Injury 52 (2021) 3555–3560

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Mangled extremity- Modern concepts in treatment

M Bumbaširević[a,b,c], S Matić[a,b], T Palibrk[a,b], I Glišović Jovanović[a,*], M Mitković[d], A Lesić[a,b]

[a] School of Medicine, University of Belgrade
[b] Clinic for orthopedic surgery and traumatology, Clinical Centre of Serbia
[c] Serbian Academy of Sciences and Arts, Belgrade
[d] Clinic for orthopedic surgery and traumatology, Clinical Centre Nis

ARTICLE INFO

Article history:
Received 5 March 2021
Accepted 9 March 2021

Keywords:
Mangled extremity
Open fractures
Limb reconstruction
Microsurgery
Salvage versus amputation

ABSTRACT

A mangled extremity is the most devastating limb injury and presents a challenge for the orthopedic surgeon. There are two main treatment options, reconstruction or amputation, but sometimes indications for either are not clear. There are many pro and contra arguments for both options. To make the decision easier numerous score systems have been introduced, but the final decision is based on the judgment and experience of the treating surgeon. Early extremity reconstruction appears to give better results than delayed or late reconstruction and should be the treatment of choice where possible. The goal in reconstruction of a lower extremity is to restore and maintain balance and ambulation, while restoration of an upper extremity's numerous functions is more demanding. In this paper the authors describe and suggest treatment approaches in patients with a severely mangled extremity, including assessment and treatment of all injured tissues, using defined protocols, with special attention to bone stabilization, revascularization, soft-tissue coverage and nerve reconstruction. These have a great impact on the outcome and function of the injured extremity. Rehabilitation and return to the preinjury level is slow and sometimes uncertain.

1. Introduction

There are numerous terms describing a compound open fracture, including semi-amputation, amputation, blast injury, mutilating injury, conquassation, while the term mangled was introduced to describe the most severe cases with partially destroyed blood vessels, nerves, muscle and bone resulting in a state beyond recognition. This presents a great challenge for treatment all over the world. [1,2,3,4] Mangling is usually caused by high energy trauma, either in civil cases or during wartime. [5]

In the treatment of a mangled extremity there is always the question whether to amputate or to reconstruct. The approach depends on whether the injury is an isolated one or part of polytraumatization, when the key is to save life before limb and any kind of limb salvage should be postponed. [3,6–9] Sometimes, early amputation is actually part of the life-saving procedure. If the patient's condition is stable, one must judge whether to amputate or save the limb. Besides local and general assessment, the surgeon must also consider other issues such as the patient's age, social and professional status. Amputation is not a simple procedure, because it must remain-obtain the adequate length and soft tissue of the stump for good prosthesis. [10] After amputation, nowadays the function of the extremity can be improved by modern osteointegrated prostheses and bionic prostheses. [11–16]

However, for the upper extremity, prostheses fail to give the same satisfactory functional and aesthetic results as those used for the lower limb. [23–26] Prosthetic devices cannot replace even a moderately functional hand and its sensibility. [27] Thus, up to 30% of such patients do not accept the prosthesis and the embodiment is poor. [8] However, bionic hand prostheses attempt to obtain sensation again. [13–16] The main characteristic of a bionic limb is that it can establish an interface between the biological residuum and an electronic device, providing not only motor control of the prosthesis but also sensitive feedback. Thus, bionic limbs can be classified into three main groups, according to the type of tissue interfaced: nerve-transferred muscle interfacing (i.e. targeted muscle reinnervation), direct muscle interfacing and direct nerve interfacing. [17–21] Targeted muscle reinnervation (TMR) involves the transfer of the remaining nerves of the amputated stump to the available muscles. [17,18] This technique is very suitable for short stumps of the upper limb and can also be used in lower limb cases. [15]. With direct muscle interfacing, intramuscular implants

* Corresponding author.
E-mail address: ivanaglisa@gmail.com (I. Glišović Jovanović).

https://doi.org/10.1016/j.injury.2021.03.028
0020-1383/

directly record muscular contractions which are then wirelessly captured through a coil integrated in the socket to actuate prosthesis movement. [19] The third group of bionic limbs involves direct interfacing of the residual nerves using implantable electrodes that enable reception of electric signals from the prosthetic sensors. [20–22] This can improve sensation in the phantom limb.

2. Treatment approach

In the past few decades, due to the increasing survival rate after high energy trauma in both civil and war cases, the number of patients with severely injured limbs has increased. Treatment of these surgical conditions has improved over time due to modern microsurgical reconstructive procedures, better resuscitation care and fixation devices. [28–31] The amputation rate has decreased to 10% compared to 60% during World War II and especially during the recent conflicts in Iraq and Afghanistan. [3,5]

Starting with a major arm replantation in a 12 year-old boy in 1962 [32], this continued in 1963 with replantation of an amputated hand, while progress in microsurgery has provided us with numerous reconstructive options. [24] Many cases of successful lower limb replantations have been reported. [25,26]

Nevertheless, there are many issues which should be considered in pro and contra arguments for treatment options concerning limb salvage or amputation. [9,33,34]

Limb salvage procedures are time- and money-consuming, because additional surgical procedures are usually needed, which result in a prolonged stay in hospital and a recovery time as long as 2 to 3 years. [3,33–36] The cost-effectiveness of such procedures is disputable, in view of an early return to work and social activities. [5] Nevertheless, based on the economic model, limb salvage should be taken into consideration as it will lead to lower costs and higher utility when compared to amputation. [37] However, the treatment may be associated with significant morbidity, leading to a delayed amputation or, in some cases a lethal outcome. [5,34,38]

3. Scoring systems and guidelines

To make decisions about treatment easier, numerous score systems and guidelines have been suggested.

