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Limb-Salvage Outcomes of Arterial Repair Beyond Time Limit at Different Lower-Extremity Injury Sites

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Manuscript Preparation E
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Background: The purpose of this study was to analyze the outcomes of revascularization exceeding 12 h after arterial injury at different sites of the lower extremity.

Materal/Methods: From January 2009 to April 2017, 58 patients with 58 lower-limb arterial injuries who underwent revascularization over 12 h after trauma were included in our study. Outcomes measured, including mortality, amputation, complications, and other parameters (gait, length discrepancy, the range of movement of the knee and ankle joint, and muscle wasting) were analyzed.

Results: External iliac artery injury (EIAI) or femoral artery injury (FAI) was affected in 4 patients, superficial femoral artery injury (SFAI) in 18, and popliteal artery injury (PAI) (including proximal gastrocnemius muscle vascular (PGMV) and proximal gastrocnemius muscle vascular [PGMV]) in 36. The median time of arterial injury was 72 h (interquartile range, 59.5). No mortality was found. Amputations were performed in 16 patients due to non-viable limbs, progressing infection, or muscle necrosis. All patients were followed up (median, 52 months; interquartile range, 5.5). Of the 42 limb-salvage patients, most had a limp, muscle wasting, or ankle and knee dysfunctions, and 26 patients with knee or ankle dysfunction underwent secondary surgery.

Conclusions: Although limited recanalization of blood vessels may lead to limb complications or amputations over time, the high success rate of limb salvage still merits the surgeon's best efforts.

MeSH Keywords: **Amputation • Femoral Artery • Iliac Artery • Leg Injuries • Popliteal Artery**

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Background

The management of lower-extremity trauma remains challenging and is highly associated with limb loss [1]. Amputation following lower-extremity trauma has been variously ascribed to extent of soft tissue damage or bone defect, ischemia-related vascular injuries, and development of compartment syndrome [2–4]. Among many associated factors, traumatic artery injury presents the most significant threat to limb survival, with amputation rates reported as high as 70% [5], particularly in resource-limited developing countries such as China, where amputation rates may be even higher. Overwhelmingly, saving the patient's life and improving the rate of limb salvage are the goals [6]. Prior studies have documented factors that affect limb salvage after arterial injury [7], of which the duration of ischemia is the most influential [8,9]. The golden time for arterial repair, widely accepted by scholars and researchers, is less than 6 h [10]. Hence, essential management for substantial improvement in limb salvage rates includes attention to minimizing delayed repair of vascular injury [11]. This is somewhat low given the fact that most of the revascularizations were done after the golden period had passed [12]. Due to technical and medical limitations or delays in diagnosis at local primary hospitals, most patients were transferred to tertiary care centers for revascularization later than 6 h after injury [13].

In addition to a higher amputation rate, delayed revascularization is associated with a poor prognosis for sensory and motor function [14]. Nonetheless, recent studies suggest that delayed intervention (later than 6 h) also presented acceptable outcomes [15,16]. Silva et al. [15] studied the retention of limb motor function after vascular time-out reconstruction (mean, 10 h) in selected cases. However, the reasons why muscles remain viable after prolonged ischemia have been largely unclear. In our institution, we found that similar traumatic violence, but in different sites of the lower extremity, resulted in different outcomes (e.g., amputation rate, limb function, limb deformity). For example, some patients with vascular injury still maintained muscle viability for 2-3 days or even 1 week, while others developed more severe muscle necrosis within 10 h. To the best of our knowledge, there have been few studies exploring how limbs undergoing revascularization with prolonged ischemia could still survive.

In the present study, we evaluated the efficacy of delayed revascularization (beyond 12 h) in patients with arterial injury and attempted to better understand the associated factors.

Material and Methods

This retrospective study was performed in the Trauma and Microsurgery Center, Wuhan University Zhongnan Hospital. The Institutional Review Board approved this study and waived the requirement of patient informed consent. Patients with lower-extremity arterial injury enrolled in this study met the following criteria: 1) patients with lower-extremity arterial injury exceeding 12 h; 2) imaging examination showed major vascular injury, but with collateral circulation; and 3) intraoperative exploration revealed vascular damage, but with a possibility of limb salvage. The exclusion criteria were: 1) amputation without vascular repair; 2) arterial injury in less than 12 h; 3) soft tissue or bone defect too extensive to repair; and 4) patients over 60 years of age with severe atherosclerosis.

