Efficacy of Staged Surgery in the Treatment of Open Tibial Fractures with Severe Soft Tissue Injury and Bone Defect

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Purpose: We aimed to report the clinical and radiological outcomes of staged surgery using the acute induced membrane technique with an antibiotic-impregnated cement spacer (ACS) and soft-tissue reconstructive surgery and to identify factors affecting clinical outcomes.

Materials and Methods: Thirty-two patients with severe open tibia fractures were treated via staged surgery from January 2014 to December 2019 and followed up for ≥1 year. In the first surgery, an ACS was inserted into the bone defect site along with debridement and irrigation and was temporarily fixed in place with an external fixator. The internal fixator was placed, and flap surgery and cement spacer changes were performed during the next surgery. In the third surgery, an autogenous bone graft was performed. Radiologic and functional results were investigated according to the Association for the Study and Application of the Method of Ilizarov (ASAMI) criteria, and factors affecting the ASAMI score were analyzed.

Results: The average bone defect width was 43.9 mm, and the size of soft-tissue defect was 79.3 cm². Bone union was achieved in all cases except one and required 9.4 months on average. Complications occurred in 10 cases (31.2%). Good or better clinical effects, in terms of ASAMI radiologic and functional scores, were observed in 29 and 24 cases, respectively. Complications and additional surgery were common factors affecting the two scores.

Conclusion: Staged surgery using the acute induced membrane technique and soft-tissue reconstructive surgery is an efficacious treatment for open tibial fractures with bone defects.

Key Words: Tibia fracture, open fracture, soft tissue injury, reconstructive surgical procedures

INTRODUCTION

Open fractures are characterized by high-energy injuries, wherein the fracture site is connected to the external environment through an open wound and exposed to the skin’s surface. Accordingly, such fractures are generally transverse, comminuted, and segmental, rather than spiral or simple fractures, and additional surgery is often required to address accompanying soft tissue damage, making them highly susceptible to infection. Particularly, if the injury is accompanied by a bone defect as a result of the wound from the time of the accident or if a significant amount of bone loss occurs while removing devitalized bone during debridement, not only infection control but also repair of the defective bone and bone union are required, making treatment highly complex. Multiple treatment options have been explored for open fractures accompanied by bone and soft tissue defects. In general, as an initial treatment for open fractures of the lower extremities of Gustilo-Anderson classification type III or higher,
an external fixator is inserted to fix the bone in place, and soft tissue defects are treated by negative-pressure wound therapy (NPWT). However, problems of infection around the pin, delayed union, malunion, and nonunion have been reported in association with maintaining the initially inserted external fixator; thus, it was replaced with an internal fixator, such as an intramedullary nail or a plate, which may pose a risk of osteomyelitis or deep infection. In addition, the damaged bone space eventually becomes a dead space, or if the bone is fixed with an external fixator, the contactable region of the main fracture site is absent or reduced, decreasing bone stability. To the best of our knowledge, no studies have ever focused on the treatment of open tibial fractures with soft tissue and bone defects.

Tibial fractures are the most common long bone fracture, and clinical manifestations vary from low-energy, low-displacement injuries to high-energy injuries with severe soft tissue and bone defects. Tibial fractures are often associated with open fractures, as the tibia has no muscle in the anteromedial region, and the bone is located directly in the subcutaneous layer. They are often accompanied by severe soft tissue injury, bone defects, compartment syndrome, and nervous or vascular tissue damage and are susceptible to infection, nonunion, and wound complications. Despite advances in soft tissue treatment methods and the variety of internal fixators, it is still very difficult to obtain satisfactory results in open tibial fracture treatment.

Therefore, this study aimed to report clinical and radiological outcomes obtained by performing a three-staged surgery for Gustilo-Anderson classification type III or more severe open tibial fractures with bone and soft tissue defects using the acute induced membrane technique to fill the bone defect and the soft tissue reconstruction surgery to restore the soft-tissue defect. In addition, we sought to identify factors affecting the clinical outcomes of open tibial fractures.

MATERIALS AND METHODS

Patients
From January 2014 to December 2019, 238 patients aged 18 years or older with tibial fractures visited our level 1 trauma center. Among them, we included in this study patients with type IIIB or more severe open fractures according to the Gustilo-Anderson classification who were surgically treated using the acute induced membrane technique and soft-tissue reconstruction because of bone and soft-tissue defects after debridement and who were followed up for ≥1 years. A retrospective analysis was conducted using patient medical records and radiographs. We excluded patients who underwent amputation as an initial treatment for severe comminuted fracture and damage (8 patients), clear brain injury (8 points or lower on the Glasgow Coma Scale on day 21 after injury or upon discharge, 15 patients), pathological fracture (2 patients), and periprosthetic fractures (3 patients). A total of 32 patients were included in this study (28 males and 4 females; median age 44.2 years, range 28–85 years). The mechanism of injury included traffic accidents in 24 patients (75%) and direct injury by heavy objects in 8 patients (25%) (Table 1). The study design and data collection were approved by the Institutional Review Board (IRB) of the Human Experimental and Ethics Committee of our hospital (IRB No: AJIRB-MED-MDB-21-032). The patients and/or their families were informed that data from their cases would be submitted for publication and provided informed consent.