The mangled extremity severity score (MESS) was introduced by Johanson in 1990. It evaluates skeletal and soft tissue injury, limb ischemia, shock and patient age. [39–42] However, in the last decade surgical possibilities have remarkably improved and decision making for patients with MESS $\geq$ 7 should be reevaluated. [43,44] The Limb Salvage Index (LSI) proposed by Russel in 1991 takes into account the time of warm ischemia and six types of tissues involved in trauma. [45] In 1994, McNamara introduced a variation of MESS that considered nerve injury, ischemia, soft tissue injury, skeletal injury, shock and patient age, known as the NISSSA score. [46] The Predictive Salvage Index (PSI) of Howe and coauthors gives attention to warm ischemia, muscle and bone damage, and to the level of vascular injury. [47] The Ganga Hospital Open Injury Score (GHOIS) was proposed in 2004 and is designed to address the outcome in IIIb injuries of the tibia without vascular deficit. It evaluates the severity of injury to three components separately, the skin, the bone and the musculotendinous structures. Seven comorbid factors are included in the score. [48,49]

With respect to fractures, there are useful classifications for lower limb trauma. Tscherne and Oester developed the Hanover fracture scale (HFS). This scale considers every detail of injury to the involved extremity and forms a checklist. Fracture type (according to AO classification), skin condition, underlying soft tissues, vascularity, neurological status, level of contamination, presence or absence of compartment syndrome, time elapsed since injury and the overall severity of the injury are summed to provide a total score. [50]

Score systems have numerous limitations. Many studies have shown that they have limited clinical utility, that MESS is not predictive [34] and that none has been proven to be valid. [51] Thus, score systems may be helpful but they are unreliable predictors for the final outcome, especially in borderline cases, the grey zone. [34,52,53] In the end, the final decision concerning treatment choice depends on the judgment and experience of the head surgeon and the specifics of the patient. [8,34,40,43,54]

Nowadays, indications for amputation are limited to unstable patients, limbs with transected nerves (sciatic nerve, tibial posterior nerve) not suitable for reconstruction [55], and a crushed extremity with an ischemia time greater than 6 h. [55–58]

General assessment is the first stage of treatment of a patient with a severely mangled extremity. Since the injury is usually caused by high energy trauma and is often part of a complex condition in a polytraumatized patient, one must consider other injuries (head, chest, abdomen) [1,3] patient age, the state of peripheral vascular vessels (presence of diabetes mellitus, atherosclerosis, drug-corticosteroid administration, immunosuppression therapy, and other comorbidities), before making a decision. [4]

4. Assessment of the extremity

The mechanism of injury is perhaps the most important predicting factor influencing the outcome of extremity reconstruction. [1] Distal, sharp (clean) injuries have a better prognosis than proximal traction, torsional and crush injuries. [28,59,60] Some cases are associated with high levels of contamination (farm, industrial locations, and war conflicts) and can involve chemical damage and burns. [5,61,62]

The duration of ischemia is also an extremely significant factor. Prolonged ischemia leads to cellular metabolic changes, especially in muscle tissue, and patients may develop serious systemic reperfusion problems, such as renal failure, following revascularization. [28] Moreover, contamination, devitalized tissue and prolonged ischemia are always associated with a high risk of infection. [5,63] This increases greatly after 6 to 12 h of cold ischemia time, while muscles are intolerant of a warm ischemic time of more than 4 to 6 h, although the hand and digits can survive up to 24 h of cold ischemia [60,64] or even for 94 h. [65]

In a hemodynamically stable patient, the vascular status of the limb is assessed through peripheral pulses, skin color, local and capillary refill. Angiography or CT angiography are not mandatory because blood vessels should be identified during surgery, which should be performed as soon as possible. [5] Doppler ultrasound and arteriography are also of limited value in this context. [66] Moreover, skeletal stability, motor and sensory deficit-impairment, soft tissue and skin loss must also be defined besides limb vascularity.

Skeletal injuries are assessed clinically and documented using plain radiography, but a CT scan is preferable for the pelvic ring and articular fractures. [1]

Nerve injures are evaluated by assessing sensory loss and motor function. For the major nerves, the clinical status is obvious, but it is sometimes difficult to examine a polytraumatized or unconscious patient, so nerve injuries may be overlooked. Nerve damage can be verified during the initial surgical debridement and precise exploration when all tissues are directly visualized. [28,60,67,68]

5. Treatment

The initial management of a major, severe limb injury should be conducted according to the Advanced Trauma Life-Support (ATLS) guidelines, with initial resuscitation and stabilization of the patient. [59,64] Bleeding from the injured limb must be controlled with pressure and a compression dressing. [9] A tourniquet is used for a severely injured limb until the vessels can be identified and ligated or repaired in the operating room. [9]

Surgical treatment is performed as a staged procedure.