From January 2009 to April 2017, 58 patients (36 males and 22 females, mean age 36.6 years, range, 20–65 years) with 58 lower-extremity vascular injuries were enrolled in the study. Vital signs and injured limb assessments were performed prior to limb salvage. The affected limb was evaluated using the Mangled Extremity Severity Score (MESS) [17]. Limbs showing mottling were highly suspected to have necrosis; nonetheless, the judgment was further confirmed by intraoperative exploration. When vascular injury was suspected and vital signs were stable, Doppler ultrasonography or computed tomography scan angiography (CTA) were conducted, especially in patients with Arterial Pressure Index [18] (API Doppler arterial pressure distal to injury/Doppler arterial pressure in uninvolved upper extremity) of 0.9 or less. **Figure 1** shows the algorithm for evaluation of patients with possible vascular injury. Cases with undoubted artery injuries were candidates for surgical repair without further evaluation [19]. Intraoperatively, when the muscle contracted to the electrocautery, demonstrating good muscle viability, or if the muscle did not response to the electrocautery, but oozed blood, revascularization was considered. However, if the muscles showed no response or slight bleeding in response to the electrocautery, amputation was imperative.

Primary amputation was required if a non-viable limb was found within 2 weeks of the surgery. In addition, secondary amputation was necessary in one of the following occurred: 1) toxin absorption, crisis of life, and dialysis not effective, 2) systemic or local progressive infection; or 3) irreparable soft-tissue or bone defects after debridement.

After successful limb salvage, all patients were followed up. Outcomes, including mortality, amputation, complications, and sensory and motor functions, were recorded.

Statistical analysis

Outcomes were compared across 3 principal aspects: (1) vascular repair sites and mechanisms, (2) primary and secondary amputation, and (3) long-term functions of the affected limb. Data were analyzed using SPSS 19.0 statistical software. Independent-samples *t* test or one-way ANOVA was used for

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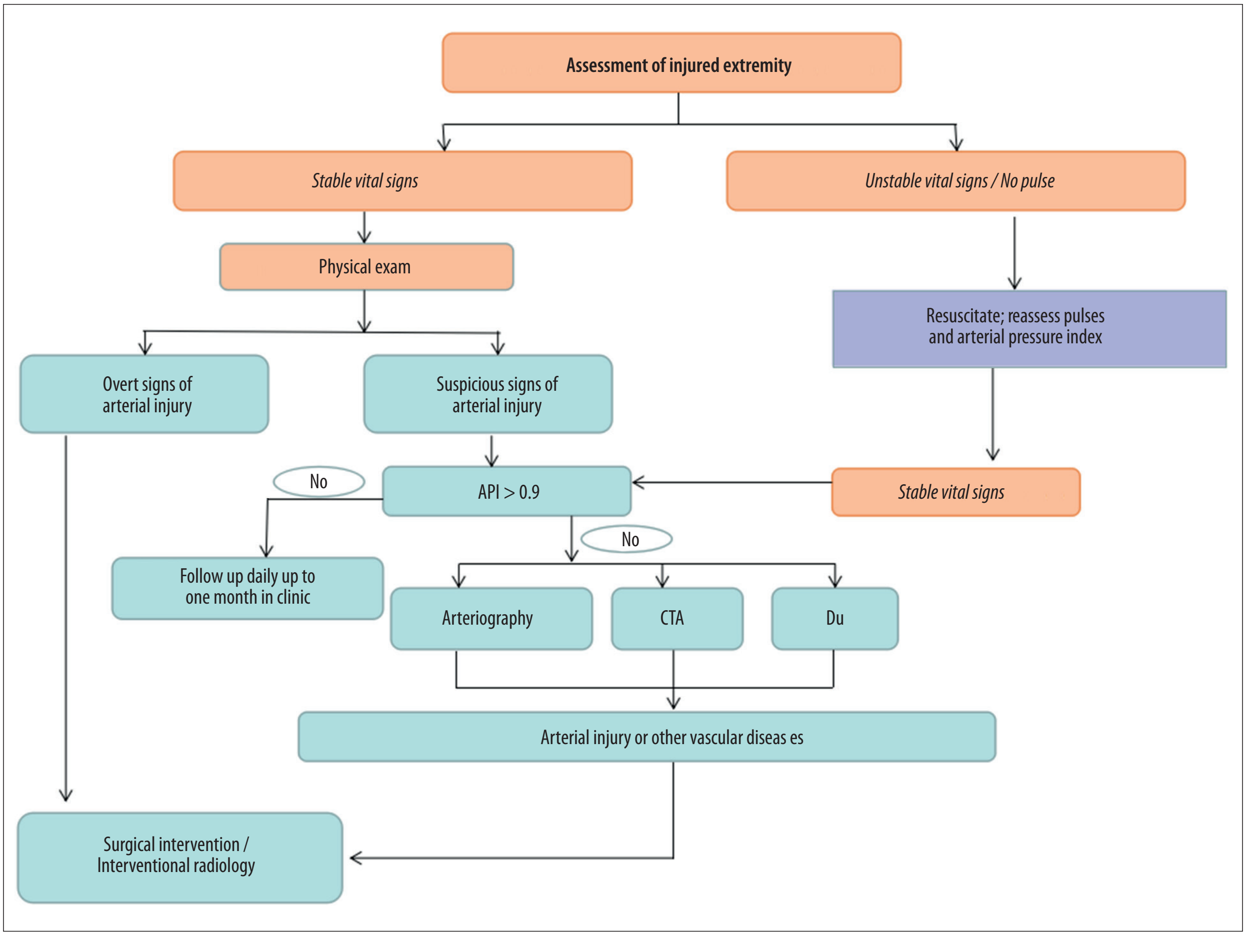

