



# Investigation and Comparison of Therapeutic Outcomes Due to Penetrating Vascular Trauma of the Upper and Lower Limbs in Patients Referred to Ahvaz Golestan Hospital

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Received 2024-07-05; Accepted 2025-06-25; Online Published 2025-08-29

## Abstract

**Introduction:** Limited research has been done on vascular traumas of the upper limb and their comparison with those of the lower limb. This research was conducted to determine and compare the therapeutic outcomes of penetrating vascular trauma of the upper and lower limbs in patients referred to Golestan Ahvaz Hospital in 2024.

**Methods:** This was a descriptive-analytical and prospective study. The sample size was determined using the census (820 participants). Information was obtained through the medical records and entered into the checklist. Primary outcomes included mortality, rehospitalization, amputation, and revascularization interventions, and other outcomes included operative complications and neurological deficits, which were compared in two groups of upper and lower limb injuries.

**Results:** The frequency of arterial involvement ( $P=0.003$ ), compartment syndrome ( $P=0.014$ ), and nerve injury ( $P=0.005$ ) was higher in the upper limb group. The duration of hospitalization in the lower limb group was significantly longer ( $P=0.003$ ). In treating penetrating arterial injuries, the rate of primary anastomosis ( $P=0.006$ ) and ligation of arterioles ( $P=0.039$ ) was significantly higher in the upper limb group. In comparison, the rate of using venous interposition graft ( $P=0.032$ ) was significantly higher in the lower limb group. In treating venous injuries, the rate of fasciotomy ( $P=0.031$ ) was significantly higher in the lower limb group. Mortality rate ( $P=0.023$ ), amputation ( $P=0.001$ ), need for reoperation ( $P=0.041$ ), and need for therapeutic fasciotomy ( $P=0.001$ ) in the lower limb group were significantly higher. At the same time, the frequency of nerve damage ( $P=0.003$ ) was significantly higher in the upper limb group.

**Conclusions:** The results show a difference between the initial manifestations, management, and surgery and the outcomes of penetrating injury of the upper and lower limbs, which suggests that attention to penetrating injury seems necessary to prevent mortality and morbidity.

**Keywords:** Extremity, Artery, Vein, Trauma.

## Introduction

Traumatic injuries are a leading cause of death among the youth population, accounting for 59% of all deaths in individuals under 45 years of age<sup>1</sup>. Vascular injuries are particularly deadly when they occur in central body areas, such as the chest or abdomen. However, traumatic vascular injuries involving limbs often have a high chance of survival<sup>2,3</sup>. While peripheral vascular trauma is associated with much lower mortality rates, these

injuries rarely occur in isolation and are often accompanied by simultaneous long bone fractures and complex nerve injuries<sup>4</sup>.

Due to these complex injury patterns, vascular trauma to the limbs presents unique challenges for injury management and is associated with significant complications. Survivors often experience poor functional outcomes and long-term disabilities<sup>5</sup>.

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Penetrating injuries to the upper and lower limbs have been on the rise worldwide in recent years. Depending on the energy imparted to the tissues, they can lead to complex injuries. Although high-energy injuries are more common in military settings, they can also occur in civilian environments, particularly after altercations involving sharp objects, traffic accidents, and terrorist attacks<sup>6</sup>. In civilian environments, penetrating injuries to the limbs account for 5% to 15% of cases based on trauma registry data from the United States, Germany, and Sweden<sup>7-9</sup>, though the number of injuries may be higher in some other countries. Stab wounds are the most common cause of injuries in Europe, while gunshot injuries prevail in countries where firearms are more commonly used. Shotgun injuries account for 5% of cases causing vascular injuries<sup>10</sup>. Clinical assessment of the injured limb following penetrating vascular trauma is crucial. Vascular injury signs are typically categorized as "hard" or "soft" signs. Hard signs include active hemorrhage, rapidly expanding hematoma, and loss of pulse, pallor, paresthesia, pain, paralysis, and bruit. Soft signs include a history of arterial bleeding at the injury site, decreased unilateral distal pulse, small hematoma, neurological deficit, or an abnormal Ankle-Brachial Index (ABI) of less than 0.913.

