scientific reports

OPEN

Impact of delayed amputation on clinical outcomes compared to that of early amputation in patients with blunt polytrauma

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Delayed amputation after failed limb salvage can lead to negative clinical and functional outcomes due to complications, including re-amputation. This study aimed to compare clinical outcomes and identify risk factors according to the timing of amputation. A retrospective review of lower-extremity injuries managed between January 2016 and December 2022 at a level 1 trauma center was conducted. Outcomes were compared between early amputation (within 48 h) and delayed amputation (beyond 48 h) groups. The primary outcome was the risk of a more proximal amputation level according to the timing of amputation. Secondary outcomes included trauma-related complications and clinical outcomes. Trauma-related complications were more common in the delayed amputation group, with no significant differences in 30-day mortality. Delayed amputation and deep surgical infection at the stump site were associated with higher odds of a more proximal amputation level than initially predicted. The overall hospital stay was significantly longer in the delayed amputation group. While there is no established standard for deciding between limb salvage and amputation strategies, delayed amputation could be a risk factor for shorter limb stumps owing to re-amputation, and patients may experience more trauma-related complications and prolonged hospitalization.

Abbreviations

ATLS	Advanced trauma life support
LEAP	Lower extremity assessment project
EMR	Electrical medical records
ISS	Severity score
AIS	Abbreviated injury scale
GCS	Glasgow coma scale
CT	Computed tomography
MESS	Mangled extremity severity score
ICU	Intensive care unit
LOS	Length of stay
IRB	Intuitional review board
PRC	Packed red cell
SD	Standard deviation
IQR	Inter-quartile range
SSI	Surgical site infection
OR	Odds ratio

Historically, amputation has been regarded as the treatment for severe extremity trauma, and whether primary amputation or challenging limb salvage should be performed remains a topic of debate[1,2]. In the study of the prevalence of limb amputation in the United States, trauma accounts for 45% of extremity amputations. In South Korea, the most common cause of lower extremity amputation is trauma, accounting for over 75% of cases[3,4]. A large number of patients with mangled extremities are relatively young and healthy people. Therefore, given the nature of limb amputation as a “life-changing” operation, physicians and patients might want to avoid

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amputation. Since the latest reconstructive techniques and medical treatment are available, we can attempt a limb salvage strategy[5,6].

Severe lower-extremity trauma is a life-threatening event. Trauma surgeons are faced with emergencies in which amputation should be considered for hemorrhagic control in the operating room as part of the initial resuscitation according to the Advanced Trauma Life Support (ATLS) guidelines[7]. In addition, the outcomes of challenging limb salvage are still debated. Previous studies, including the Lower Extremity Assessment Project (LEAP), insisted that limb salvage did not improve functional outcomes and showed a higher complication rate, resulting in prolonged hospital stays or multiple procedures. Delayed amputation, which involves limb salvage, was associated with more frequent major complications than early amputation[8–10].

The length of the residual limb is an essential outcome of treating the mangled extremity, which indicates the amputation level, and it may have a decisive effect on functional outcomes. Longer residual limbs have mechanical advantages and are associated with quality of life. However, re-amputation could be necessary because of the sequelae of postoperative complications, which cannot be handled through non-operative methods, and a shorter residual limb contributes to more significant physical strain. Therefore, re-amputation may affect functional outcomes in patients who have undergone previous amputations[11,12].

For trauma surgeons responsible for the initial resuscitation of patients with severe polytrauma, deciding the timing of amputation is vital for establishing a treatment strategy. Nonetheless, most previous studies have been conducted in trauma patients with relatively lower ISS, and studies on the association between the timing of amputation and re-amputation for severely injured patients are scarce[8,13–15]. We hypothesize that the timing of amputation could affect clinical outcomes and the rate of re-amputation, which may cause changes in amputation level.

Therefore, this study aimed to compare clinical outcomes and the final amputation level and identify risk factors that change to a more proximal level according to the timing of the amputation.

Materials and methods

We performed a retrospective study of patients presenting with a mangled lower extremity at a single level 1 trauma center over 7 years (2016–2022) using the electronic medical records (EMR) of the patients included in this study.

We included adults aged 18 years or older with lower extremity injuries caused by blunt trauma. According to a previously published approach, a mangled extremity injury is defined as (1) a severe crushing injury or (2) a major fracture combined with selected severe injuries to at least two or three of the following: soft tissue, artery, or nerve[16]. Patients who died on arrival or within 48 h of hospital presentation were also excluded because their cause of death could be associated with other severe trauma, such as thoracic or abdominal injury, rather than the timing of amputation. Patients who underwent only midfoot or toe amputation or amputation for nontraumatic causes were excluded. Patients with incomplete or missing data were excluded.

After reviewing medical records, the following data were collected: patient demographics, injury characteristics, comorbidities, treatment courses, and complications. Injury characteristics were defined by injury mechanism, Injury Severity Score (ISS), and presence of concomitant severe head and neck, face, chest, abdomen, and/or pelvis injury, which is defined as an Abbreviated Injury Scale (AIS) score of > 3. We also assessed the presence of shock (a systolic blood pressure of less than 90 mmHg) and the Glasgow Coma Scale (GCS) score in the resuscitation area. Two trauma surgeons and two orthopedic surgeons evaluated lower extremity trauma regarding orthopedic, soft tissue, and vascular injury by reviewing medical records, clinical photography, radiography, and computed tomography (CT) and assessed the Mangle Extremity Severity Score (MESS)[17].