Surgical technique
In as many cases as possible, the first surgery was performed within 12 h after injury. Debridement was performed sequentially from the skin to the subcutaneous and deep tissues thoroughly and systemically, removing all contaminated skin. Since subcutaneous fat tissue and fascia have poor blood supply, any contaminated parts were thoroughly removed. Because fracture fragments are susceptible to infection, owing to relatively low blood supply (particularly those of the cortical bone in the shaft), the free cortical bone fragments not attached to soft tissue, such as the periosteum, were all removed regardless of their size. Next, tissue culture was performed around the fracture site, and an antibiotic-impregnated cement spacer (ACS, DePuy CMW 3 gentamicin bone cement, DePuy Synthes, Raynham, MA, USA) was used to reproduce the original bone shape as much as possible and inserted into the site of the bone defect (Fig. 1). Subsequently, an external fixator was installed to avoid the zone of injury. For soft-tissue defects, NPWT was performed using vacuum-assisted closure. As for injuries with severe contamination, with a delay in surgery beyond 12 h after injury or with unsatisfactory debridement, a second-look surgery was performed by debridement after evaluating viability after 48–72 h. After ensuring the stability of the fracture through initial fixation, repetitive debridement and irrigation were performed every 2–3 days for the treatment of open wounds, and NPWT was maintained. Post debridement culture was performed at all stages, and according to the culture results, the type and duration of administered antibiotics were determined in consultation with an infectious medicine specialist. In most cases, efforts were made for 3 days or longer to avoid first-generation cephalosporin.

After the soft-tissue condition improved and the patient generally recovered through repetitive wound cleaning and NPWT, a second surgery was performed to place an internal fixator for the fracture site and reconstruct the soft tissue. The second surgery (fix and flap) was generally performed within 2 weeks after the first surgery. During the surgery, the cement inserted into the bone defect site was first removed, followed by meticulous debridement, and an internal fixator and ACS were placed. Intramedullary nailing that could cover the entire length of the tibia with biomechanical superiority was first considered. When intramedullary nailing was difficult because of a frac-
| Patient # | Age | Sex   | Past history | Injury mechanism | Injury site | Combined injury | Injury severity score | Gustilo-Anderson classification | AO-OTA classification | Bone defect type | Bone defect size (mm) | Soft tissue defect size (cm²) |
|-----------|-----|-------|--------------|------------------|-------------|----------------|----------------------|-------------------------|----------------------|----------------|---------------------|-----------------------------|
| 1         | 28  | Female | None         | Pedestrian TA    | Rt          | Liver contusion | 13                   | II A                   | 42-C3                | Segmental        | 100                 | 220                         |
| 2         | 47  | Male   | None         | Motorcycle TA   | Rt          | L3 compression fracture | 13                   | II B                   | 42-B3                | Partial           | 25                  | 34                          |
| 3         | 30  | Male   | None         | Motorcycle TA   | Rt          | SDH            | 25                   | II B                   | 42-C3                | Segmental        | 35                  | 110                         |
| 4         | 39  | Male   | None         | Direct injury   | Lt          | None           | 9                    | II A                   | 42-C3                | Segmental        | 60                  | 56                          |
| 5         | 51  | Male   | None         | Direct injury   | Rt          | None           | 9                    | II A                   | 42-B3                | Partial           | 10                  | 88                          |
| 6         | 74  | Male   | HTN, DM      | Direct injury   | Rt          | None           | 9                    | II A                   | 42-C3                | Partial           | 38                  | 48                          |
| 7         | 34  | Male   | None         | Motorcycle TA   | Lt          | EDH, Pneumocephalus, Femur neck fracture | 38                   | II B                   | 42-C3                | Segmental        | 20                  | 36                          |
| 8         | 44  | Female | None         | In car TA       | Lt          | None           | 19                   | II B                   | 42-C3                | Segmental        | 45                  | 58                          |
| 9         | 49  | Male   | None         | Pedestrian TA   | Rt          | None           | 9                    | II B                   | 42-B3                | Partial           | 75                  | 120                         |
| 10        | 35  | Male   | Panic disorder, MDD | Motorcycle TA  | Lt          | MRF, hemopneumothorax | 13                   | II B                   | 42-C3                | Segmental        | 44                  | 65                          |
| 11        | 51  | Female | None         | HTN, DM         | Pedestrian TA | Rt          | None           | 9                    | II B                   | 42-C3                | Segmental        | 52                  | 58                          |
| 12        | 85  | Male   | None         | Motorcycle TA   | Rt          | SDH, MRF, Pneumothorax | 29                   | II B                   | 42-C3                | Segmental        | 35                  | 93                          |
| 13        | 45  | Male   | None         | Motorcycle TA   | Lt          | Aortic dissection | 25                   | II B                   | 42-C3                | Segmental        | 40                  | 46                          |
| 14        | 20  | Male   | None         | Direct injury   | Rt          | None           | 9                    | II B                   | 42-C3                | Segmental        | 85                  | 72                          |
| 15        | 55  | Male   | None         | Pedestrian TA   | Rt          | Spleen injury, EDH | 25                   | II B                   | 42-B3                | Partial           | 35                  | 136                         |
| 16        | 53  | Male   | Systemic psoriasis, mental retardation | Bicycle TA      | Rt          | Lt. pelvic bone fracture | Femur neck open fracture, Lung contusion both, T2, 3, 4, 5, 7, 9 spinous fracture | 18 | II B | 42-B3 | Partial | 15 | 42 |
| 17        | 33  | Male   | None         | In car TA       | Rt          | Nasal bone fracture | 11                   | II B                   | 42-B3                | Partial           | 41                  | 69                          |
| 18        | 29  | Male   | None         | Motorcycle TA   | Lt          | Lt. clavicle fracture, Lt. Kidney injury, spleen injury | 18 | II B | 42-B3 | Partial | 17 | 63 |
| 19        | 63  | Male   | DM           | In car TA       | Lt          | MRF, hemorax | 18 | II B | 42-C3 | Partial | 38 | 54 |
| 20        | 46  | Male   | None         | Direct injury   | Lt          | Rt. Tibia shaft fracture | 9 | II B | 41-C3 | Partial | 77 | 146 |
| 21        | 69  | Male   | None         | Pedestrian TA   | Rt          | Lt. distal tibia and fibula open fracture, MRF, hematoma, SDH | 18 | II B | 42-C3 | Partial | 9 | 38 |
| 22        | 39  | Male   | None         | In car TA       | Rt          | SDH, pneumothorax, kidney injury | 17 | II B | 42-C3 | Partial | 32 | 68 |
| 23        | 42  | Male   | None         | Pedestrian TA   | Rt          | Pelvic bone fracture, lung contusion, EDH | 18 | II B | 42-C3 | Segmental | 48 | 72 |
| 24        | 58  | Male   | None         | Motorcycle TA   | Rt          | Spleen injury, kidney injury hemopneumothorax, rib fracture | 22 | II B | 42-B3 | Partial | 41 | 98 |
| 25        | 48  | Male   | HTN          | Direct injury   | Lt          | None           | 9                    | II B                   | 42-C3                | Segmental        | 72                  | 148                         |
| 26        | 28  | Female | None         | Pedestrian TA   | Rt          | None           | 9                    | II B                   | 42-B3                | Partial           | 30                  | 46                          |
| 27        | 36  | Male   | None         | Motorcycle TA   | Lt          | SDH, hemopneumothorax | 22 | II B | 42-C3 | Segmental | 51 | 76 |
| 28        | 27  | Male   | None         | Pedestrian TA   | Rt          | None           | 9                    | II B                   | 42-C3                | Partial           | 34                  | 58                          |
| 29        | 42  | Male   | None         | Direct injury   | Rt          | None           | 9                    | II B                   | 42-C3                | Partial           | 56                  | 72                          |
| 30        | 26  | Male   | None         | Motorcycle TA   | Rt          | Spleen injury   | 11                   | II B                   | 42-B3                | Segmental        | 32                  | 56                          |
| 31        | 46  | Male   | None         | Motorcycle TA   | Lt          | Rt. tibia shaft fracture | 9 | II B | 42-B3 | Segmental | 73 | 130 |
| 32        | 33  | Male   | None         | Direct injury   | Rt          | None           | 9                    | II B                   | 42-B3                | Segmental        | 42                  | 60                          |