1. Irrigation and radical debridement of all damaged tissues are mandatory. Treatment begins with copious gravity irrigation with saline solution, but high pressure irrigation is not preferable [69,70]. This procedure removes foreign material and frees devitalized from healthy tissues and should be performed within 24 h. Second- and third-look debridement surgery is often necessary during hospitalization, at 24 and 36 h. [3,31,71,72] Bacterial culture swabs are taken from the damaged tissue, and antibiotics should be administered immediately, inside 2 h, to decrease the infection rate. [73,74] Usually it is first generation cephalosporin, aminoglycosides, gentamicin, while high doses of penicillin and metronidazole are given when anaerobic bacterial contamination is suspected. [75] Tetanus prophylaxis is mandatory. As in tumor surgery, extensive debridement is done in the operating room when nerves should be identified and spared wherever possible, while other devascularized tissues, including skin, fascia, bone and muscle, need to be removed until brisk bleeding appears at the debrided ends. Damaged blood vessels should be debrided, ligated or prepared for reconstruction. [1,9] At this stage one can also decompress the fascial compartments, particularly in the forearm and hand, but also in the lower leg. [10,66,67]
2. The next step is skeletal stabilization. In cases with major soft tissue damage, as part of damage control orthopedics, temporary external fixation is the treatment of choice. [3,5,53,62,76] Stable fixation enables soft tissue reconstruction, especially vascular repair. Regarding the long bone, external fixation can be replaced by internal fixation, since external fixation leads to nonunion in 50% of cases. [9] Moreover, besides external fixation, plating and intramedullary fixation are reasonable options. Stable internal fixation does not result in a higher infection rate. [3,40,65,77] When a limited length of bone is destroyed, shortening is allowed and direct internal bone fixation can be done, which also facilitates primary end-to-end arterial anastomoses and direct suture of the nerves. The humerus can be shortened up to 5 cm, and the forearm up to 4 cm. [62] On the other hand, for the lower limb the length of the extremity should be restored. A stable bone autograft or allograft (up to 4 cm) is the method for substitution of large bone defects. [62] For those of 6 cm or more, a vascularized autograft, such as a free vascularized fibula graft, is mostly used. [78–80] Also, when there is a large bone defect, the Ilizarov method of distraction osteogenesis can be applied. [81] In some circumstances, a frame may be placed, followed by simultaneous shortening (resection of devitalized bone) and lengthening by corticotomy and distraction. [82] Also, the bone loss can be treated by the induced membrane technique, [83,84] as well as with different biomaterials and new biologic adjuvants. [85–92]
3. If possible, intra-articular fractures must be anatomically reduced and stabilized, the goal being to enable early joint motion. Joint replacement may be a treatment option for larger joints. On the other hand, stability is more important than mobility, and primary fusion may be the best option for some wrist, ankle and foot joints. [5,93]
4. In the presence of vascular injury, reconstruction is mandatory. Arteries are sutured first. Vein grafts can be used where there is a vessel defect. Reversed saphenous vein grafts are a common option. Longer defects may also be reconstructed with a peroneal artery graft. [94] Smaller diameter vein grafts can be obtained from the dorsum of the hand, superficial forearm veins and from the spare parts in the mutilated extremity. [95] Veins should be reconstructed wherever there is any doubt about adequate venous drainage. [1]
5. Tendon repair and tendomuscular reconstruction is the next step. Although tendons can be sutured later, early primary tendon restoration is advisable whenever possible. In the case of tendon defect or tissue destruction, one should use a graft such as the palmaris longus or another tendon. Tendon transfers can also be done at a late stage [1,96], and side-to-side tenodeses can also yield good results. However, passive or active silicone tendon rods should be used to reduce any problems associated with scar tissue when one needs to perform delayed or staged reconstructions. [34] Another possibility is to use free microsurgical functional muscle transfers, such as *latissimus dorsi, gracilis, tensor fascia latae, rectus femoris, medial gastrocnemius and serratus anterior*. [29,97]
6. Nerve reconstruction is important and probably the most demanding surgical procedure with the least predictable result. [1] Meticulous surgical repair is important, but the functional outcome depends on a variety of other non-surgical factors, including the age of the patient, the extent and site of the injury (more proximal - less predictable), the kind of nerve damage, associated diseases, the mechanism of the particular injury and the size of the possible nerve gap. [98] It is preferable to carry out nerve exploration and reconstruction (when possible) during initial surgery, because scar tissue makes late exploration and reconstruction very difficult. Moreover, axon regeneration progressively fails over time and the outcome is much worse after late reconstruction. The best results are achieved with direct end-to-end epineural repair. Smaller nerve gaps can be resolved by mobilizing the nerve ends, through proximal nerve transpositions, or by using bridging veins, nerve conduits, silicone and absorbable tubes. [99–101] Primary nerve transfers can be performed in multiple nerve injuries, for example an anterior interosseous nerve transferred to the motor ulnar nerve, or the sensory branch of the radial nerve moved to the digital nerves for the first two digits. [102,103] Larger nerve gaps need conventional nerve grafting. [3,104]
7. Timing and type of wound closure are still controversial issues. In war injuries immediate closure is not advisable, but exposed bone, tendons and blood vessels should be covered to decrease infection using negative wound pressure for less than 7 days [5]. In the presence of major soft tissue defects, when primary closure is impossible, different flaps are an option. The concept of early coverage of soft-tissue defects is becoming widely accepted, [1,31,72,105–111] because vascularized flaps have the capacity to promote healing biologically under the coverage, with a simultaneously decreased infection rate. Numerous pedicle or free vascularized flaps are used in practice, from less aggressive, such as local muscle flaps, [112,113] to more demanding and extensive surgical procedures, such as free flaps. [114,115] When second debridement is necessary, one should consider the “Closed-Open-Close free flap technique”, which allows early wound covering even if it is contaminated. [72] In any case, wounds (or flaps) must never be closed tightly, due to the risk of ischemic changes. [1,31,72] The choice of graft is determined by the size and location of the defect and follows the ”reconstructive ladder” principles. [108] Recent advances in the treatment of soft tissue use dermal regenerate templates and extracellular matrix scaffolds. [5]