The patients were divided into two groups according to the timing of amputation: early or delayed. Patients who underwent amputation within 48 h of injury were classified into the early amputation group. Delayed amputation was defined as any amputation that occurred 48 h after the injury with the intention of limb salvage. For lower limbs, the amputation level was classified into five levels: trans-tarsal, below knee, through knee (knee disarticulation), above knee, and hip disarticulation. The predicted amputation level was defined as the expected amputation level if lower extremity amputation was performed within 48 h of injury and evaluated by four trauma specialists, including two orthopedic surgeons and two trauma surgeons. A proximal change in the amputation level was defined as any category change between the predicted and final amputation level with the final amputation level being more proximal than the predicted level. One of the two trauma surgeons is a cardiovascular specialist. Four trauma specialists retrospectively reviewed the EMR images, clinical photographs, and initial lower-extremity CT angiography (Fig. 1). After the review, any disagreements about the predicted amputation level were discussed among the specialists.

Our primary outcome was to compare the final amputation level and identify the risk factors that changed to a more proximal amputation level according to the timing of the amputation. The secondary outcomes are the outcomes of patients with lower extremity mangled injury, including development of complications, mortality, hospital stay, and Intensive Care Unit (ICU) length of stay (LOS).

Our institution is a tertiary academic hospital that operates a level 1 trauma center serving a region with a population of 10 million. Further according to the Korean Trauma Data Bank, our trauma center admits approximately 4000 acutely injured patients annually. In our institution, initial assessment and resuscitation for polytrauma patients is conducted according to the ATLS guidelines by the trauma team, which includes well-trained and dedicated general trauma surgeons, cardiovascular surgeons, and emergency medicine specialists. On arrival, all patients with mangled lower extremities are assessed by the trauma team. During the initial assessment in the trauma bay, routine vascular examination is conducted including pulse palpation and Doppler assessment, and first generation antibiotics are administered to patients according to our guidelines. For suspected bone, soft tissue, tendon or ligamentous injuries, orthopedic surgeons in the trauma bay adopt a

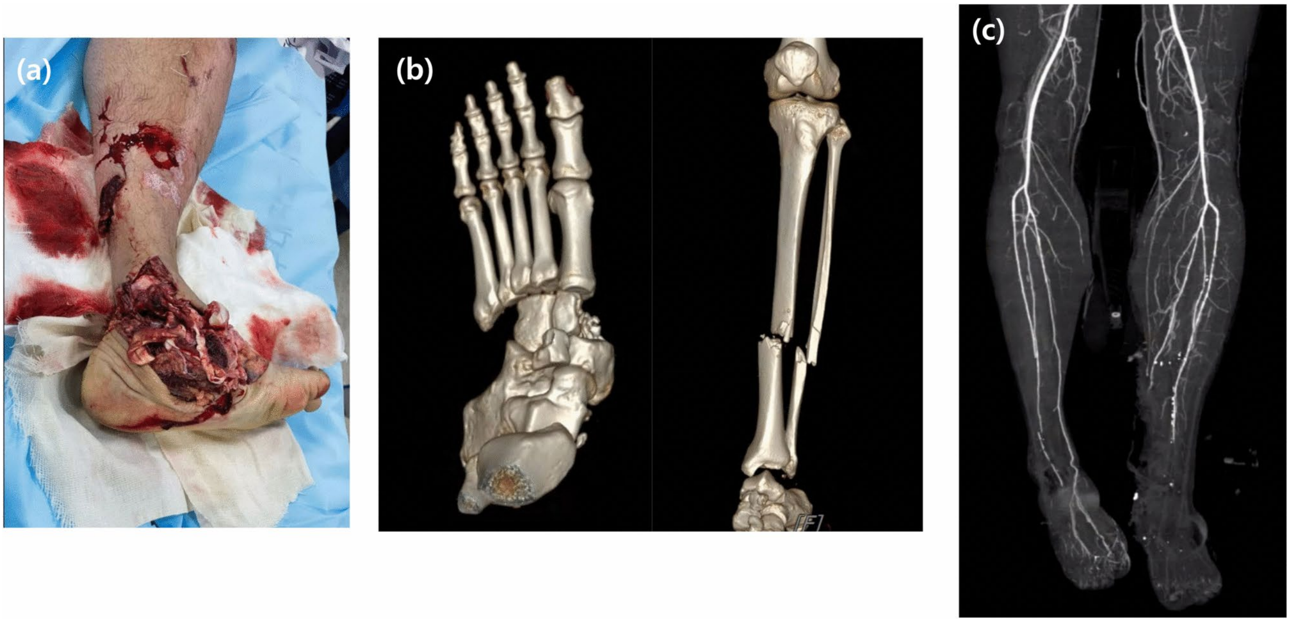


Fig. 1. A 35-year-old man presented to the trauma center following a motorcycle collision with a left lower extremity injury. The predicted amputation level was below knee. (**a**) Left-sided pulseless "mangled" lower leg, ankle and foot injuries. (**b**) Computed tomography (CT) scan shows left tibiofibular shaft fracture and dislocation of the tibiotalar and Lisfranc joints. (c) CT angiography demonstrates injury of the left dorsalis pedis artery and posterior tibial artery.