AO-OTA, Arbeitsgemeinschaft für Osteosynthesefragen/Orthopedic Trauma Association; TA, traffic accident; HTN, hypertension; DM, diabetes mellitus; MDD, major depressive disorder; Rt, right; Lt, left; SDH, subdural hemorrhage; EDH, epidural hemorrhage; MRF, multiple rib fracture.
ture concentrated in the proximal or distal part, plating was performed (Fig. 2). Reconstruction was performed by a microsurgery specialist, and either a free or rotation flap was selected according to the condition of the soft tissue around the fracture, age of the patient, and general condition. When the condition of the reconstructed soft tissue improved, the patients were asked to begin joint range, quadriceps femoris muscle strengthening, and straight leg raise exercises. Initiation of weight-bearing exercise was dependent on the type of fixator used. When nailing was performed for fixation, immediate full weight-bearing exercise was allowed if the patient could tolerate this. In the case of fixation with plating, partial weight-bearing exercise was allowed when pain disappeared, while full weight-bearing exercise was allowed 6 weeks after surgery. The patients were allowed to return to daily life after discharge from the hospital for outpatient follow-up if they had no fever, if the flap site was viable without redness, swelling, or flush at the surgical site, and if there was no evidence of infection, such as a sudden rise in C-reactive protein levels or white blood cell count.

After approximately 3 months, when the condition of the flap site was adequate and networking of collateral vessels around the flap was observed, a third surgery was performed to remove the cement from the bone defect site and an autogenic bone graft with bone obtained from the anterior or posterior iliac crest was applied. If the autogenic bone was insufficient, it was mixed with a demineralized bone matrix (DBM) for insertion. Augmented plating was performed, depending on the site, to enhance fixation in the bone defect area.

**Evaluation and follow-up**

In this study, to evaluate the fracture site severity of patients who underwent final operation according to the protocol, we examined the injury mechanism, past history, injury site, associated injuries, injury severity score upon hospital visit, Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association classification to determine fracture location and degree of fracture, and Gustilo-Anderson classification for the evaluation of open fractures. Bone defects were classified as partial when there was contact between the main fracture sites and as segmental when there was no contact with...
the main fracture sites. Bone defect size was identified by calculating the radiographic apparent bone gap, as suggested by Haines, et al. The area of the soft-tissue defect was defined as the product of the distance between two vertices in the diagonal direction (cm$^2$) after completion of the first surgery by selecting four vertices with the longest side of the defect as the vertex.

A follow-up evaluation was conducted to investigate reoperation and bone union status during a follow-up period >1 year. Radiologic and functional results were evaluated based on the Association for the Study and Application of the Method of Ilizarov (ASAMI) criteria. Radiologic evaluation was conducted to evaluate bone union, timing, and alignment. Bone union was defined as a case in which more than 3/4 of the cortical bone was formed at the fracture site on both anteroposterior and lateral images on simple radiography at follow-up, every 4 weeks after surgery, with no clinical abnormalities, such as pain and claudication, during walking (weight-bearing). Malalignment was defined as a case in which deformation, including varus and valgus deformation, was as severe as 10° or more on radiographic examination; the measurement was performed adopting Milner’s method. Shortening was defined as a decrease of ≥10 mm in length relative to the healthy side. Nonunion was defined as a case in which complete bone union was not observed at the fracture site on simple radiographs, performed more than 6 months after surgery, or as a case in which bone union did not progress at the 3-month follow-up. Clinically, there was pain or claudication at the fracture site. Joint stiffness was defined as a decrease in the range of motion of the knee or ankle joint on the injured side by >20% compared with the range of motion of a healthy joint.

