

MANAGEMENT OF THE HIGH ENERGY TRAUMATISM OF THE LIMBS

R.D. NECULA¹ I. ŞAMOTĂ¹ G. TUDOSE²
A. PANAIT² O. NISTOR² B.R. NECULA¹

Abstract: *The management of high energy traumatism is complex and must be done by a multidisciplinary team. In this review we have tried to discuss and to divide the treatment in three steps, based on the moment of performing it. Soon after the traumatism, the team performs the primary evaluation, plans the future interventions and administer the antibiotic prophylaxis. Secondly, the orthopaedic surgeon, together with the plastic surgeons, and other specialists from the team, perform the first surgical management. Last step is going to be performed especially in Gustilo-Anderson fractures type III and is represented by the secondary surgical management.*

Key words: *High energy traumatism, Open fracture*

1. Introduction

Severe limb traumatism represents a challenge for specialists that treat those kinds of injuries. The treatment aims to preserve the injured limb, but the severity of the wound may endanger the patient's life so that the limb amputation becomes the lifesaving procedure. In order to maximise the chance of success there should be a multidisciplinary team consisting of emergency medicine doctors, orthopaedic, plastic and vascular surgeons and intensive care specialists.

In successive stages the team will act to resuscitate the patient and to preserve the limb anatomy and function. Following high energy trauma, the first 7 days are crucial. We have summarised general treatment principles for open fractures and structured them into 3 notable stages.

2. Initial Evaluation

After cardiovascular and haemodynamic resuscitation – according to Advance Trauma Life Support (ATLS) [6] – it is of utmost important to obtain crucial

¹ Transilvania University of Brasov, Faculty of Medicine

² Brasov County Emergency Clinic Hospital

*corresponding author: radu.necula@unitbv.ro

information about the aetiology of the traumatism. Furthermore, the specialists can collect data about the energy of the trauma, exposure of the wound to contamination factors, etc. [24]. The wound and soft tissue lesion should be evaluated and classified so that surgeons can easily share information and consult each other about the management [57]. If an extensive wound with soft tissue defect is present, the situation must be evaluated directly by the plastic surgeon. Primary evaluation should consist of vascular assessment, neurological exam of the peripheric nerves, soft tissue damage estimation and fracture type classification.

First of all, we evaluate the limb vascularisation, even though those injuries are present in only 3% of cases, they are associated with high complication rate and morbidity [40]. If we diagnose as soon as possible the wound, the outcome will be better. Vascular lesions can be evident, massive bleeding, suggestive for penetrating damage of the arteries. Also, there can be present just clinical indirect evidence of a vascular injury such as skin of the injured limb is paler than the other one or there is a developing hematoma or the artery pulse is lowered compared to unimpaired extremity. While the situation develops late vessel related pathology can appear, for example pseudo-aneurysm, thrombosis or arterio-venous fistulae. When the patient has signs and symptoms suggestive for vascular traumatism, the specialist can evaluate the damage of an artery by two methods. Doppler echography is faster, non-invasive and cheaper, but is more susceptible to false diagnosis because it depends on the person who performs it [40]. The gold

standard is the Computed Tomography angiography, so that it is recommended to scan any patient whose clinical presentation is suggestive for vascular injury [44].

For a polytraumatised patient is important to assess the peripheric nerves integrity. To diagnose any deficiency is difficult to do in this context and using the electrical stimulation is not commonly used [44]. Based on the clinical findings and traumatic mechanism – history taking – those lesions can be classified using Seddon and Sunderland classifications of nerve injuries [3], [30]. Further information will be collected during primary surgical management.

Regarding the soft tissue, specialists should assess the gross contamination with any substance and think of possible microbial contamination i.e. dirt – *Clostridium tetani*. Some years ago, it was thought that before any procedure, one or more swabs should be taken from the wound site. Even if the tests can identify some microorganisms it is not sure that those will cause infections. At this moment, it has been proven that predebridement bacterial cultures are not useful [13], [34].

