategy by discussing the preoperative patient evaluation, determining the critical-sized defects, and elaborating on some reconstruction options.

A. Preoperative Evaluation and Patient Optimization

Optimum preoperative planning is paramount for reconstructing STBD; some factors are beyond surgeons' control, such as the presence of the previous infection, patient age, patient comorbidities, mental status, inadequate social support, and financial obstacle; however, they should be optimized as possible (7, 11).

1- Physiologic Status: The decision to reconstruct the defect or to go for a salvage procedure depends partially on the physiological status of the patient; various classification systems consider the physiological status in making the treatment decision, such as the Cierny classification system of osteomyelitis which is based on systemic factors of the patient (11). Usually, reconstructing STBD might need multiple surgeries; therefore, patients' general condition should be optimized to withstand this burden and limit complications. For example, some modifiable risk factors have been shown to affect bone healing, such as smoking, peripheral vascular disease, metabolic bone diseases, protein malnutrition, and low vitamin D levels (11, 12).

2- Mental Status: This mainly includes considering the patient's mental function and his/her willingness to experience a complex management option, furthermore participation in deciding the management plan, and further care during the follow-up period (11).

3- Social Status: Most reconstructive procedures, especially for larger defects, might require a more extended period; this could be stressful for the patients



and their caregivers (13). A reconstruction free of external fixators is assumed to be better for patients lacking social support or having mental health issues (11). It has been shown that poor social support resulted in lower outcomes after bone defect reconstruction or amputation (14).

B. Defect Size Issues

A critical-sized STBD is defined as a defect that is not expected to heal unless a secondary surgical intervention is used (15). However, there is no agreement on the exact size of a defect to be considered a critical one (16, 17). According to Court-Brown, it is a defect that involves 50% of the cortical diameter with a minimum length of one cm (18). This definition was used in the SPRINT trial by Bhandari et al. to prospectively evaluate intramedullary nails (IMN) in managing tibial fractures (19); later the same group found that 47% of the defects defined as critical according to the previous definition healed spontaneously with no additional procedures, indicating that controversy still present in defining what a critical defect is (16). A survey was carried out among the Orthopedic Trauma Association members to evaluate the various perceptions of a critical-sized segmental bone defect; however, no solid definition or criteria could be reached (20).

Various other factors will affect what defines a critical-sized bone defect, such as considering the absolute or relative size of the defect, anatomical location, soft tissue envelop status (periosteum and muscles), is the soft tissue loss circumferential or not, and the physiological status of the patient (4, 17).

In a study evaluating the results of exchange nailing for managing aseptic tibial fracture non-union, the authors defined a defect of 2 cm in length and affecting 50% of the tibial circumference to be the critical value to achieve union, where 61.5% of the defects below these values achieved union. In contrast, none of the defects above these values united (21).

Nauth et al. reported that a paucity of evidence was present to agree on definitive guidelines for considering a defect to be critical as this decision was usually multifactorial; they agreed that defect sized 1 to 2.5 cm had a good chance of healing without secondary intervention and an autogenous bone graft worked well in these cases, but defects greater than 2.5 cm had a poor natural history; furthermore, there was no clear management strategy (22).

C. Defect Reconstruction Options

Reconstruction should be viewed as soft tissue management and coverage options, bone defect filling options, and fixation methods utilized during various reconstruction techniques.

1- Biological Options: Besides bone grafts (autograft and allograft), various biological materials were introduced as options to manage defects or as a supplement for other treatment strategies, including the bone marrow aspirate and platelet-rich plasma (PRP) (22).

1- Autogenous Iliac Bone Graft: This could be considered a suitable option for defects less than five cm or supplementary for other reconstruction options. High failure rates were reported with this method when the defect was larger than five cm (23).

II- Papineau's Technique (Direct Open Cancellous Grafting of Granulation Bed): In this technique, a cancellous autograft is placed within the granulation tissue bed created after excision of the diseased segment; however, the main disadvantage of this technique is that the cancellous bone has weak mechanical structure (24).

III- Bone Marrow Aspirate Concentrate: Concentrated bone marrow aspirate that could be harvested from the iliac bone and concentrated in the operating theater contains viable osteoprogenitor cells with osteogenesis (25). The aspirate could be carried on an osteoconductive substrate or scaffold such as demineralized bone matrix (DBM), collagen sponges, and porous hydroxyapatite ceramics (26). Hernigou et al. reported high union rates after managing bone defects up to 3-4 cm in length using a bone marrow aspirate combined with DBM (25).

