31 Surgical Management: Management of Traumatic Bone Defects

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Learning Goals

- Definition and epidemiology of traumatic bone defects.
- Initial management of the polytrauma patient.
- Reconstruction versus early amputation for the severely injured limp.
- Treatment principles for skeletal fixation and soft tissue coverage.
- Definition of "critical"-sized bone defect.
- Options for managing traumatic bone defects.

31.1 Introduction

Segmental bone defects can be the result of either severe trauma, infection, or malignancy. Traumatic bone defects can occur either during the initial injury (high energy impact, penetrating trauma, blast injuries) or following debridement of devitalized bone fragments related to open fractures or infected non-unions.

Currently, there are reliable methods to successfully reconstruct large defects that in the past were treated even with primary amputation. Reconstruction of large bone defects can cause significant disabilities and represent a challenging situation for the surgeon. They carry a substantial burden of disease, a high rate of complications and reoperations, as long as a significant economic impact.

Autologous bone grafting remains the gold standard for the reconstruction of small defects, while distraction osteogenesis, acute shortening, vascularized grafts, the induced membrane technique, titanium mesh cages, and arthroplasty—in selected cases—are useful alternatives for the management of the larger bone defects.

31.1.1 Epidemiology

Only a small minority of all fractures are associated with bone loss and critical size bone defects, and these are mostly open injuries. In a prospective audit of admissions to the Edinburgh Orthopaedic Trauma Unit in 10 years, fractures with bone loss accounted only for 0.4% of all fractures. Bone loss, though, was present in 11.4% of open fractures. The most common ana-

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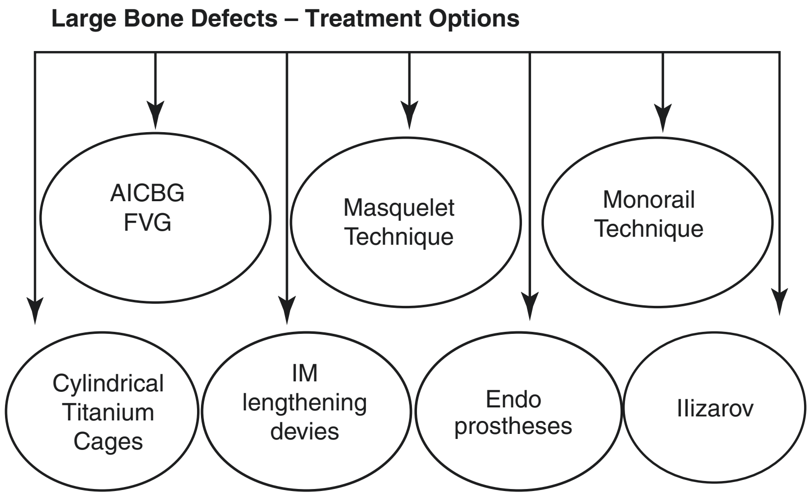


Fig. 31.1 Treatment options for large bone defects. **AICBG* Autologous iliac crest bone graft; **FVG* Fibula vascularized graft

tomical site sustaining bone loss following trauma was the tibia [1] (Fig. 31.1).

