



The Outcomes of Open Ankle Fractures in Patients Managed by Early or Delayed Definitive Fixation: A Comparative Analysis of 73 Patients

Raghavendra Kaganur, Bhaskar Sarkar*, Pragadeeshwaran Jaisankar*, Nirvin Paul*,
Md Quamar Azam*, Anurag Bhakhar*

Department of Orthopedics, AIIMS Patna, Bihar, *Department of Trauma Surgery and Critical Care, AIIMS Rishikesh, Uttarakhand, India

Purpose: Ankle fracture fixation is the gold standard of treatment but it does have its own complications. There is inadequate data regarding the comparative effectiveness of early vs. delayed fixation for open ankle fracture outcomes. This study compares the clinical and functional outcomes of open ankle fractures treated by early or delayed definitive fixation and identifies the limitations of both methods.

Materials and Methods: All 73 patients enrolled in the study underwent surgical intervention within 24 hours of injury. The early fixation group (group A) consisting of 39 patients underwent definitive fixation as an index procedure, while the delayed fixation group (group B) consisted of 34 patients who underwent debridement and external fixator application as an index procedure and definitive fixation when soft tissue condition was conducive. All patients were evaluated at 2, 6, and 12 weeks postoperatively and then three monthly for a year.

Results: Enneking and American Orthopaedic Foot and Ankle Society scores were markedly higher in the early fixation group at 6 months postoperatively (p-values <0.001 and 0.011, respectively). However, no discernible intergroup difference was evident at 12 months postoperatively. Between 6 and 12 months, group functional outcome scores were significantly different. At 6 months, there was a substantial difference in dorsiflexion between the two groups (p-values 0.001 and <0.001, respectively), but no difference was observed at 12 months postoperatively. At 6 and 12 months, group average plantar flexions were non-significantly different.

Conclusion: Early definitive fixation of complex ankle fractures using a targeted approach produced promising results for lower grade open fractures (grades 1 and 2), and delayed definitive fixation, after initial external fixation to allow for soft tissue stabilization, produced promising results for higher grade open fractures (grades 3A and 3B). At 12-month follow-ups, clinical and functional outcomes achieved using these strategies were equivalent.

Key Words: Open ankle fracture, Early fixation, Delayed definitive fixation, Debridement

INTRODUCTION

Open ankle fractures, which account for 2%~5% of all ankle fractures, have much greater morbidity rates hampering day to day activities of individuals than closed ankle fractures.¹⁾ Open ankle fractures frequently result in significant soft tissue damage to the surrounding skin and ligaments,

which has a poor functional outcome. Although minor trauma causes open ankle fractures in elderly patients, high-energy injuries like those from collisions with vehicles are the most common cause of injury in young individuals.²⁾ Evidence regarding patient characteristics that are associated with an increased risk of complications and poor functional outcomes would help us plan treatment options and targeted care for patients with ankle fractures.

According to data from a thorough review of ankle fracture outcomes, results worsen with age, mostly because of diminished physiological reserves, comorbidities, and diminished muscle mass and power.³⁾ Open fractures are associated with 33%~50% more complications than closed fractures.⁴⁾

There is a lack of information regarding the outcome of

Received July 4, 2023 Revised January 10, 2024

Accepted January 26, 2024

Corresponding Author: Nirvin Paul

Department of Trauma Surgery, AIIMS Rishikesh, Virbhadrā Road, Rishikesh, Uttarakhand 249203, India

Tel: 91-135-2462503, E-mail: drnirvinpaul@gmail.com

ORCID: <https://orcid.org/0000-0001-7081-8332>

Financial support: None.

Conflict of interest: None.

Copyright © 2024 Korean Foot and Ankle Society.

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

open ankle fractures based on whether fixation was early or delayed depending on the severity of the injury and complications associated with both modes of fixation. Recent research on the management of open ankle fractures has focused on early definitive fixation, which has been demonstrated to be similarly successful as staged fixation with similar complication rates and functional outcomes.^{5,6)} A tailored, patient-centered strategy becomes crucial for treating open ankle fractures because it is absolutely necessary to do so, on a case-by-case basis. We wish to investigate the potential for treating low and high-grade open fractures using two different treatment modalities. This study compares the clinical and functional outcomes of open ankle fractures treated with early vs. delayed definitive fixation, as well as the drawbacks of each group.