Statistical analysis
Statistical analysis was performed using SPSS (SPSS for Windows release 16.0, SPSS, Chicago, IL, USA) to analyze the effect of various factors on ASAMI score. The Kruskal-Wallis test
was performed for continuous data, whereas the chi-square and Fisher’s exact tests were performed for categorical data. Statistical significance was set at $p$-values$<$0.05.

RESULTS

With regard to internal fixation in the second surgery, the type of fixation included intramedullary nailing in 24 patients and plating in 8. The average size of the bone defect was 43.9 mm (9–100 mm), and the area of the soft-tissue defect was 79.3 cm² (34–220 cm²). The average time interval from the first to the second surgery (fix and flap surgery) was 10.4 days (5–17 days), and that to the third surgery (bone graft) was 101.6 days (61–158 days). Soft-tissue coverage included a rotational flap in 11 patients and a free flap in 21. Bone union (96.9%) was achieved in all patients except one. The average time to bone union was 9.4 months (4–16 months), and the average follow-up period was 19.1 months (12–41 months) (Table 2).

Microorganisms were cultured in 12 cases (37.5%), where Staphylococcus aureus and Acinetobacter baumannii accounted for the highest proportion (Table 3). Complications occurred in 10 patients (31.2%), including three with superficial infection, three with deep infection, two with partial flap skin necrosis, one with malalignment, and one with joint stiffness. Of these, superficial infection was treated by debridement and antibiotic administration without removal of the internal fixator. In one of the three patients (case 13), deep infection occurred after bone union, which was recovered via internal fixator removal, debridement, and antibiotic administration. Another patient with deep infection (case 16) was treated by replacing the internal fixator with an external fixator and performing debridement and osteotomy for bone transport. Lastly, in another patient with deep infection (case 12), the infection recurred, even after internal fixator removal and debridement, and the patient’s general condition was poor; thus, below-knee amputation was performed (Fig. 3). Two cases of partial flap skin necrosis were treated using a split-thickness skin graft. In the case of malalignment, conservative treatment was performed with the patient’s consent as the symptoms were mild. Arthrolysis was performed for joint stiffness.

Good or better clinical effects were observed in 29 patients (90.6%) in terms of ASAMI radiologic score and 24 patients (75%) in terms of functional score. Radiologic analysis revealed that factors affecting ASAMI score were size of the soft-tissue defect, type of soft-tissue coverage, complications, and additional surgery. Functional results showed significant correlations with injury severity score, types of internal fixation and complications, and additional surgery (Table 4).

DISCUSSION

This study demonstrates that staged surgery using the acute induced membrane technique and soft-tissue reconstruction may be performed for very unstable high-energy open tibial fractures with bone and soft-tissue defects to achieve a high bone union rate and functional recovery. In this study, patients who experienced complications and underwent additional surgeries showed poor radiologic and functional outcomes. In particular, infection was the most common complication.21

Lack, et al.24 reported that deep infection occurred in 24 (17.5%) of 137 patients with type III open tibial fractures. Mohseni, et al.25 reported that infection occurred in 16% and 32% of patients treated with intramedullary nailing and an external fixator, respectively. In the present study, the complication rate was 31.2% (10 patients), and the range of complications was strictly defined in this study. There were only three patients (9.4%) with deep infections, for which amputation or salvage was considered.

In this study, functional outcomes were significantly influenced by the type of internal fixator used. This was interpreted by timing discrepancies in return to daily life between the two internal fixators. Nailing allows for a rapid return to daily life because it is commonly used for tibial shaft fractures, placed inside the bone, requires less amount of bone graft (as much as the width of the nail), and allows for full weight-bearing immediately after the second surgery.11 On the other hand, plate fixation was found to yield lower scores, owing to the relatively late timing of standing and weight-bearing because of the relatively larger amount of bone graft and inevitable direct exposure to the external environment due to extramedullary fixation.26 The authors attempted to perform fixation with nailing in as many cases as possible, and plate fixation was performed only for cases in which fixation with nailing was challenging because the fracture site was located in the proximal or distal tibia.

In addition, patients with higher injury severity scores had severe trauma extending to the lower extremity, resulting in poor prognosis owing to a prolonged stay in bed and slow rehabilitation therapy progression, because of which their functional scores seemed to become statistically significantly low. Interestingly, the influencing factors of the ASAMI radiologic results included soft tissue injuries, such as the defect size and coverage type of soft tissue; this is because a more severe injury to soft tissue is associated with a lower blood supply and poorer conditions around the bone. This leads to a vulnerability to non-union and infection.