IV- PRP: There is no solid evidence of the efficacy of PRP in managing segmental bone defects; however, some studies showed that when it was used as an adjuvant with other materials or local bone graft, it could boost the healing potential with an improvement in the quality of bone regeneration (22).

2- Induced Membrane (Masquelet) Techniques:

Suppose a trauma surgeon chooses to use massive bone grafting. In that case, a Masquelet technique could be ideal for achieving the goal of defect reconstruction, as it first allows management of dead space as well as eradication of infection if present, and the formed biologically active membrane helps in stimulating bone defect healing (22, 23, 27, 28).

The procedure comprises two stages; the first lasts for 6 to 8 weeks, including adequate debridement, bone stabilization, and application of a cement spacer which could be loaded with antibiotics in infected cases (preventing fibrous tissue ingrowth within the defect). The second stage involves applying a bone graft inside the membrane formed after cement spacer removal (27). However, the results of this technique are controversial; although the healing rate could reach up to 90% (29), infection rates reached up to 50% (30).

3- Reamer-Irrigator-Aspirator (RIA) System: The space created after the Masquelet technique could be filled by bone graft obtained from the femur through the RIA technique (which is obtaining massive bone grafting from the femoral medullary cavity). The graft obtained was shown to be biologically active and prosperous in mesenchymal/progenitor cells (31). RIA has the advantage of less donor site morbidity and pain, unlike the autogenous iliac bone graft (32). Stafford and Norris reported high union rates of segmental bone defect treated by a combined Masquelet technique and RIA grafting, reaching up to 90% at one year in their series of 25 patients having an average defect size of 5 cm (33).

4- Titanium Mesh Cage: This is used in combination with plate fixation or IMN. The cage could be filled by autogenous or allogenic bone graft; it allows new bone formation through its fenestration, increases the biomechanical stability of the fixation devices used, enables partial weight-bearing, and helps restore the bone length with a proper near-normal soft tissue tension. However, it still carries the risk of infection related to its large metal surface area and is not suitable in cases with active infection or with soft tissue defect (34).

Cobos et al. first described and reported on the use of a cylindrical titanium mesh cage for managing tibial segmental bone defect in two patients (8.5 and 9.5 cm defects). They used a cage filled with cancellous grafts combined with IMN fixation; both attained complete bony union and accepted function by one-year follow-up (35). In a more recent study by Attias et al., the authors adopted the same technique to manage segmental bone defects in long bone in 17 patients (nine tibias) with a mean defect length of

8.4 cm by a 55-month follow-up; 94% of the patients achieved defect filling and union to the native bone ends (34).

5- Bone Transport [Distraction Osteogenesis (DO)]:

Another technique to manage STBD is the bone transport concept or DO, which is a dynamic process performed by cutting in healthy bony tissue and transferring this segment toward the defect site, slowly allowing the bone healing process to fill the gaps (2). Bone transport could be achieved through two main strategies; first, by acute or gradual shortening and compression at the defect site, then a cortectomy is performed through which lengthening is carried out and acute shortening of 3 to 4 cm could be performed safely in the tibia. The second strategy entails performing a cortectomy at a healthy level and transporting this segment to close the defect (36).

This technique was commonly performed by applying a circular external fixator (Ilizarov) which showed promising results in various reports (37); however, it still carries the risk of pin tract infection and prolonged management periods (38). This fixation method was replaced by other methods aiming at the shortening of the external fixator time; some authors introduced a concept of bone transport using a monolateral external fixator in combination with other fixation modalities such as locking plate and IMN, or even bone transport over IMNs or plates and using auto distractors that serve to shorten the fixation time (22).