The hypothesis of the study was “Early definitive fixation for low-grade open fractures and delayed definitive fixation for high-grade open fractures would result in lower complications and better functional outcomes”. The null hypothesis is that functional outcomes and complications don’t change significantly depending on the severity of open fractures and the type of fixation.

MATERIALS AND METHODS

1. Patient selection

All patients with mature skeletons who had been treated for open ankle fractures at our level 1 trauma centre between January 2019 and January 2022 were retrospectively reviewed. During the course of the study, all participants who experienced unstable (bimalleolar and trimalleolar) ankle fractures were included. Group A consisted of patients who were managed by delayed definitive fixation and group B had patients who underwent definitive fixation as the index procedure (Fig. 1).

Patients with open ankle fractures who are under the age of 18 and those who are over 60, patients with associated fractures of other extremities. Following surgery, all patients were evaluated at 2 weeks, 6 weeks, 12 weeks, and every 3 months for a year. Patients who did not complete 1 year of follow-up or those patients that missed follow-up visits were excluded from the study.

2. Objectives

The primary objective was to identify differences in the clinical and functional outcomes of the patients with open ankle fractures managed by immediate definitive fixation and delayed definitive fixation, which was measured at 6 months and 1 year. The incidence of infection and wound dehiscence (wound gaping or breakdown in the postoperative period due to any cause) requiring debridement and wound closure by suturing in both primary fixation and delayed definitive fixation groups, which was evaluated at 2, 6, and 12 weeks, was the secondary objective. The tertiary objective was to look for the incidence of other complications like implant failure, peri-implant fracture, deep infection, and osteomyelitis at 1-year follow-up.

The Gustilo-Anderson classification was used to categorize each patient who presented to our trauma centre with an open ankle fracture and the Weber classification was used to categorize the fractures based on the pattern and level of lateral malleolus fracture.

3. Treatment protocol

Ankle fractures that were subluxated or dislocated were treated with reduction and splinting. According to hospital policy, open fractures were given, and tetanus prophylaxis, analgesics, and intravenous antibiotics were started. In the emergency room, a wound wash was performed, and an aseptic non-adherent bandage was applied. Within 24 hours, all patients were operated on after being transported as fast as possible to the emergency surgery. Debridement and external fixator application were used to treat patients with grade III open fractures, followed by definitive fixation when soft tissue condition permitted or after soft tissue coverage in cases of skin defects requiring primary or revision debridement. However, patients with grade I and II open fractures were treated by primary debridement and definitive fixation if the skin was in good enough condition at the time of presentation.

At the time of definitive fixation, several techniques were utilized to treat ankle fractures. If the patient had a syndesmotic injury, the fibula was fixed with a pre-contoured 1/3 tubular plate and a syndesmotic screw through the plate. Depending on the fracture anatomy, recon plate, cancellous screws, or tension band wiring were used to fix the medial

malleolus.

Three doses of antibiotics were given post-operatively to each patient. As soon as feasible following surgery, ankle range-of-motion exercises were encouraged. However, mobilization with partial weight-bearing began at 6 weeks and progressed to full weight-bearing once signs of union were noted. Patients had their postoperative pain evaluated using the visual analogue scale (VAS) score at 6 and 12 months, their limb function was graded using the Enneking system, and their ankle function was graded using the American Orthopaedic Foot and Ankle Society (AOFAS) score. The range of motion was measured using a goniometer at 6 and 12 months by the principal investigator.

4. Statistical analysis

Radiological parameters and functional outcome scores before and after the surgery were compared using paired t-tests. An independent t-test was used to compare data between the 2 groups. A p-value of less than 0.05 was considered significant. All collected data was statistically analyzed using SPSS software version 26.0 (IBM SPSS Statistics; IBM Corp.).

RESULTS

1. Selection of the study population and their characteristics

In the study duration, our level 1 trauma centre received 96 total cases of open ankle fractures. Of these 23 cases were excluded as they did not meet the inclusion criteria (2 were children less than 18 years, 5 presented beyond 24 hours, 4 did not complete 1 year of follow-up and 12 patients had associated foot or pilon fractures or other system involvement that would have confounded results). To conduct the analysis, a total of 73 patients (39 with delayed definitive fixation [group A] and 34 with early definitive fixation [group B]) were included.