The induced membrane technique, also known as the Masquelet technique, was initiated by performing a wide resection of the infected bone and filling the defect site with ACS, followed by bone grafting for chronic osteomyelitis or post-traumatic septic nonunion.27 Based on satisfactory clinical outcomes, the histological and biochemical characteristics of the membrane formed around the cement were examined. The
| Patient # | Implant of definitive surgery | Time between 1st and 2nd surgery (days) | Time between 2nd and 3rd surgery (days) | Soft tissue coverage | Union time (months) | Follow-up (months) | ASAMI score (bony results) | ASAMI score (functional results) | Complication | Additional surgery |
|-----------|-----------------------------|----------------------------------------|----------------------------------------|---------------------|---------------------|-------------------|------------------------|-----------------------------|--------------|-------------------|
| 1         | IM nailing                  | 5                                      | 61                                     | Free flap           | 12                  | 13                | Excellent              | Good                        | None          | None              |
| 2         | IM nailing                  | 8                                      | 78                                     | Rotational flap     | 8                   | 25                | Excellent              | Good                        | None          | None              |
| 3         | Plating                     | 12                                     | 97                                     | Free flap           | 14                  | 12                | Good                   | Fair                        | Knee joint stiffness | Arthrolysis |
| 4         | IM nailing                  | 7                                      | 93                                     | Rotational flap     | 6                   | 17                | Excellent              | Excellent                    | None          | None              |
| 5         | IM nailing                  | 10                                     | 88                                     | Free flap           | 6                   | 22                | Good                   | Excellent                    | None          | None              |
| 6         | IM nailing                  | 14                                     | 110                                    | Rotational flap     | 13                  | 31                | Excellent              | Excellent                    | None          | None              |
| 7         | IM nailing                  | 14                                     | 121                                    | Rotational flap     | 6                   | 17                | Excellent              | Good                        | Graft site partial necrosis | I&D, STSG |
| 8         | Plating                     | 11                                     | 99                                     | Free flap           | 14                  | 22                | Excellent              | Good                        | None          | None              |
| 9         | IM nailing                  | 12                                     | 87                                     | Free flap           | 8                   | 25                | Good                   | Good                        | Superficial infection       | I&D         |
| 10        | IM nailing                  | 15                                     | 78                                     | Free flap           | 6                   | 16                | Excellent              | Fair                        | Graft site partial necrosis | I&D, STSG |
| 11        | IM nailing                  | 12                                     | 123                                    | Free flap           | 7                   | 19                | Good                   | Excellent                    | None          | None              |
| 12        | Plating                     | 10                                     | 93                                     | Rotational flap     | 12                  | 12                | Fair                   | Poor                        | Deep infection            | BK amputation |
| 13        | Plating                     | 9                                      | 111                                    | Free flap           | 9                   | 22                | Poor                   | Poor                        | Deep infection            | Salvage operation |
| 14        | Plating                     | 10                                     | 91                                     | Rotational flap     | 8                   | 17                | Excellent              | Excellent                    | None          | None              |
| 15        | IM nailing                  | 12                                     | 77                                     | Rotational flap     | 12                  | 19                | Excellent              | Good                        | None          | None              |
| 16        | IM nailing                  | 7                                      | 132                                    | Free flap           | Nonunion           | 27                | Poor                   | Poor                        | Deep infection            | Salvage operation |
| 17        | IM nailing                  | 17                                     | 158                                    | Free flap           | 9                   | 41                | Excellent              | Excellent                    | None          | None              |
| 18        | IM nailing                  | 10                                     | 125                                    | Free flap           | 9                   | 12                | Excellent              | Fair                        | 10 degrees valgus deformity | None        |
| 19        | Plating                     | 17                                     | 119                                    | Free flap           | 6                   | 17                | Good                   | Fair                        | None          | None              |
| 20        | IM nailing                  | 10                                     | 124                                    | Free flap           | 4                   | 21                | Good                   | Good                        | None          | None              |
| 21        | IM nailing                  | 9                                      | 125                                    | Free flap           | 16                  | 31                | Excellent              | Excellent                    | None          | None              |
| 22        | IM nailing                  | 5                                      | 113                                    | Free flap           | 10                  | 14                | Excellent              | Excellent                    | None          | None              |
| 23        | IM nailing                  | 9                                      | 126                                    | Free flap           | 13                  | 19                | Excellent              | Excellent                    | None          | None              |
| 24        | IM nailing                  | 6                                      | 89                                     | Free flap           | 12                  | 16                | Good                   | Excellent                    | None          | None              |
| 25        | IM nailing                  | 10                                     | 93                                     | Free flap           | 14                  | 18                | Good                   | Good                        | None          | None              |
| 26        | IM nailing                  | 13                                     | 97                                     | Rotational flap     | 10                  | 17                | Excellent              | Excellent                    | None          | None              |
| 27        | IM nailing                  | 8                                      | 106                                    | Free flap           | 11                  | 16                | Good                   | Good                        | Superficial infection       | I&D         |
| 28        | IM nailing                  | 9                                      | 98                                     | Rotational flap     | 9                   | 13                | Excellent              | Excellent                    | None          | None              |
| 29        | Plating                     | 16                                     | 111                                    | Free flap           | 8                   | 15                | Excellent              | Fair                        | Superficial infection       | I&D         |
| 30        | Plating                     | 9                                      | 83                                     | Rotational flap     | 6                   | 18                | Excellent              | Excellent                    | None          | None              |
| 31        | IM nailing                  | 14                                     | 91                                     | Free flap           | 9                   | 13                | Excellent              | Excellent                    | None          | None              |
| 32        | IM nailing                  | 12                                     | 68                                     | Rotational flap     | 7                   | 15                | Excellent              | Excellent                    | None          | None              |
results indicated that the membrane was a vascularized layer rich in growth factors, such as vascular endothelial growth factor (VEGF), transforming growth factor β (TGF-β), and bone morphogenetic protein-2 (BMP-2), which increased mechanical strength. The use of cement, which is significantly stronger than bone, may enhance mechanical stability, unlike making the site of the bone defect a dead space and leaving fibrotic tissue. In combination with an internal fixator, such as a plate or nail, patients can return to daily life even before autogenous bone graft. Rehabilitation treatment was initiated after the second surgery and was a significant advantage of staged surgery, as this was not possible with other surgical options.

