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*Original Article / Özgün Makale*

# Histopathological evaluation of the arterial wall damage in upper limb injuries

*Üst ekstremite yaralanmalarında arter duvarı hasarının histopatolojik değerlendirmesi*

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## ABSTRACT

***Background:*** This study aims to evaluate the upper limb crush injuries according to the histopathological changes in the arterial vessel and to report the early and late clinical outcomes.

***Methods:*** We retrospectively analyzed of prospectively collected data of 12 patients (9 males, 3 females; mean age 33.3±11.7 years; range 18 to 57 years) with an upper extremity crush injury between February 2011 and November 2013. All the patients had a Mangled Extremity Severity Score of ≥7 and all had strong signs of vascular injury. Vascular reconstruction was performed after orthopedic stabilization. Digital subtraction angiography was routinely performed after hemodynamic stabilization. During the revascularization procedure, injured arterial vessels were harvested and stored in the formalin solution. The presence of endothelial swelling, intimal thickening, cellular vacuolization in the muscle layer, edema in the tunica media, and extent of the necrosis were evaluated.

***Results:*** Injuries were due to work-related accidents in five patients and motor vehicle accidents in seven patients. Vein graft interposition was performed in all patients (12; 100%). Primary patency rate was 75% and one patient died (30-day mortality 8.3%). Three amputations were performed 12 patients. The median follow-up was 3.2 (range: 2.1 to 3.7) years. Microscopic examination of the specimens collected revealed vascular congestion and thrombus formation, progressive subintimal dissection, and rupture of the membrane of elastic interna.

***Conclusion:*** Our study results suggest performing limb salvage procedures, even if the Mangled Extremity Severity Scores indicate amputation.

***Keywords:*** Crush injury; pathological examination; upper limb revascularization.

## ÖZ

***Amaç:*** Bu çalışmada, üst ekstremite ezilme yaralanmaları arter duvarındaki histopatolojik değişikliklere göre değerlendirildi ve erken ve geç dönem klinik sonuçlar bildirildi.

***Çalışma planı:*** Şubat 2011 - Kasım 2013 tarihleri arasında üst ekstremite ezilme yaralanması olan 12 hastanın (9 erkek, 3 kadın; ort. yaş 33.3±11.7 yıl; dağılım 18-57 yıl) prospektif olarak toplanan verileri retrospektif olarak incelendi. Hastaların tümünün Ezilmiş Ekstremite Şiddet Skoru ≥7 idi ve tümünde ciddi vasküler yaralanma bulguları vardı. Ortopedik stabilizasyon sonrasında vasküler rekonstrüksiyon yapıldı. Hemodinamik stabilizasyon sonrasında, rutin olarak dijital substraksiyon anjiyografi çekildi. Revaskülarizasyon işlemi sırasında, hasarlı arter damarları çıkarıldı ve formalin solüsyonunda saklandı. Endotelyal şişme, intimal kalınlaşma, kas tabakasındaki hücresel vaküolizasyon, tunika medyadaki ödem ve nekrozun derecesi değerlendirildi.

***Bulgular:*** Yaralanma beş hastada işe bağlı kazalar ve yedi hastada motorlu araç kazaları ile ilişkiliydi. Tüm hastalara ven greft interpozisyonu uygulandı (12; %100). Primer açıklık oranı %75 idi ve bir hasta kaybedildi (30 günlük mortalite %8.3). On iki hastada üç amputasyon yapıldı. Medyan takip süresi 3.2 (dağılım: 2.1-3.7) yıl idi. Alınan örneklerin mikroskopik incelemesinde vasküler konjesyon ve trombüs oluşumu, ilerleyici subintimal diseksiyon ve elastik internanın membranında yırtılma olduğu belirlendi.

***Sonuç:*** Çalışma sonuçlarımız Ezilmiş Ekstremite Şiddet Skoruna göre amputasyon endikasyonu olsa da, ekstremite kurtarma işlemlerinin uygulanmasını önermektedir.