The next step is the fracture evaluation. Based on the previous assessments, wound dimensions, soft tissue defect, mechanism of production, the surgeon can classify the case using Gustilo-Anderson scoring system. In order to check the bone discontinuity, we must perform a set of radiographs for isolated fracture. Extensively check of the pelvic bones or spinal cord must be done using computed tomography. CT scans must be done for every polytraumatic patient. The

X-Rays offers further information about the intensity of the mechanism – AO type C fracture suggest important intensity even when the integumentary tissue may look just slightly injured. In this case the multidisciplinary team should proceed with caution because secondary soft tissue necrosis may develop.

The method to predict the patient's evolution is to categorise the injuries. To do that we use two scoring systems Gustilo-Anderson (GA) and Mangled Extremity Severe Score (MESS). GA has been developed for classifying the traumatism during the surgery, but now it is also use as initial score system, before operation. Using GA we can predict the probability of infection and osseous union. All information about the complications must be presented to the patient prior to any intervention, while obtaining the informed consent. An important aspect to be mentioned is the new GA III B plus which means that the vascular lesion is present partially as at least one main artery is intact and irrigates the injured limb [56]. MESS is useful when we need to choose whether to do an amputation or to try the limb salvage surgery.

Surgical management can be adapted for each patient individually because of this 4-point evaluation. For the first step, the team can choose between a damage control therapy or a treatment option suitable for the wound type. Even if at this stage the patient is still in the emergency room, the treatment has begun already.

Microbial contamination of the lesion can appear during the wound production, but not only, as patients are susceptible to nosocomial infections. There are many ways to reduce the contamination of the

wound, for example debridement and lavage, and we will present them later in this paper. The very first step is to start the antibiotic therapy. It has been proven that the infectious risk is diminished to 16.6% if the antibiotic is administered within 3 hours since the traumatism [44]. The antibiotic therapy should start as soon as the drug is available and the venous route of administration is patent [27], [51]. It has been successfully studied that the infectious risk varies according to the GA classification. While GA type I has a risk of infection ranging from 0 to 2%, the advanced ones like type III have A 7%, B with 10% and C 20-50% [7]. Another research has found that GA type I and II fracture are more prone to develop infections because of Gram-positive pathogens, while GA type III present more Gram-negative microorganisms [16]. The best choice of antibiotic therapy (which should be broad spectrum) is intravenous Co-amoxiclav (1.2g every 8 hours) or second generation cephalosporins – Cefuroxime (1,5g every 8 hours), up to 24 hours after primary closure or maximum 72 hours after traumatism [43]. The tetanus prophylaxis must be initiated in the emergency room and it depends on vaccination history, severity of the wound and latest vaccination date. The two types of prophylaxis are toxoid or immunoglobulin, both are administered intramuscularly.

3. Primary Surgical Management

When proceeding to the operation room with the patient, some well selected patients may benefit from the damage control technique, prioritising the life-

threatening injury treatment to limb salvage procedures. An experienced surgeon is the best person to do initial debridement because poorly planned incisions can affect the next reconstructive therapeutic options and eventually the quality of patients' life [17].

Primary debridement should be done by the plastic surgeons until vascularized soft tissue is touched. The recommendation of doing this intervention within 6 hours from the traumatism is no longer supported, but it must be done within the first 24 hours [58]. It should be highlighted that for GA type I and II, if the surgery can not be performed in proper conditions during the night, it can be postponed until the morning [57]. During the first debridement it is advised to administer another dose of one of the above-mentioned antibiotics plus gentamicin (1.5mg/kg) [43]. In our practice we use another protocol. For GA type III we start as soon as possible with ampicillin/sulbactam – begin 1.5g before surgery and postoperative dosage 0.75g/ 6 hours – combined with gentamicin – 80mg before surgery and after 3mg/kg dose twice in 48 hours. If we suspect MRSA infection or Beta lactam allergy, we use vancomycin – 15mg/kg before surgery and 10mg/kg every 8 hours – plus metronidazole – 7mg/kg before surgery, followed by 7mg/kg every 8 hours – and combined with gentamicin – 3mg/kg twice in 48 hours.