Hatashita, et al. recently reported that good clinical outcomes were obtained by the “acute Masquelet technique,” where ACS was used for open lower limb fractures accompanied by bone loss. However, in their study, there were only three cases of tibial fractures, and deep infection occurred in one case. Due to the anatomical structure of the tibia, the anteromedial region is a subcutaneous layer, and soft-tissue damage is frequently caused by open fractures. Here, blood supply is relatively lower than that in the humerus and femur. Moreover, it is difficult to perform staged treatment when there is a higher risk of infection. In such conditions, the success rate could be improved by utilizing the three-stage treatment devised in this

### Table 3. Micro-Organisms in Severe Open Tibia Fractures

| Organism                         | Number of cases |
|----------------------------------|-----------------|
| Methicillin-susceptible *S. aureus* | 3               |
| Methicillin-resistant *S. aureus*  | 1               |
| Acinetobacter baumannii          | 3               |
| *Staphylococcus epidermidis*      | 1               |
| *Klebsiella pneumoniae*           | 1               |
| *Pseudomonas aeruginosa*          | 2               |
| *Enterococcus faecium*            | 1               |
| No growth                        | 20              |

Fig. 3. Failure case of staged surgery for tibia open fracture. (A) An 85-year-old male patient with hypertension and diabetes (case 12) was admitted to the trauma center because of a motorcycle accident. The patient had bone loss after distal tibia open fracture (GA type III-B) and debridement. (B) For this patient, an external fixator was inserted, and antibiotic-coated cement spacer insertion was performed for the bone defect. In addition, negative pressure wound therapy was conducted for soft tissue defects. (C) Since the general conditions and soft tissues were stable after 10 days, plating and cement changing were performed along with reverse sural rotational flap for the posteromedial aspect. (D) In the third surgery, an autogenous bone graft was performed for the bone defect area, followed by plate augmentation. (E) However, surgical wound redness, swelling, and fever manifested a month after the third surgery. With suspicion of infection, repetitive I&D was applied. (F) However, since the general condition deteriorated accompanied by continuous fever and pneumonia, below knee amputation was performed. G-A, Gustilo-Anderson classification; I&D, irrigation and debridement.
study, which comprises sufficient examination and careful operation of the bone and soft-tissue conditions.

In general, bone defect treatment is determined by considering the size of the defect. Several studies have reported that bone defects <5 cm can be treated with autogenous bone grafts, while bone defects >5 cm may be treated using the induced membrane technique (Masquelet technique), distraction osteogenesis, and vascularized fibular transfer. However, there are no experimental and biomechanical criteria regarding size, and this rule appears to have been formulated considering the donor-site morbidity in autogenous bone grafts. Distraction osteogenesis requires using an external fixator long-term, with a risk of infection and daily life inconveniences. Vascularized fibular transfer has a low survival rate, as it is technically difficult to perform microsurgery. As long as there is sufficient autogenous bone, the induced membrane technique

| Variable                  | Poor | Fair | Good | Excellent | Total | p value |
|---------------------------|------|------|------|-----------|-------|---------|
| Age (yr)                  | 49.0±5.7 | 85 | 48.0±10.1 | 40.5±13.3 | 44.5±14.3 | 0.057   |
| Sex                       |      |      |      |           |       | 0.906   |
| Female                    | 0 (0) | 0 (0) | 1 (25.0) | 3 (75.0) | 4     |         |
| Male                      | 2 (7.1) | 1 (3.6) | 8 (28.6) | 17 (60.7) | 28    |         |
| Past medical history      |      |      |      |           |       | 0.484   |
| None                      | 1 (4.0) | 1 (4.0) | 6 (24.0) | 17 (68.0) | 25    |         |
| Yes                       | 1 (14.3) | 0 (0.0) | 3 (42.9) | 3 (42.9) | 7     |         |
| Injury mechanism          |      |      |      |           |       | 0.747   |
| Pedestrian                | 0 (0) | 0 (0) | 2 (25.0) | 6 (75.0) | 8     |         |
| Motorbike                 | 2 (16.7) | 1 (8.3) | 3 (25.0) | 6 (50.0) | 12    |         |
| In car                    | 0 (0) | 0 (0) | 1 (25.0) | 3 (75.0) | 4     |         |
| Direct                    | 0 (0) | 0 (0) | 3 (37.5) | 5 (62.5) | 8     |         |
| Combined injury           |      |      |      |           |       | 0.564   |
| None                      | 0 (0) | 0 (0) | 4 (30.8) | 8 (66.7) | 12    |         |
| Yes                       | 2 (10.0) | 1 (5.0) | 5 (25.0) | 12 (60.0) | 20    |         |
| ISS                       | 21.5±5.0 | 29 | 14.7±6.9 | 14.3±7.2 | 15.3±7.4 | 0.171   |
| Fracture type             |      |      |      |           |       | 0.846   |
| Wedge                     | 1 (10.0) | 0 (0) | 3 (30.0) | 6 (60.0) | 10    |         |
| Complex                   | 1 (4.5) | 1 (4.5) | 6 (27.3) | 14 (63.6) | 22    |         |
| G-A type                  |      |      |      |           |       | 0.906   |
| IIIA                      | 0 (0) | 0 (0) | 1 (25.0) | 3 (75.0) | 4     |         |
| IIIB                      | 2 (7.1) | 1 (3.6) | 8 (28.6) | 17 (60.7) | 28    |         |
| Bone defect               |      |      |      |           |       | 0.774   |
| Partial                   | 1 (6.3) | 0 (0) | 5 (31.3) | 10 (62.5) | 16    |         |
| Segmental                 | 1 (6.3) | 1 (6.3) | 4 (25.0) | 10 (62.5) | 16    |         |
| Soft tissue defect size (cm²) | 44.0±2.8 | 93.0 | 99.8±34.5 | 72.9±43.3 | 79.3±41.2 | 0.036   |
| RABG (mm)                 | 27.5±17.7 | 35.0 | 50.1±22.1 | 43.3±22.6 | 44.0±21.9 | 0.457   |
| Implant                   |      |      |      |           |       | 0.265   |
| IM nail                   | 1 (4.2) | 0 (0) | 7 (29.2) | 16 (66.7) | 24    |         |
| Plate                     | 1 (12.5) | 1 (12.5) | 2 (25.0) | 4 (50.0) | 8     |         |
| Soft tissue coverage      |      |      |      |           |       | 0.020   |
| Rotational flap           | 0 (0) | 1 (8.1) | 0 (0) | 10 (90.9) | 11    |         |
| Free flap                 | 2 (9.5) | 0 (0) | 9 (42.9) | 10 (47.6) | 21    |         |
| Complication              |      |      |      |           |       | 0.050   |
| None                      | 0 (0) | 0 (0) | 6 (27.3) | 16 (72.7) | 22    |         |
| Yes                       | 2 (20.0) | 1 (10.0) | 3 (30.0) | 4 (40.0) | 10    |         |
| Additional surgery        |      |      |      |           |       | 0.023   |
| No                        | 0 (0) | 0 (0) | 6 (26.1) | 17 (73.9) | 23    |         |
| Yes                       | 2 (22.2) | 1 (11.1) | 3 (33.3) | 3 (33.3) | 9     |         |