Figure 1. Algorithm for evaluation of patient with possible vascular injury. DU – Doppler ultrasonography; API – Doppler arterial pressure distal to injury/Doppler arterial pressure in uninvolved upper extremity.

comparison of variables; a *P* value of <0.05 was considered a statistically significant difference.

Results

All 58 patients were diagnosed with artery injuries accompanied by prolonged ischemia at least 12 h after trauma (median, 72 h; interquartile range, 59.5). The external iliac artery injury (EIAI) and femoral artery injury (FAI) were involved in 4 patients (6.90%), superficial femoral artery injury (SFAI) in 18 patients (31.03%), and popliteal artery injury (PAI) in 36 patients (62.07%). In the PAI group, 15 cases of arterial injury occurred in the proximal part of the gastrocnemius muscle vasculature (PGMV) and 21 cases of arterial injury occurred in the distal part of the gastrocnemius muscle vasculature (DGMV) (**Figure 2**). Mechanisms of injury were categorized as blunt trauma in 79.31%, stab wound in 15.52%, and gunshot wound in 5.17%. No significant differences existed between these groups (*P*>0.05) (**Table 1**). Most patients (87.93%) had concomitant fractures, nerve, or (and) deep vein injuries. There were no statistically significant differences among the groups of patients with concomitant injury (*P*>0.05).

There was no pre- or post-operative mortality. Three patients (1 SFAI, 1 PGMVI, and 1 DGMVI) presented with non-viable limbs and underwent primary amputation. Primary amputation was not significantly different between the 4 groups (*P*>0.05). Secondary amputation occurred in 11 patients (24.14%), including 6 patients in the PGMVI group and 1 patient in the DGMVI group because of infection and muscle necrosis, respectively, 2 cases in the EIAI or FAI group due to muscle necrosis, and 2 cases in the SFAI group owing to progressing infection. The secondary amputation rate in the DGMVI group was significantly lower than in the other 3 groups (*P*<0.05).

Among the 44 patients with limb salvage, 26 had related complications, including 6 patients (15.38%) with chronic osteomyelitis, 3 patients (7.69%) with nonunion, 10 patients with soft-tissue infection, and 7 patients with muscle necrosis, respectively. Compared with the other 3 groups, the DGMV group had the lowest complication rate (*P*<0.05) (**Table 1**).