multidisciplinary approach. Patients presenting with hemorrhagic shock proceed to the operation room (OR), where they undergo hemorrhagic control or revascularization by cardiovascular surgeons and stabilization of orthopedic injuries using fixators by orthopedic surgeons after revisualization, if necessary. We also routinely perform massive irrigation and debridement for injured limbs to promptly remove any nonviable tissue and contaminants. The amputation vs. limb salvage decision is established by the multidisciplinary trauma team in the trauma bay or the OR based on the patient's overall burden of injury, physiology (to prioritize patient survival), socioeconomic status, and opinions[18,19]. For hemodynamically stable patients, CT angiography is conducted to investigate the presence of vascular injuries, including the anatomic site and extent according to the AAST-WSES guideline[20]. Negative-pressure wound therapy is commonly used to reduce infection and assist wound management and negative-pressure dressings are usually changed every 48–72 h. Our trauma team conducts regular wound inspections and performs repeated irrigation and debridement based on wound appearance, including assessment of tissue viability and infection status. Additionally, our trauma center holds a weekly multidisciplinary conference involving trauma, orthopedic, and plastic surgeons, as well as wound care nurses, to facilitate effective communication between care professionals and establish comprehensive treatment strategies.

The normality assumption was tested using the Shapiro–Wilk test. When departures from normality were significant, the Mann–Whitney U test was used as a non-parametric method. When the data followed a normal distribution, a two-sample *t*-test was used for the analysis. Continuous variables are presented as mean ± standard deviation (SD) and median interquartile range (IQR). Dichotomous variables were compared using the chi-square test or Fisher's exact test, as appropriate, and expressed as proportions. Considering the results of univariate analysis, the variables with $P < 0.05$ were included as candidates in the multivariable logistic regression analysis using a stepwise selection to identify the risk factors for changes at a more proximal amputation level than the predicted level. All statistical analyses were conducted using R software, version 4.1.2. A P-value < 0.05 was considered significant.

The study was approved by the Institutional Review Board of our institution (IRB No. AJOUIRB-DB-2023-270), the requirement for informed consent was waived owing to the observational nature of this study. This study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Guidelines for Observational Studies[21].

Results

A total of 199 patients were included in the analysis, of whom 132 (66.3%) underwent early amputation, and 67 (33.7%) were treated by delayed amputation. 24 patients were excluded from analysis (Fig. 2). The baseline characteristics of the patients are summarized in Table 1. Most patients in both groups were male, with an average age of 53 years, and had similar initial systolic blood pressure and GCS scores. There were no significant differences in the proportions of smokers and underlying diseases, except for hypertension. All patients experienced blunt trauma, and the ISS and mechanism of injury were not significantly different between the two groups (Table 1).

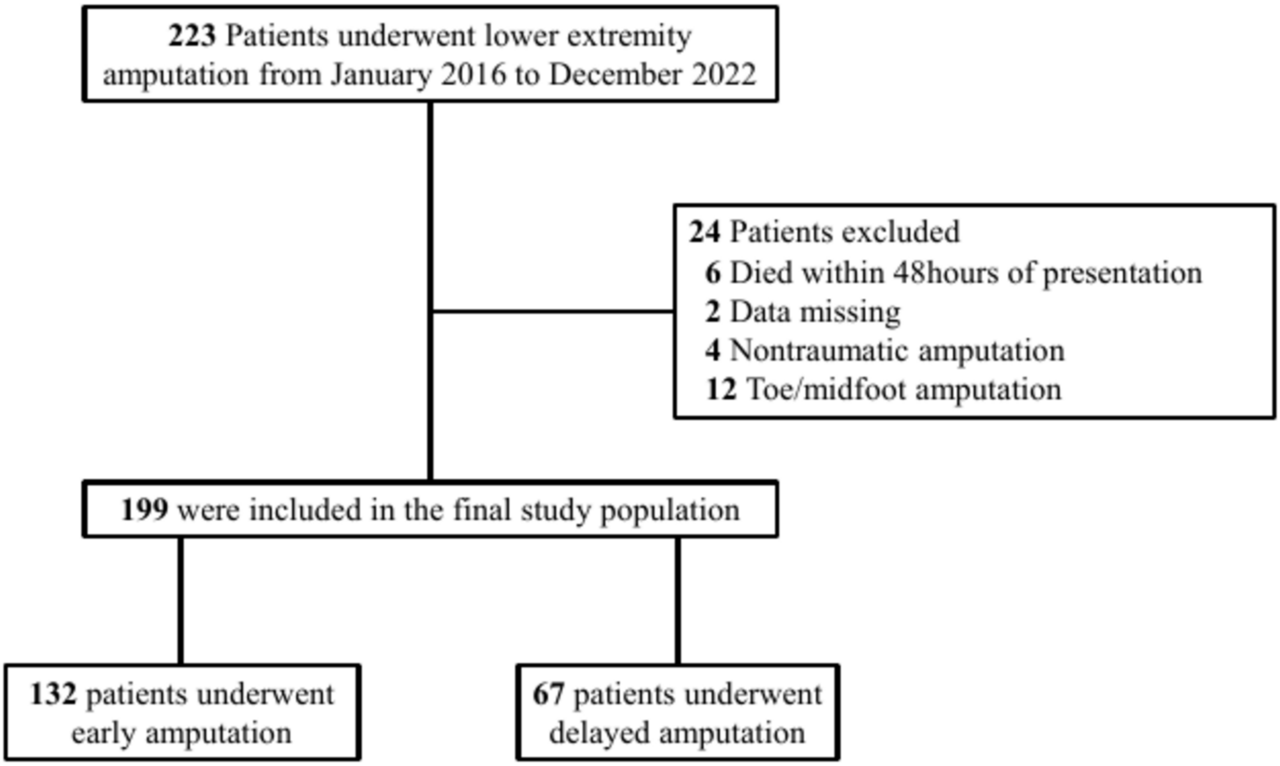


Fig. 2. Flow chart of the Study Population.