***Anahtar sözcükler:*** Ezilme yaralanması; patolojik değerlendirme; üst ekstremite revaskülarizasyonu.

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Upper limb injuries cause serious problems in terms of functionality. In contrast to penetrating trauma, which is usually characterized by limited damage within a limited area and few accompanying lesions, blunt trauma is more frequently associated with higher energy damage and leads to a significant higher rate of disability. More importantly, injuries may be associated with major organ damages which may lead life-threatening conditions that require urgent interventions.[1,2]

Previous studies have shown that limb salvage or primary amputation are potential treatment options.[2-4] The treatment is usually chosen according to the Mangled Extremity Severity Score (MESS) which is obtained based on the extremity examination on four clinical conditions: skeletal/soft tissue injury, ischemic time, shock, and age.[3,4]

As well, vascular pathology of the injured vessels may also predispose patients for treatment. In trauma patients, vascular injuries are classified as contusion, intimal disruption, puncture, lateral disruption, arteriovenous fistulae and pseudoaneurysms. Nevertheless, the key for arterial injury treatment may be to locate the injured artery precisely and to describe it accurately based on the histopathological characteristics of the arterial wall injury, including vascular congestion and thrombus formation, progressive subintimal dissection, and rupture of the membrane of elastic interna.[3]

In the present study, we aimed to evaluate the histology of the surgically harvested upper extremity injured arteries prior to the intervention and to identify an evidence of trauma which may contribute to crush injury management.

## PATIENTS AND METHODS

Between February 2011 and November 2013, we analyzed the records of prospectively collected data of 12 patients (9 males, 3 females; mean age 33.3±11.7 years; range 18 to 57 years) with an upper extremity crush injury. All specimens were excised during the surgical intervention, and all were fixed in 10% formalin, captured, and examined in detail by a senior pathologist specialized in cardiovascular diseases (U.H.). The study protocol was approved by the Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Committee. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The MESS was used to evaluate the limb damage for considering the treatment algorithm and to evaluate the severity of the injury. All the patients had a MESS of ≥7 and had strong signs of vascular injury such as active hemorrhage, lack of pulse, expanding hematoma, and ischemic symptoms. Therefore, the diagnosis was made only based on clinical examination findings.

All operations were performed under general anesthesia. Surgery was initiated with the plenty of irrigation to remove the foreign materials and removal of devitalized tissue from the healthy tissue. Due to the availability of orthopedic team, in all patients, vascular reconstruction was performed after orthopedic stabilization without any time lost. Digital subtraction angiography (DSA) was routinely examined after hemodynamic stabilization. During the revascularization of the upper limb, the injured arterial vessels were harvested for histopathological examination. Injured arterial vessel materials were stored in the formalin solution. In all patients, nerve injuries were scheduled to repair in the next session. After debridement was completed, the vascular structures exposed were surrounded by the muscle and fascia. Gauze with antibiotic or negative pressure wound therapy was used to assist in wound care and to reduce the infection rate. Vascular injuries were reconstructed with saphenous vein grafts. For the patients with suspected inadequate venous drainage, venous reconstruction was performed.

Data collection included demographic parameters, mechanism of injury, location and type of injury, presence of ischemia, presence of concomitant vein, nerve and/or bone/joint injuries, details of arterial reconstruction and follow-up results (Table 1). The sections of the dissected tissues were sent for histological examination. All paraffin-embedded sections were stained with Hematoxylin-Eosin (Table 2). To evaluate clinical outcome, perioperative mortality (30-day mortality), limb-salvage rate, primary and secondary patency of arterial reconstruction, and early and late vascular reinterventions were considered study endpoints (Table 3).