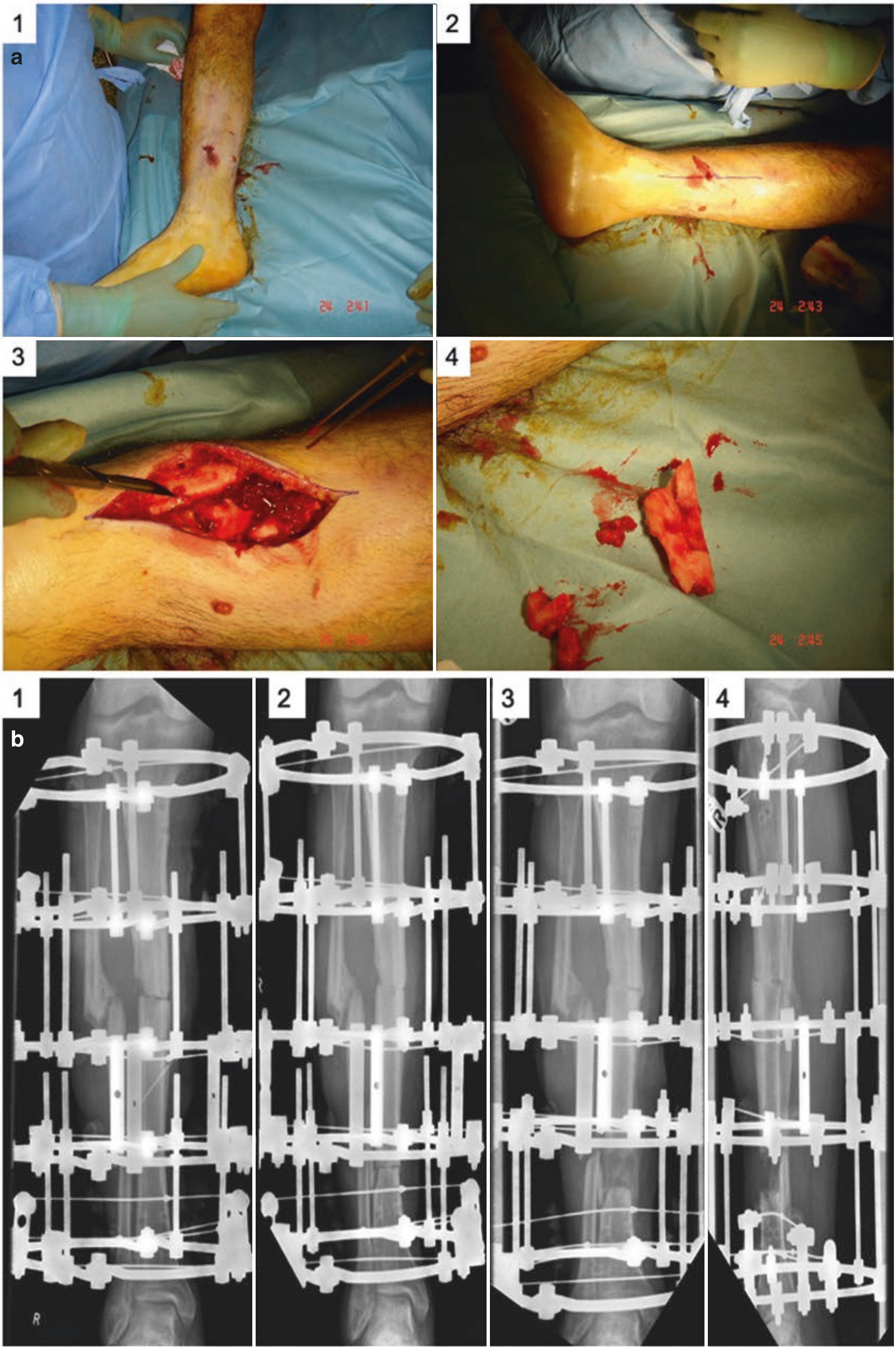
31.1.2 Initial Patient Management

Early evaluation of the patient according to the ATLS protocol is mandatory [2] in all trauma cases. Initial procedures in the context of poly-trauma must be of life-saving nature in order to maintain the function of vital organs such as the brain, heart, and lung. Volume replacement and interventions to stop the bleeding, restoring hae-modynamic stability are essential. The dogma save life, save the limb, limit disability continues to dictate the management of patients presenting with multiple injuries.

Once the primary assessment has been completed, and the patient is physiologically stable, a detailed assessment of any open wound should take place, and all findings documented. Photography is also beneficial for documentation and for multidisciplinary team communication. The wound should not be explored in the emergency setting and handled only for gross contamination removal; it must then be covered until formal exploration occurs in the operating room and under sterile conditions. A detailed neurovascular examination and documentation of the findings are also of paramount importance (Fig. 31.2).

When necessary and within the concept of "damage control orthopaedics", a spanning external fixation can be applied to stabilize orthopaedic injuries avoiding additional physiological stress-related insults to the patient [3]. Pin site and implant placement should be carefully selected to allow for definite fixation and stabilization of the defect at a later stage.

Fig. 31.2 A 38-year-old male patient presented with a pelvic, spinal, and right tibia open fracture following a motorbike accident. After resuscitation and restoration of physiology, the patient was taken to the operating theatre. (**a**) 1: Open wound of the right tibia. 2: Wound was extended as shown. 3: Wound inspected underneath and debrided. 4: Non-vital fragments removed. (**b**) 1: AP right tibia radiograph showing bone shortening occurred and compression of fracture at the injury site. 2: AP right tibial radiograph showing distal corticotomy performed 7 days later for bone transport to address the bone loss incurred. 3: AP radiograph showing bone transport. 4: Lateral radiograph showing the degree of bone transport. (**c**) 1: AP radiograph; 2: Lateral radiograph showing the formation of regenerate bone at the distraction site at 4 months. 3: AP radiograph; 4: Lateral radiograph demonstrating osseous healing at 6 months following the injury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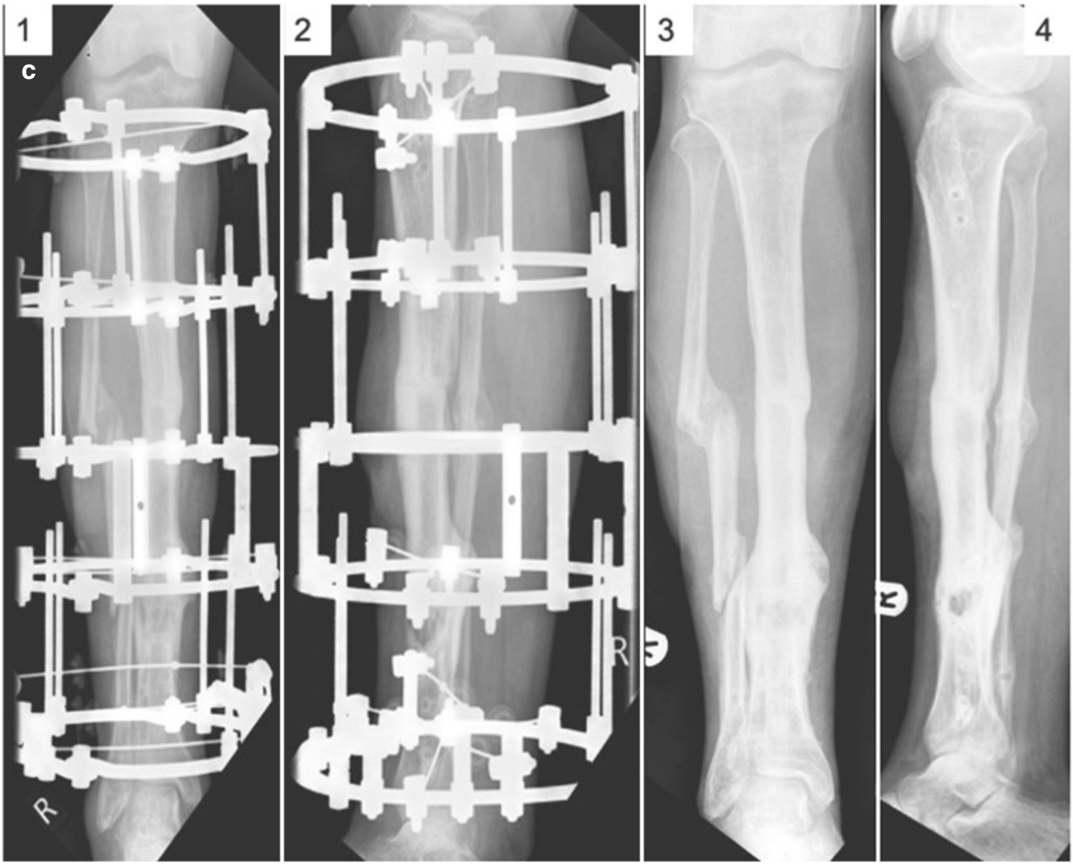