In groups A and B, the mean ages were 41.97 ± 13.35 and 42.35 ± 13.80 years, respectively, with a p-value of 0.91. In group A there were 25 males and 14 females and group B had 24 males and 10 females. Injury to hospital presentation time for all patients was less than 8 hours (5.10 ± 1.52 hours for group A; 4.79 ± 1.70 hours in group B). The injury to surgery

duration was less than 24 hours for all patients in the study (13.87 ± 4.00 hours in group A; 13.38 ± 3.62 hours in group B). The average delay between the damage control surgery and definitive fixation was 22.78 ± 5.43 days. There was a significant difference in the total duration of hospital stay between the two groups, where group A had an average stay of 11.67 ± 2.06 days and group B was 4.09 ± 1.38 days (Table 1).

According to the Gustilo Anderson's grading, 14 patients in group A had grade 3A injuries, of which 9 needed split thickness skin grafting, while 25 had grade 3B injuries, and all of them required flap coverage. 15 patients in group B had grade 1 injuries, while 19 patients had grade 2 injuries and none of them needed any procedure for soft tissue coverage. According to the Weber's classification, group A consisted of 5 infra-syndesmotic, 23 syndesmotic, and 11 supra-syndesmotic injuries. Group B had 21 syndesmotic, 4 infra-syndesmotic, and 9 supra-syndesmotic injuries (Table 2).

2. Outcome comparison between the two groups

Enneking and AOFAS scores showed substantial differences between the two groups at the 6-month mark (p-value <0.01 , 0.011 respectively), with the early definite fixation group scoring higher. However, there was no discernible difference between the two groups at the 1-year follow-up (p-value 0.87 , 0.94 respectively). Functional outcome scores in both groups significantly differed between follow-up periods of 6 months and 1 year, with both groups achieving better functional outcomes at 12 months than they did at 6 months (Table 3). Enneking and AOFAS scores between six and twelve months in group A had p-values of 0.008 and 0.001 , respectively, while in group B, they had p-values of <0.001 , respectively (Table 4). There was no discernible difference in the VAS scores between the two groups at 6 months and at the final follow-up (p-value 0.23 , 0.65 respectively) (Table 3).

At the 6-month and 1-year follow-ups, the mean dorsiflexion attained in group A was $0.29^\circ \pm 1.71^\circ$ and $8.38^\circ \pm$

Table 1. Total Hospital Stay

Serial no.	Group	Total stay (d)	p-value
1	A	11.67 ± 2.06	<0.001
2	B	4.09 ± 1.38	

Values are presented as mean \pm standard deviation.

Table 2. Demography

Serial no.	Demographic data	Group A	Group B	p-value
1	Age (yr)	41.97±13.35	42.35±13.80	0.91
2	Sex (male:female)	25:14	24:10	-
3	Injury to presentation duration (hr)	5.10±1.52	4.79±1.70	0.42
4	Presentation to surgery duration (hr)	13.87±4.00	13.38±3.62	0.49
5	Webers A (%)	5 (12.83)	4 (11.76)	0.89
6	Webers B (%)	23 (53.97)	21 (61.76)	0.87
7	Webers C (%)	11 (28.20)	9 (26.47)	0.81
8	Comorbidities (%)	11 (28.20)	13 (38.23)	0.37

Values are presented as mean±standard deviation or number (%).

Table 3. Outcome Measures Group A vs. Group B

Score	Group A	Group B	p-value
Enneking 6 months	12.85±1.05	24.95±2.58	<0.01
Enneking 1 year	27.82±4.63	27.77±4.66	0.87
AOFAS 6 months	35.88±7.47	67.36±12.24	0.01
AOFAS 1 year	76.59±11.94	76.18±11.91	0.94
Ankle dorsiflexion 6 months (°)	0.29±1.71	5.64±5.02	0.001
Ankle dorsiflexion 1 year (°)	8.38±4.03	8.21±4.37	0.91
Ankle plantarflexion 6 months (°)	21.03±6.60	21.79±6.64	0.57
Ankle plantarflexion 1 year (°)	26.47±6.46	26.67±6.62	0.90
VAS score at 6 months	2.82±0.76	2.38±0.85	0.23
VAS score at 1 year	1.62±0.54	1.56±0.50	0.65

Values are presented as mean±standard deviation.

AOFAS: American Orthopaedic Foot and Ankle Society, VAS: visual analogue scale.