### Histopathological evaluation

Pathological vessel tissues were re-examined in all patients by the surgeons and pathologist. Microscopically, we evaluated the presence of endothelial swelling, intimal thickening, smooth muscle vacuolization, edema in tunica media and the extent of necrosis. A total damage scoring system reflecting the damage to the vein wall was established as follows: the absence of a pathological finding was scored as 0, while the presence was scored as 1. As an exception, necrosis was scored 0-2 depending on its

**Table 1. Demographic and operative characteristics of the patients**

| Patient | Age/Gender | Level | Nerve damage | Muscle bellies damage | Vein graft | Fasciotomies | Initial repair successful | Muscle necrosis |
|---|---|---|---|---|---|---|---|---|
| 1 | 34/M | UA+RA | MN | 3 | Yes | Yes | Yes | No |
| 2 | 29/M | UA+RA | RN | 4 | Yes | Yes | Yes | Yes |
| 3 | 57/F | BA | MN | 2 | Yes | No | Yes | No |
| 4 | 25/M | UA+RA | MN | 3 | Yes | No | Yes | Yes |
| 5 | 18/M | UA+RA | UN | 3 | Yes | Yes | No | Yes |
| 6 | 43/M | BA | MN | 2 | Yes | Yes | Yes | No |
| 7 | 49/F | UA+RA | UN+MN | 4 | Yes | Yes | No | Yes |
| 8 | 24/M | BA | MN | 2 | Yes | Yes | Yes | No |
| 9 | 21/M | UA+RA | UN | 3 | Yes | Yes | No | Yes |
| 10 | 28/M | BA | MN | 2 | Yes | Yes | Yes | No |
| 11 | 33/F | BA | MN | 4 | Yes | Yes | Yes | Yes |
| 12 | 38/M | UA+RA | MN | 1 | Yes | No | Yes | No |

UA: Ulnar artery; RA: Radial artery; BA: Brachial artery; MN: Median nerve; RN: Radial nerve; UN: Ulnar nerve.

extent, due to its relative importance in the evaluation of tissue damage. Finally, a total damage score was calculated using the sum of scores based on the pathological findings (Table 2).

### Statistical analysis

Statistical analysis was performed using the PASW for Windows version 17.0. software (SPSS Inc., Chicago, IL, USA). Continuous variables were presented in mean ± standard deviation (SD) or median (min-max) values. Categorical variables were presented in number and frequency (%). All p values were two-sided and a p value of ≤0.05 was considered statistically significant.

## RESULTS

Demographic findings are shown in Table 1 and the injury levels and interventions for the patients are listed in Figure 1 and Table 1. Injuries were due to work-related accidents in five patients (41.6%) and motor vehicle accidents in seven patients (58.3%). In seven patients, both the radial and ulnar arteries were injured, while only brachial artery injury was detected in five patients.

Five patients underwent saphenous vein interposition procedure for brachial artery injury. In addition, five had saphenous vein interposition for radial and ulnar artery injuries, and two patients had Y configuration bypass procedure for combined radial and ulnar artery injuries (Figure 1). There was no intraoperative mortality; however, one patient died within one month after a serious traffic accident and upper extremity arterial repair (30-day mortality rate: 8.3%).

Three arterial reconstructions failed postoperatively (primary patency rate: 75%), and these three combined radial and ulnar artery graft occlusions were successfully revised (Cases 5, 7, and 9). The injured vessel, initial procedure, day of revision and type of secondary repair in patients with early occlusions are summarized in Table 3. At the time of discharge, all arterial repairs were patent (secondary patency rate: 100%). Three amputations were performed following surgical revision procedure. After a median follow-up time of 3.2 years (range: 2.1 to 3.7), clinical follow-up data were available in eight (75%) of 11 patients who survived with successful limb salvage initially.