Fig. 31.2 (continued)

31.1.3 Reconstruction Versus Amputation

In these complex injuries, a decision whether to proceed with salvage procedures or primary amputation should take place early in the process. Several algorithms have been proposed to guide the management [4–6] and scoring systems such as the mangled extremity severity scale (MESS); the limp salvage index (LSI), and the predictive salvage index (PSI) [7–9] are useful but need to be interpreted with caution as such a decision is always difficult and rarely clear. The Lower Extremity Assessment Project (LEAP) a multicenter study for severe lower extremity trauma in the US population, investigated the functional outcomes of a salvaged versus amputated-prosthetic lower extremity. The Sickness Impact Profile Score was used to evaluate the outcomes of prospectively collected data from patients with Gustillo grade IIIB and IIIC fractures. It was concluded that at 2- and 7-year follow-up; there was no difference in functional outcome between patients who underwent either limb salvage surgery or amputation. Long-term outcomes following major limp trauma were poor for both groups, and approximately 50% of patients in each group were able to return to work. Patient characteristics predicting poor outcome included older age, non-white race, lower level of education, poverty, smoking, poor self-reported preinjury health status, and involvement in disability compensation litigation.

Indications for early amputation in adults include significant nerve and vascular injury beyond the limits of repair. Relative indications are severe soft tissue damage, absence of plantar sensation, warm ischemia of more than 6 h and life-threatening trauma. Noteworthy, the extend of bone loss that prevents limb salvage is yet to be determined.

Finally, it is also vital that the patient understands the potential need for future surgical procedures and prolonged rehabilitation, and his compliance needs to be carefully evaluated to the degree that this is possible within the limits of an acute major trauma situation.

31.2 Skeletal Fixation and Soft Tissue Coverage

Traumatic bone defects are often associated with open fractures with potential severe soft tissue involvement, so successful management requires collaboration from several specialities (orthopaedics, plastics, vascular) to optimize the outcome. Wound debridement, stabilization, defect reconstruction, and soft tissue coverage must all be planned in conjunction.

The aim of treatment is skeletal stabilization, soft tissue management, restoration of length and alignment, and preservation of limp function.

The initial debridement or serial debridements, if required, are of paramount importance to reduce the bacterial load and remove necrotic tissue. The defect can be provisionally filled with a PMMA-antibiotic spacer or antibiotic-impregnated PMMA beads [10]. This can be exchanged during debridements, and it is aiming to reduce infection rates and create a clean aseptic environment for future bone reconstruction procedures. Alternatively, it can be maintained for a period of 4–6 weeks if the induced membrane technique is planned.

In the presence of temporary spaning fixation (external fixator), conversion to definite fixation should take place as soon as possible to minimize the risk of pin site infection (ideally within the first 10–14 days) [9].

Managing the soft tissues in conjunction with the bone defect is crucial, and the reconstruction ladder, as described in the literature, provides the plan of action for this challenging situation [11, 12].

For the treatment of diaphyseal bone loss, interlocking nails have become the treatment of choice. They offer excellent stability; the soft tissues can be easily addressed over a nail, and joints can be early mobilized. Nails are not the treatment of choice when distraction osteogenesis is planned unless an intramedullary lengthening device is used. Plates have biomechanical disadvantages in the presence of bone loss due to cantilevering, but they are useful for metaphyseal or articular defects. External fixators can be used in almost any location and offer the advantage of deformity correction and bone lengthening (distraction osteogenesis) [1].

31.3 Management of Bone Defects

31.3.1 Definition of "Critical"-Sized Bone Defect

There is no single definition of a "critical"-sized bone defect. In general, defects that are not expected to heal without intervention and despite stabilization are considered as "critical". In the literature bone defects of more than >1–2 cm, greater than twice the diameter of the diaphysis or >50% loss of the circumference, are considered "critical" [1, 13–15]. Parameters that could impact the outcome of the defect reconstruction include biomechanical related issues, the potency of local biology, the overall state of the soft tissue envelope, the age and comorbidities of the patient, nutrition, glycemic control, smoking habits, and development of infection [16, 17].

The anatomical location of the bone defect is also related to the overall prognosis as some areas display better vascularity and osteogenic potential [1, 14]. Poor outcomes have been reported for defects in the tibia more than 1–2 cm and >50% circumference [14]. Interestingly, spontaneous healing of traumatic segmental defects of the femur up to 15 cm long has been reported in the literature [18].

31.3.2 Autologous Bone Grafts

For small defects <5 cm, with adequate soft tissue coverage, autologous bone graft remains the gold standard [13]. Autograft is the only material that possesses all three properties of osteogenesis, osteoinduction, and osteoconduction [19]. Other advantages are its low cost and the fact that it carries no risk of disease transmission and immunologic rejection. The graft can be harvested from several sites, such as the ilium, the femur, the tibia, the radius, and the ribs. The iliac crest remains the most common harvesting source. The ilium can provide both cancellous and cortical bone as well as a vascularized graft; the technique is well familiar by most surgeons and can take place in the supine position, which makes it accessible in most trauma-related scenarios. Disadvantages of autologous bone grafting are donor site morbidity and the limited volume that can be obtained in cases of large defects. Both the anterior and the posterior crests can be harvested with the anterior being the most common. Anterior crest harvesting has been associated with higher rates of infection, haematoma, fractures, and hypertrophic scar wherareas donor site pain and sensory disturbances were lower when compared to the posterior iliac crest harvesting [20].