I- The Monolateral Rail Fixation System: In a study by Mudiganty et al., where the authors evaluated the use of the Rail System (which is a uniplanar, dynamized external fixator system) for DO as an alternative to circular external fixator in the management of femoral and tibial defects after infected non-union, the fixator was applied for an average of 13.6 months, and after a mean follow-up of 22.56 months, they reported bone union free of infection in 97.5% of their patients, and the mean length of regenerated bone was 7.17 cm (8). In a study by Bhardwaj et al., comparing the use of Rail Fixator System and Ilizarov in managing long bone fracture non-union through DO, 25 patients were included in each group with an average bone defect of 7.76 cm in the Ilizarov group and 5.78 cm in Rail Fixator group. The mean duration of external fixator application was significantly lower with Rail Fixator compared to Ilizarov (11.56 months vs. 17 months, respectively, $P < 0.01$). The mean union time was significantly shorter with the Rail Fixator compared to Ilizarov (14.08 ± 4.31 months vs. 17.64 ± 4.79 months, respectively, $P < 0.01$). The authors concluded that the Rail Fixator was less cumbersome, and better accepted by patients. They would prefer and recommend its use in managing such cases (39).

II- Bone Transport over IMN: Bas et al. in a study evaluated the results of managing tibial and femoral bone defects by bone transport over an IMN in association with a monolateral external fixator for the femur cases while a circular external fixator was used for tibia cases, aiming at reducing the application time of the external fixators. For the tibial cases (21 patients), the mean defect length was 8.36 cm, the mean length of bone transport was 9.24 cm, and the mean consolidation time was 305.71 days; however, the mean external fixator time was 142.29 days. The authors reported excellent and good functional results in all patients; however, docking site non-union was reported in two patients (40).

Lengthening over an IMN introduced various advantages to the technique of DO for bone defect management; it helped overcome the disadvantages of

external fixators, such as eliminating the pin tract infection, soft tissue fixation, scarring, re-fracture after removal, and the prolonged application time (41). In a study by Olesen et al., the authors evaluated using lengthening IMN combined with plates (motorized lengthening nails and locking plates) for managing tibial segmental bone defect, which they called plate-assisted bone segment transport (PABST) in nine patients (including four tibias with a mean defect of 8.9 cm). All patients in their study reached complete bony consolidation after a mean of 10 months (41).

In a study by Eralp et al., where the authors compared using external fixation alone or combined with IMN for bone transport to manage STBD resulting from chronic osteomyelitis, the authors proved that both techniques worked with no difference in non-union rates, deformity, LLD, and functional results. Although the external fixation time was significantly shorter in the combined group than the external fixation alone group (5.5 vs. 14.0 months, respectively), they reported higher rates of infection reactivation in the combined group when the tibial lengthening needed was more than nine cm (1).

III- Bone Transport over a Plate: Some authors described the technique of bone transport over a plate, where the tibia is fixed using a plate (preferably a locked plate), then a cortectomy is performed in a healthy segment which is then distracted with the help of a monolateral external fixator to close the defect while keeping the plate in place (42).

6- Free Vascularized Fibular Graft (FVFG): Yokoyama et al. carried out a direct comparison between FVFG and DO for tibial bone defect reconstruction; four patients were included in each group, with a mean defect size of 7.3 cm in the FVFG group and 4.6 cm in the DO group. The external fixation period was 176 days and 261 days for the FVFG and DO groups, respectively. One septic non-union after re-fracture of the grafted fibula occurred in the FVFG group. Regarding the cost, FVFG and DO cost 68505 and 109242 United States (US) dollars, respectively. The authors could not detect a clear difference between the two groups owing to the limited number of included patients (43).

In a more extensive study by El-Gammal et al. comparing 12 patients treated by DO (by Ilizarov) and 13 treated by FVFG, the authors reported that all cases united by the last follow-up; however, the operative time and blood loss were significantly higher in the FVFG group (1.3 vs. 10.6 hours and 190 vs. 766 cc). The external fixator time was longer in the DO group, but they reported no difference in the functional outcome or complication rate. They found that the defect size was the most important for the results where defect length of 12 cm or more was better treated by an FVFG, while DO was better for defects less than 12 cm. They recommended FVFG for defects more than 12 cm on condition of the presence of an experienced surgical team (44).

7- Tibialisation of the Fibula: It includes the medial transport of the fibula with peroneal and anterior tibial muscles on a pedicle of peroneal vessels, to be placed instead of the defective tibia. This technique is considered biological, which allows shorter consolidation time. It has been noted that the translated fibula hypertrophy with time to be about twice its original size (45, 46).

8- Tibiofibular Synostosis: This is performed through bone graft placement on the superior and inferior margins of the tibial defect between the tibia and fibula, above the interosseous membrane; however, it carries the risk of eccentric loading and decreased ankle motion (47).