**Table 2. Pathological grade scores as total damage score of the injured arterial vessels**

| Patient | ES | N | EoTM | VoSM | IT | Total |
|---|---|---|---|---|---|---|
| 1 | 1 | 1 | 1 | 1 | 1 | 5 |
| 2 | 0 | 1 | 1 | 1 | 1 | 4 |
| 3 | 1 | 0 | 1 | 1 | 1 | 4 |
| 4 | 1 | 1 | 1 | 1 | 1 | 5 |
| 5 | 1 | 2 | 1 | 1 | 1 | 6 |
| 6 | 1 | 1 | 1 | 1 | 0 | 4 |
| 7 | 1 | 2 | 1 | 1 | 1 | 6 |
| 8 | 1 | 0 | 1 | 1 | 1 | 5 |
| 9 | 1 | 2 | 1 | 0 | 1 | 6 |
| 10 | 1 | 2 | 0 | 1 | 1 | 5 |
| 11 | 1 | 2 | 0 | 1 | 1 | 5 |
| 12 | 1 | 1 | 1 | 0 | 1 | 5 |

Total damage score ranges between 0 to 6. ES: Endothelial swelling-(Absent: 0, Present: 1); N: Necrosis-(Absent: 0, Focal: 1, Widespread: 2); EoTM: Edema of tunica media-(Absent: 0, Present: 1); VoSM: Vacuolization of smooth muscle-(Absent: 0, Present: 1); IT: Intimal thickening-(Absent: 0, Present:1).

**Table 3. Patient outcomes, reinterventions, and total damage scores**

| Patient | Localization | Initial surgery | Day of occlusion | Pathological score | Surgery revision |
|---|---|---|---|---|---|
| 1 | UA+RA | Graft interposition | 0 | 5 | No |
| 2 | UA+RA | Graft interposition | 0 | 4 | No |
| 3 | BA | Graft interposition | 0 | 4 | No |
| 4 | UA+RA | Graft interposition | 0 | 5 | No |
| 5 | UA+RA | Graft interposition | 2 | 6 | Embolectomy |
| 6 | BA | Graft interposition | 0 | 4 | No |
| 7 | UA+RA | Graft interposition | 1 | 6 | Graft interposition |
| 8 | BA | Graft interposition | 0 | 5 | No |
| 9 | UA+RA | Graft interposition | 2 | 6 | Graft interposition |
| 10 | BA | Graft interposition | 0 | 5 | No |
| 11 | BA | Graft interposition | 0 | 5 | No |
| 12 | UA+RA | Graft interposition | 0 | 5 | No |

UA: Ulnar artery; RA: Radial artery; BA: Brachial artery; UN: Ulnar nerve.

Furthermore, DSA was performed to all of the patients in the early postoperative period to evaluate the patency of the anastomosis (Figure 2). In addition, in all patients, viability of tissues and ischemic symptoms were evaluated using Doppler ultrasonography. Three patients had vascular thrombosis at the repair site, and embolectomy procedure was made in one patient and the vessels were re-anastomosed in the remaining two patients. Unfortunately, due to sepsis, wide tissue damage, and limb salvage failure, secondary amputation was made in three patient. The level of amputation was performed at the transhumeral level in this patients.

Moreover, three patients had concomitant injuries. Two of them had chest trauma, while the other had head trauma. All patients were treated in the intensive care unit ranging from 3 to 7 days. During follow-up, vascular surgery, orthopedics, plastic surgery, and physical therapy clinics worked in collaboration with each other. During this period, except one, all patients with successful limb salvage did not undergo secondary amputation.

As the term of crush injury refers to three functional components of the limb, vascular injury is frequently underestimated in the microscopic level. After the assessment of the injured arterial segments, a major damage was observed (Table 2). Microscopic examination of the specimens revealed vascular congestion and thrombus formation, progressive subintimal dissection, and rupture of membrane of elastic interna (Figure 2).