Autologous bone graft can also be obtained from the long bone intramedullary cavity and particularly the femur. The "reamer-irrigator-aspirator" (RIA) is a recent development that was originally designed to address the issues of fat emboli and thermal necrosis associated with reaming during long bone nailing procedures. Although clinical evidence is still lacking to support that fully, RIA indications have expanded to include bone graft harvesting for the management of non-unions and bone defects as it can provide a significant volume of bone graft up to 25–90 cm^3 [21]. Reamings obtained with RIA have been shown to have greater enrichment in mesenchymal stem cells than the iliac crest bone graft [16] (Fig. 31.3).

Evidence suggests that RIA is relatively safe, with a fairly low overall complication rate of about 6% [20]. However, there are unique complications associated with the use of RIA, such as femoral neck fracture, anterior femoral cortex perforation, heterotropic ossification, and hypertrophic scar, which can be avoided with meticulous surgical technique [22].

Though autologous bone graft remains the gold standard for small size defects, larger than 5 cm defects require other reconstruction options as the resorption caused by revascularization produces significant mechanical weakening at the construct and failure of osteogenesis.

31.3.3 Distraction Osteogenesis (Ilizarov Technique)

Large bone defects can be managed with this technique which involves transporting a free bone segment with either an external fixator or an intramedullary device. Distraction osteogenesis was pioneered by Ilizarov in 1950 [23], and since then, it has been successfully used to treat long bone fractures, non-unions, bone defects, and deformities. This technique has the advantage of not only addressing the bone defect issue but also correcting any shortening, malalignment, joint contractures, or soft tissue loss at the same time. It is mainly based on the use of a circular fixator and on the principle that tissue can be generated under controlled applied tension between corticotomy surfaces. Histologically, this process strongly resembles intramembranous ossification, as seen in the periosteum [24]. In traumatic segmental bone defects, this method can be applied in two ways, acute shortening followed by lengthening to restore the original length or by bone transportation.

Acute limb shortening is a fast and straightforward way of management bone defects. It consists of closing and compressing the bony defect, followed by distraction. It offers the advantage of early soft tissue management and tension-free wound closure. Soft tissues and neurovascular status will dictate the amount of shortening as loss of perfusion caused by artery kinking is one of the complications. A safe limit for acute shortening before neurovascular compromise is about 3–5 cm in the femur and 2–3 cm in the tibia [25]. Greater shortening can be achieved if this is performed gradually instead of acutely.

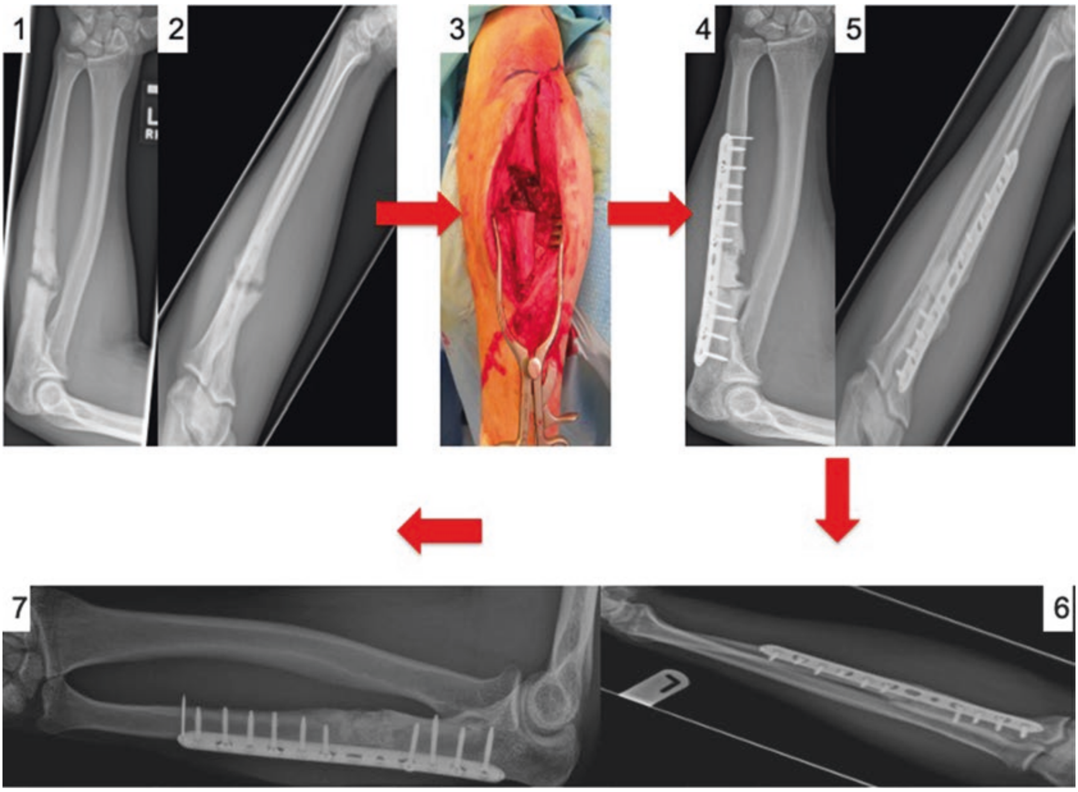

Fig. 31.3 A 40-year-old male presented with a left proximal ulna non-union which was originally plated, but the patient developed an infection and the plate was removed. 1: AP view left forearm; 2: Lateral view left forearm demonstrating a proximal ulna infected non-union. 3: Intraoperative picture showing the bone defect created following debridement of the infected bone. 4: AP radiograph; 5:Lateral radiograph of the left forearm showing that the fracture has been stabilized with a plate, and a cement spacer has been inserted in the bone defect area for the induction of the induced membrane. 6: Lateral radiograph; 7: AP radiograph of left forearm, 4 months after the second stage of the induced membrane technique demonstrating osseous bone healing of the previous bone defect

