Predictors of secondary amputation in patients with grade IIIC lower limb injuries
A retrospective analysis of 35 patients

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Abstract
The aim of this study was to identify risk factors for failure of limb salvage surgery in grade IIIC lower extremity injuries. A single-institution, retrospective review was performed of all patients with grade IIIC lower limb injuries presenting from January 2009 to April 2014. We gathered the data on each patient who underwent limb salvage and analyzed the final outcome for these patients (limb salvage vs secondary amputation).

Grade IIIC lower limb injuries were identified in 41 patients. Primary amputation was performed in 6 patients (15%) as the initial procedure. Thirty-five patients (85%) underwent vascular reconstruction and other surgical procedures to salvage the limb. Limb salvage was successful in 23 patients (66%); 12 patients (34%) ultimately underwent secondary amputation. The median time from injury to secondary amputation was 22.5 days (range 4–380 days). The mean Mangled Extremity Severity Score (MESS) was 7.2 ± 1.5 (range 5–10). The MESS was significantly higher in the secondary amputation group compared with the limb salvage group. Additionally, statistical testing revealed that the limb ischemia time, complex fractures, rate of fasciotomy, and number of vascular reconstructions were significantly higher in the secondary amputation group. Muscle necrosis and extensive soft tissue defect were the main reasons for secondary amputation.

The findings indicate that MESS of 7 or greater, complex fractures, limb ischemia time equal to or greater than 6 hours, and osteofascial compartment syndrome were associated with an increased risk of delayed amputation. The MESS is highly prognostic but not perfect; decision-making in patients with an MESS of 7 or greater should be re-evaluated for clinical use.

Abbreviations: ISS = Injury Severity Score, MESS = Mangled Extremity Severity Score.

Keywords: grade IIIC, limb salvage, MESS, predictors, secondary amputation, severe lower limb injuries

1. Introduction
With the expansion of vehicular traffic, the morbidity of severe lower limb injury caused by high-energy collisions is rising.[1,2] These patients often have extensive soft tissue damage and vascular injuries, with serious complications and sequelae.[3,4] Even for experienced surgeons, these injuries are challenging to treat. In the past several decades, limbs with Gustilo type grade IIIC injuries (open fractures of the lower limb associated with vascular injury) have been difficult to salvage and have been treated by primary amputation. With the advancement of surgical technique, especially the use of microsurgery, the salvage rate for grade IIIC lower limb fractures is rising, and the rates of attempted limb salvage are also increasing.[3] Many patients have undergone successful limb salvage.[4] Unfortunately, some patients must undergo secondary amputation for various reasons, enduring additional surgery, longer hospital stays, greater expense, and more pain resulting from complications. This is a heavy psychologic and physiologic blow to patients. Therefore, the aim of this study was to identify the predictors that help surgeons determine which patients with grade IIIC lower limb fractures should undergo primary amputation.

2. Methods
Permission for this study was obtained from the Medical Ethics Committee of Shandong Provincial Hospital Affiliated to Shandong University.

We analyzed all patients with grade IIIC limb fractures who were treated in our institution from January 2009 to April 2014. We gathered the following data on each patient who underwent limb salvage: gender, age, injury mechanism, fracture type, Injury Severity Score (ISS),[5] Mangled Extremity Severity Score (MESS),[6] number of associated organ injuries, limb ischemia time, management of fractures, time to secondary amputation, reason of secondary amputation, site of amputation, skin avulsion injury, presence or absence of osteofascial compartment syndrome, treatment course, and complications.

There are several classification systems for limb fractures. We used the AO system to classify the bony injury: type A, simple
fracture; type B, wedge fracture; and type C, complex fracture. Many criteria are used to assess patients with lower-extremity trauma. MESS is widely accepted; therefore, we used that system to predict the risk of amputation. We applied the ISS to assess the trauma severity; a major trauma (or polytrauma) is defined as a score being equal to or greater than 16.²³

We identified 41 patients with Gustilo grade IIC open lower limb fractures; 6 patients underwent primary amputation. The other 35 patients had limb salvage and were grouped according to the outcome: limb salvage was successful in 23 patients (group I) and 12 patients underwent secondary amputation (group II).