The postoperative rehabilitation program is very important because it promotes early movement of the joints and tendons, preventing joint contractures and formation of scar tissue around tendons. [1] Patients also benefit from psychological support and social assistance because post-traumatic stress disorder and depression are common following these catastrophic injuries. [9,116]

6. Complications and secondary reconstructions

One must be aware of numerous complications occuring in a severely injured extremity. The most serious are arterial or vein thrombosis, pulmonary embolism, [117] deep infection, osteomyelitis, loss of tissue flaps. [45,59,118] The most common are wound infection (28.3%), nonunion (23.7%) and osteomyelitis (7.7%). [119] Some authors have had to perform secondary reconstructions for failed primary procedures in 45% of hand and digital replant patients. [120] Secondary procedures can include simple adhesiolysis, tenolysis, capsulotomies, Z-lengthening of contracted scars, local flaps, nerve grafting, and tendon transfers. [121,122] Absence of the thumb can be overcome by pollicization of the second digit or through the Morrison procedure. [123]

7. Conclusion

Treatment of a mangled extremity is very difficult and represents a challenge for orthopedic surgeons. The efficiency of a particular treatment depends on numerous conditions and one must choose the correct care at the right time for each patient, as well as considering cost efficiency. [5] In some cases one chooses life before limb, but in others one needs to decide between limb saving or amputation. Limb salvage procedures are lengthy and associated with significant morbidity, reoperations, financial expense and social impairment. For a functional extremity, movement and sensation must be restored but after any reconstruction, the functional result can never match the function of an uninjured limb. However, in the future, functional results may possibly be improved with cadaveric tissue transplants. [124–126]

If it is impossible to reconstruct the mangled extremity, limb amputation should be done with the awareness that there are bionic types of prosthesis. Adding sensory feedback to prosthetic devices dramatically improves functionality and embodiment. However, the final decision about when to save or when to amputate is still up to the surgeon.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

Funding

There is no funding source.