Discussion

A recent systematic review by Klifto et al. evaluated various techniques for managing tibial bone defects (traumatic or post-traumatic osteomyelitis) and concluded that a non-vascularized bone graft should be considered the first line for tibial bone defect less than 5 cm regardless of the etiology of the defect. A vascularized fibular graft should be considered the first line for more than 5 cm defects, while bone transport should be the second line in managing all defect sizes regardless of the etiology (6).

Bezstarosti et al. carried out a systematic review to evaluate the results of managing critical-sized tibial defects resulting from fracture-related infection. They evaluated 1530 patients from 43 studies where 82% of the included patients had a tibial affection; all the defects were more than one cm with an average of 6.6 cm. Various methods were reported in managing the defects (non-vascularized bone graft, RIA, vascularized bone grafts, synthetic grafts) and different techniques were utilized (primary graft, induced membrane technique, bone transport). The authors reported that 94% of the included patients achieved bony healing; however, they could not get solid evidence on the difference between all techniques included in the evaluation (15).

McClure et al. proposed an algorithm for tibial defect reconstruction depending on the defect size, where they considered defects less than 7 cm to be small defects, from 7 to 12 cm moderated defects, and large defects if more than 12 cm. This classification depended on the definition by Enneking et al. in 1980 (48), where defect sized 7.5 cm was considered as the transition zone at which non-vascularized graft would have high failure rates. The authors indicated that a Masquelet technique, bone transport over an IMN, and a titanium cage filled with bone graft could work for almost all partial defects. Furthermore, lengthening over an IMN worked for all defects regardless of their size or location (proximal, middle, or distal) (7).

Conclusion

Reconstructing segmental tibial bone defects poses a challenge to the trauma surgeon. Multiple reconstruction techniques are available, and selecting the most appropriate technique should consider patient, defect, and surgeon factors. Fixation by IMN, plates, monolateral external fixator, or a combination could safely replace the need for a circular external fixator with good results.

Conflict of Interest

The authors declare no conflict of interest in this study.