Table 2 demonstrates the MESS score used to assess the severity of lower-extremity management injury. MESS was significantly higher in the early amputation group (7.1 ± 1.5 vs. 6.0 ± 1.5, *P* < 0.001). In the early amputation group, most patients were injured by a very high-energy injury mechanism, significantly higher than the delayed amputation group (88.6% vs. 47.8%, *P* < 0.001). Compared with the delayed amputation group, the early amputation group demonstrated a greater prevalence of severe limb ischemia, whereas the number of patients with ischemia longer than 6 h was notably higher in the delayed amputation group (Table 2).

Delayed amputation was defined as any amputation that occurred more than 48 h after the injury; however, the mean time to amputation in this group was 11.9 ± 7.3 days (Table 3). Among the 67 cases of delayed amputation, the most significant causes of delayed amputation were infection and tissue necrosis (n = 48), followed by surgical delay due to the patient's refusal for early amputation (n = 6), vascular reconstruction failure (n = 5), flap failure (n = 3), and a conflict between the patient's desire for amputation and the evaluation of a possibility of limb salvage (n = 2). Although the proportion of patients requiring packed red cell (PRC) transfusion units was not significantly higher in the early amputation group (89.4% vs. 79.1%, *P* = 0.079), the rate of massive transfusion was significantly higher in that group (54.5% vs. 32.8%, *P* = 0.004). Vascular procedures were more frequently performed in the delayed amputation group (10.6% vs. 26.9%, *P* = 0.003). In the delayed amputation group, the most commonly performed vascular procedure was vascular reconstruction, whereas ligation of the vessels was the most frequent procedure in the early amputation group. Ipsilateral fractures above amputation level were more common in the delayed amputation group (20.5% vs. 35.8%, *P* = 0.019). There were no statistically significant differences in the rates of re-amputation, predicted amputation level, final amputation level, and overall stump complications (Table 3).

However, there was a significant change in the predicted and final amputation levels between the two groups. The delayed amputation group showed a significantly greater final amputation level change rate (14.4% vs. 35.8%, *P* < 0.001*)* to a more proximal level than initially predicted, whereas the predicted and final amputation levels were the same in 85.6% of patients in the early amputation group. (Fig. 3).

Despite the lack of significant differences in the 30-day mortality rate between the two groups, the delayed amputation group experienced significantly more complications related to trauma and rhabdomyolysis (38.6% vs. 59.7%, *p* = 0.005, 38.2% vs. 55.2%, *P* = 0.022, respectively) (Table 4). The delayed amputation group experienced significantly more compartment syndrome on the injured limb (0% vs. 13.4%, *P* < 0.001) and decubitus ulcer (9.1% vs. 23.9%, *P* = 0.003). Osteomyelitis was observed more often in the delayed amputation group (0.8% vs. 7.5%, *P* = 0.017) (Table 4).

Between the two groups, ICU length of stay (LOS) (4 days [IQR, 2,9] vs. 7 days [IQR, 3,14], *P* = 0.060) was not significantly different, whereas ventilator days (3 days [IQR, 1,8] vs. 5 days [IQR, 2,13.5], *P* = 0.033) and hospital LOS (37.5 [IQR, 18,55.3] vs. 48 [IQR, 26.5,70.5], *P* = 0.005) showed significant differences (Table 5a). A similar result was observed when patients were stratified according to an ISS < 15 (Table 5b). On the contrary, among patients with an ISS of > 15, there were no significant differences between the two groups (Table 5c).