References

[1] Bumbasirevic M, Stevanovic M, Lesic A, Atkinson HD. Current management of the mangled upper extremity. Int Orthop 2012;36(11):2189–95.
[2] Gregory RT, Gould RJ, Peclet M, Wagner JS, Gilbert DA, Wheeler JR. The mangled extremity syndrome (M.E.S.): a severity grading system for multisystem injury of the extremity. J Trauma 1985;25(12):1147–50.
[3] Prasarn ML, Helfet DL, Kloen P. Management of the mangled extremity. Strategies Trauma Limb Reconstr 2012;7(2):57–66.
[4] Wolinsky PR, Webb LX, Harvey EJ, Tejwani NC. The mangled limb: salvage versus amputation. Instr Course Lect 2011;60:27–34.
[5] McKinley TO, D Alleyrand SC, Valerio I, Tetsworth K, Elster EA. Management of the mangled extremities and orthopaedic war injuries. J Orth Trauma 2018;32(3):S37–42.
[6] Covey DC. Blast and fragment injuries of the musculoskeletal system. J Bone Joint Surg [Am] 2002;84A(7):1221–34.
[7] Okike K, Bhattacharyya T. Trend in the management of the open fractures, a critical analysis. J Bone Joint Surg [Am] 2006;88(12):2739–48.
[8] Tindle S, Baechler M, Nanos PG, Forsberg JA, Potter BK. Traumatic and trauma-related amputations. J Bone Joint Surg 2010;92:2934–45.
[9] Miller EA, Iannuzzi NP, Kennedy SA. Management of the mangled upper extremity. J Bone Joint Surg 2018;6(4):1–12.
[10] Fisher MT, Riehl JT. Orthopaedic tips: the mangled extremity. J Bone Joint Surg 2017;5(2):1–4.
[11] Muderis MA, Tetsworth K, Khemka A. The osteointegration Group of Australian Accelerated Protocol (OGAAP-1) for two-stage osteointegrated reconstruction of amputated limbs. J Bone Joint Surg 2016;98-B:952–60.
[12] Muderis MA, Khemka A, Lord SJ, et al. Safety of osteointegrated implants for transfemoral amputees: a two-center prospective cohort study. J Bone Joint Surg Am 2016;98:900–9.
[13] Bumbasirevic M, Lesic A, Palibrk T, Georgescu A, Matei IR, Vucetic C. What microsurgeon, orthopedic and plastic surgeon should know about bionic hand. Injury 2019;50(5):137–40.
[14] Petrini FM, Valle G, Bumbasirevic M, Barberi F, Bortolotti D, Čvančara P, et al. Enhancing functional abilities and cognitive integration of the lower limb prosthesis. Sciencia Translational Medicine 2019;11(512):eaav 8939.
[15] Petrini FM, Bumbasirevic M, Valle G, Ilić V, Mijović P, Čvančara P, et al. Sensory feedback restoration in leg amputees improves walking speed, metabolic cost and phantom pain. Nature Med 2019;25:1356–63.
[16] Bumbaširević M, Lesic A, Palibrk T, Milovanovic D, Zoka M, Kravić-Stević T. The current state of bionic limbs from the surgeon's viewpoint. EFORT Open Rev 2020;5(2):65–72.
[17] Kuiken TA, Miller LA, Lipschutz RD, et al. Targeted reinnervation for enhanced prosthetic arm function in a woman with a proximal amputation: a case study. Lancet 2007;369:371–80.
[18] Hargrove LJ, Simon AM, Young AJ, et al. Robotic leg control with EMG decoding in an amputee with nerve transfers. N Engl J Med 2013;369:1237–42.
[19] Pasquina PF, Evaangelista M, Carvalho AJ, et al. Firts in-in-man demonstration of fully implanted myoelectric sensor systems to control an advanced electromechanical prosthetic hand. J Neurosci Methods 2015;244:85–93.
[20] Weber DJ, Friesen R, Miller LE. Interfacing the somatosensory system to restore touch and proprioception: essential considerations. J Mot Behav 2012;44:403–18.
[21] Navarro X, Krueger TB, Lago N, Micera S, Stieglitz T, Dario P. A critical review of interfaces with the peripheral nervous system for the control of neuroprostheses and hybrid bionic systems. J Peripher Nerv Syst 2005;10:229–58.
[22] Rossini PM, Micera S, Benvenuto A, et al. Double nerve intraneuralinterface implant on a human amputee for robotic hand control. Clin Neurophysiol 2010;121:777–83.
[20] Bosse MJ, MacKenzie EJ, Kellam JF, Burgess AR, Webb LX, Swiontkowski MF. An analysis of outcomes of reconstruction or amputation after leg-threatening injuries. N Engl J Med 2002;347(24):1924–31.
[24] Rickard RF, Hudson DA. A history of vascular and microvascular surgery. Ann Plast Surg 2014;73(4):465–72.
[25] Chen ZW, Zeng BF. Replantation of the lower extremity. Clinics Plastic Surg 1983;10:103–13.
[26] Bumbaširević M, Lešić A, Palibk T, Georgescu AV, Matei IR, Tabaković D. Lower limb replantation: 27 years follow up. Injury 2020;51(Suppl 4):S77–80.
[27] Peacock K, Tsai TM. Comparison of functional results of replantation versus prosthesis in a patient with bilateral arm amputation. Clin Orthop Relat Res 1987;214:153–9.
[28] Bueno RA Jr, Neumeister MW. Outcomes after mutilating hand injuries: review of the literature and recommendations for assessment. Hand Clin 2003;19:193–204.
[29] Stevanovic M, Gutow AP, Sharpe F. The management of bone defects of the forearm after trauma. Hand Clin 1999;15(2):299–318.
[30] Brown JB, Cannon B, Graham B, Davis WB. Restoration of major defects of the arm by combination of plastic, orthopedic and neurologic surgical procedures. Plast Reconstr Surg 1949;4(4):337–40.
[31] Bumbasirevic M, Lesic A, Mitkovic M, Bumbasirevic V. Treatment of blast injuries of the extremity. J Am Acad Orthop Surg 2006;14(10):77–81.
[32] Malt RA, Mc Khann C. Replantation of severe arms. JAMA 1964;189:716–22.
[33] Hansen ST Jr. The type IIIc tibial fracture. Salvage or amputation. J Bone Joint Surg Am 1987;69(6):799–800.
[34] Korompilias AV, Beris AE, Lykissas MG, Vekris MD, Kontogeorgakos VA, Soucacos PN. The mangled extremity and attempt for limb salvage. J Orthop Surg Res 2009;13(4):4.
[35] Langer V. Management of major limb injuries. Sci World J 2014;2014:640430.
[36] Probe RA. Orthopaedic trauma mythbusters: is limb salvage the preferred method of treatment for the mangled lower extremity? Instr Course Lect 2013;62:35–40.
[37] Chung KC, Saddawi-Konefka D, Haase SC, Kaul G. Cost-utility analysis of amputation versus salvage for Gustilo type IIIB and IIIC open tibial fractures. Plast Reconstr Surg 2009;124(6):1965–73.
[38] Bondurant FJ, Cotler HB, Buckle R, Miller-Crotchett P, Browner BD. The medical and economic impact of severely injured lower extremities. J Trauma 1988;28(8):1270–3.
[39] Slauterbeck JR, Britton C, Moneim MS, Clevenger FW. Mangled extremity severity score: an accurate guide to treatment of the severity injured upper extremity. J Orthop Trauma 1994;8(4):282–5.
[40] Johansen K, Daines M, Howey T, Helfet D, Hansen ST Jr. Objective criteria accurately predict amputation following lower extremity trauma. J Trauma 1990;30:568–73.
[41] Helfet DL, Howey T, Sanders R, Johansen K. Limb salvage versus amputation. preliminary results of the Mangled Extremity Severity Score. Clin Orthop Relat Res 1990;256:80–6.