Bone transportation consists of gradually moving a free segment of viable bone together with the soft tissue envelope from an adjacent area into the defect. A corticotomy is performed away from the injury, and an external fixator is usually used to transport the bone segment in a mechanically stable and controlled manner. The procedure is divided into three phases, latency, distraction, and consolidation. Following the latency period which is usually 7 days from the osteotomy, distraction is being applied at a rate of 1 mm/day (0.25 mm four times a day). During this phase, a gradually elongated bone gap is produced, and as the apparatus creates tension, bone formation occurs within the callus. The soft tissue envelope is also increasing (distraction histogenesis). When the transported segment reaches the end of the defect, it is compressed for several weeks, and the distraction gap is allowed to bridge and corticalize. For large defects bifocal (corticotomy at either side of the defect), distraction osteogenesis can be performed.

A major drawback of this method is the length of the time required for the reconstruction to be completed, leading to prolonged use of an external fixator. The most common complication is pin tract infection which carries the risk of septic arthritis for pins inserted closed to a joint. Other complications are joint stiffness, refractures, malunions, neurovascular complications, and amputation.

In a systematic review by Papakostidis et al., union rates to about 94% were reported. It was though highlighted that a significant risk of refractures exists for defects >8 cm long. The risk of neurovascular complications was 2.2% and amputations 2.9%, with half of them being voluntary. This finding highlighted the tolerance that patients can demonstrate related to this method, and the authors suggested that careful patient selection is essential to avoid such a complication [26].

31.3.4 Vascularized Bone Grafts (VBG)

Vascularized bone grafts can be obtained from several donor areas (fibula, iliac crest, ribs) [17, 27]. They have the advantage due to the preserved circulation (vascular pedicle) to maintain cell viability (osteocytes) compared to non-vascularized grafts. VBGs do not undergo creeping substitution during incorporation, so potentially they preserve their biomechanical properties, and they display better healing properties and reaction to stress [28]. VBGs can also contribute to the revascularization of necrotic bone [29]. They are also useful in combined soft-tissue/bone reconstruction as skin paddles, muscles, tendon, nerves, and other tissues can be harvested at the same time. VBGs are useful in unfavourable healing environments and/or impaired absent blood flow (scarred soft tissue envelop, irradiated or avascular bone bed) and in the cases of concomitant infection [30, 31]. The disadvantages of vascularized grafts are donor site morbidity, prolonged operating times, and the fact that they represent technically challenging procedures requiring microvascular expertise.

Historically, the fibula is the most commonly used vascularized bone graft. It can provide up to 25 cm of bone with minimal donor site morbidity [17]. It can be harvested 4 cm from the fibular head and 6 cm from the ankle without compromising either the proximal tibiofibular joint or the ankle stability [13, 32].

Vascularized grafts are generally used for the management of bone defects greater than 6 cm. However, in a recent review article, it was concluded that it is uncertain if there is enough evidence to support this 6 cm rule and that further research is required to avoid patients undergoing more complex procedures [33]. VBGs can also be used in smaller defects where poor biology is present (atrophic non-unions, infections, scarred soft tissue envelop, irradiated bone, avascular bone).

Union rates of >95% have been reported with a vascularized fibular graft [34, 35].

31.3.5 Induced Membrane Technique (IMT)

Masquelet et al. developed a two-stage technique using induced biologic membranes in combination with cancellous autograft for the treatment of large segmental defects. They reported 100% union rates in 35 patients with defects up to 25 cm [36].

The first stage consists of aggressive bone/soft tissue debridement to remove all areas of necrosis and reduce the risk of subsequent infection. It is vital at that stage that multiple tissue samples are sent for microbiology analysis. A methyl-methacrylate (PMMA) cement spacer is then inserted into the defect, overlying the periosteum at both ends. Antibiotics can be added to the cement, either targeted or empirical. Stabilization can take place with various methods (IM nail, plate, external fixator) and will remain in place for 4–8 weeks. Soft tissue reconstruction takes place in the first stage, and inflammatory markers are carefully monitored to exclude infection.

At the second stage, the pseudomembrane is carefully incised (maintaining integrity and vascularity), and the cavity is filled with cancellous bone autograft. The graft can be taken from the iliac crest, or the Reamer-Irrigator-Aspirator (RIA) can be used. Graft expanders (cancellous allografts, demineralized bone matrix (DBM), bone morphogenetic proteins (BMPs)) may be used if a greater volume is needed. The bone edges will require further debridement to permit graft incorporation, and the medullary canal should be opened when possible, allowing endosteal communication. It is important to avoid dense graft impaction, and the membrane is finally sutured. Stable fixation at the end of the second stage, either with internal or external (circular frame), is important [37].

Complications of the IMT are infection (either from inadequate initial debridement or de novo), hardware failures, malalignment, soft tissue healing problems, and delayed stress fractures [38, 39].

Since the first study published by Masquelet et al., several case reports and retrospective case series reported an overall success rate of 86% [37]. In the largest published series of 84 post-traumatic diaphyseal long bone reconstructions, Karger et al. reported union rates in 90% of cases, at a mean of 14.4 months. The size of the treated defects ranged from 2 to 23 cm, with 57% being larger than 5 cm [40].