4.03° respectively. The mean dorsiflexion attained in group B was 5.64° ± 5.02° and 8.21° ± 4.37° respectively, during the 6-month and 1-year follow-ups. At 6 months, there was a substantial difference in dorsiflexion between the two groups (p-value 0.001), but there was no difference at the 1-year follow-up (p-value 0.91). At 6 months and 1 year, the average plantar flexion achieved by both groups did not significantly differ (p-value 0.57 and 0.90 respectively). At six months, group A's plantar flexion was 21.03° ± 6.60°, whereas group B's was 21.79° ± 6.64°. Plantar flexion was 26.47° ± 6.46° in group A at 12 months, compared to 26.67° ± 6.62° in group B (Table 3).

In groups, A and B, 11 and 13 patients, respectively, had comorbid conditions such as diabetes, obesity, and dependence on substances. Both groups experienced complications at a rate of 20.51% and 20.59%, respectively. Complications were noticed only in patients with co morbid illnesses

Table 4. Outcome Measure 6 Months vs. 1 Year

Serial no.	Group	Score	p-value
1	A	Enneking	0.008
2	A	AOFAS	0.001
3	B	Enneking	<0.001
4	B	AOFAS	<0.001

AOFAS: American Orthopaedic Foot and Ankle Society.

Table 5. Comorbidities

Serial no.	Comorbidities	Group A	Group B
1	Morbid obesity	5	4
2	Alcoholic	9	11
3	Diabetes	5	6
4	Hypertension	4	3
5	Smoking	7	9
6	Substance abuse	1	2

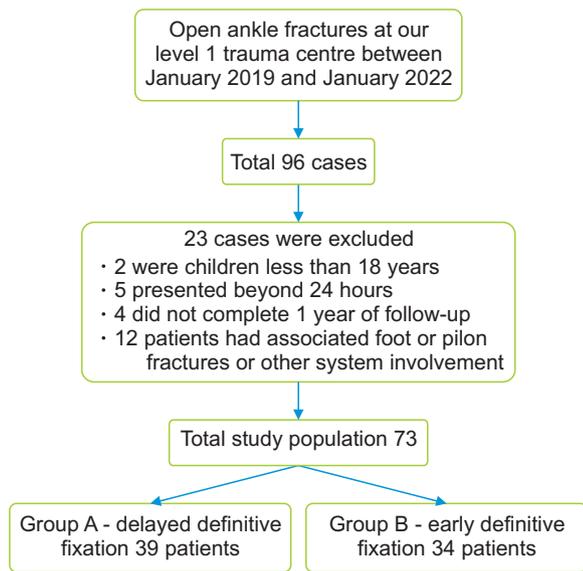
(Table 5). At 2 week follow up, one patient in group A and 3 patients in group B had wound dehiscence which was managed conservatively with regular dressing. Superficial infection was noticed in 2 patients from group A and group B respectively at 6 weeks, which was managed conservatively with antibiotics and wound dressing. At the 6 week follow-up, 3 patients in group A had deep infections which required surgical debridement. At 3 month follow-up 1 patient in group A had a superficial infection that was managed with wound care and oral antibiotics, whereas, one patient in group B developed a deep infection necessitating surgical management. One patient from each group had nonunion at the final follow-up and we noticed that both had continued smoking after definitive surgery. None of the study participants had implant failure, peri-implant fracture or osteomyelitis at the final visit (Table 6).

DISCUSSION

In this study, we found that there was a significant difference in clinical and functional outcomes between the two groups at 6 months. However, there was no discernable difference in clinical outcomes that were measured using range of movement and post-operative pain at 1 year. The functional outcomes assessed using the Enneking score and AOFAS score were significantly improved at the final follow up. Therefore, the employment of a targeted treatment strat-

Table 6. Complications

Serial no.	Complications	Group A	Comorbidity	Group B	Comorbidity
1	Wound dehiscence	1	Diabetes	3	Diabetes 2, morbid obesity & hypertension 1
2	Superficial infection	3	Diabetes 1, morbid obesity & hypertension 2	2	Diabetes 1, morbid obesity 1
3	Deep infection	3	Substance abuse & alcoholic 1, diabetes 2	1	Substance abuse & alcoholic 1
4	Nonunion	1	Smoking 1	1	Smoking 1
	Total	8		7	

**Figure 1.** Algorithm of patient selection for the study.

egy with early definitive fixation for low grade (grade 1 and 2) fractures and delayed definitive fixation for higher grade (3A and 3B) fractures produced good functional outcomes while minimizing the risk of complications.

As mentioned earlier, there are studies which advocate the use of early definitive fixation for all open fractures irrespective of the severity of injury and they have reported a good outcome. However, there is substantial evidence to suggest that staged delayed fixation of open ankle fractures is effective as early fixation with lesser long term ankle swelling compared to early fixation group.^{7,8)} We were interested in discussing a targeted strategy to patients with respect to the grade of open ankle fracture as there are no clear guidelines about whether early or delayed treatment is advantageous.