[42] Kiran Kumar M, Badole CM, Patond KR. Salvage versus amputation: utility of mangled extremity severity score in severely injured lower limbs. Indian J Orthop 2007;41(3):183–7.
[43] Loja MN, Sammann A, DuBose J, Li CS, Liu Y, Savage S. The mangled extremity score and amputation: time for revision. J Trauma Acute Care Surg 2017;82(3):518–23.
[44] Fochtmann A, Binder H, Rettl G, Starlinger J, Asymann O, Sarahrudi K. Third degree open fractures and traumatic sub-/total amputations of the upper extremity: outcome and relevance of the mangled extremity severity score. Orthop Trumatol Surg Res 2016;102(6):785–90.
[45] Russell WL, Sailors DM, Whittle TB, et al. Limb salvage versus traumatic amputation: a decision based on a seven-part predictive index. Ann Surg 1991;213:473–80.
[46] 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(2):81–7.
[47] JrJr Howe HR, Poole GV, Hansen KJ, Clark T, Plonk GW, LA Koman. Salvage of lower extremities following combined orthopedic and vascular trauma. a predictive salvage index. Am Surg 1987;53(4):205–8.
[48] Rajasekaran S, Sabapathy SR, Dheenadhayalan J, Sundararajan SR, Venkataramani H, Devendra A. Ganga hospital open injury score in management of open injuries. Eur J Trauma Emerg Surg 2015;41(1):3–15.
[49] Rajasekaran S, Giannoudis PV. Open injuries of the lower extremity. Injury 2012;43:1783–4.
[50] Rüedi TP, Buckley RE, Moran CG. AO principles of fracture management. In: Fracture reduction (p 166). Stuttgart New York: Georg Thieme Verlag; 2007. p. 164–86.
[51] Scalea TM, DuBose J, Moore EE, West M, Moore FA, McIntyre R. Western Trauma Association critical decisions in trauma: management of mangled extremity. J Trauma Acute Care Surg 2012;72(1):86–93.
[52] Schirò GR, Sessa S, Piccioli A, Maccauro G. Primary amputation vs limb salvage in mangled extremity: a systematic review of the current scoring system. BMC Musculoskelet Disord 2015;16:372.
[53] Durham RM, Mistry BM, Mazuski JE, Shapiro M, Jacobs D. Outcome and utility of scoring systems in the management of the mangled extremity. Am J Surg 1996;172(5):569–74.
[54] Dirschl DR, Dahners LE. The mangled extremity: when should it be amputated? J Am Acad Orthop Surg 1996;4:182–90.
[55] Lange RH, Bach AW, Hansen ST Jr, Johansen KH. Open tibial fractures with associated vascular injuries: prognosis for limb salvage. J Trauma 1985;25(3):203–8.
[56] Barla M, Gavanier B, Mangin M, Parot J, Bauer C, Mainard D. Is amputation a viable treatment option in lower extremity trauma? Orthop Traumatol Surg Res 2017;103(6):971–5.
[57] Fodor L, Sobec R, Sita-Alb L, Fodor M, Ciuce C. Mangled lower extremity: can we trust the amputation scores? Int J Burns Trauma 2012;2(1):51–8.
[58] Hertel R, Strebel N, Ganz R. Amputation versus reconstruction in traumatic defects of the leg outcome and costs. J Orthop Trauma 1996;10:223–9.
[59] Neumeister MW, Brown RE. Mutilating hand injuries: principles and management. Hand Clin 2003;19:1–15.
[60] Graham B, Adkins P, Tsai TM, Firrel J, Breidenbach WC. Major replantation versus revision amputation and prosthetic fitting in the upper extremity: a late functional outcomes study. J Hand Surg [Am] 1998;23:783–91.
[61] Gorche TS, Wood MB. Mutilating corn-picker injuries of the hand. J Hand Surg Am 1988;13(3):423–7.
[62] Ring D, Jupiter JB. Mangling upper limb injuries in industry. Injury 1999;30(Suppl 2):B5–13.
[63] Green DP, Rowland SA. Fractures and dislocations of the hand. In: Rockwood CA, Green DP, Bucholz RW, editors. Rockwood and Green's Fractures in Adults. Philadelphia: JB Lippincott Co 1991:441–561.
[64] Bernstein ML, Chung KC. Early management of the mangled upper extremity. Injury 2007;38(Suppl 5):S3–7.
[65] Wei FC, Chang YL, Chen HC, Chuang CC. Three successful digital replantations in a patient after 84, 86 and 94h of cold ischemia time. Plast Reconstr Surg 1988;82(2):346–50.
[66] McGee DL, Dalsey WC. The mangled extremity. compartment syndrome and amputations. Emerg Med Clin North Am 1992;10(4):783–800.
[67] Burkhalter W. Mutilating injuries of the hand. Hand Clin 1986;2(1):45–68.
[68] Brown PW. The fate of exposed bone. Am J Surg 1979;137(4):464–9.
[69] 3rd Boyd JI, MD Wong Wongworawat. High-pressure pulsatile lavage causes soft tissue damage. Clin Orthop Relat Res 2004;427:13–17.
[70] Hassinger SM, Harding G, Wong Wongworawat MD. High-pressure pulsatile lavage propagates bacteria in to soft tissue. Clin Orthop Relat Res 2005;439:27–31.
[71] Byrd HS. Discussion of microvascular soft-tissue transplantation for reconstruction of acute open tibial fractures: Timing of coverage and long-term functional results. Plast Reconstrct Surg 1992;89:488–9.
[72] Bumbasirevic M, Palibrk T, Georgescu AV, Soucacos P, Matei IR, Vucetic M. Close-open-close free flap technique" for the cover of severely injured limbs. Injury 2019;Suppl 50(5):S29–31.
[73] Penn-Barwell JG, Murray CK. Venke JC early anitbiotics and the debridement independently reduce infection in an open fracture model. J Bone Joint Surg [Br] 2012;94(1):107–12.
[74] Wd Lack, Karanukan MA, Angerame MR, Seymour RB, Sims S, Kellam JF. Type III open tibial fracture: immediate antibiotic prophylaxis minimize infection. J Orthop Trauma 2015;29:1–6.