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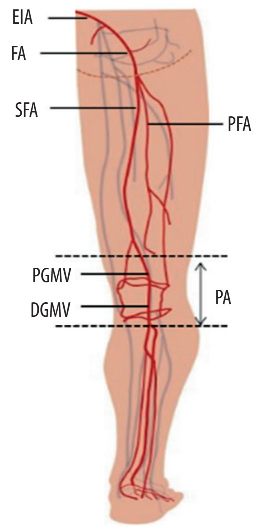

Figure 2. Schematic illustration of vascular injury sites in lower extremity. EIA – extemal iliac artery; FA – femoral artery; PFA – profounda femoral artery; SFA – superficial femoral artery; PA – popliteal artery; PGMV – proximal gastrocnemius muscle vascular; DGMV – distal gastrocnemius muscle vascular.

In the long-term follow-up, the sensory and motor functions of most patients with limb salvage were seriously affected (**Table 2**). Motor dysfunctions, including limp, length discrepancy, RMK, RMA, and muscle wasting, were noted in all 4 groups. Except that KRM in DGMVI group was superior to the other 3 groups ($P<0.05$), there was no significant difference in other motor deficits among the 4 groups ($P>0.05$). Sensory dysfunctions were observed in all 4 groups, and the difference was not statistically significant ($P>0.05$).

Finally, for patients with partial knee or ankle joint loss due to muscle necrosis or fibrosis, further surgeries were required by 2 patients in the EIAI (**Figure 3**) or FAI group, 3 patients in the SFAI group (**Figure 4**), 4 patients in the PGMVI group, and 8 patients in the DGMVI group (**Figure 5**).

Discussion

Based on the replantation time of the amputated limb, the optimal golden time of revascularization was less than 6 h [12,20]. Unlike amputated limbs, which may resist up to a typical 6 h of ischemia because of complete disruption of blood supply, limbs with arterial injuries could survive longer due to collateral circulation. However, prolonged ischemia of an injured limb (longer than 6 h) is associated with a 4-fold increased risk of secondary amputation [10]. Therefore, whether revascularization is worth more than 6 h after arterial injury has been a controversial issue. Prior studies have reported that limbs with revascularization later than 24 h (or even one week) after arterial injury could be salvaged successfully [12,21], but the reasons why the limbs that underwent revascularization with prolonged ischemia time can survive is less well understood.

After the trunk vascular injury, the tissue blood supply is seriously reduced and insufficient, which makes the tissue enter into the ischemic tolerance period. At this point, collateral circulation begins to play a critical role in pathophysiological processes, providing a small amount of blood supply to tissue metabolism. In other words, collateral circulation, to a certain extent, determines the prospects of limb salvage in patients with delayed revascularization after vascular injury. In the lower extremity, the abundance of collateral branches varies in different anatomical sites, which indicates that delayed vascular repair after trunk vascular injury at different anatomical sites may present distinct limb salvage effects. Perkins et al. [8] identified the anatomical site of the arterial injury as a risk factor for amputation after a meta-analysis reviewing the prognostic factors for surgical repair of lower-extremity vascular trauma. In our study, we classified the vascular injury of lower limbs according to the anatomic sites to explore the limb-salvage outcomes after revascularization for more than 12 h.

Accordingly, we found that compared with EIAI, FAI, and PGMVI, SFAI and DGMVI presented encouraging limb salvage outcomes with lower rates of primary and secondary amputation, which is consistent with the literature [22,23] Traupe et al. [24] quantified function of collateral arteries by balloon occlusion of the superficial femoral artery, and concluded that the superficial femoral artery has abundant collateral circulation, which plays a key role in the pathophysiological process of limb ischemia. Indeed, the superficial femoral artery and the profunda femoris artery form a collateral bed between the ileo-femoral segment and the popliteal artery. Consequently, among patients with SFAI lasting more than 12 h, the majority (94.44%) had successful revascularization and avoided primary amputation. Due to anatomic factors of the thigh, prophylactic and therapeutic osteofascial operations are generally not required, which reduces the incidence of complications such as infection and osteomyelitis, resulting in a low rate (11.11%) of secondary amputation. Therefore, compared with popliteal artery injury, superficial femoral artery injury has the innate advantage of limb salvage. Inevitably, superficial femoral arterial injury was followed by the disruption of blood supply to the calf muscles. So, in our study, as the result of the anterior and posterior muscles ischemic necrosis or nerve injury, some patients lost most of their knee and ankle joint functions, and developed clubfoot deformity.