Statistical analysis was performed with SPSS Statistics for Windows, Version 12.0 (SPSS Inc., Chicago, IL). Mean, standard deviation, median with minimum, and maximum values were calculated for continuous and discrete variables. All categorical variables were presented as number of patients. Differences between 2 groups were tested by Fisher exact test. A 2-sided significance level of 0.05 was used for all statistical tests.

3. Results

There were 41 patients identified with grade IIC lower limb fractures, all of whom were treated in our institution between January 2009 and April 2014. Primary amputation was performed in 6 patients (15%) as the initial procedure. Thirty-five (85%) patients underwent vascular reconstruction and other surgical procedures to salvage the limb; however, salvage was achieved in 23 patients (66%), and 12 patients (34%) ultimately underwent secondary amputation. We gathered the data for each patient who underwent limb salvage.

Demographic information and trauma scoring were listed in Table 1. The main mechanism of lower limb fracture was motor vehicle injury; it accounted for 63% of 35 patients (n=22). The mean ISS was 15.8±3.9 (range 8–23), 13 patients were equal to or greater than 16 in group I, and 7 patients were equal to or greater than 16 in group II. When we compared the ISS between the 2 groups, there was no significant difference. The mean MESS was 7.2±1.5 (range 5–10), 9 patients were equal to or greater than 7 in group I, 11 patients were equal to or greater than 7 in group II. When the MESS of the 2 groups was compared, the MESS in group II was higher than for group I, and the difference was significant (P=0.01). The mean limb ischemia time for all patients was 5.5±2.6 hours (range 2–12 hours), 5 patients were equal or greater than 6 hours in group I, 8 patients were equal or greater than 6 hours in group II. There was a significant difference in comparing the limb ischemia time between the 2 groups (P=0.024).

All patients underwent initial vascular reconstruction. Vein grafting was performed in 18 patients (10 in group I and 8 in group II). Arterial incision and embolectomy was performed in 12 patients (10 in group I and 2 in group II). End-to-end anastomosis was performed in 5 patients (3 in group I and 2 in group II). Twenty-six patients had 1 vascular reconstruction procedure (20 in group I and 6 in group II). Eight patients underwent 2 vascular repair procedures (3 patients in group I and 5 in group II). There was only 1 patient (group II) who underwent 3 vascular reconstruction surgeries. When we compared the number of vascular reconstruction procedures between the 2 groups, the number for group II was higher than for group I (P=0.045).

Five patients had simple tibial shaft fractures (14%) in group I and none in group II. Eleven patients had wedge fractures (31%), 9 in group I and 2 in group II. Nineteen patients had complex fractures (54%), 9 in group I and 10 in group II. The rate of complex fractures in group I was lower than in group II; there was a significant difference between the 2 groups (P=0.035). Thirty-four open tibia fractures in the 2 groups were treated initially with external fixation followed wound debridement. One patient was treated with an interlocking nail. In the course of treatment, 18 patients experienced bone loss, 13 in group I and 5 in group II. These patients were treated with autologous bone grafting or bone removal.

Two patients were treated with fasciotomy in group I and 5 in group II. The fasciotomy rate was significantly higher in group II than in group I; there was a significant difference between the 2 groups (P=0.03). Four patients in group I and 6 in group II underwent flap repair for soft tissue defect coverage, with the median time being 10.0 days (range 7–31 days). However, 3 patients experienced flap necrosis. Ten patients in group I and 7 in group II underwent split-thickness skin grafting. Vacuum-assisted closure was used in patients whose wounds could not be repaired primarily; flap repair or split-thickness skin grafting was performed until granulation tissue appeared. Predictors of secondary amputation by univariate analyses are listed in Table 2.

Secondary amputation was performed in 12 patients, and the median time was 22.5 days (range 4–380 days). Muscle necrosis and extensive soft tissue defect were the main reasons for secondary amputation (n=8). Two patients were diagnosed with sepsis and 1 with gas gangrene. One patient underwent amputation because of osteomyelitis and a nonhealing chronic ulcer after 380 days. All patients underwent transtibial amputation except 1 patient who underwent knee exarticulation (Table 3).