[75] Hoffman RD, Adams BD. Antimicrobial management of mutilating hand injuries. Hand Clin 2003;19(1):33–9.
[76] Hildebrand F, Giannoudis P, Kretteck C, Pape HC. Damage control: extremities. Injury 2004;35(7):678–89.
[77] Shea KG, Fernandez DL, Casillas M. Fixation methods in contaminated wound and massive crush injuries of the forearm. Hand Clin 1997;13(4):737–43.
[78] Bumbasirevic M, Stevanovic M, Bumbasirevic V, Lesic A, Atkinson HD. Free vascularised fibular grafts in orthopaedics. Int Orthop 2014;38(6):1277–82.
[79] Beris AE, Lykissas MG, Korompilias AV, Vekris MD, Mitsionis GI, Malizos KN. Vascularized fibula transfer for lower limb reconstruction. Microsurgery 2011;31(3):205–11.
[80] Soucacos PN, Korompilias AV, Vekris MD, Zoubos A. Beris AE The free vascularized fibular graft for bridging large skeletal defects of the upper extremity. Microsurgery 2011;31(3):190–7.
[81] 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 Joint J 2013;95-B(12):1673–80.
[82] Gulsen M, Ozkan C. Angular shortening and delayed gradual distraction of the treatment of asymmetrical bone and soft tissue defects of tibia: a case series. J Trauma 2009;66:E61–6.
[83] Masquelet AC, Bégué T. The concept of induced membrane for reconstruction of long bone defects. Orthop Clin N Am 2010;41:27–37.
[84] Giannoudis PV, Faour O, Goff T, Kanakaris N, Dimitriou R. Masquelet technique for the treatment of bone defects: tips-tricks and future directions. Injury 2011;42:591–8.
[85] Pountos I, Giannoudis PV. Is there a role of coral bone substitutes in bone repair? Injury 2016;47(12):2606–13.
[86] Alt V, Borgman B, Eicher A, Heiss C, Kanakaris NK, Giannoudis PV. Effects of recombinant human Bone Morphogenetic Protein-2 (rhBMP-2) in grade III open tibia fractures treated with unreamed nails - A clinical and health-economic analysis. Injury 2015;46(11):2267–72.
[87] Giannoudis PV, medicine Einhorn TA Bone morphogenetic proteins in musculoskeletal. Injury 2009;40(Suppl 3):S1–3.
[88] Giannoudis PV . fracture healing and bone regeneration: autologous bone grafting or BMPs? Injury. 2009; 40(12): 1243–4.
[89] Giannoudis PV, Dinopoulos H, Tsiridis E. Bone substitutes: an update. Injury 2005;36(Suppl 3):S20–7.
[90] Dimitriou R, Giannoudis PV . Discovery and development of BMPs. Injury. 2005; 36 Suppl 3: S28–33.
[91] Winkler T, Sass FA, Duda GN, Schmidt-Bleek K. A review of biomaterials in bone defect healing, remaining shortcomings and future opportunities for bone tissue engineering: the unsolved challenge. Bone Joint Res 2018;7(3):232–43.
[92] Bilic R, Simic P, Jelic M, Stern-Padovan R, Dodig D, Pompe van Meerdervoort H. Osteogenic protein-1 (BMP-7) accelerates healing of scaphoid non-union with proximal pole sclerosis. Int Orthop 2006;30(2):128–34.
[93] Heller L, Levin S. In: Bucholz RW, Heckman JD, Court-Brown C (eds). Bone and soft tissue reconstruction in Rockwood and Green's fractures in adults, 6th ed. Lippincott Co, Philadelphia, pp. 497–547.
[94] Plecha EJ, Seabrook GR, Bandyk DF, Towne JB. Determinants of successful peroneal artery bypass. J Vasc Surg 1993;17(1):97–105.
[95] Brown Re WTY. Use of "spare parts" in mutilated upper extremity injuries. Hand Clin 2003;19(1):73–87.
[96] Brown HC, Williams HB, Woolhoise FM. Principles of salvage in mutilating hand injuries. J Trauma 1968;8:319–32.
[97] Garcia RM, Ruch DS. Free flap functional muscle transfers. Hand Clin 2016;32(3):397–405.
[98] Lundborg G, Dahlin L, Danielsen N, Zhao Q. Trophism, tropism, and specificity in nerve regeneration. J Reconstr Microsurg 1994;10(5):345–54.
[99] Weber RA, Breidenbach WC, Brown RE, Jabaley ME, Mass DP. A randomized prospective study of polyglycolic acid conduits for digital nerve reconstruction in humans. Plast Reconstr Surg 2000;106(5):1036–45.
[100] Stanec S, Stanec Z. Reconstruction of upper-extremity peripheral-nerve injuries with ePTFE conduits. J Reconstr Microsurg 1998;14(4):227–32.
[101] Mackinnon SE, Dellon AL. Clinical nerve reconstruction with a bioabsorbable polyglycolic acid tube. Plast Reconstr Surg 1990;85(3):419–24.
[102] Moucharafieh RC, Badra MI, Boulos KA, Mansour JI, Daher JC, Wardani HM. Nerve transfers in the upper extremity: a review. Injury 2020;51(12):2804–10.
[103] Ozcelik IB, Yildiran G, Mersa B, Sutcu M, Celik ZE, Ozalp T. A novel nerve transfer: the first palmar interosseous motor branch of the ulnar nerve to the recurrent motor branch of the median nerve. Injury 2020;51(Suppl 4):S81–3.
[104] Stancic MF, Eskinja N, Bellinzona M, Nicovic V, Stosic A, Tomljanovic Z. The role of interfascicular nerve grafting after gunshot wounds. a report of 44 cases. Int Orthop 1996;20(2):87–91.
[105] Godina M. Early microvascular reconstruction of complex trauma of extremities. Plast Reconstrct Surg 1986;78:285–92.
[106] Francel TJ, Ca Vander Kolk, Hoopes JE, Manson PN, Yaremchuk MJ. Microvascular soft-tissue transplantation for reconstruction of acute open tibial fractures: timing of coverage and long-term functional results. Plast Reconstr Surg 1992;89(3):478–87.
[107] Faibisoff B, Daniel RK. Management of severe forearm injuries. Surg Clin North Am 1981;61:287–301.
[108] Levin LS. The reconstructive ladder. an orthoplastic approach. Orthop Clin North Am 1993;24(3):393–409.