Variables	Early amputation (n = 132)	Delayed amputation (n = 67)	*p*-value
Age, mean ± SD (years)	53 ± 13.8	53.2 ± 18.5	0.949
Sex, n (%)			
Male	102 (77.3)	58 (86.6)	0.119
Female	30 (22.7)	9 (13.4)	
Mechanism of injury, n (%)			
Free fall	4 (3)	1 (1.5)	0.176
Motor vehicle accident	27 (20.5)	11 (16.4)	
Motorcycle accident	24 (18.2)	18 (26.9)	
Bicycle/Pedestrian	55 (41.7)	23 (34.3)	
Machinery	14 (10.6)	4 (6)	
Other blunt injury	8 (6.1)	10 (14.9)	
Arrived from, n (%)			
Scene	107 (81.1)	36 (53.7)	< 0.001
Outside Hospital	25 (18.9)	31 (46.3)	
Initial SBP, n (%)			
< 90 mmHg	117 (88.6)	55 (82.1)	0.203
≥ 90 mmHg	15 (11.4)	12 (3.4)	
Initial GCS, mean ± SD	13.7 ± 3	13.4 ± 3.4	0.629
Initial lactic acid (mmol/L), median (IQR)	3.8 (2.1, 5.2)	2.6 (1.7, 4.1)	0.011
Known associated injuries, AIS ≥ 3, n (%)			
Head and neck	14 (10.6)	8 (11.9)	0.777
Face	2 (1.5)	0 (0)	0.551
Chest	60 (45.5)	29 (44.3)	0.771
Abdomen	20 (15.2)	13 (19.4)	0.446
Pelvis	8 (6.1)	11 (16.4)	0.019
ISS, median (IQR)	19 (10,26)	18 (9, 24.5)	0.458
ISS < 15	39 (29.5)	27 (40.3)	0.128
ISS ≥ 15	93 (70.5)	40 (59.7)	
Underlying diseases, n (%)	45 (34.1)	28 (41.8)	0.287
Cardiovascular disease	4 (3)	0 (0)	0.303
Peripheral disease	0 (0)	2 (3)	0.112
Cerebrovascular disease	7 (5.3)	0 (0)	0.098
Diabetes Mellitus	23 (17.1)	11 (16.4)	0.859
CKD	0 (0)	1 (1.5)	0.337
Liver disease	2 (1.5)	1 (1.5)	> 0.999
HTN	27 (20.5)	26 (38.8)	0.006
Current smoker, n (%)	60 (45.5)	29 (43.3)	0.771

Table 1. Baseline characteristics of patients with mangled extremity underwent lower extremity amputation, subdivided by the time of amputation. SD, standard deviation; SBP, systolic blood pressure; GCS, Glasgow Coma Scale; IQR, interquartile ranges; AIS, abbreviated injury scale; ISS, injury severity scale; CKD, chronic kidney disease; HTN, hypertension

Table 6 presents the risk factors for changes at a more proximal amputation level than the predicted level based on multivariate logistic regression analysis. The odds of delayed amputation after 48 h of injury were 2.95 times higher among the participants (adjusted odds ratio [OR] 2.95; 95% CI 1.38–6.24; $P = 0.006$). In addition, preexisting underlying disease (OR 2.26; 95% CI 1.07–4.79; $P = 0.032$) and deep surgical site infection of the amputation stump (OR 3.56; 95% CI 1.58–8.07; $P = 0.002$) were statistically significant risk factors for changes at a more proximal amputation level than the predicted level (Table 6).

Discussion

Despite significant advancements in limb salvage techniques, such as surgical stabilization, vascular repair, microsurgical free tissue transfer, and antibiotic therapy, the question of whether to amputate or attempt limb salvage remains. The treatment strategy depends on isolated lower extremity injury, polytrauma, or coexisting hemorrhagic shock[22,23]. Therefore, a multidisciplinary approach to mangled lower extremities, especially in collaboration with trauma surgeons, orthopedic surgeons, and plastic surgeons, is mandatory based on patients' medical conditions to provide optimal treatment.

Variables	Early amputation (n = 132)	Delayed amputation (n = 67)	p-value
MESS score, mean ± SD	7.1 ± 1.5	6.0 ± 1.5	< 0.001
Skeletal/soft-tissue injury (%)			
Low energy	0 (0)	2 (3)	< 0.001
Medium energy	5 (3.8)	15 (22.4)	
High energy	10 (7.6)	18 (26.9)	
Very high energy	117 (88.6)	39 (47.8)	
Limb ischemia (%)			
Reduced pulse but normal perfusion	35 (26.5)	37 (55.2)	< 0.001
Pulseless, paresthesia, slow capillary refill	25 (18.9)	10 (14.9)	
Cool, paralysis, numb/insensate	72 (54.5)	20 (29.9)	
Limb ischemia for > 6 h (%)	11 (8.3)	18 (26.9)	< 0.001
Shock (%)			
SBP > 90 mmHg consistently	57 (43.2)	38 (56.7)	0.190
Transient hypotension	46 (34.8)	17 (25.4)	
Persistent hypotension	29 (22)	12 (17.9)	
Age (%)			
< 30yrs	23 (17.4)	11 (16.4)	0.118
30–50yrs	36 (27.3)	10 (14.9)	
> 50yrs	73 (55.3)	46 (68.7)	

Table 2. Injury severity of lower extremity mangled injury according to MESS score. MESS, mangled extremity severity score; SBP, systolic blood pressure.

However, previous studies have not demonstrated ISS. Furthermore, most studies have a relatively low ISS in the study population, and few studies have been conducted in patients with lower extremity mangled injuries combined with multiple severe traumas[6,8,13–15,24]. In this study, the majority (67%) of the population had an ISS > 15, and only 8.5% of patients were identified with an ISS < 9, indicating our study includes a relatively larger number of blunt polytraumatized injured patients compared to previous studies.

Although vascular injuries to the extremities are rare in civilian settings, blunt trauma is a major cause of vascular trauma and contributes to increased mortality and morbidity. Therefore, aggressive hemorrhage control should follow the ATLS guidelines, including resuscitation and surgical approaches[25,26]. In the present study, the early amputation group showed more severe limb ischemia, implying peripheral vascular injury; hence, massive transfusion was more frequently required, which means that some early amputations were inevitably performed as part of the primary resuscitation for hemorrhagic control. In contrast, vascular reconstruction was more likely to occur in the delayed amputation group.