One patient was lost to follow-up after the limb was successfully salvaged; another patient died of lung cancer 2 years after successful limb salvage. Thirty-three patients were followed, with a median time of 23.0 months (range 14–29 months). Patients in the limb salvage groups were observed until they could stand and walk with or without a cane. Patients in the secondary amputation group were observed until they used an artificial limb. The complications from the artificial limb were observed, too; follow-up was complete if a patient did not have a plan to use an artificial limb in the short term. None of the patients could return to their previous work. In group I, 10 patients presented with peroneal paresis; 8 patients improved after treatment with nerve nutrition medicine, and 2 patients had permanent peroneal paresis. Most of the patients with successful limb salvage had knee joint dysfunction; 5 patients could stand and walk without a cane after rehabilitation, and the other patients had to use a cane to help with prolonged standing and walking. In group II, 6 patients used an artificial limb well and had a good quality of life, but 1 patient had ulceration of the residual limb and was ultimately cured by surgery. The other 6 patients did not use an artificial limb and were aided by wheelchair or cane.
Lange et al[11] reviewed 23 cases and suggested that complex fractures were associated with a bad outcome. Our results support this conclusion; the number of patients with complex fractures was higher in the delayed amputation group than in the limb salvage group. Complex fractures imply that high-energy forces were exerted on the lower limb, and the fracture segments could increase the risk of arterial injury, and severe soft tissue injuries could lead to a bad outcome. There has been great progress in the management of fractures,[12,13] even with bone loss, several treatment options are available for fractures and bone loss. In our study, we applied autologous bone grafting and bone removal to treat bone loss and achieved good outcomes. There was no significant difference with regard to bone loss between the 2 groups.

Vascular reconstruction is another difficult management problem. The primary care of grade IIIIC lower limb injuries is critical for the success of a limb salvage procedure. Twenty-three patients with open tibial fractures complicated by limb-threatening vascular injuries were reviewed; the amputation rate was 61%.[11,12] The acknowledged issue is that a limb ischemia time equal to or greater than 6 hours is associated with a bad outcome.[14-16] Simmons et al[17] however, reviewed data for 51 patients and concluded that a limb ischemia time equal to or greater than 6 hours was not predictive of amputation. Our conclusions support the traditional view. The rate of delayed vascular reconstruction was significantly higher in the secondary amputation group. Interestingly, we found that the number of vascular repair procedures in the secondary amputation group was higher than in the successful limb salvage group. Normally, we can diagnose penetrating arterial injuries immediately, while the diagnosis of blunt vascular injuries is usually neglected.[18] This leads to many patients requiring multiple revascularization procedures, and the best time to improve limb ischemia might be missed. In our experience, secondary or multiple revascularizations are associated with a bad outcome.

Compartment syndrome is a surgical emergency; the dangerously high pressure in compartment syndrome could impede the flow of blood to and from the affected tissues, exacerbating limb ischemia and leading to permanent injury. Therefore, fasciotomy must be performed early.[19] However, the window for optimal management is often missed because of the lack of diagnostic clarity. Once the best time is missed, patients may face secondary amputation, and even death caused by severe complications. In our study, 20 patients (80%) underwent fasciotomy; the rate of fasciotomy was higher in the secondary amputation group than in the limb salvage group. Additionally, compartment syndrome usually develops when revascularization of an ischemic limb is delayed because of reperfusion (re-oxygenation) injury.[20] Sheridan and Matsen[21] reviewed 66 cases and reported that 68% of the patients recovered when the fasciotomy was performed early, and 8% of the patients recovered when the procedure was delayed. In our experience, prophylactic fasciotomy was necessary for patients who had lower limb fractures combined with vascular injuries.

It has been reported that the severity of soft tissue injury is the greatest factor in deciding between limb salvage or amputation.[31] Similarly, our results showed that the main reason for secondary amputation was muscle necrosis and extensive soft tissue defect. The focus is often on vascular reconstruction at the beginning of treatment, and soft tissue injuries are often neglected. Other studies also revealed that patients with severe soft tissue injuries underwent secondary amputation.[14,22] Additionally, we observed that delayed vascular reconstruction was related to soft