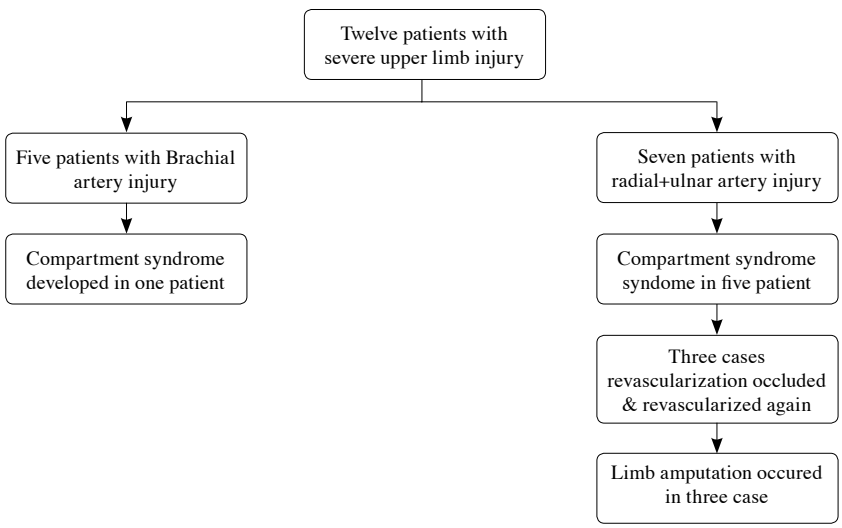


**Figure 1.** Treatment algorithm.

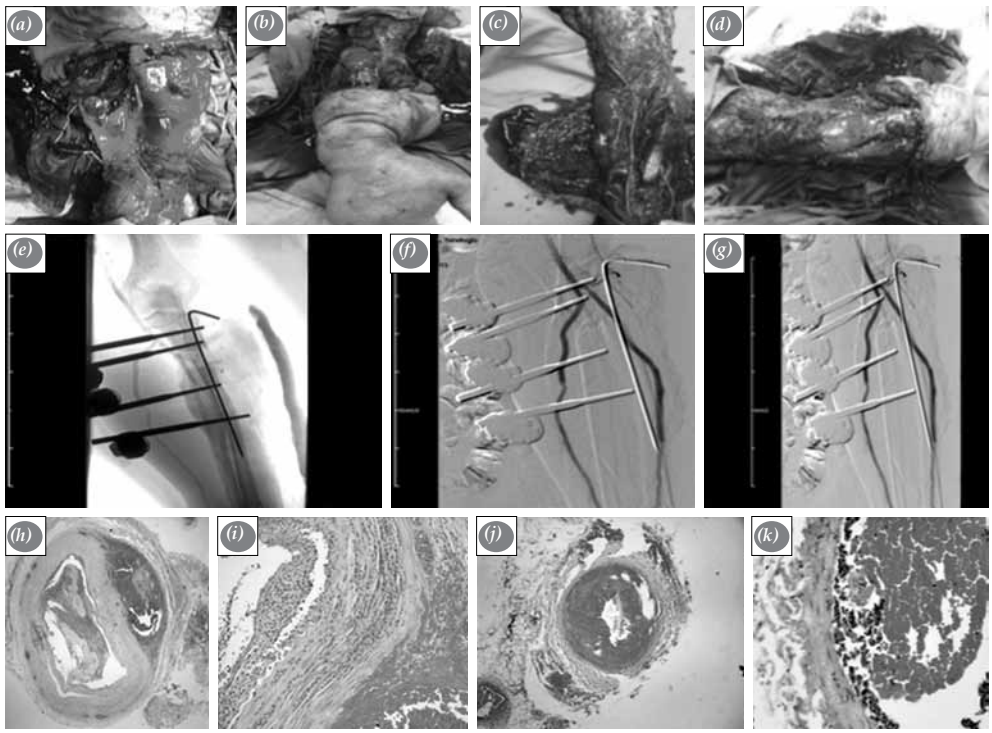


**Figure 2.** A 29-year-old male was admitted to the emergency service after a crush injury occurred in a pressing machine. **(a)** Antecubital region was clearly seen. **(b)** Skin of the right upper limb was stripped. **(c)** Both radial and ulnar arteries were injured. **(d)** The mangled extremity including nerve and soft tissue damage. **(e, f, g)** Stabilization was achieved and DSA revealed patency of the saphenous vein bypasses. **(h)** The injured radial artery was harvested for histopathological examination. Intramural hemorrhage and luminal fibrinous deposits in H-E with ×40 magnified examination with light microscope. **(i)** Dissection of the internal elastic membrane and progression of hemorrhage. **(j)** Harvested ulnar artery demonstrated vascular congestion and a thrombosed lumen (H-E×40). **(k)** Endothelial swelling and intimal vacuolar changes. Dissection of the luminal structure and presence of luminal fibrionuos formation (H-E×400).

## DISCUSSION

The treatment of a mangled extremity is challenging for both the patient and the surgeon. A multidisciplinary approach should be applied for these injuries. The prognosis of mangled extremity injuries are greatly affected by cooperation of the orthopedists, plastic surgeons, and vascular surgeons. Currently, by the help of the advances in microsurgery and technology, limb salvage procedures are encouraged to be made rather than extremity amputation.[4,5] However, unsuccessful limb salvage attempts can cause multiple surgical procedures, prolong the duration of hospitalization, and create a huge financial and psychological distress to the patient.[6] Therefore, patients and their families should be informed about the possible results of unsuccessful limb salvage.

Our study results are consistent with previous reports showing that crush injury is frequently associated with major musculoskeletal injuries.[7] In our cohort, skeletal and nerve injuries were most frequently seen in brachial artery lesions, where all patients had either nerve or orthopedic lesions.

In our routine practice, we commonly use vascular access for exposure of the artery and do not accept a compromise due to other procedures planned. The site of injury is inspected after proximal and distal control of the artery, or an endoluminal balloon occlusion is used. We also avoid the use of intraluminal shunts. Systemic anticoagulation using heparin can be also initiated, if not contraindicated. Alternatively, local instillation of diluted heparin to the artery can be considered. Surgical repair is principally dependent on the severity and extent of damage: Lateral suture patch angioplasty, tension-free end-to-end anastomosis or graft interposition may be considered. In other series with a high