31.3.6 Titanium Mesh Cages

The cylindrical mesh cage technique was first described by Cobos et al. in 2000 [41]. It utilizes the use of cylindrical titanium cages typically used in spinal surgery to bridge the defect by surrounding it. This technique is a one-stage procedure and can be adapted in diaphyseal as well as meta-diaphyseal defects. Following debridement, an appropriately sized cage is selected and packed with graft (cancellous allograft). The construct is reinforced by internal rings placed at both ends and then stabilized for protection [42]. Initially, intramedullary nails were used in combination with titanium mesh-allograft reconstruction though this can also be achieved with plates or external fixators [43].

This technique is characterized by some advantageous biological properties which promote defect reconstitution. The principal among these biological advantages is the actual cage with its biocompatible (titanium) material and its hollow fenestrated design. The fenestrations limit the amount of metal and also permit diffusion of host nutrients and enhance the vascular ingrowth into the defect [42].

The titanium mesh cage technique can be used as an alternative or as salvage to the other described techniques for the treatment of large bone defects. It offers the advantage of an easy single-stage procedure achieving immediate limp stability with no donor site morbidity. It has the disadvantage of metalwork placement in an open fracture which might carry a greater risk of infection. Moreover, the results of treatment are not uniform.

31.3.7 Arthroplasty—Megaprosthesis

Arthroplasty can also provide surgical solutions especially in the presence of large traumatic metaphyseal and periarticular defects. The prosthesis design and technology has evolved, and several options currently exist to manage the underlying bone loss. The vast majority of the existing research, data, and outcomes come from the arthroplasty field, but the same principles can be applied to trauma patients.

Mild metaphyseal bone loss can be managed via arthroplasty with cement (with or without screws supplementation), impaction grafting or metal augmentation. Larger defects will require sleeves, trabecular metal cones, or bulk structural allografts. For the massive bone loss, a megaprosthesis has made it possible for orthopaedic surgeons to replace entire limps [44–46]. In the young and lower risks patients, an Allograft Prosthesis Composite (APC) can also be considered which is a revision type of prosthesis combined with an allograft [47].

Megaprostheses were initially designed for the management of oncologic bone loss; however, their indications have expanded to include also non-neoplastic situations such as trauma (with severe bone loss or poor bone quality), complex non-unions (septic and aseptic), bone loss in revision arthroplasty surgery and periprosthetic fractures around unstable implants with inadequate bone stock. These implants offer the advantage of replacing large skeletal segments, providing immediate mechanical stability that allows early weight bear, good functional recovery, improved compliance, and lower cost of surgery [48–50], so they can be considered as a limb salvage option in the absence of other surgical solutions. In 2008, a classification system was developed to guide treatment for patients with post-traumatic non-union and bone defects (Non-Union Scoring System—NUSS), taking into account not only the radiological features of the injury and the bone quality but also general risk factors as long as the soft tissue status. A patient's score over 75 points indicates that a more definitive treatment, such as amputation, arthrodesis, or replacement with megaprosthesis might be beneficial [51, 52]. It is essential, though, to understand that these patient groups (post-trauma, infective, failed arthroplasty) have different characteristics than oncologic patients and also life expectancy differs [48, 53]. The patient's age, overall condition, other comorbidities, soft tissue status, previous procedures, or previous infection must be carefully evaluated when considering megaprosthesis replacement. Ideally, these procedures should be performed in specialized centres, and the surgical technique and implantation should be meticulous to ensure the longevity of the prosthesis [53].

De Gori et al. in their study over the use of megaprosthesis in non-neoplastic patients (87 patients) found an overall survival rate of 69.1% at 10 years [48]. In two recent systematic reviews regarding the use of megaprosthesis for non-oncological patients, an overall midterm survival rate of 76% for proximal femoral prostheses and 83% for distal femoral prostheses were reported, respectively. The most common complication was dislocation for the proximal femoral replacements and infection for the distal [54–56]. The overall complications and survival rates of megaprosthesis implantation for non-neoplastic conditions are inferior when compared to primary arthroplasty of the hip and knee, but comparable or even better than those in the neoplastic patients [56].

31.4 Conclusion

Traumatic bone defects remain a challenging problem for the orthopaedic surgeon and the patient. These complex injuries carry a substantial burden of disease; they lead to prolonged rehabilitation times and are associated with a high complication rate. A multidisciplinary approach to optimize the outcomes is of significant value.

Numerous techniques are presently available to offer solutions. Further research is required to improve our understanding of these injuries, to define what constitutes a critical-sized bone defect and the extent of bone loss that prevents limb salvage and finally to rate each technique and guide treatment accordingly.

Key Concepts

- Life-saving procedures, resuscitation, and restoration of physiology remain the priority of early management in patients with polytrauma and injuries associated with open fractures and bone loss.
- Debridement, soft tissue coverage, fixation, and bone reconstruction must all be planned in conjunction, within a multidisciplinary approach, to optimize the outcome.
- Bone defects of more than >1–2 cm, greater than twice the diameter of the diaphysis or > 50% loss of the circumference, are considered "critical".
- For small defects <5 cm, with adequate soft tissue coverage, autologous bone grafting (ABG) remains a good solution for bone healing.
- Ilizarov bone transfer technique, vascularized fibular grafts, and the induced membrane technique are currently the most commonly used techniques for bone defect reconstruction.
- Arthroplasty can provide solutions in selected cases, especially around the metaphysis.

Take Home Message

Autologous bone graft remains the gold standard for small defects. For larger defects, several techniques have been described. Historically, the vascularized fibular graft and the Ilizarov technique have been the mainstays of treatment. Although good clinical results have been reported for both methods, they are also associated with complications and significant drawbacks. Distraction osteogenesis is a lengthy procedure with a risk of infection especially when pins are used close to a joint (septic arthritis), whereas vascularized fibula allograft is a technically demanding procedure requiring prolonged operating times and has donor site morbidity. The Masquelet technique is an increasingly utilized method with satisfactory results; it requires though a two-stage approach. The use of titanium mesh cages can potentially provide an alternative; nonetheless, the results of treatment are not consistent. Arthroplasty and megaprosthesis replacement can also be an option in selected cases, especially in the metaphyseal/periarticular area. The treatment method should be carefully chosen for the correct indication and the right patient in order to optimize the results of treatment.