For muscle debridement the 4 “C” must be checked: consistency, colour, contractility and circulation [7]. During debridement, intensive lavage of the tissue should be done at low pressure [8]. For lavage it is recommended to choose a

solution (normal saline) that is readily available in large quantities and which is also cheap because 3 litres multiplied by the grade of the fracture are used for one intervention i.e. for GA type III 3 litres multiplied by 3 [21], [48]. Massive contamination is a moment when the specialist can choose the local antibiotic therapy combined with the systemic one. The drug of choice for local treatment has been pearl gentamicin, tobramycin and vancomycin; currently on the market are present many formulations, some of them are combinations with osteoinduction molecules. It has been observed a reduction by 11.9% of the risk of infection when local therapy has been added to certain wounds [41].

The next step is fracture fixation. Several methods can be found while meticulously searching the literature. If the cardiovascular status of the patient is unstable, the lesion is considered susceptible to infection or serious injured (GA IIIA-IIIIC), it is preferred to use an external fixator [17]. The position of the external fixator should occupy less space so that further interventions can be performed to the wound place, for example second debridement, skin flaps etc. Perfect positioning requires a highly skilled surgeon.

There are some exceptions. It has been observed that some selected cases of III A shaft fractures can be managed like GA type I, II – intramedullary nailing being performed during the first surgery [23]. Some papers have assessed that in tibial shaft fracture it is better to do osteosynthesis as soon as possible, recommended during the first surgical intervention. Promptly using the

intramedullary nailing has some advantages such as lowering the necessity of second intervention, lowering the risk of infection and faster rehabilitation [25], [39]. This outcome has been noted also in GA III traumatism of the tibial shaft [23].

Regarding intramedullary nailing, extensive discussions have existed whether to ream or not the medullary channel before inserting the nail. This debate has appeared because in theory the endosteal circulation promotes the bone formation and reaming inside the centromedular channel would destroy this source of vascularisation. While some studies observe no difference between reamed and unreamed [28], [38], others have noticed a better outcome in the reamed cohort [22], [39].

Large bone defects may be present because of high energy traumatism. During this stage, Masquelet technique can be initiated by inserting the bone spacer [55]. Bone grafting will be done later after soft tissue healing and when the infectious risk is lowered [37], but this is not the subject of this review.

To diminish the ischaemia of the limb the surgeon may need to perform patching of a main vessel, vascular graft or even bypass. If the patient presents signs and symptoms of compartment syndrome, intercompartmental pressure must be checked. If it is above 35-40 mmHg, the fasciotomy must be performed.

Another lesion that can be dealt with during the primary surgical management is the peripheral nerves injuries. This is the best moment to check the nerves integrity. The gold standard treatment for

traumatic injury is the direct nerve repair – different suture techniques [30]. If the lesion is sharp, transecting the nerve structure – Sunderland grade 5, the reconstruction must be done within 72 hours from the traumatism [10]. Moreover, the perineurial repair will be done in combination with bone shortening so that the two ends of the nerve will not be under tension.

Covering the soft tissue defect is a complex topic and more opinions can be found throughout the literature. It is generally approved that the intervention must be done rather sooner than later. The wounds without underlying soft tissue injury are better closed within the first hours from traumatism as the infection rate of the lesion rises from 3.5% in the first 20 minutes to 22% after 10 hours.[7] For GA type III it has been shown that the late closure of the wound is associated with higher rates of infections [35].