incidence of blunt trauma, the majority of arterial injuries were treated with vein graft interposition rather than primary anastomosis[7] and this was also the method of arterial repair most frequently used in our cohort due to the extensive vessel damage. In principle, the use of autologous vein grafts from lower limbs is preferred. Whenever possible, we also perform a completion arteriography to visualize the arterial run-off and to document the initial technical success of revascularization. Primary nerve repair is preferentially performed at the next session, as our priority is the arterial repair.

In terms of the procedure-related mortality and early limb loss, our study results showed that perioperative mortality due to upper extremity trauma was rare and limb loss after reconstruction could be avoided in most patients. Similar results were also published previously;[7] however, controversial results can be obtained in other studies including patients with irreversible tissue damages. In addition, primary amputation should be considered in case of life-threatening events, and decisions must follow the 'life before limb' rule.

There are significant differences between the approaches to the lower and upper mangled extremities. Functional and aesthetic results of upper limb prostheses are worse, compared to lower limb prostheses. Late functional outcomes of reconstruction procedures of upper extremity was shown to be superior upper limb prosthesis.[7,8] Furthermore, bad hand is more functional than a good prosthesis.[7]

According to the Evidence-based Orthopedic Trauma Working Group, the psychological outcomes are much better in limb salvage group than the amputation group.[7] The collateral circulation in the upper extremities is higher than in the lower extremities, which provides a better ischemic time and more promising results in the upper extremity.

On the other hand, paying attention only to the vascular component in severe upper extremity injuries may be misleading for the decision for limb salvage or primary amputation. Even after performing successful vascular repair in our three patients, amputation was required due to extensive tissue damage and sepsis. Due to extensive tissue damage in the mangled extremity, the most appropriate treatment for vascular injuries would be graft interposition. Embolectomy may cause intimal damage, as the harvested specimens revealed in our study. This procedure may be useless and harmful in the crushed extremity injuries accompanied by acute ischemia.