ISS, injury severity score; G-A, Gustilo-Anderson classification; RABG, Radiographic Apparent Bone Gap.
Data are presented as mean±standard deviation or n (%).
is the safest and most reliable method for filling bone defects. Therefore, the authors performed an iliac bone graft for defect sites >5 cm. If the amount of autogenic bone was insufficient, it was mixed with a DBM for insertion. As Cho, et al. suggested, circumferential bone grafting was performed around an absorbable gelatin sponge core inserted into the intramedullary area to reduce the amount of autogenous bone required.

The timing of bone grafting is an important factor. In this study, an autogenous bone graft was performed at the last surgery. Some authors have reported a high success rate by performing internal fixation and bone grafting at the same time. However, performing autogenous bone graft in addition to fix and flap surgery lengthens the operation time excessively, resulting in a higher risk of infection. Moreover, the risk of aftereffects is higher when the surgery fails because of limited donor site and high morbidity. Therefore, in this study, bone grafting

| Table 4. Statistical Analysis of Factors Influencing Association for the Study and Application of Methods of Ilizarov (ASAMI) Scores (Continued) |
|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| Variable         | Poor             | Fair             | Good             | Excellent        | Total            | p value          |
| Age (yr)         | 53.3±23.2        | 42.3±14.8        | 42.5±9.0         | 43.9±14.4        | 44.5±14.3        | 0.834            |
| Sex              |                  |                  |                  |                  |                  | 0.515            |
| Female           | 0 (0)            | 0 (0)            | 2 (50.0)         | 2 (50.0)         | 4                |
| Male             | 4 (14.3)         | 4 (14.3)         | 6 (21.4)         | 14 (50.0)        | 28               |
| Past medical history |              |                  |                  |                  |                  | 0.433            |
| None             | 3 (12.0)         | 2 (8.0)          | 6 (24.0)         | 14 (56.0)        | 25               |
| Yes              | 1 (14.3)         | 2 (28.6)         | 2 (28.6)         | 2 (28.6)         | 7                |
| Injury mechanism |                  |                  |                  |                  |                  | 0.324            |
| Pedestrian       | 0 (0)            | 0 (0)            | 3 (37.5)         | 5 (62.5)         | 8                |
| Motorbike        | 4 (33.3)         | 2 (16.7)         | 2 (16.7)         | 4 (33.3)         | 12               |
| In car           | 0 (0)            | 1 (25.0)         | 1 (25.0)         | 2 (50.0)         | 4                |
| Direct           | 0 (0)            | 1 (12.5)         | 2 (25.0)         | 5 (62.5)         | 8                |
| Combined injury  |                  |                  |                  |                  |                  | 0.292            |
| None             | 0 (0)            | 1 (8.3)          | 3 (25.0)         | 8 (66.7)         | 12               |
| Yes              | 4 (20.0)         | 3 (15.0)         | 5 (25.0)         | 8 (40.0)         | 20               |
| ISS              | 24.3±4.6         | 14.5±4.4         | 18.0±10.2        | 11.9±4.3         | 15.3±7.4         | 0.018            |
| Fracture type    |                  |                  |                  |                  |                  | 0.832            |
| Wedge            | 1 (10.0)         | 2 (20.0)         | 2 (20.0)         | 5 (50.0)         | 10               |
| Complex          | 3 (13.6)         | 2 (9.1)          | 6 (27.3)         | 11 (50.0)        | 22               |
| G-A type         |                  |                  |                  |                  |                  | 0.634            |
| IIIA             | 0 (0)            | 0 (0)            | 1 (25.0)         | 3 (75.0)         | 4                |
| IIIB             | 4 (14.3)         | 4 (14.3)         | 7 (25.0)         | 13 (46.4)        | 28               |
| Bone defect type |                  |                  |                  |                  |                  | 0.432            |
| Partial          | 1 (6.3)          | 3 (18.8)         | 3 (18.8)         | 9 (56.3)         | 16               |
| Segmental        | 3 (18.8)         | 1 (6.3)          | 5 (31.3)         | 7 (43.8)         | 16               |
| Soft tissue defect size (cm²) | 72.8±44.0 | 63.5±7.4 | 111.7±59.2 | 65.7±23.9 | 79.3±41.2 | 0.147 |
| RABG (mm)        | 31.3±11.1        | 38.8±16.3        | 59.4±26.1        | 40.8±20.1        | 44.0±21.9        | 0.172            |
| Implant          |                  |                  |                  |                  |                  | 0.034            |
| IM nail          | 1 (4.2)          | 2 (8.3)          | 7 (28.2)         | 14 (58.3)        | 24               |
| Plate            | 3 (37.5)         | 2 (25.0)         | 1 (12.5)         | 2 (25.0)         | 8                |
| Soft tissue coverage |            |                  |                  |                  |                  | 0.231            |
| Rotational flap  | 1 (9.1)          | 0 (0.0)          | 2 (18.2)         | 8 (72.7)         | 11               |
| Free flap        | 3 (14.3)         | 4 (19.0)         | 6 (28.6)         | 8 (38.1)         | 21               |
| Complication     |                  |                  |                  |                  |                  | <0.001           |
| None             | 0 (0)            | 1 (4.5)          | 5 (22.7)         | 16 (72.7)        | 22               |
| Yes              | 4 (40.0)         | 3 (30.0)         | 3 (30.0)         | 0 (0.0)          | 10               |
| Additional surgery |              |                  |                  |                  |                  | <0.001           |
| No               | 0 (0)            | 2 (8.7)          | 5 (21.7)         | 16 (69.6)        | 23               |
| Yes              | 4 (44.4)         | 2 (22.2)         | 3 (33.3)         | 0 (0.0)          | 9                |