The outcome the multidisciplinary team tries to avoid is amputation of the limb, which may be seen, in this case, as a failure. An amputation represents a psychological challenge for both sides, for the patient, but also for the surgeons. The option of performing an amputation can be guided by scoring system, but must be taken by judging the clinical situation, patient's occupation, patient's general status, age etc. It has been observed that the presence of the infection alone is not a predictive factor for mortality or amputation [52]. Even though it might be seen as a failure, sometimes it is the only method to save the patient's life, for example when the haemorrhage is massive and can not be controlled or patients suffering from Ischaemia-

Reperfusion injury [7]. Even if the team is focused to treat a focal lesion, they must not forget to check the patient's general status regularly. This can be done by clinical and paraclinical examination.

The complexity of the wound generates a wide range of complications and because of this the fractures classified as GA type I and II rarely present any problem [9]. Most of them can be avoided by an experienced surgeon, but some of them depend only on the patient status. Severe traumatism can lead also to renal insufficiency for patient that present crush syndrome or Bywaters' syndrome. Rhabdomyolysis followed by myoglobinuria have been also present during compartment syndrome or reperfusion of the limb [12]. A patient who suffers from acute renal insufficiency must be treated by Intensive Care Unit specialists.

4. Secondary Surgical Management

If high contamination or vascular/microvascular injury – high energy traumatism – are present, it is recommended to do a second debridement surgery after 24 hours from the first one, but not more than 48 hours [26]. Following this step, the soft tissue damage should be reduced and the lesion should be covered. Some groups suggest closing the wound or covering the one that present also tissue defect, during the initial intervention [31], [42]. This idea is not generally accepted and some specialists have observed that the best moment to close the wound is between 72 hours and 7 days from the traumatism [20]. British Orthopaedic Association

(BOA) and British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS) guidelines observed the best outcome when the tissue closure has been done within 72 hours [2]. Over 7 days it has been demonstrated a higher infection risk and non-union of the fracture, so that it should be avoided if possible [47].

Final osteosynthesis should be performed in approximatively same interval as wound closure. It is preferred to keep the external fixator for not more than 72 hours and after that to convert to an internal fixation method [19]. Another study has showed that the conversion from external to internal fixation should be done as soon as the general status of the patient improves or the soft tissues quality allow intrafocal osseous manipulation [36], [49]. An exception from external to internal conversion is represented by fractures with important osseous defects that necessitate external fixator reconstruction, for example external circular fixator Ilizarov [1], [39]. This conversion is done in order to prevent several complications. Tibial shaft fractures are more prone to non-union compared to other area of fracture [18]. Pseudarthrosis appearance depends on the local factors i.e. type osseous fixation used or presence of infection. Non-union can appear also because of some factors that depend on the patient such as smoking, diabetes, obesity etc.

Another aspect that should be mentioned is the fact that a multidisciplinary team, orthopaedic surgeons and plastic surgeons, have a better timing when comes to closure than just the orthopaedic team alone. While the last team performs the definitive

surgery at around 6 days, the combined team needs an average of 3.5 days [54]. The experience of both specialists aids in identifying the suitable moment earlier.

Unfortunately, not always the amputation is done as a primary option, but later, after several procedures aiming to save the limb which fail to do so. Approximately 7% of patient with tibial fracture GA type III have needed eventually an amputation [45]. Another study has shown that up to 50% of GA type IIIC will need an amputation eventually [7]. MESS score over 7, over 6 hours of limb ischaemia and compartment syndrome have been associated with high risk of necessitating secondary amputation [53]. When needed, the secondary amputation must be done within the first 72 hours since the traumatism.

If the local vascularization does not allow the surgeon to perform primary closure, the negative pressure devices have been developed to support and protect the wound until final suture can be done [32]. The benefits of using this system are the improvement of local tissue perfusion, promoting the granulation tissue appearance and protection against bacteria [4], [11]. Important to highlight that there is no evidence to support using vacuum devices for treatment of the deep infections. Tissue perfusion and granulation tissue improve the local conditions allowing for skin graft or skin flap surgery to be performed in a facile way, fact that has been proven on GA type IIIB [50]. Keeping the patch under 7 days has been demonstrated to have great outcome especially when vacuum device is

combined with plastic surgery techniques for covering the soft tissue or skin defect [33]. If it is necessary to use more than 7 days the vacuum device, the patch must be changed before the 7 days threshold, because above this point the risk of amputation and infection rises [29].