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References

- Eralp L, Kocaoglu M, Polat G, Bas A, Dirican A, Azam ME. A comparison of external fixation alone or combined with intramedullary nailing in the treatment of segmental tibial defects. *Acta Orthop Belg.* 2012;78(5):652-9. [PubMed: 23162962].
- Lu Y, Ma T, Ren C, Li Z, Sun L, Xue H, et al. Treatment of segmental tibial defects by bone transport with circular external fixation and a locking plate. *J Int Med Res.* 2020;48(4):300060520920407. doi: 10.1177/0300060520920407. [PubMed: 32351151]. [PubMed Central: PMC7218946].
- Borzunov DY, Balaev PI, Subramanyam KN. Reconstruction by bone transport after resection of benign tumors of tibia: A retrospective study of 38 patients. *Indian J Orthop.* 2015;49(5):516-22. doi: 10.4103/0019-5413.164042. [PubMed: 26538757]. [PubMed Central: PMC4598542].
- Nauth A, McKee MD, Einhorn TA, Watson JT, Li R, Schemitsch EH. Managing bone defects. *J Orthop Trauma.* 2011;25(8):462-6. doi: 10.1097/BOT.0b013e318224cafo. [PubMed: 21738065].
- Amoozadeh Omrani F, Elahi M, Sarzaeem MM, Sayadi S, Farzaneh H. Infection rate of reamed versus unreamed intramedullary nailing in open tibia fractures. *J Orthop Spine Trauma.* 2020;5(2):29-31. doi: 10.18502/jost.v5i2.3749.
- Klifto KM, Azoury SC, Klifto CS, Mehta S, Levin LS, Kovach SJ. Treatment of posttraumatic tibial diaphyseal bone defects: A systematic review and meta-analysis. *J Orthop Trauma.* 2022;36(2):55-64. doi: 10.1097/BOT.0000000000002214. [PubMed: 34633778].
- McClure PK, Abouei M, Conway JD. Reconstructive options for tibial bone defects. *J Am Acad Orthop Surg.* 2021;29(21):901-9. doi: 10.5435/JAAOS-D-21-00049. [PubMed: 34288887].
- Mudiganty S, Daolagupu AK, Sipani AK, Das SK, Dhar A, Gogoi PJ. Treatment of infected non-unions with segmental defects with a rail fixation system. *Strategies Trauma Limb Reconstr.* 2017;12(1):45-51. doi: 10.1007/s11751-017-0278-6. [PubMed: 28236034]. [PubMed Central: PMC5360676].
- Grivas TB, Magnissalis EA. The use of twin-ring Ilizarov external fixator constructs: application and biomechanical proof of principle with possible clinical indications. *J Orthop Surg Res.* 2011;6:41. doi: 10.1186/1749-799X-6-41. [PubMed: 21834985]. [PubMed Central: PMC3178515].
- Moss DP, Tejwani NC. Biomechanics of external fixation: A review of the literature. *Bull NYU Hosp Jt Dis.* 2007;65(4):294-9. [PubMed: 18081548].
- McClure PK, Alrabai HM, Conway JD. Preoperative evaluation and optimization for reconstruction of segmental bone defects of the tibia. *J Orthop Trauma.* 2017;31(Suppl 5):S16-S19. doi: 10.1097/BOT.0000000000000983. [PubMed: 28938385].
- Brinker MR, O'Connor DP, Monla YT, Earthman TP. Metabolic and endocrine abnormalities in patients with nonunions. *J Orthop Trauma.* 2007;21(8):557-70. doi: 10.1097/BOT.0b013e31814d4dc6. [PubMed: 17805023].
- Richard HM, Nguyen DC, Birch JG, Roland SD, Samchukov MK, Cherkashin AM. Clinical implications of psychosocial factors on pediatric external fixation treatment and recommendations. *Clin Orthop Relat Res.* 2015;473(10):3154-62. doi: 10.1007/s11999-015-4276-z. [PubMed: 25828943]. [PubMed Central: PMC4562937].
- Bosse MJ, MacKenzie EJ, Kellam JF, Burgess AR, Webb LX, Swiontkowski MF, et al. An analysis of outcomes of reconstruction or amputation after leg-threatening injuries. *N Engl J Med.* 2002;347(24):1924-31. doi: 10.1056/NEJMoa012604. [PubMed: 12477942].
- Bezstarosti H, Metsemakers WJ, van Lieshout EMM, Voskamp LW, Kortram K, McNally MA, et al. Management of critical-sized bone defects in the treatment of fracture-related infection: A systematic review and pooled analysis. *Arch Orthop Trauma Surg.* 2021;141(7):1215-30. doi: 10.1007/s00402-020-03525-0. [PubMed: 32860565]. [PubMed Central: PMC8215045].
- Sanders DW, Bhandari M, Guyatt G, Heels-Ansdell D, Schemitsch EH, Swiontkowski M, et al. Critical-sized defect in the tibia: Is it critical? Results from the SPRINT trial. *J Orthop Trauma.* 2014;28(11):632-5. doi: 10.1097/BOT.0000000000000194. [PubMed: 25233157].
- Schemitsch EH. Size matters: Defining critical in bone defect size! *J Orthop Trauma.* 2017;31(Suppl 5):S20-S22. doi: 10.1097/BOT.0000000000000978. [PubMed: 28938386].
- Court-Brown CM, Keating JF, Christie J, McQueen MM. Exchange intramedullary nailing. Its use in aseptic tibial nonunion. *J Bone Joint Surg Br.* 1995;77(3):407-11. [PubMed: 7744925].
- Bhandari M, Guyatt G, Tornetta P, III, Schemitsch EH, Swiontkowski M, Sanders D, et al. Randomized trial of reamed