Conflict of Interest There are no conflicts of interest.

References

1. Keating JF, Simpson AHRW, Robinson CM. The management of fractures with bone loss. J Bone Joint Surg Series B. 2005;87:142.
2. Trauma A, Support L. Atls 2018. Atls. 2018.
3. Roberts CS, Pape HC, Jones AL, Malkani AL, Rodriguez JL, Giannoudis PV. Damage control orthopaedics: evolving concepts in the treatment of patients who have sustained orthopaedic trauma. Instr Course Lect. 2005;54:447.
4. Lange RH. Limb reconstruction versus amputation decision making in massive lower extremity trauma. Clin Orthop Relat Res. 1989;243:92.
5. Mommsen P, Zeckey C, Hildebrand F, Frink M, Khaladj N, Lange N, et al. Traumatic extremity arterial injury in children: epidemiology, diagnostics, treatment and prognostic value of mangled extremity severity score. J Orthop Surg Res. 2010;5:25.
6. Court-Brown CM, Heckman JD, McQueen MM, Ricci WM, Tornetta P, McKee MD. Rockwood and Green's fractures in adults. 2015.
7. Bosse MJ, MacKenzie EJ, Kellam JF, Burgess AR, Webb LX, Swiontkowski MF, et al. A prospective evaluation of the clinical utility of the lower-extremity injury-severity scores. J Bone Joint Surg Ser A. 2001;83:3.
8. McNamara MG, Heckman JD, Corley FG. Severe open fractures of the lower extremity: a retrospective evaluation of the mangled extremity severity score (mess). J Orthop Trauma. 1994;8:81.
9. Pape H-C, Sanders R, Borrelli J, GmbH S-V. The poly-traumatized patient with fractures a multidisciplinary approach. 2016.
10. Adams K, Couch L, Cierny G, Calhoun J, Mader JT. In vitro and in vivo evaluation of antibiotic diffusion from antibiotic- impregnated polymethylmethacrylate beads. Clin Orthop Relat Res. 1992;278:244.
11. Levin LS, Condit DP. Combined injuries—soft tissue management. Clin Orthop Relat Res. 1996;327:172.
12. Janis JE, Kwon RK, Attinger CE. The new reconstructive ladder: modifications to the traditional model. Plast Reconstr Surg. 2011;127:2055.
13. Mauffrey C, Barlow BT, Smith W. Management of segmental bone defects. J Am Acad Orthop Surg. 2015;23:143.
14. Nauth A, Schemitsch E, Norris B, Nollin Z, Watson JT. Critical-size bone defects. J Orthop Trauma [Internet]. 2018;32:S7–11. http://journals.lww.com/00005131-201803003-00002
15. Roddy E, DeBaun MR, Daoud-Gray A, Yang YP, Gardner MJ. Treatment of critical-sized bone defects: clinical and tissue engineering perspectives. Eur J Orthop Surg Traumatol. 2018;28:351.
16. Obremskey W, Molina C, Collinge C, Nana A, Tornetta P, Sagi C, et al. Current practice in the management of open fractures among orthopaedic trauma surgeons. Part A: initial management. A survey of orthopaedic trauma surgeons. J Orthop Trauma. 2014;28:e198.
17. Lasanianos NG, Kanakaris NK, Giannoudis PV. Current management of long bone large segmental defects. Orthop Trauma. 2010;24:149.
18. Hinsche AF, Giannoudis PV, Matthews SE, Smith RM. Spontaneous healing of large femoral cortical bone defects: does genetic predisposition play a role? Acta Orthop Belg. 2003;69:441.
19. Bauer TW, Muschler GF. Bone graft materials: an overview of the basic science. Clin Orthop Relat Res. 2000;371:10.