ISS: injury severity score; G-A, Gustilo-Anderson classification; RABG, Radiographic Apparent Bone Gap. Data are presented as mean±standard deviation or n (%).
was not performed during soft-tissue reconstruction; the bone graft was performed using autologous iliac bone after confirming that the soft tissue had healed and no infection was found, which took an average of 3 months. This treatment was based on observations by Salmi, et al. who reported that microvas- cularization took approximately 3 months after flap surgery. In clinical observations, the cluster around the wound was completely healed approximately 3 months after soft-tissue recon- struction. Therefore, in this study, an autogenous bone graft was performed after ensuring that there were no complications, such as infection and soft-tissue necrosis, through the course of staged surgery.

While the methods of covering soft-tissue defects include free flap and rotational flap in open fractures, it is difficult to create a rotational flap using the surrounding soft tissue because an open fracture causes serious damage to the surrounding soft tissue. Therefore, in this study, soft tissue restoration with a free flap was preferred. In terms of reconstruction timing, Godina reported that performing flap surgery within 72 h after injury was effective for the prevention of infection. Gopal, et al. reported that performing flap surgery within 72 h resulted in a bone infection rate reduction of approximately 3%. However, due to the high-energy and multiple injuries in most patients, there is a risk of prolonged surgery and anaesthesia with flap surgery at an early stage. There are also several limitations, as emergency flap surgery requires many experi- enced medical staff members and facilities. There is an ongoing controversy regarding the timing of flap surgery for soft-tissue restoration. A recent study by D’Alleyrand, et al. also reported that there was no significant difference in the risk associated with flap surgery within 7 days; however, after that, the risk of complications, such as infection, increased by 16% each day. There was no failure of flap surgery in this study, but there were two cases of split-thickness skin graft due to partial necrosis. Both cases occurred in patients for whom it took more than 14 days after the injury until flap surgery.

This study has some limitations. First, the number of participants was relatively small, as only patients with open tibial fractures accompanied by soft-tissue and bone defects were included, and there was no control group. Second, patient compliance was not considered. Third, the follow-up period was relatively short (approximately 1 year). Therefore, there are limitations in determining the incidence and recurrence of infection in patients. However, considering that the average outpatient follow-up period was 19.1 months and that severe complications from open fractures generally appear within 1 year, we believe there is sufficient evidence for the efficacy of this staged surgery. Finally, this retrospective study analyzed the efficacy of staged surgery based on clinical and radiological results. Therefore, there is a need for a prospective randomized study to corroborate our results.

In conclusion, despite many advances in the treatment of open tibial fractures with extensive soft-tissue and bone defect injuries in terms of soft-tissue reconstruction and lower limb salvage, treatment of open tibial fractures remains challenging. The vital goals to optimal treatment of such injuries include infection removal, bone stability restoration, and soft tissues reconstruction. Staged surgery using the acute induced membrane technique and soft-tissue reconstructive surgery proposed in this study appears to be a safe and feasible treatment for open tibial fractures with soft-tissue and bone defects.

AUTHOR CONTRIBUTIONS

Conceptualization: Yong-Cheol Yoon and Hyung Keun Song. Data curation: Youngwoo Kim and Young Hyun Yoon. Formal analysis: Hyung Keun Song. Funding acquisition: Young Hyun Yoon. Investi- gation: Hyung Keun Song. Methodology: Yong-Cheol Yoon. Project administration: Hyung Keun Song. Resources: Young Hyun Yoon. Software: Hyung Keun Song. Supervision: Hyung Keun Song. Validation: Youngwoo Kim. Visualization: Youngwoo Kim. Writing—original draft: Yong-Cheol Yoon. Writing—review & editing: Yong-Cheol Yoon and Hyung Keun Song. Approval of final manuscript: all authors.

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