[109] Lenarz CJ, Watson JT, Moed BR, Israel H, Mullen JD, MacDonald JB. Timing of wound closure in open fractures based on cultures obtained after debridement. J Bone Joint Surg 2010;92A:1921–6.
[110] Liu DS, Sofiadellis F, Ashton M, MacGill K, Webb A. Early soft tissue coverage and negative pressure wound therapy optimizes patient outcomes in lower limb trauma. Injury 2012;43(6):772–8.
[111] Crowley DJ, Kanakaris NK, Giannoudis PV. Debridement and wound closure of open fractures: the impact of the time factor on infection rates. Injury 2007;38(8):879–89.
[112] Pu LL. Soft-tissue coverage of extensive mid-tibial wound with the combined medial gastrocnemius and medial hemisoleus muscle flaps: the role of local muscle flaps revisited. Plast Reconstr Aesthet Surg 2010;63(8):605–10.
[113] Bhatti A, Adeshola A, Ismael T, Harris N. Lower leg flaps comparison between free versus local flaps. Internet J Plast Surg (ISPUB.COM) 2006;3(2):1–8.
[114] Jordan DJ, Malahias M, Hindocha S, Juma A. Flap decision and options in soft tissue coverage of the lower limb. Open Orthop J 2014;8:423–32.
[115] Tu YK, Yen CY, Ch Ma, Yu SW, Chou YC, al Lee MSand. Soft-tissue injury management and flap reconstruction for mangled lower extremities. Injury 2008;39(4):75–95.
[116] Grunert BK, Smith CJ, Devine CA, Fehring BA, Matloub HS, al Sanger JRand. Early psychological aspects of severe hand injury. J Hand Surg Br 1988;13(2):177–80.
[117] Freitas D, Warnack E, DiMaggio C, Frangos S, Klein M, Berry C. Embolism but not deep venous thrombosis: results from the trauma quality improvement program database. J Surg Res 2020;248:7–13.
[118] Granchi T, Schmittling Z, Vaszquez J, Schreiber M, Wall M. Prolonged use of intraluminal arterial shunts without systemic anticoagulation. Am J Surg 2000;180(6):493–6.
[120] Harris AM, Althausen PL, Kellam J, Bosse MJ, Castillo R. Lower Extremity Assessment Project (LEAP) study group complications following limb-threatening lower extremity trauma. J Orthop Trauma 2009;23:1–6.
[119] Lutz BS, Klauke T, Dietrich FE. Late results after microvascular reconstruction of severe crush and avulsion injuries of the upper extremity. J Reconstr Micosurg 1997;13(6):43–9.
[121] Jupiter JB, Pess GM, Bour CJ. Results of flexor tendon tenolysis after replantation in the hand. J Hand Surg Am 1989;14(1):35–44.
[122] Russel RC, Bueno RA Jr, Wu TY. Secondary procedures following mutilating hand injuries. Hand Clin 2003;19(1):149–63.
[123] Morrison WA, Macleod AM, O'Brien BM. Digital reconstruction in the mutilated hand. Ann Plast Surg 1982;9(5):392–9.
[124] Shores JT, Imbriglia JE, Lee WP. The current state of hand transplantation. J Hand Surg Am 2011;36:1862–7.
[125] Siemionow M, Ozer K. Advances in composite tissue allograft transplantation as related to the hand and upper extremity. J Hand Surg Am 2002;27:565–80.
[126] Foroohar A, Elliot RM, Kim TW, Breidenbach W, Shaked A, Levin LS. The history and evolution of hand transplant. Hand Clin 2011;27:405–9.