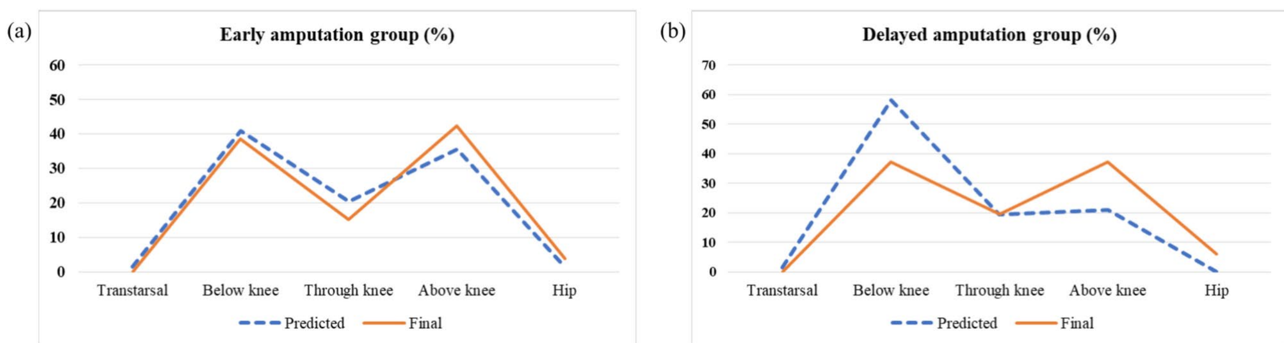
The LEAP study reported a higher incidence of complications in the late amputation group, including wound infection, osteomyelitis, and residual limb complications. In addition, the severity of soft tissue injury may be the most important factor in decision-making regarding amputation or limb salvage[5,10,13]. Urrechaga et al. suggested that the high-energy mechanism of blunt trauma is associated with a significant rate of limb loss[14]. A high-energy soft tissue injury stimulates the inflammatory process and microvascular cascade, which causes tissue hypoxia and further tissue injury[25]. Those crushing injuries induce muscle cell damage and release diverse substances, including creatine phosphokinase, myoglobin, and potassium, into the systemic circulation. This process is defined as rhabdomyolysis and can lead to various complications, such as compartment syndrome and acute kidney injury[27]. The compartment syndrome develops with increased pressure within the osseofascial space, leading to microvascular compromise and tissue injury[28]. Interestingly, our study showed that delayed amputation was associated with a higher incidence of rhabdomyolysis and compartment syndrome in the injured extremities, and tissue necrosis on the stumps and osteomyelitis were more common. Half of the patients in the delayed amputation group experienced rhabdomyolysis, whereas none in the early amputation group experienced compartment syndrome.

In the present study, there was no association between delayed amputation and mortality; however, delayed amputation increased the overall incidence of trauma-related complications. Although not statistically significant, the incidence of renal replacement therapy was higher in the delayed amputation group, which may have been due to the relatively increased incidence of rhabdomyolysis. Delayed amputation is also associated with the occurrence of decubitus ulcers. Applying plaster splints, immobilization of patients, and poor tissue perfusion results in medical conditions that could be important etiologies of decubitus ulcers, prolonging hospital length of stay and causing financial burden[29,30]. In addition, despite being statistically insignificant, the incidences of urinary tract infection and severe sepsis were relatively higher in the delayed amputation group in our study.

Our study also revealed a tendency toward increased hospital LOS and mechanical ventilator days in the delayed amputation group, indicating that patients with delayed amputation may require a longer period for additional surgeries and handling of complications. When we stratified the results according to ISS, we observed a similar pattern for ISS < 15, whereas early amputation did not have an advantage for ICU LOS and hospital LOS for ISS > 15. Tillmann et al. reported that the limb salvage strategy for mangled lower extremity patients could

Variables	Early amputation (n = 132)	Delayed amputation (n = 67)	*p*-value
Timing of definitive amputation, mean ± SD (days)	0.2 ± 0.7	11.9 ± 7.3	< 0.001
Total numbers of operation	2.5 ± 1.8	4.4 ± 3.0	< 0.001
PRC transfusion, n (%)	118 (89.4)	53 (79.1)	0.079
Transfusion within 24 h, median (IQR)	8 (4,15)	5 (3,15)	0.137
Massive transfusion[£], n (%)	72 (54.5)	22 (32.8)	0.004
Other orthopedic injury, n (%)	79 (59.8)	21 (31.3)	< 0.001
Ipsilateral fractures above amputation level, n (%)	27 (20.5)	24 (35.8)	0.019
Vascular procedure to ipsilateral leg, n (%)	14 (10.6)	18 (26.9)	0.003
Thrombectomy only	1 (7.1)	1 (5.6)	
Reconstruction	4 (28.6)	12 (66.7)	
Vessel ligation	9 (64.3)	5 (27.8)	
Open amputation, n (%)	15 (11.4)	6 (9)	0.601
Re-amputation, n (%)	26 (19.7)	7 (10.4)	0.097
Predicted amputation level, n (%)			
Transtarsal	2 (1.5)	1 (1.5)	
Below knee	54 (40.9)	39 (58.2)	
Through knee	27 (20.5)	13 (19.4)	0.112
Above knee	47 (35.6)	14 (20.9)	
Hip	2 (1.5)	0 (0)	
Final amputation level, n (%)			
Below knee	51 (38.6)	25 (37.3)	
Through knee	20 (15.2)	13 (19.4)	0.703
Above knee	56 (42.4)	25 (37.3)	
Hip	5 (3.8)	4 (6)	
Stump complication, n (%)	71 (53.8)	35 (52.2)	0.836
Deep SSI	24 (18.2)	15 (22.4)	0.480
Superficial SSI	2 (1.5)	0 (0)	0.551
Dehiscence/wound breakdown	3 (2.3)	4 (6)	0.228
Tissue necrosis	58 (43.9)	17 (25.4)	0.011
Hematoma	3 (2.3)	5 (7.5)	0.122