A study that compares between standard wound dressing versus vacuum patches by following the patients up to 12 months has shown no difference between the groups [15]. Another paper states that the patient treated with vacuum devices undergo the final internal fixation procedure and also the final wound closure earlier than the other group. They have noticed an improvement in the rehabilitation of the patients within the vacuum group compared to the standard dressing cohort [5].

Correlated to open fractures can appear complex regional pain syndrome (CRPS), thromboembolism and renal insufficiency. CRPS appears usually after fractures at the level of the forearm, followed in incidence by the tibial fractures. Some studies estimate that up to about 30% of compound tibial fracture present CRPS as late complication [18].

Thromboembolism is one of the most common complication of orthopaedic surgery. It is estimated that pulmonary embolism and thrombosis are present in 2% up to 58% of the patient who have suffered a compound fracture [7]. Venous thrombosis risk can be reduced by early mobilisation of the patient.

Even if the treatment is prolonging with this secondary surgical management, the antibiotic must be administered according to general rules, which have been presented in primary evaluation topic. The

therapy should be continued up to 72 hours since the traumatism [43]. Long term administration has no advantageous outcome as it has been showed that continuation of therapy for 5-7 days can affect the saprophyte flora and leave space for exogenous bacterial flora and nosocomial pathogens [14], [46].

5. Conclusion

To sum up, this review has divided the treatment of the open fractures in three consecutive steps. Primary evaluation should be done as soon as possible after the traumatism in order to choose the best therapy – which injury treatment should be prioritised – and to administer the antibiotic drugs.

Primary surgical management consists of debridement and osseous fixation – temporary or final – so that it is advisable to perform it by a multidisciplinary team – plastic and orthopaedic surgeons. During the primary surgical management, the team treats also associate lesions i.e. arterial damage by the vascular surgeon. Patient must be periodical evaluated in order to observe any aggravation of the general status as soon as it happens. Patients whose limb has been crushed or patients presenting polytraumatism should be admitted to the Intensive Care Unit.

Unless any deterioration is present, the primary surgical management can be enough – GA I, II or selected cases GA type IIIA. Gustilo-Anderson type III B or C necessitate a two-step surgical management.

References

1. Ajmera, A., Verma, A., et al.: *Outcome of Limb Reconstruction System in Open Tibial Diaphyseal Fractures*. In: *Indian J Orthop*, 2015, 49(4), p. 429-35.
2. Ali, A., McMaster, J., et al.: *Experience of managing open fractures of the lower limb at a major trauma centre*. In: *Ann R Coll Surg Engl*, 2015, 97(4), p. 287–290.
3. Althagafi, A., Nadi, M.: *Acute Nerve Injury*. In: *StatPearls* [Internet], StatPearls Publishing, Treasure Island (FL), 2020.
4. Angelis, S., Apostolopoulos, A. P., et al.: *The Use of Vacuum Closure-assisted Device in the Management of Compound Lower Limb Fractures with Massive Soft Tissue Damage*. In: *Cureus*, 2019, 11(7), e5104.
5. Arti, H., Khorami, M., et al.: *Comparison of Negative Pressure Wound Therapy (NPWT) & Conventional Wound Dressings in the Open Fracture Wounds*. In: *Pak J Med Sci*, 2016, 32(1), p. 65-9.
6. ATLS Subcommittee; American College of Surgeons' Committee on Trauma; International ATLS working group. *Advanced Trauma Life Support (ATLS®): The Ninth Edition*. In: *J Trauma Acute Care Surg*, 2013, 74(5), p. 1363-6.
7. Azar, F. M., Canale, S. T., et al.: *Open Fractures*. In: *Campbell's operative orthopaedics*, 2017, p. 2662-2673. Philadelphia. Elsevier.
8. Bhandari, M., Jeray, K. J., et al.: *A Trial of Wound Irrigation in the Initial Management of Open Fracture*