In contrast, the occurrence of limb salvage effects like SFAI in EIAI or FAI seems relatively rare. As a consequence of the

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Table 1. Demographic data of different vascular injure site.

Variables	EIAI or FAI (N=4)	SFAI (N=18)	PAI: PGMVI (N=15)	PAI: DGMVI (N=21)	Sum (N=58)	P value
Age (y)	21.8±10.5	36.9±12.6	38.9±13.4	37.6±11.0	36.6±12.5	0.096
M: F	3: 1	9: 9	11: 4	13: 8	36: 22	0.531
Smoker	2	5	4	7	16	0.814
CA	1	3	3	5	12	0.950
Comorbidities						
Diabetes	0	0	1	0	1	0.405
Hypertension	0	2	3	1	6	0.443
VI	0	0	0	1	1	0.616
CVDs	0	0	1	2	3	0.556
Atherosclerosis	0	0	2	1	3	0.356
Mechanism of injury						
Blunt wound	4	11	12	19	46 (79.31%)	0.342
Stab wound	0	5	2	2	9 (15.52%)	
Gunshot wound	0	2	1	0	3 (5.17%)	
MESS	10–12 10.8±1.0	4–12 7.1±2.4	4–13 8.4±2.5	5–12 8.3±2.1	4–13 8.1±2.4	0.033
Concomitant injuries						
Multiple arterial injury	0	2	3	4	9	0.698
Vein injury	2	7	6	9	24	0.978
Nerve injury	2	5	4	6	16	0.999
Bone fracture	3	16	13	19	51	0.850
Duration of Ischemia (h)	12–27 19.2±7.4	28–149 75.8±37.9	24–108 65.7±28.3	24–165 83.2±36.4	12–165 72.0±36.7	0.007
Arterial repair						
Saphenous vein graft	4	12	9	10	35 (60.3%)	0.226
End-to-end	0	6	6	11	23 (39.7%)	
Outcome						
Mortality	0	0	0	0	0	
Amputation						
Primary amputation	0	1 (5.56%)	1 (6.67%)	1 (4.76%)	3 (5.17%)	0.96
Secondary amputation	2 (50.00%)	2 (11.11%)	6 (40.00%)	1 (4.76%)	11 (18.97%)	0.01
Complications						
Soft tissue infection	0	3	7	0	10	0.005
Muscle necrosis	2	3	0	2	7	
Osteomyelitis	0	0	2	4	6	
Nonunion	1	1	0	1	3	

M – Male; F – Female; CA – chronic alcoholism; VI – venous insufficiency; VI – venous diseases.

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Table 2. Long-term follow-up of limb salvage patients with arterial injury at different sites.

Variables	EIAI or FAI (N=2)	SFAI (N=15)	PAI		P value
			PGMVI (N=8)	DGMVI (N=19)	
Follow-up time (M)	32–122	36–48	46–59	32–63	
Motor dysfunctions					
Limp	1	13	6	16	0.589
Length discrepancy (N/cm)	1/0.5	10/1.13±0.19	5/1.20±0.15	7/1.07±0.10	0.396
RMK (degree)	82.00±5.66	89.93±39.88	80.50±8.26	115.32±2.11	0.027
RMA (degree)	12.50±6.61	25.33±15.30	16.88±16.62	24.79±15.89	0.224
Muscle wasting (cm)	1.20±0.28	1.09±0.76	1.25±0.70	0.94±0.73	0.313
Sensory dysfunctions	2	3	3	3	0.052

KRM – range of motion of knee joint; ARM – range of motion of ankle.

absence of corresponding collateral circulation in the proximal femoral artery and the external iliac artery, high amputation rates, especially in secondary amputation, occurred in our series. Accordingly, in 4 EIAI or FAI patients, 2 had amputation due to massive toxin absorption, with no remission on dialysis. Although the other 2 patients had their limbs salvaged after hemodialysis and multiple debridements, their knee and ankle functions were almost completely lost**.** Hence, in this scenario, revascularization should be performed as early as possible, especially where there is little collateral circulation.