- and unreamed intramedullary nailing of tibial shaft fractures. *J Bone Joint Surg Am.* 2008;90(12):2567-78. doi: [10.2106/JBJS.G.01694](https://doi.org/10.2106/JBJS.G.01694). [PubMed: [19047701](https://pubmed.ncbi.nlm.nih.gov/19047701/)]. [PubMed Central: [PMC2663330](https://pubmed.ncbi.nlm.nih.gov/PMC2663330/)].
20. Obremesky W, Molina C, Collinge C, Tornetta P 3rd, Sagi C, Schmidt A, et al. Current practice in the management of open fractures among orthopaedic trauma surgeons. Part B: Management of segmental long bone defects. A survey of Orthopaedic Trauma Association members. *J Orthop Trauma.* 2014;28(8):e203-e207. doi: [10.1097/BOT.0000000000000034](https://doi.org/10.1097/BOT.0000000000000034). [PubMed: [26057886](https://pubmed.ncbi.nlm.nih.gov/26057886/)].
 21. Buchholz RW, Heckman JD, Tornetta P, McQueen MM, Ricci WM. Rockwood and Green's fractures in adults. Philadelphia, PA: Lippincott Williams & Wilkins; 2010. p. 1275.
 22. Nauth A, Schemitsch E, Norris B, Nollin Z, Watson JT. Critical-size bone defects: is there a consensus for diagnosis and treatment? *J Orthop Trauma.* 2018;32(Suppl 1):S7-S11. doi: [10.1097/BOT.0000000000001115](https://doi.org/10.1097/BOT.0000000000001115). [PubMed: [29461395](https://pubmed.ncbi.nlm.nih.gov/29461395/)].
 23. Masquelet AC, Begue T. The concept of induced membrane for reconstruction of long bone defects. *Orthop Clin North Am.* 2010;41(1):27-37. doi: [10.1016/j.ocl.2009.07.011](https://doi.org/10.1016/j.ocl.2009.07.011). [PubMed: [19931050](https://pubmed.ncbi.nlm.nih.gov/19931050/)].
 24. Canale ST, Beaty JH. Campbell's operative orthopaedics e-book: Expert consult premium edition - Enhanced online features. Philadelphia, PA: Elsevier/Mosby; 2012.
 25. Hernigou P, Poignard A, Beaujean F, Rouard H. Percutaneous autologous bone-marrow grafting for nonunions. Influence of the number and concentration of progenitor cells. *J Bone Joint Surg Am.* 2005;87(7):1430-7. doi: [10.2106/JBJS.D.02215](https://doi.org/10.2106/JBJS.D.02215). [PubMed: [15995108](https://pubmed.ncbi.nlm.nih.gov/15995108/)].
 26. Jager M, Jelinek EM, Wess KM, Scharfstadt A, Jacobson M, Keyv SV, et al. Bone marrow concentrate: A novel strategy for bone defect treatment. *Curr Stem Cell Res Ther.* 2009;4(1):34-43. doi: [10.2174/157488809787169039](https://doi.org/10.2174/157488809787169039). [PubMed: [19149628](https://pubmed.ncbi.nlm.nih.gov/19149628/)].
 27. Pelissier P, Masquelet AC, Bareille R, Pelissier SM, Amedee J. Induced membranes secrete growth factors including vascular and osteoinductive factors and could stimulate bone regeneration. *J Orthop Res.* 2004;22(1):73-9. doi: [10.1016/S0736-0266\(03\)00165-7](https://doi.org/10.1016/S0736-0266(03)00165-7). [PubMed: [14656662](https://pubmed.ncbi.nlm.nih.gov/14656662/)].
 28. Canavese F, Khan A. Chronic osteomyelitis in children treated with antibiotic-laden cement: A preliminary report. *J Orthop Spine Trauma.* 2016;2(2):e5283. doi: [10.17795/jost-5283](https://doi.org/10.17795/jost-5283).
 29. Karger C, Kishi T, Schneider L, Fitoussi F, Masquelet AC. Treatment of posttraumatic bone defects by the induced membrane technique. *Orthop Traumatol Surg Res.* 2012;98(1):97-102. doi: [10.1016/j.otsr.2011.11.001](https://doi.org/10.1016/j.otsr.2011.11.001). [PubMed: [22244249](https://pubmed.ncbi.nlm.nih.gov/22244249/)].