- Wounds. In: N Engl J Med, 2015, 373(27), p. 2629-41.
9. Bonneville, P.: *Operative Treatment of Early Infection After Internal Fixation of Limb Fractures (Exclusive of Severe Open Fractures)*. In: Orthop Traumatol Surg Res, 2017, 103(1S), S67-S73.
 10. Campbell, W.W.: *Evaluation and Management of Peripheral Nerve Injury*. In: Clin Neurophysiol, 2008, 119(9), p. 1951-65.
 11. Chandewar, M. M., Singh, S., et al.: *Outcome analysis of vacuum assisted closure application in open fractures of long bones*. In: International Journal of Research in Orthopaedics, 2018, 4(1), p. 146-153.
 12. Chavez, L. O., Leon, M., et al.: *Beyond muscle destruction: a systematic review of rhabdomyolysis for clinical practice*. In: Crit Care, 2016, 20(135), p. 1-11.
 13. Cherian, J. J., Lobo, J. O., et al.: *Comparative Study of Bacteriological Culture Results Using Swab and Tissue in Open Fractures: A Pilot Study*. In: J Orthop Case Rep, 2019, 9(1), p. 33-36.
 14. Cooper, R. A.: *Surgical Site Infections: Epidemiology and Microbiological Aspects in Trauma and Orthopaedic Surgery*. In: Int Wound J., 2013, 1(-), p. 3-8.
 15. Costa, M. L., Achten, J., et al.: *Effect of Negative Pressure Wound Therapy vs Standard Wound Management on 12-Month Disability among Adults with Severe Open Fracture of the Lower Limb: The WOLLF Randomized Clinical Trial*. In: JAMA, 2018, 319(22), p. 2280-2288.
 16. Cross, W.W., Swiontkowski, M.F.: *Treatment principles in the management of open fractures*. In: Indian J Orthop, 2008, 42(4), p. 377-386.
 17. Diwana, A., Eberlinb, K. R., et al.: *The principles and practice of open fracture care*. In: Chinese Journal of Traumatology, 2018 21(-), p. 187-192.
 18. Elniel, A. R., Giannoudis, P. V.: *Open Fractures of the Lower Extremity: Current Management and Clinical Outcomes*. In: EFORT Open Rev, 2018, 3(5), p. 316-325.
 19. Fernandez, M. A., Nanchahal, J., et al.: *Open tibial fractures*. In: Major trauma, 2017, 31(2), p. 125-132.
 20. Fernandez, M., Wallis, K., et al.: *The impact of a dedicated orthoplastic operating list on time to soft tissue coverage of open lower limb fractures*. In: Ann R Coll Surg Engl, 2015, 97(6), p. 456-459.
 21. Giglio, P. N., Cristante, A. F., et al.: *Advances in treating exposed fractures*. In: Rev Bras Ortop, 2015, 50(2), p. 125-130.
 22. Gill, S. P., Raj, M., et al.: *Early Conversion of External Fixation to Interlocked Nailing in Open Fractures of Both Bone Leg Assisted With Vacuum Closure (VAC) - Final Outcome*. In: J Clin Diagn Res, 10(2), 2016.
 23. Giovannini, F., Palma, L. D., et al.: *Intramedullary Nailing Versus External Fixation in Gustilo Type III Open Tibial Shaft Fractures: A Meta-Analysis of Randomised Controlled Trials*. In: Strategies Trauma Limb Reconstr, 2016, 11(1), p. 1-4.