Open ankle fractures have a 9.4 times greater chance of developing a superficial infection, which is typically treated with meticulous debridement and antibiotics based on wound culture for three weeks.⁹⁾ However, 5% of patients

experience a profound infection that necessitates multiple debridement and flap reconstruction.^{2,4)} In the current study, we found 7.69% superficial infections in group A and 8.82% superficial infections in group B respectively that was managed conservatively with 3 weeks of antibiotic treatment based on wound culture to eradicate it. Furthermore, 7.7% of the patients in group A experienced deep infections that required debridement and flap coverage, while 2.9% patients in group B had profound infections that required only surgical debridement and not flap coverage.

Comorbidities such as obesity with a body mass index >30 , diabetes, alcohol use, and illicit drug use have all been linked to an increased risk of postoperative complications such as infection.^{2,10)} In contrast to patients without comorbidities, these conditions were not observed to increase the incidence of infections, non-union, implant failure, or post-traumatic arthritis in open ankle fractures.¹¹⁾ In this study, we found no difference between early versus delayed fixation for open ankle fractures in terms of comorbidities and complications.

Early weight bearing and ankle mobilization were discovered to be beneficial for improving ankle range of motion, functional outcomes, returning to daily activities, and reducing osteoporosis.¹²⁾ The functional outcome for patients with early vs. late weight-bearing in open ankle fractures was not significantly different during long-term follow-up.¹²⁻¹⁴⁾ As part of a standard procedure, all patients commenced range-of-motion exercises on the second day following definitive fixation and early weight bearing after suture removal at 2 weeks. Our study shows that early weight bearing and physiotherapy following definitive fixation were associated with a good functional outcome at the final follow up with no additional risk of loss of fixation or requirement for intervention.

Open ankle fractures from high-energy accidents were treated based on the grade of the fracture; for example, grade 3B fractures that required flap reconstruction were

treated in two stages, typically by a team comprising orthopaedic surgeons and plastic surgeons at the time of definitive fixation, which improves outcomes.^{15,16} At the time of the final follow-up, the delayed fixation group, which was used in our study for all 3A and 3B injuries, had outcomes that were just as favourable as those of the early fixation group. Our results indicate that delayed definitive fixation in higher grade injuries was more advantageous in terms of improving outcome and reducing complications, as both groups had comparable functional and clinical outcome at 12 months.

Open ankle fractures represent a significant challenge in orthopaedic surgery and require prompt and meticulous management. The complexity of these injuries requires a multidisciplinary approach involving orthopaedic surgeons, plastic surgeons, infectious disease specialists, and physical therapists. Moreover, individualized treatment plans tailored to the patient's specific needs, considering their overall health status, wound condition, and associated comorbidities, are paramount. We recommend early definitive fixation for lower grade injuries (Gustilo Anderson I and II), and, using a phased surgical approach with delayed definitive fixation for higher grade injuries (Gustilo Anderson 3A and 3B). This should be followed by early physiotherapy and weight bearing to improve clinical and functional outcomes following open ankle fractures.

The limitation of our study is that it is a retrospective study with short follow up time. Sample size is small to draw any definitive conclusions. Large multicentric randomized controlled trial can be done to further validate the study.

CONCLUSION

Low grade open ankle fracture patients who received early definitive fixation had better dorsiflexion and functional ratings at 6 months compared to high grade open fracture patients who received delayed definitive fixation. However, both groups had comparable clinical and functional outcomes at 12 months. Hence, we recommend the above approach for management of open ankle fractures. A randomised control study would help to further validate our findings in future research.