Among all vascular injuries in the lower limbs, popliteal artery injury is considered to be the most serious threat to limb survival [25]. In our study, according to the anatomical positions between the popliteal artery and the gastrocnemius, popliteal artery injuries were classified into PGMVI and DGMVI. Since the popliteal artery has relatively few branching loops before entering the gastrocnemius, popliteal artery injury in PGMV has significant and severe symptoms of lower-limb ischemia. If the PGMVI were missed or delayed in repair, the likelihood of amputation would be very high. In most cases, popliteal artery injury, which often resulted from high-energy injury, is frequently associated with the knee fracture, dislocations, and severe tissue swelling. In this context, anastomotic vessels are prone to embolize again. Moreover, most patients had to undergo prophylactic and therapeutic fasciotomy, which can increase the risk of osteomyelitis and aggravating infections. Logically, it can be assumed that the secondary amputation rate increased because of the above complications, and this may account for the high amputation rates in patients with PGMVI. However, due to the abundant collateral circulation of the popliteal artery in the gastrocnemius segment, when the popliteal artery is injured at DGMV, even in the posterior deep muscle, the blood supply is still not completely interrupted. In our study, following vascular anastomosis, the amputation rate (9.52%) in the DGMV group was lower than that in the PGMV group (46.67%), which was attributed to better vascular bed. Moini et al. [25] assessed the outcomes of delayed vascular repair from 3 aspects: motor loss, sensory loss, and muscle viability. They concluded that a high success rate of vascular recanalization and limb salvage would be achieved in the presence of viable gastrocnemius muscle after popliteal artery injury. Jagdish et al. [12] also determined that delayed revascularization after popliteal injury in some cases resulted in improved sensory and motor functions under the condition of gastrocnemius vitality. In our study, due to popliteal artery injury, the posterior tibial muscle had ischemic necrosis, which more or less affected the lower-extremity motor function of patients, such as foot deformity, limp, and limited joint activity.

Several studies have delineated factors affecting sensor functions after vascular injury; time to revascularization is one of the crucial factors [26]. In our series, we observed 4 groups of varying degrees of sensory impairment. Since sensory dysfunction is mainly caused by nerve injury, and some patients had nerve injury on admission, we cannot accurately judge the effect of delayed vascular repair at different sites on sensory function. Therefore, early vascular repair may avoid aggravating sensory dysfunctions.

Additionally, modern techniques have made limb salvage possible, but many people have been skeptical about the long-term disability it brings [27]. Although major advances in medicine have improved the technical capacity to reconstruct severely injured limbs, concurrent development of bioengineering in prosthetics also can provide good function for amputees [28]. Therefore, patients with severe trauma may face the challenge of choosing between amputation and limb salvage. Attempts to save limbs necessitate multiple operations, often resulting in partial or complete loss of functions, which imposes a greater financial and psychological burden on patients. However, some patients still prefer limb salvage because of psychological

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Figure 3. A typical example of delayed repair of EIAI (27 h): A 10-year-old boy sustained a car accident, open pelvic fracture, and extensive avulsion of the abdomen and right thigh. After local hospital debridement, the patient was transferred to our hospital. As a result of intractable hypotension, exploratory surgery was immediately prepared. We found a rupture in the right external iliac artery, and then revascularized the damaged artery using a saphenous vein graft (SVG). After 1 week of dialysis, 4 debridements, and a skin graft, his life and lower limbs were saved. At the 10^{th} year of follow-up, there were many scars in his inguinal region and right thigh (**A**). His motor function was severely impaired, including a maximum knee flexion of 80 degrees (**B**) and a clubfoot deformity (**C**). Achilles tendon release surgery and subtalar-talonavicular joint fusion were performed to correct the deformities (**D**).