In our study, we preferred vena saphena magna as an autogenous graft. For both radial and ulnar artery injuries, we performed individual or Y anastomosis for arterial revascularization. Harvesting an adequate length of the greater saphenous vein is not time-consuming and allows adequate debridement of the injured artery and the creation of secure, tension-free anastomosis with the preservation of all collaterals. In our study, trauma requiring complex vascular reconstructions was associated with an increased risk of limb loss, which was due to the severity of injuries (100% caused by high energy transfer with associated injuries in all of the cases) rather than to the procedure itself. In addition, the primary patency rate of arterial repair was 75%, which is similar to previously published results.[8,9] Manord et al.[9] reported a primary patency rate of 88% and they concluded that there might be a relatively high technical error rate and broader tissue damage in patients with blunt injuries.

In our series, three arterial reconstructions occluded postoperatively, and all were located in the radial and ulnar artery. All graft occlusions occurred on the first and second day following repair. After a median follow-up period of more than three years, only two patients were diagnosed with late graft occlusions, and both patients were asymptomatic. Our study results suggest that there is a considerable risk of arterial thrombosis perioperatively, whereas the risk of late occlusion is low. As suggested previously, the main reasons for early graft occlusions are technical errors, poor graft quality and/or insufficient anticoagulation.

We assumed that the arterial wall damage during the crush injury affects the occlusion rates rather than technical errors. The histopathological evidences of our cohort also suggest the presence of necrosis, dissected arterial segments which may easily ignored during the procedure. The zone of the injured vessel segment may be larger than the surgeon predicts. These features of the damage vessel may influence the occlusion rates and success of the limb salvage.

In our patients, vascular injury diagnosis was made based on the physical examination due to extensive tissue damage and a long ischemic time. In addition, postoperative vascular DSA was performed to assess the blood flow and the quality of the anastomosis.

Furthermore, the majority of the mangled extremity cases are borderline; that is why it is often difficult to decide in terms of making limb salvage or amputation. Wrong decisions may cause unnecessary amputation or unsuccessful limb salvage attempts.[9,10] To date,

several scoring systems have been developed to help physicians in making this decision. The most widely used scoring system in this area is the MESS system. When the score is ≥7, amputation is recommended. In the literature, it is stated that MESS scoring gives more accurate results in the lower limbs and in pediatric cases.[11,12] However, there are still debates about the use of MESS scoring in the upper limb. According to Slauterbeck et al.,[6] MESS scoring is as a good predictor for amputation in the upper extremity injuries.[5,13-15] However, clinical experience and the skills of the surgeon are more critical than the scoring systems in the upper extremity crush injuries.[6,8,15-18] This is probably the result of several contributing factors.[8,18-20]

Due to the complexity of the artery injury and the limitations of the imaging studies, it is still difficult to reveal all lesions of the interested arteries in certain cases. All these factors contribute to the difficulty in determining the arterial damage and injury severity in the upper extremity crush injuries.[21-24] The severity of the arterial injury can be assessed more accurately with the combination of imaging data, histopathological assessment, and the direct intraoperative visualization.[19,20] Optimal treatment can be also suggested accordingly, which should be the priority of the developing treatment guidelines for the artery injuries.

In conclusion, limb salvage procedures have better functional results than upper limb prostheses. Although long-term results for limb salvage procedures are missing, we recommend limb salvage procedures without calculating scoring systems, unless life-threatening factors are present. Injury patterns which involve high energy transfer are also associated with an increased risk of limb loss. Time-saving by prompt transportation and temporary arterial shunting is essential. Swift and adequate reconstruction of arterial injuries is critical to achieve optimal results. Efforts should be concentrated on early diagnosis and treatment of complications such as graft failure, development of compartment syndrome and infection. However, associated nerve injuries still remain the primary causes of long-term functional disability.

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