 30. Morris R, Hossain M, Evans A, Pallister I. Induced membrane technique for treating tibial defects gives mixed results. *Bone Joint J.* 2017;99-B(5):680-5. doi: [10.1302/0301-620X.99B5.BJJ-2016-0694.R2](https://doi.org/10.1302/0301-620X.99B5.BJJ-2016-0694.R2). [PubMed: [28455479](https://pubmed.ncbi.nlm.nih.gov/28455479/)].
 31. Sagi HC, Young ML, Gerstenfeld L, Einhorn TA, Tornetta P. Qualitative and quantitative differences between bone graft obtained from the medullary canal (with a Reamer/Irrigator/Aspirator) and the iliac crest of the same patient. *J Bone Joint Surg Am.* 2012;94(23):2128-35. doi: [10.2106/JBJS.L.00159](https://doi.org/10.2106/JBJS.L.00159). [PubMed: [23224383](https://pubmed.ncbi.nlm.nih.gov/23224383/)].
 32. Dawson J, Kiner D, Gardner W, Swafford R, Nowotarski PJ. The reamer-irrigator-aspirator as a device for harvesting bone graft compared with iliac crest bone graft: Union rates and complications. *J Orthop Trauma.* 2014;28(10):584-90. doi: [10.1097/BOT.0000000000000086](https://doi.org/10.1097/BOT.0000000000000086). [PubMed: [24625833](https://pubmed.ncbi.nlm.nih.gov/24625833/)].
 33. Stafford PR, Norris BL. Reamer-irrigator-aspirator bone graft and bi Masquelet technique for segmental bone defect nonunions: A review of 25 cases. *Injury.* 2010;41(Suppl 2):S72-S77. doi: [10.1016/S0020-1383\(10\)70014-0](https://doi.org/10.1016/S0020-1383(10)70014-0). [PubMed: [21144933](https://pubmed.ncbi.nlm.nih.gov/21144933/)].
 34. Attias N, Thabet AM, Prabhakar G, Dollahite JA, Gehlert RJ, DeCoster TA. Management of extra-articular segmental defects in long bone using a titanium mesh cage as an adjunct to other methods of fixation: A multicentre report of 17 cases. *Bone Joint J.* 2018;100-B(5):646-51. doi: [10.1302/0301-620X.100B5.BJJ-2017-0817.R2](https://doi.org/10.1302/0301-620X.100B5.BJJ-2017-0817.R2). [PubMed: [29701099](https://pubmed.ncbi.nlm.nih.gov/29701099/)].
 35. Cobos JA, Lindsey RW, Gugala Z. The cylindrical titanium mesh cage for treatment of a long bone segmental defect: Description of a new technique and report of two cases. *J Orthop Trauma.* 2000;14(1):54-9. doi: [10.1097/00005131-200001000-00011](https://doi.org/10.1097/00005131-200001000-00011). [PubMed: [10630804](https://pubmed.ncbi.nlm.nih.gov/10630804/)].
 36. Mekhail AO, Abraham E, Gruber B, Gonzalez M. Bone transport in the management of posttraumatic bone defects in the lower extremity. *J Trauma.* 2004;56(2):368-78. doi: [10.1097/01.TA.0000057234.48501.30](https://doi.org/10.1097/01.TA.0000057234.48501.30). [PubMed: [14960982](https://pubmed.ncbi.nlm.nih.gov/14960982/)].
 37. Bernstein M, Fragomen AT, Sabharwal S, Barclay J, Rozbruch SR. Does integrated fixation provide benefit in the reconstruction of posttraumatic tibial bone defects? *Clin Orthop Relat Res.* 2015;473(10):3143-53. doi: [10.1007/s11999-015-4326-6](https://doi.org/10.1007/s11999-015-4326-6). [PubMed: [25940337](https://pubmed.ncbi.nlm.nih.gov/25940337/)] [PubMed Central: [PMC4562932](https://pubmed.ncbi.nlm.nih.gov/PMC4562932/)].
 38. Yin P, Zhang L, Zhang L, Li T, Li Z, Li J, et al. Ilizarov bone transport for the treatment of fibular osteomyelitis: A report of five cases. *BMC Musculoskelet Disord.* 2015;16:242. doi: [10.1186/s12891-015-0708-x](https://doi.org/10.1186/s12891-015-0708-x). [PubMed: [26342841](https://pubmed.ncbi.nlm.nih.gov/26342841/)]. [PubMed Central: [PMC4561167](https://pubmed.ncbi.nlm.nih.gov/PMC4561167/)].