24. Griffin, M., Malahias, M., et al.: *Update on the Management of Open Lower Limb Fractures*. In: *Open Orthop J*, 2012, 6(-), p. 571-7.
25. Halawi, M. J., Morwood, M. P.: *Acute Management of Open Fractures: An Evidence-Based Review*. In: *Orthopedics*, 2015, 38(11), e1025-33.
26. Hierner, R., Nast-Kolb, D., et al.: *Degloving Injuries of the Lower Limb*. In: *Unfallchirurg*, 2009, 112(1), p. 55-62.
27. Hoff, W. S., Bonadies, J. A., et al.: *East Practice Management Guidelines Work Group: Update to Practice Management Guidelines for Prophylactic Antibiotic Use in Open Fractures*. In: *J Trauma*, 2011, 70(3), p. 751-4.
28. Hofmann, A., Dietz, S.-O., et al.: *The Role of Intramedullary Nailing in Treatment of Open Fractures*. In: *Eur J Trauma Emerg Surg*, 2015, 41(1), 39-47.
29. Hou, Z., Irgit, K., et al.: *Delayed Flap Reconstruction with Vacuum-Assisted Closure Management of the Open IIIB Tibial Fracture*. In: *J Trauma*, 2011, 71(6), p. 1705-8.
30. Hussain, G., Wang, J., et al.: *Current Status of Therapeutic Approaches against Peripheral Nerve Injuries: A Detailed Story from Injury to Recovery*. In: *Int J Biol Sci*, 2020, 16(1), p. 116-134.
31. Jenkinson, R. J., Kiss, A., et al.: *Delayed Wound Closure Increases Deep-Infection Rate Associated With Lower-Grade Open Fractures: A Propensity-Matched Cohort Study*. In: *J Bone Joint Surg Am*, 2014, 96(5), p. 380-6.
32. Jordan, D. J., Malahias, M., et al.: *The Ortho-Plastic Approach to Soft Tissue Management in Trauma*. In: *The Open Orthopaedics Journal*, 2014 8(1), p. 399-408.
33. Kim, Y. H., Hwang, K. T., et al.: *What Is the Ideal Interval Between Dressing Changes During Negative Pressure Wound Therapy for Open Traumatic Fractures?* In: *J Wound Care*, 2015, 24(11), p. 536- 542.
34. Lingaraj, R., Santoshi, J.A., et al.: *Predebridement wound culture in open fractures does not predict postoperative wound infection: A pilot study*. In: *J Nat Sci Biol Med*, 2015, 6(Suppl 1), S63–S68.
35. Matos, M. A., Lima, L. G., et al.: *Predisposing factors for early infection in patients with open fractures and proposal for a risk score*. In: *J Orthop Traumatol*, 2015, 16(3), p. 195–201.
36. Matsumura, T., Takahashi, T., et al.: *Clinical outcome of conversion from external fixation to definitive internal fixation for open fracture of the lower limb*. In: *Journal of Orthopaedic Science*, 2019, 24(5), 888-893.
37. McCall, T.A., Brokaw, et al.: *Treatment of Large Segmental Bone Defects with Reamer-Irrigator-Aspirator Bone Graft: Technique and Case Series*. In: *Orthopedic Clinics of North America*, 2010, 41(1), p. 63-73.
38. Metsemakers, W.-J., Handojo, K. et al.: *Individual Risk Factors for Deep Infection and Compromised Fracture Healing After Intramedullary Nailing of Tibial Shaft Fractures: A Single Centre Experience of 480 Patients*. In: *Injury*, 2015, 46(4), p. 740-5.