Table 3. Procedures, and complications related to lower extremity amputation. SD, standard deviation: PRC, packed red cells; SSI, surgical site infection; IQR, interquartile ranges; £, Defined as transfusion of ≥ 10 units of PRC within 24 h or 4 units of RBC in 4 h.



Variables	Early amputation (n=132)	Delayed amputation (n=67)	*p-value*
Comparison of the final amputation level to the predicted level, n (%)			*<0.001*
Identical	113 (85.6)	43 (64.2)	
Changed to more proximal level	19 (14.4)	14 (35.8)	

Fig. 3. Comparison of the final amputation level to the predicted level.

Variables	Early amputation (n = 132)	Delayed amputation (n = 67)	p-value
30-day mortality, n (%)	7 (5.3)	0 (0)	0.098
Hospital disposition, n (%)			
Death	11 (8.3)	1 (1.5)	0.070
Inpatient rehab	93 (70.5)	56 (83.6)	
Home with or without home care	28 (21.2)	10 (14.9)	
Received mechanical ventilation, n (%)	87 (65.9)	39 (58.2)	0.287
Mode of ambulation at discharge			
Crutches	22 (18.2)	10 (15.2)	0.828
Rolling walker	1 (0.8)	0 (0)	
Wheelchair	93 (76.9)	52 (78.8)	
Bed rest	5 (4.1)	4 (6.1)	
Prosthetic use, n (%)			
Prosthetic use	77 (64.2)	43 (66.2)	0.563
Follow up loss	30 (25)	18 (27.7)	
Rhabdomyolysis, n (%)	50 (38.2)	37 (55.2)	0.022
Complications related to trauma, n (%)	51 (38.6)	40 (59.7)	0.005
AKI, n (%)	9 (6.8)	5 (7.5)	> 0.999
ARDS, n(%)	4 (3)	4 (6)	0.446
Cardiac arrest, n(%)	4 (3)	5 (7.5)	0.167
Decubitus ulcer, n (%)	12 (9.1)	16 (23.9)	0.005
Deep SSI, n (%)[a]	8 (6.1)	8 (11.9)	0.149
Superficial SSI, n (%)[a]	2 (1.5)	2 (3)	0.604
Compartment syndrome, n (%)[b]	0 (0)	9 (13.4)	< 0.001
DVT, n (%)	12 (9.1)	7 (10.4)	0.149
Flap failure, n (%)	0 (0)	2 (3)	0.112
VAP, n (%)	19 (14.4)	11 (16.4)	0.706
PTE, n (%)	6 (4.5)	3 (4.5)	> 0.999
Organ/Space surgical infection, n (%)[a]	0 (0)	1 (1.5)	0.337
Stroke, n (%)	0 (0)	2 (3)	0.112
Unplanned intubation, n (%)	2 (1.5)	3 (4.5)	0.338
Urinary tract infection, n (%)	3 (2.3)	6 (9.0)	0.063
CRABSI, n (%)	2 (1.5)	1 (1.5)	> 0.999
Osteomyelitis, n (%)[b]	1 (0.8)	5 (7.5)	0.017
Unplanned return to OR, n (%)	10 (7.6)	9 (13.4)	0.184
Unplanned return to the ICU, n (%)	7 (5.3)	5 (7.5)	0.543
Severe sepsis, n (%)	7 (5.3)	7 (10.4)	0.240
Renal replacement therapy, n (%)	5 (3.8)	6 (9.0)	0.187

Table 4. Patient outcomes. AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; SSI, surgical site infection; DVT, deep vein thrombosis; VAP, ventilator associated injury; PTE, pulmonary thromboembolism; CRABSI, catheter related blood stream infection; OR, operation room; ICU, intensive care unit. [a]Excluding the amputation site. [b]Data related to the lower extremity amputation site only.

elevate the risk of AKI and prolong ICU and hospital stays; however, it did not affect mortality for multisystem injuries[6]. Although delayed amputation costs 2.5 times more than primary amputation, according to Bondurant et al., this treatment strategy could provide additional time for patients and families with failed limb reconstruction to provide opportunities for psychological preparation, leading to satisfactory outcomes[31–34].