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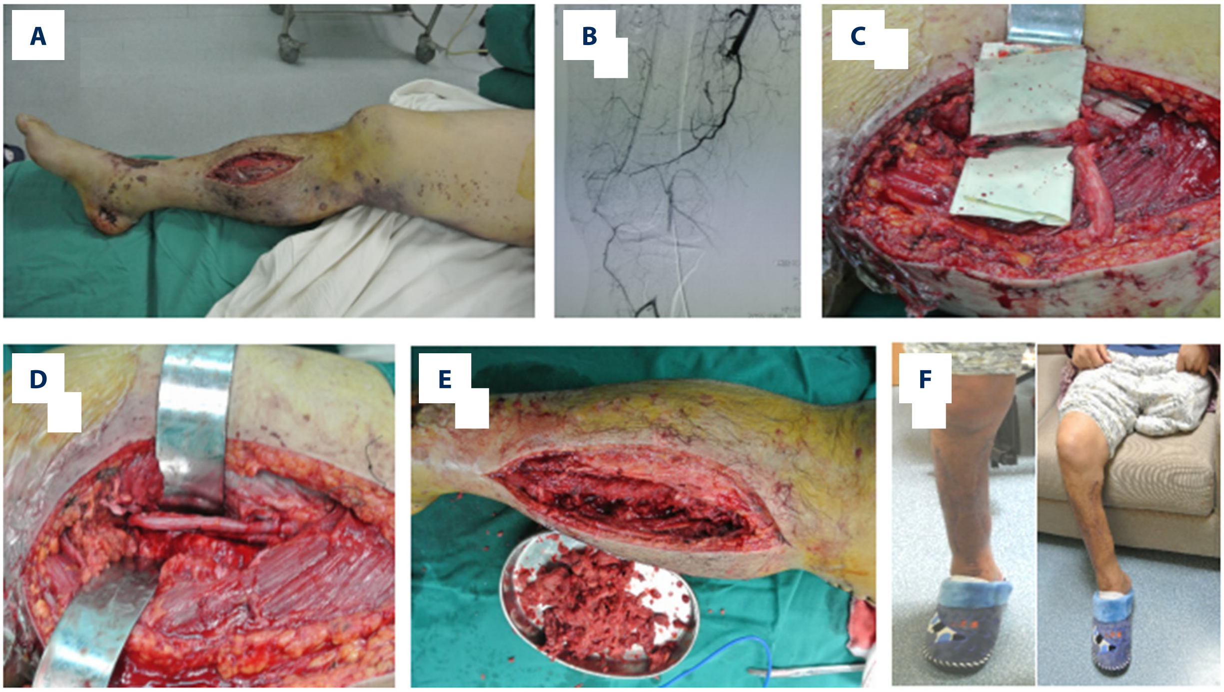

Figure 4. A typical example of delayed repair of SFAI (72 h). A 41-year-old man was struck by a car. In a local hospital, a closed dislocation of his right knee joint was reduced 8 h after the injury and an amputation was performed in his left leg due to the severity of the injury. Three days later, the patient was transferred to our hospital to treat the limb ischemia. A few mottling and some muscle-necrosis wounds were found on his foot (**A**). The angiography demonstrated injury to the superficial femoral artery, but the lateral branches of the deep femoral artery and the anterior and posterior tibial arteries were clearly presented (**B**). Intraoperatively, SFAI with long-segment embolus (**C**) was revascularized by SVG (**D**). After multiple debridements to remove necrotic tissue (**E**), the incision of the decompression of compartment was sutured. Lower extremity follow-up at 32 months showed good ankle and knee functions (**F**).

rejection of prosthetic limbs. Several studies also have reported significant disability following limb salvage of such injuries, with patients often complaining of severe pain while walking, difficulty returning to work, and, in some cases, permanent disability [29,30]. Mitchell et al. [30] observed the outcomes of amputation versus limb salvage following major lower-extremity trauma and found that the functional prognosis of amputees after wearing a prosthesis was better than that of patients with limb salvage. If such patients can return to normal activities after amputation and early postoperative prosthesis, avoiding the sufferings of poor limb function after limb salvage, this is in line with the concept of accelerated rehabilitation. The purpose of surgery is to obtain the best limb function outcome in patients with severe limb injury that is not life threatening. Therefore, amputation and early postoperative prosthesis may be a consideration for lower-extremity vascular injury with poor prognostic function if patients can accept the prosthesis psychologically.

The outcomes of delayed repair of damaged vasculature are closely related to collateral circulation at the sites of vascular injury. Abundant vascular branches could provide the possibility of limb salvage beyond the time limit after arterial injury, but poor sensory and motor function may ultimately still be unavoidable. Therefore, in the face of vascular injury, it is important to complete revascularization as early as possible if limb salvage is planned.