39. Mir, F. R., Mehta, R.: *Management Protocol for Open Fractures of Tibia*. In: JK-Practitioner, 2015, 20(3-4), p. 18-25.
40. Montorfano, M. A., Pla, F., et al.: *Point-of-care Ultrasound and Doppler Ultrasound Evaluation of Vascular Injuries in Penetrating and Blunt Trauma*. In: Crit Ultrasound J, 2017, 9(1), 5.
41. Morgenstern, M., Vallejo, A., et al. The Effect of Local Antibiotic Prophylaxis When Treating Open Limb Fractures: A Systematic Review and Meta-Analysis. In: Bone Joint Res, 2018, 7(7), p. 447-456.
42. Nambi, G. I., Salunke, A. A., et al. Single stage management of Gustilo type III A/B tibia fractures: Fixed with nail & covered with fasciocutaneous flap. In: Chinese Journal of Traumatology, 2017, 20(2), p. 99-102.
43. Nanchahal, J., Nayagam, S., et al.: *Standards for the management of open fractures of the lower limb*. London. Royal Society of Medicine Press Ltd., 2009.
44. Nemoto, M.: *Multidisciplinary Management of Severe Extremity Injuries*. In: Limb Amputation, 2019, 1-16. Nagasaki. IntechOpen.
45. Neto, F.C., Canal, M. D., et al.: *Analysis of the characteristics of patients with open tibial fractures of Gustilo and Anderson type III*. In: Rev Bras Ortop, 2016, 51(2), p. 143-149.
46. O'Brien, C.L., Menom, M., et al.: *Controversies in the Management of Open Fractures*. In: The Open Orthopaedics Journal, 2014 8(1), p. 178-84.
47. Olesen, U. K., Juul, R., et al.: *A Review of Forty-Five Open Tibial Fractures Covered With Free Flaps. Analysis of Complications, Microbiology and Prognostic Factors*. In: Int Orthop, 2015, 39(6), p. 1159-66.
48. Olufemi, O. T., Adeyeye, A. I.: *Irrigation Solutions in Open Fractures of the Lower Extremities: Evaluation of Isotonic Saline and Distilled Water*. In: SICOT J, 2017, 3(7), p. 1-6.
49. Pairon, P., Ossendorf, C., et al.: *Intramedullary Nailing After External Fixation of the Femur and Tibia: A Review of Advantages and Limits*. In: Eur J Trauma Emerg Surg, 2015, 41(1), p. 25-38.
50. Park, C. H., Shon, O. J., et al.: *Negative Pressure Wound Therapy for Gustilo Anderson Grade IIIb Open Tibial Fractures*. In: Indian J Orthop, 2016, 50(5), p. 536-542.
51. Prokuski, L.: *Prophylactic Antibiotics in Orthopaedic Surgery*. In: J Am Acad Orthop Surg, 2008, 16(5), p. 283-93.
52. Schlatterer, D. R., Hirschfeld, A. G., et al.: *Negative Pressure Wound Therapy in Grade IIIB Tibial Fractures: Fewer Infections and Fewer Flap Procedures?* In: Clin Orthop Relat Res, 2015, 473(5), 1802-11.
53. Song, W., Zhou, D., et al.: *Predictors of secondary amputation in patients with grade IIIC lower limb injuries, a retrospective analysis of 35 patients*. In: Medicine (Baltimore), 2017, 96(22), e7068.
54. VandenBerg, J., Osei, D., et al.: *Open Tibia Shaft Fractures and Soft-Tissue Coverage: The Effects of Management by an Orthopaedic Microsurgical*

- Team*. In: *J Orthop Trauma*, 2017, 31(6), p. 339-344.
55. Wong, T.M., Lau, T. W., et al.: *Masquelet Technique for Treatment of Posttraumatic Bone Defects*. In: *The Scientific World Journal*, 2014(-), 710302.
56. Yim, G.H., Hardwicke, J.T.: *The Evolution and Interpretation of the Gustilo and Anderson Classification*. In: *J Bone Joint Surg Am*, 2018, 100(-), e152(1-8).
57. You, D. Z., Schneider, P. S.: *Surgical timing for open fractures: Middle of the night or the light of day, which fractures, what time?* In: *OTA International*, 2020, 3(1), e067.