| Table 2 | Univariate analyses of predictors of secondary amputation. |
|----------|-------------------------------------------------|
| Covariate | Group I | Group II | P |
| Age, y | 39.61 (21–62) | 40.42 (17–67) | .875 |
| Sex | | | .200 |
| Male | 20 | 8 | |
| Female | 3 | 4 | |
| Accident mechanism | | | .272 |
| Motor vehicle injury | 15 | 7 | |
| Fall | 3 | 0 | |
| Crush injury | 1 | 3 | |
| Heavy equipments accident | 3 | 2 | |
| Pedestrian-struck by vehicle | 1 | 0 | |
| ISS | | | .100 |
| ≥16 | 13 | 7 | |
| <16 | 10 | 5 | |
| MESS | | | .004 |
| ≥7 | 9 | 11 | |
| <7 | 14 | 1 | |
| Associated injuries | | | .342 |
| None | 3 | 2 | |
| 1 | 9 | 6 | |
| 2 | 10 | 2 | |
| ≥3 | 1 | 3 | |
| AO classification | | | .035 |
| 42 A1–3 | 5 | 0 | |
| 42 B1–3 | 9 | 2 | |
| 42 C1–3 | 9 | 10 | |
| Osteosynthesis | | | .575 |
| External fixation | 22 | 12 | |
| Interlocking nail | 1 | 0 | |
| Limb ischemia time | | | .024 |
| ≥6h | 5 | 8 | |
| <6h | 18 | 4 | |
| Number of vascular reconstructions | | | .045 |
| 1 | 20 | 6 | |
| 2 | 3 | 5 | |
| ≥3 | 0 | 1 | |
| Fasciotomy | | | .033 |
| Absent | 21 | 7 | |
| Present | 2 | 5 | |
| Bone loss | | | 1.000 |
| Absent | 16 | 8 | |
| Present | 7 | 4 | |

ISS=Injury Severity Score, MESS=Mangled Extremity Severity Score.

4. Discussion

With surgical innovations, we have reached a consensus that extremity salvage for grade IIIC fractures of the lower limb is not impossible.[31] Attempted limb salvage has a higher risk for a longer hospital stay, more expense, a greater number of surgeries, and significantly higher rates of complications.[11-3,7] However, some patients may undergo secondary amputation because of failure in limb salvage. The reported rate of amputation is as high as 78%,[31] and the secondary amputation rate reaches 15% in grade IIIC fractures of the lower limb.[31] Predicting which patients should forego limb salvage and undergo amputation is a challenge to surgeons. Many investigators have reported on various amputation predictors for patients with grade IIIA or grade IIIB fractures of the lower limb.[1,2,9,10] but there are comparatively few studies on grade IIIC fractures of the lower limb. The aim of this study was to gather cases in our hospital and analyze the amputation predictors for patients with severe lower limb injuries.
Table 3
Details of secondary amputation group.

| Age, sex, fracture | Accident ISS MESS | Primary surgical treatment | No of associated organ injuries | TA | No of VR | Surgical procedures | Reasons for secondary amputation | Amputation site, no. operations |
|-------------------|-------------------|---------------------------|--------------------------------|----|---------|---------------------|--------------------------------|----------------------------------|
| 57 Female C3      | MVC ISS 10 MESS 9 | EXF, VR, VAC              | 1                              | 380| 1       | Free microvascular flap, STSG, septic revisions | Osteomyelitis, soft tissue infection | Lower leg 10                      |
| 44 Male C3        | MVC, ISS 21, MESS 8 | EXF, VR, fasciotomy, VAC  | 3                              | 48 | 2       | STSG, septic revisions                                | Muscle necrosis, soft tissue infection | Lower leg 5                      |
| 50 Male C3        | MVC, ISS 16, MESS 9 | EXF, VR, fasciotomy, VAC  | 2                              | 16 | 2       | STSG, septic revisions                                | Muscle necrosis, vessel occlusion, soft tissue infection | Lower leg 3                      |
| 17 Male C3        | MVC ISS 17 MESS 6 | EXF, VR                   | 1                              | 8  | 3       | STSG, vascular reconstruction, surgical revisions    | Soft tissue defect                       | Lower leg 4                      |
| 39 Female C3      | MVC ISS 22 MESS 10 | EXF, VR                   | 3                              | 56 | 1       | Free microvascular flap, STSG, septic revisions      | Muscle necrosis, vessel occlusion, soft tissue infection | Lower leg 7                      |
| 34 Female C3      | MVC ISS 18 MESS 10 | EXF, VR, fasciotomy       | 2                              | 51 | 1       | STSG, vascular reconstruction, surgical revisions    | Muscle necrosis, vessel occlusion, soft tissue infection | Lower leg 7                      |
| 31 Male B2        | Crush injury ISS 14 MESS 8 | EXF, VR                  | 1                              | 11 | 1       | Vascular reconstruction, surgical revisions         | Soft tissue defect, septic revisions    | Lower leg 3                      |
| 17 Male C3        | Crush injury ISS 9 MESS 7 | EXF, VR, fasciotomy       | 0                              | 4  | 2       | Septic revision                                      | Soft tissue infection, gaseous gangrene | Knee exarticulation 2             |
| 52 Male B3        | Crush injury ISS 12 MESS 9 | EXF, VR, VAC              | 0                              | 6  | 2       | Vascular reconstruction, surgical revisions         | Soft tissue defect, soft tissue infection | Lower leg 2                      |
| 26 Female C3      | MVC ISS 16 MESS 8 | EXF, VR                   | 1                              | 23 | 1       | Vascular reconstruction, surgical revisions         | Muscle necrosis, vessel occlusion, soft tissue defect | Lower leg 6                      |
| 67 Male C2        | Heavy equipment accident ISS 18 MESS 10 | EXF, VR                  | 1                              | 45 | 2       | Free microvascular flap, vascular reconstruction, STSG | Soft tissue defect                       | Lower leg 6                      |
| 51 Male C3        | Heavy equipment accident ISS 15 MESS 8 | EXF, VR, fasciotomy, VAC  | 1                              | 28 | 1       | Vascular reconstruction, surgical revisions, septic revisions | Muscle necrosis, soft tissue defect | Lower leg 5                      |