Conclusions

Early diagnosis and timely revascularization are still the basic principles in the treatment of vascular injury. Vascular recanalization beyond the time limit is not necessarily an absolute indication for amputation. In terms of limb salvage, once a lower-limb arterial injury is diagnosed, even delayed revascularization can still be actively considered because of the relatively high success rate. However, considering the unsatisfactory functions of the limb after limb salvage, this is still a dilemma that patients have to face.

Conflict of interest

None.

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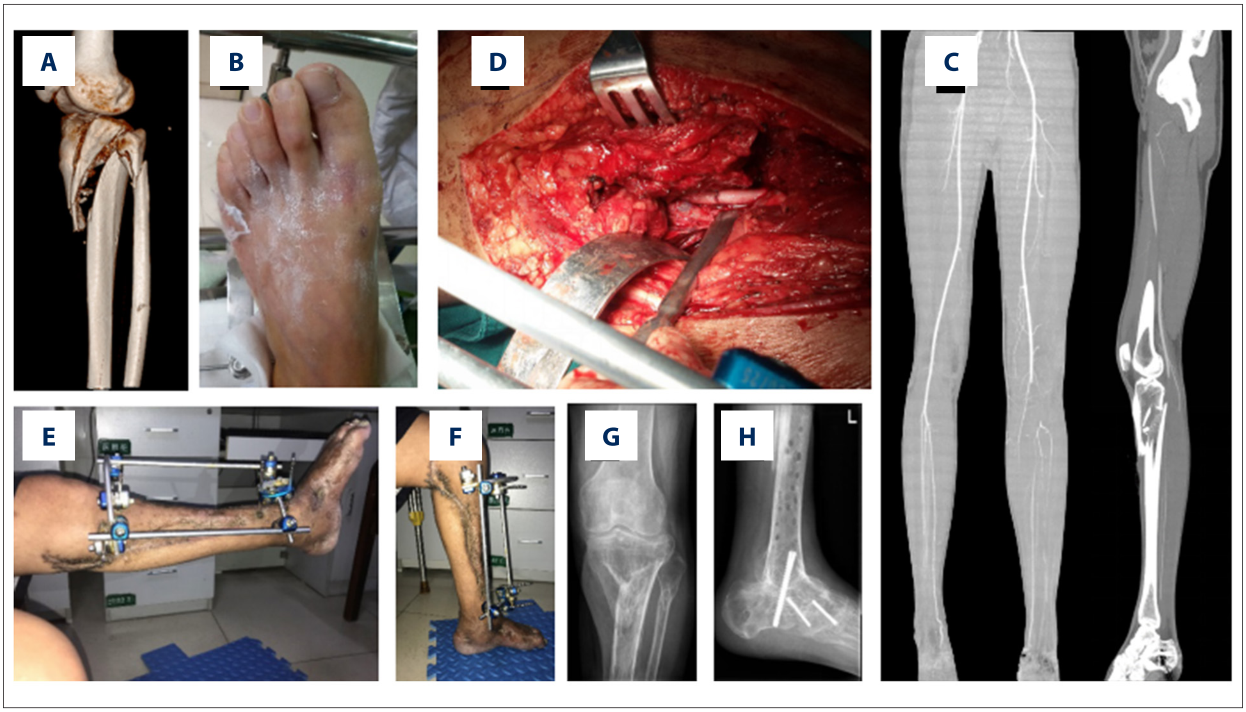

Figure 5. A typical example of delayed repair of PAI at DGMV (60 h). A 41-year-old man was admitted to a local hospital due to a traffic accident, suffering tibia and fibula fractures with a popliteal artery injury of his left leg (**A**). At 2 days after trauma, the patient was transferred to our hospital. The skin color of the left foot seemed normal but there was no pulse (**B**). CTA revealed popliteal artery embolization at DGMV, but the blood signal of the gastrector artery, the calf artery, and the collateral circulation were very clear (**C**). The PAI was confirmed intra- operatively, and revascularization was performed by end-to-end anastomosis (**D**). After external fixation of the fracture, good knee function was presented (**E, F**). However, 1 year after fracture healing, poor ankle function (clubfoot deformity) was corrected by four-joint fusion (**G, H**).

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