Shorter residual limbs are associated with physiological strain. Therefore, adequate soft tissue and stump lengths are essential for better functional outcomes. The selection of the anatomical level for amputation depends on the patient's clinical status, including hemodynamics, vascular condition, soft tissue injury, and activity level[12]. Unfortunately, clinical decisions may not always be appropriate; re-amputation to a higher level is required for some patients with trauma, which can lead to worsening clinical and functional outcomes. Overall, 10.5% of patients required re-amputation in the present study due to trauma-related complications during the initial admission. There is a lack of studies on the re-amputation rate for mangled extremity injuries; it is surprising considering approximately 19% ipsilateral and contralateral re-amputation rates for patients with diabetes at one year[35]. Ebskov et al. suggested that ipsilateral re-amputation results from an inappropriate choice of the initial amputation level or postoperative complications, including infection[11]. These serial processes could be associated with changes in the amputation level in patients with delayed amputation by accelerating secondary damage to the soft tissue of the injured limb. Interestingly, our study demonstrated that the presence of deep

(a) Entire population	Early amputation (n = 132)	Delayed amputation (n = 67)	*p* value
ICU LOS, days, median (IQR)	4 (2, 9)	7 (3, 14)	0.060
Ventilator days, median (IQR)	3 (1, 8)	5 (2, 13.5)	0.033
Hospital LOS, days, median (IQR)	37.5 (18, 55.3)	48 (26.5, 70.5)	0.005
(b) ISS < 15	**Early amputation (n = 39)**	**Delayed amputation (n = 27)**	***P* value**
ICU LOS, days, median (IQR)	3 (2, 4)	4 (2, 8.5)	0.097
Ventilator days, median (IQR)[a]	1 (1, 2)[a]	5 (4.3, 12.5)[b]	< 0.001
Hospital LOS, days, median (IQR)	21 (14.5, 35.5)	42 (25.5, 63)	< 0.001
(c) ISS ≥ 15	**Early amputation (n = 93)**	**Delayed amputation (n = 40)**	***P* value**
ICU LOS, days, median (IQR)	6 (3, 13)	7.5 (3.8, 14.3)	0.114
Ventilator days, median (IQR)	4 (1, 13)[a]	5 (2, 13)[b]	0.416
Hospital LOS, days, median (IQR)	44 (20, 66)	49.5 (29.8, 72.5)	0.102

Table 5. ICU LOS, MV days and Hospital LOS. CI, Confidence Interval; ICU, intensive care unit; LOS, length of stay; IQR, Interquartile range. (b): [a]n = 20; [b]n = 10 (c): [a]n = 67; [b]n = 29

Variables	Odds ratio	95% CI	*p*-value
Underlying disease	2.26	1.07–4.79	0.032
Presentation at the hospital 6 h after trauma	2.04	0.78–5.20	0.138
Delayed amputation (48 h)	2.95	1.38–6.42	0.006
Stump Deep SSI	3.56	1.58–8.07	0.002

Table 6. Risk factors for changes at a more proximal amputation level than the predicted level. SSI, surgical site infection;

surgical site infection of stump and delayed amputation could be associated with re-amputation to a higher level, with approximately a threefold higher risk (Table 6).

Our study had several strengths. We included a relatively large number of patients with severe multiple trauma compared to previous studies that considered ISS. Therefore, we hope that our study will help in the decision-making process for patients with severe polytrauma in level 1 or level 2 trauma centers. In addition, this study included only patients who were severely injured because of blunt trauma. Trauma specialists, including well-trained trauma surgeons, especially cardiovascular surgeons, were responsible for the primary survey and included initial resuscitation. Orthopedic trauma surgeons are also available for trauma resuscitation. Therefore, errors related to ineffective communication among specialties or unnecessary delays due to inappropriate procedures or imaging studies can be minimized[18].

However, this study had several limitations due to the data's retrospective nature. First, this was a single-center retrospective study; therefore, the generalizability of our results may be limited. Second, although this study was retrospective in design, assessing the predicted amputation level was difficult. To overcome this limitation, we retrospectively reviewed four trauma specialists based on all available clinical information, including EMR, clinical photographs, and CT angiography. In our trauma center, clinical photographs are routinely taken for all trauma patients as part of recording clinical information in the resuscitation area at the time of arrival. Third, we excluded patients who died within 48 h of hospital presentation because the cause of death could be other severe injuries such as traumatic brain injury or abdominal trauma. Fourth, our findings are solely representative of civilian trauma; therefore, the results may not be generalizable to combat-inflicted injuries. Finally, as long-term follow-up is not available in tertiary hospitals because of the healthcare delivery system in South Korea, we could not assess functional outcome scores using Lower Extremity Functional Scale. Despite several limitations, this was the first study to assess the risk factors for changing the final amputation level. We found that delayed amputation and deep SSI on the stump could be important risk factors.

Conclusion
In our study, delayed amputation may have been a risk factor for shorter limb stumps due to re-amputation. Although we found no difference in overall mortality, delayed amputation to limb salvage could result in more trauma-related complications and prolonged hospital and ICU LOS. However, owing to the limitations of retrospective studies, there is a need for future multicenter prospective research on this topic. We expect our results to provide useful information for managing lower extremity injuries.

Data availability
The datasets used and analyzed during the current study available from the corresponding author on reasonable request.

Received: 22 January 2024; Accepted: 6 March 2025
Published online: 10 March 2025

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Author contributions

J. K., W. C.[1] (Wanseon Choi), W. C.[2] (Wontae Cho) and J. M. were involved in the conception and design of the study. All authors performed data collection and analysis. J. K. and J. M. performed interpretation, writing the manuscript, and critical revision. All authors approved the final manuscript.

Declarations

Competing interests
The authors declare no competing interests.

Additional information
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