ORCID

Raghavendra Kaganur, <https://orcid.org/0009-0003-7506-2855>

Bhaskar Sarkar, <https://orcid.org/0000-0002-1317-534X>

Pragadeeshwaran Jaisankar, <https://orcid.org/0000-0002-8177-650X>

Md Quamar Azam, <https://orcid.org/0000-0003-4313-153X>

Anurag Bhakhar, <https://orcid.org/0000-0002-3291-198X>

REFERENCES

1. Court-Brown CM, Bugler KE, Clement ND, Duckworth AD, McQueen MM. *The epidemiology of open fractures in adults. A 15-year review. Injury.* 2012;43:891-7. doi: 10.1016/j.injury.2011.12.007.
2. Ovaska MT, Madanat R, Honkamaa M, Mäkinen TJ. *Contemporary demographics and complications of patients treated for open ankle fractures. Injury.* 2015;46:1650-5. doi: 10.1016/j.injury.2015.04.015.
3. Toole WP, Elliott M, Hankins D, Rosenbaum C, Harris A, Perkins C. *Are low-energy open ankle fractures in the elderly the new geriatric hip fracture? J Foot Ankle Surg.* 2015;54:203-6. doi: 10.1053/j.jfas.2014.10.015.
4. Simske NM, Audet MA, Kim CY, Vallier HA. *Open ankle fractures are associated with complications and reoperations. OTA Int.* 2019;2:e042. doi: 10.1097/OI9.000000000000042.
5. Lee JY, Cho YJ, Kang SW, Cho YM, Choi HB. *Outcomes of immediate operative treatment of ankle trimalleolar open fractures. J Korean Foot Ankle Soc.* 2020;24:25-30. doi: 10.14193/jkfas.2020.24.1.25.
6. Hong-Chuan W, Shi-Lian K, Heng-Sheng S, Gui-Gen P, Ya-Fei Z. *Immediate internal fixation of open ankle fractures. Foot Ankle Int.* 2010;31:959-64. doi: 10.3113/FAL.2010.0959.
7. Bray TJ, Endicott M, Capra SE. *Treatment of open ankle fractures. Immediate internal fixation versus closed immobilization and delayed fixation. Clin Orthop Relat Res.* 1989;(240):47-52.
8. Peterson DL, Schuurman M, Geamanu A, Padela MT, Kennedy CJ, Wilkinson J, et al. *Early definitive care is as effective as staged treatment protocols for open ankle fractures caused by rotational mechanisms: a retrospective case-control study. J Orthop Trauma.* 2020;34:376-81. doi: 10.1097/BOT.0000000000001734.
9. Näsell H, Ottosson C, Törnqvist H, Lindé J, Ponzer S. *The impact of smoking on complications after operatively treated ankle fractures--a follow-up study of 906 patients. J Orthop Trauma.* 2011;25:748-55. doi: 10.1097/BOT.0b013e318213217.
10. Shao J, Zhang H, Yin B, Li J, Zhu Y, Zhang Y. *Risk factors for surgical site infection following operative treatment of ankle fractures: a systematic review and meta-analysis. Int J Surg.* 2018;56:124-32. doi: 10.1016/j.ijsu.2018.06.018.
11. Martin CW, Ryan JC, Bullock TS, Cabot JH, Makhani AA, Griffin LP, et al. *Surgical site complications in open pronation-abduction ankle fracture-dislocations with medial tension failure wounds. J Orthop*

- Trauma*. 2021;35:e481-5. doi: 10.1097/BOT.0000000000002128.
12. **Smeeing DP, Houwert RM, Briet JP, Kelder JC, Segers MJ, Verleisdonk EJ, et al.** Weight-bearing and mobilization in the postoperative care of ankle fractures: a systematic review and meta-analysis of randomized controlled trials and cohort studies. *PLoS One*. 2015;10:e0118320. doi: 10.1371/journal.pone.0118320.
 13. **Keene DJ, Williamson E, Bruce J, Willett K, Lamb SE.** Early ankle movement versus immobilization in the postoperative management of ankle fracture in adults: a systematic review and meta-analysis. *J Orthop Sports Phys Ther*. 2014;44:690-701, C1-7. doi: 10.2519/jospt.2014.5294.
 14. **Sernandez H, Riehl J, Fogel J.** Do early weight-bearing and range of motion affect outcomes in operatively treated ankle fractures: a systematic review and meta-analysis. *J Orthop Trauma*. 2021;35:408-13. doi: 10.1097/BOT.0000000000002046.
 15. **Chummun S, Wright TC, Chapman TW, Khan U.** Outcome of the management of open ankle fractures in an ortho-plastic specialist centre. *Injury*. 2015;46:1112-5. doi: 10.1016/j.injury.2014.12.017.
 16. **Al-Hourani K, Fowler T, Whitehouse MR, Khan U, Kelly M.** Two-stage combined ortho-plastic management of type IIIB open diaphyseal tibial fractures requiring flap coverage: is the timing of debridement and coverage associated with outcomes? *J Orthop Trauma*. 2019;33:591-7. doi: 10.1097/BOT.0000000000001562.