 39. Bhardwaj R, Singh J, Kapila R, Boparai RS. Comparison of ilizarov ring fixator and rail fixator in infected nonunion of long bones: A retrospective followup study. *Indian J Orthop.* 2019;53(1):82-8. doi: [10.4103/ortho.IJOrtho_77_17](https://doi.org/10.4103/ortho.IJOrtho_77_17). [PubMed: [30905986](https://pubmed.ncbi.nlm.nih.gov/30905986/)]. [PubMed Central: [PMC6394165](https://pubmed.ncbi.nlm.nih.gov/PMC6394165/)].
 40. Bas A, Daldal F, Eralp L, Kocaoglu M, Uludag S, Sari S. Treatment of tibial and femoral bone defects with bone transport over an intramedullary nail. *J Orthop Trauma.* 2020;34(10):e353-e359. doi: [10.1097/BOT.0000000000001780](https://doi.org/10.1097/BOT.0000000000001780). [PubMed: [32304473](https://pubmed.ncbi.nlm.nih.gov/32304473/)].
 41. Olesen UK, Nygaard T, Prince DE, Gardner MP, Singh UM, McNally MA, et al. Plate-assisted bone segment transport with motorized lengthening nails and locking plates: A technique to treat femoral and tibial bone defects. *J Am Acad Orthop Surg Glob Res Rev.* 2019;3(8):e064. doi: [10.5435/JAAOSGlobal-D-19-00064](https://doi.org/10.5435/JAAOSGlobal-D-19-00064). [PubMed: [31592010](https://pubmed.ncbi.nlm.nih.gov/31592010/)]. [PubMed Central: [PMC6754216](https://pubmed.ncbi.nlm.nih.gov/PMC6754216/)].
 42. Girard PJ, Kuhn KM, Bailey JR, Lynott JA, Mazurek MT. Bone transport combined with locking bridge plate fixation for the treatment of tibial segmental defects: A report of 2 cases. *J Orthop Trauma.* 2013;27(9):e220-e226. doi: [10.1097/BOT.0b013e31827069b9](https://doi.org/10.1097/BOT.0b013e31827069b9). [PubMed: [22955338](https://pubmed.ncbi.nlm.nih.gov/22955338/)].
 43. Yokoyama K, Itoman M, Nakamura K, Tsukamoto T, Saita Y, Aoki S. Free vascularized fibular graft vs. Ilizarov method for post-traumatic tibial bone defect. *J Reconstr Microsurg.* 2001;17(1):17-25. doi: [10.1055/s-2001-12684](https://doi.org/10.1055/s-2001-12684). [PubMed: [11316280](https://pubmed.ncbi.nlm.nih.gov/11316280/)].
 44. El-Gammal TA, Shiha AE, El-Deen MA, El-Sayed A, Kotb MM, Addosooki AI, et al. Management of traumatic tibial defects using free vascularized fibula or Ilizarov bone transport: a comparative study. *Microsurgery.* 2008;28(5):339-46. doi: [10.1002/micr.20501](https://doi.org/10.1002/micr.20501). [PubMed: [18537173](https://pubmed.ncbi.nlm.nih.gov/18537173/)].
 45. Rahimnia A, Fitoussi F, Pennecot G, Mazda K. Treatment of segmental loss of the tibia by tibialisation of the fibula: A review of the literature. *Trauma Mon.* 2012;16(4):154-9. doi: [10.5812/kowsar.22517464.3184](https://doi.org/10.5812/kowsar.22517464.3184). [PubMed: [24749092](https://pubmed.ncbi.nlm.nih.gov/24749092/)]. [PubMed Central: [PMC3989564](https://pubmed.ncbi.nlm.nih.gov/PMC3989564/)].
 46. Tuli SM. Tibialization of the fibula: A viable option to salvage limbs with extensive scarring and gap nonunions of the tibia. *Clin Orthop Relat Res.* 2005;431:80-4. [PubMed: [15685059](https://pubmed.ncbi.nlm.nih.gov/15685059/)].
 47. Shiha AE, Khalifa AR, Assaghir YM, Kenawey MO. Medial transport of the fibula using the Ilizarov device for reconstruction of a massive defect of the tibia in two children. *J Bone Joint Surg Br.* 2008;90(12):1627-30. doi: [10.1302/0301-620X.90B12.21378](https://doi.org/10.1302/0301-620X.90B12.21378). [PubMed: [19043136](https://pubmed.ncbi.nlm.nih.gov/19043136/)].
 48. Enneking WF, Eady JL, Burchardt H. Autogenous cortical bone grafts in the reconstruction of segmental skeletal defects. *J Bone Joint Surg Am.* 1980;62(7):1039-58. [PubMed: [7000788](https://pubmed.ncbi.nlm.nih.gov/7000788/)].