20. Dimitriou R, Mataliotakis GI, Angoules AG, Kanakaris NK, Giannoudis PV. Complications following autologous bone graft harvesting from the iliac crest and using the RIA: a systematic review. Injury. 2011;42:S3-15.
21. Pfeifer R, Kobbe P, Knobe M, Pape H-C. The reamer-irrigator-aspirator (RIA) system. Oper Orthop Traumatol. 2011;23(5):446–52.
22. Cox G, Jones E, McGonagle D, Giannoudis PV. Reamer-irrigator-aspirator indications and clinical results: a systematic review. Int Orthop. 2011;35:951.
23. Ilizarov GA. The tension-stress effect on the genesis and growth of tissues. Part I. The influence of stability of fixation and soft-tissue preservation. Clin Orthop Relat Res. 1989;238:249.
24. Aronson J, Johnson E, Harp JH. Local bone transportation for treatment of intercalary defects by the Ilizarov technique: biomechanical and clincial considerations. Clin Orthop Relat Res. 1989;243:71.
25. Wozasek GE, Zak L. Acute shortening and then lengthening. In: Rozbruch SR, Hamdy R, editors. Limb lengthening and reconstruction surgery case atlas [internet]. Cham: Springer International Publishing; 2015. p. 1–9. https://doi.org/10.1007/978-3-319-02767-8_153-1.
26. Papakostidis C, Bhandari M, Giannoudis PV. Distraction osteogenesis in the treatment of long bone defects of the lower limbs: effectiveness, complications and clinical results; a systematic review and meta-analysis. Bone and Joint Journal. 2013;95-B:1973.
27. Lin CH, Wei FC, Chen HC, Chuang DCC. Outcome comparison in traumatic lower-extremity reconstruction by using various composite vascularized bone transplantation. Plast Reconstr Surg. 1999;104:984.
28. Shin EH, Shin AY. Vascularized bone grafts in orthopaedic surgery. JBJS Rev. 2017;5:e1.
29. Gonzalez del Pino J, Gomez Castresana F, Benito M, Weilan DAJ. Role of free vascularized bone grafts in the experimentally-induced ischemic necrosis of the femoral head. J Reconstr Microsurg. 1990;6:151.
30. Friedrich JB, Moran SL, Bishop AT, Wood CM, Shin AY. Free vascularized fibular graft salvage of complications of long-bone allograft after tumor reconstruction. J Bone Joint Surg Ser A. 2008;90:93.
31. Friedrich JB, Moran SL, Bishop AT, Wood CM, Shin AY. Vascularized fibula flap onlay for salvage of pathologic fracture of the long bones. Plast Reconstr Surg. 2008;121:2001.
32. Khira YM, Badawy HA. Pedicled vascularized fibular graft with Ilizarov external fixator for reconstructing a large bone defect of the tibia after tumor resection. J Orthop Traumatol. 2013;14:91.
33. Allsopp BJ, Hunter-Smith DJ, Rozen WM. Vascularized versus nonvascularized bone grafts: what is the evidence? Clin Orthop Relat Res. 2016;474:1319.
34. Cavadas PC, Landín L, Ibáñez J, Nthumba P. Reconstruction of major traumatic segmental bone defects of the tibia with vascularized bone transfers. Plast Reconstr Surg. 2010;125:215.
35. Zhen P, Hu YY, Luo ZJ, Liu XY, Lu H, Li XS. One-stage treatment and reconstruction of gustilo type III open tibial shaft fractures with a vascularized fibular osteoseptocutaneous flap graft. J Orthop Trauma. 2010;24:745.
36. Masquelet AC, Fitoussi F, Begue T, Muller GP. Reconstruction of the long bones by the induced membrane and spongy autograft. Ann Chir Plast Esthet. 2000;45:346.
37. Masquelet A, Kanakaris NK, Obert L, Stafford P, Giannoudis PV. Bone repair using the Masquelet technique. J Bone Joint Surg (Am Vol). 2019;101:1024.
38. Taylor BC, French BG, Ty Fowler T, Russell J, Poka A. Induced membrane technique for reconstruction to manage bone loss. J Am Acad Orthop Surg. 2012;20:142.
39. Morelli I, Drago L, George DA, Gallazzi E, Scarponi S, Romanò CL. Masquelet technique: myth or reality? A systematic review and meta-analysis. Injury [Internet]. 2016;47:S68–76. https://linkinghub.elsevier.com/retrieve/pii/S0020138316308427
40. 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;98:97.
41. 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;14:54.
42. Lindsey RW, Gugala Z. Cylindrical titanium mesh cage for the reconstruction of long bone defects. Osteosynthesis Trauma Care. 2004;12(03):108–15.
43. Gugala Z, Lindsey RW, Gogolewski S. New approaches in the treatment of critical-size segmental defects in long bones. Macromol Symp [Internet]. 2007;253(1):147–61. https://doi.org/10.1002/masy.200750722.
44. Sheth NP, Bonadio MB, Demange MK. Bone loss in revision total knee arthroplasty: evaluation and management. J Am Acad Orthop Surg. 2017;25:348.
45. Kamath AF, Lewallen DG, Hanssen AD. Porous tantalum metaphyseal cones for severe tibial bone loss in revision knee arthroplasty: a five to nine-year follow-up. J Bone Joint Surg Am. 2015;97:216.
46. Panegrossi G, Ceretti M, Papalia M, Casella F, Favetti F, Falez F. Bone loss management in total knee revision surgery. Int Orthop. 2014;38:419.
47. Gautam D, Malhotra R. Megaprosthesis versus allograft prosthesis composite for massive skeletal defects. J Clin Orthop Trauma. 2018;9:63.
48. De Gori M, Scoccianti G, Frenos F, Bettini L, Familiari F, Gasparini G, et al. Modular endoprostheses for nonneoplastic conditions: midterm complications and survival. Biomed Res Int. 2016;2016:2606521.
49. Capanna R, Scoccianti G, Frenos F, Vilardi A, Beltrami G, Campanacci DA. What was the survival of Megaprostheses in lower limb reconstruc-

tions after tumor resections? Clin Orthop Relat Res. 2015;473:820.
50. Calori GM, Colombo M, Ripamonti C, Malagoli E, Mazza E, Fadigati P, et al. Megaprosthesis in large bone defects: opportunity or chimaera? Injury. 2014;45(2):388–93.
51. Calori GM, Albisetti W, Agus A, Iori S, Tagliabue L. Risk factors contributing to fracture non-unions. Injury. 2007;38:S11.
52. Calori GM, Phillips M, Jeetle S, Tagliabue L, Giannoudis PV. Classification of non-union: need for a new scoring system? Injury. 2008;39(Suppl.2):S59–63.
53. Calori GM, Colombo M, Malagoli E, Mazzola S, Bucci M, Mazza E. Megaprosthesis in post-traumatic and periprosthetic large bone defects: issues to consider. Injury. 2014;45:S105.
54. Korim MT, Esler CNA, Ashford RU. Systematic review of proximal femoral arthroplasty for non-neoplastic conditions. J Arthroplast. 2014;29:2117.
55. Korim MT, Esler CNA, Reddy VRM, Ashford RU. A systematic review of endoprosthetic replacement for non-tumour indications around the knee joint. Knee. 2013;20:367.
56. Vaishya R, Thapa SS, Vaish A. Non-neoplastic indications and outcomes of the proximal and distal femur megaprosthesis: a critical review. Knee Surg Relat Res. 2020;32:18.