EXF = external fixation, ISS = Injury Severity Score, MESS = Mangled Extremity Severity Score, MVC = motor vehicle injury, STSG = split-thickness skin graft, TA = time till secondary amputation, VAC = vacuum assisted closure, VR = vascular reconstruction.
tissue infection. A study performed by Pelissier et al²²³ reported similar findings. Delayed vascular reconstruction accompanied by prolonged warm ischemic time of muscle provides ideal conditions for bacterial growth and can lead to severe infection.

In our study, ISS is not a predictor in the decision to amputate or salvage an injured limb; there was no significant difference between the 2 groups. This conclusion is different from the study by Dua et al.,¹² which suggested a correlation between a higher ISS and a higher likelihood of amputation. We also noted the number of injured organs and found no significant difference between the 2 groups. We suggested the application of multidisciplinary can explain this phenomenon. Additionally, the principle “life before limb” should be used in everyday clinical.

In the 1990s, Helfet et al⁶ first described the MESS system, which includes the degree of injury, time of limb ischemia, presence or absence of shock, and patient age. Amputation was recommended for patients having an MESS score equal to or greater than 7. MESS has been widely used and analyzed, with some studies revealing a good correlation between an MESS higher than 7 and amputation,¹¹ ¹³ ²⁴ ²⁵ while others did not.¹⁸ ²⁷ ²⁸ In our study, MESS in the secondary amputation group was higher than in the limb salvage group, revealing that MESS was a stronger predictor for secondary amputation. Doucet et al.²³ concluded that successful limb salvage was still possible in most patients with an MESS of 7 or greater, and our results support this conclusion. In our study, 20 patients had scores equal to or greater than 7, and limb salvage was attempted; this was successful in 9. The remaining patients underwent secondary amputation. The main reason for this success is the advancement of surgical techniques in the past decades, especially in microsurgical technique that makes successful limb salvage a possibility in patients with severe limb injuries. O’Sullivan et al.²⁶ found that the score should not be considered absolutely reliable because the patients with an MESS equal to or greater than 7 had limb salvage with an acceptable functional outcome, similar to our study, in which all patients with limb salvage had acceptable function.

The first limitation of our study is its retrospective nature. The other limitation is that our study was conducted on a small number of patients, so the conclusions of the study are limited.

In conclusion, patients with grade IIIC lower limb injuries are at high risk for amputation. An MESS equal to or greater than 7, complex fractures, time from injury to operation equal to or greater than 7 hours, and osteofascial compartment syndrome were associated with an increased risk of secondary amputation. From our data, MESS was the strongest predictor of secondary amputation; however, we recognize that the group of patients undergoing limb salvage contained 9 patients in whom the MESS was equal to or greater than 7, which is different from the traditional view. New methods in decision-making for limb salvage or amputation in the mangled extremity are needed.

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