Routine imaging has no established role in penetrating limb trauma<sup>3,4</sup>. However, when computed tomography (CT) is available and the patient's physiology allows for further assessment, computed tomography angiography (CTA) has become the gold standard for diagnosing vascular injuries and determining whether open surgery or endovascular techniques are needed<sup>12</sup>.

In lower limb penetrating vascular trauma, mortality rates are higher for common and superficial femoral artery injuries (4.8%) compared to popliteal or tibial artery injuries (1.4%). However, popliteal artery injuries are more likely to result in limb amputation<sup>3</sup>. The rate of secondary amputation following lower limb penetrating trauma is approximately 5%<sup>9</sup>.

Prognostic factors for limb amputation following surgical repair of lower limb trauma include multiple arterial injuries, significant soft tissue damage and fractures, compartment syndrome, ischemia lasting longer than 6 hours, and age over 55 years. In contrast, mortality and limb amputation following penetrating injuries to the upper limb, such as injuries to the axillary and brachial arteries, are rare<sup>6</sup>. The vast majority of existing studies on peripheral vascular trauma focus on arterial injuries of the lower limb<sup>10-12</sup>, with limited studies addressing penetrating vascular trauma of the upper limb and comparing it to lower limb injuries. Consequently, identifying risk factors, clinical management, morbidity and mortality assessment, and treatment outcomes for arterial injuries in the upper limbs are often based on the guidelines for lower limb

vascular injuries. However, upper limb injuries account for approximately 30 to 40% of all peripheral arterial injuries. This has resulted in a significant gap in the direct assessment of the similarities and differences between penetrating vascular trauma of the upper and lower limbs. As the incidence of all types of penetrating traumatic vascular injuries continues to rise over time<sup>5</sup>, there is an increasing need for a comprehensive study on penetrating vascular trauma of both the upper and lower limbs, comparing these two types<sup>13</sup>. Given the importance of this topic and the lack of similar research in the region, this study aimed to determine and compare the treatment outcomes resulting from penetrating vascular injuries of the upper limb with those of the lower limb in patients referred to Golestan Hospital in Ahvaz in 2024.

## Methods

This study was a descriptive-analytical prospective study. The statistical population was all patients with penetrating arterial trauma of the upper and lower limbs who presented to Golestan Hospital (the southwest trauma center of Iran) during the year 2024. The sample size was determined through a census, which included 820 patients. Inclusion criteria for the study were being over 18 years of age, having penetrating arterial trauma to the upper and lower limbs during the specified time that required surgical intervention, being admitted to the surgical emergency department of Golestan Hospital with vascular trauma, and consenting to participate in the study. The exclusion criterion was the unwillingness of participants to continue their cooperation. Upper limb injuries were defined as injuries to the axillary through to the ulnar artery, and lower limb injuries were defined as injuries to the femoral through to the tibial artery<sup>6</sup>. The diagnosis of penetrating peripheral vascular injury and indications for surgical intervention were determined by a specialized team of vascular surgeons who are faculty members of the university, with or without imaging studies (such as CT angiography). The same vascular surgery team performed all surgical procedures. Indications for surgical intervention included hemorrhage from the injured limb (uncontrolled bleeding at the site of injury, expanding hematoma, pseudoaneurysm, severe arterial injury, and the presence of hemorrhage based on CT angiography results) or ischemic limb injury (absence of distal pulses or Doppler signals in the injured limb, reduced ABI, and evidence of thrombosis in imaging)<sup>2</sup>. Vascular injuries were treated with arterial repair (arteriography), end-to-

end anastomosis, interposition grafting using the saphenous vein, or ligating the artery or vein. Additional interventions included primary amputation of the injured limb, concurrent fasciotomies (either preventive or therapeutic postoperatively), endovascular treatment, use of shunts, and the administration of anticoagulants during surgery<sup>6</sup>. The primary outcomes included mortality, readmission within 30 days, limb loss within 30 days, and unplanned revascularization interventions. Unplanned revascularization interventions included hematoma evacuation, thrombectomy of repaired vessels, re-evaluation of the anastomosis site, pseudoaneurysm repair, or secondary amputation.

Other outcomes included postoperative complications and neurological deficits (sensory or motor dysfunction despite intact or repaired nerves, nerve transection, or hematoma at the nerve site). Postoperative complications were defined as compartment syndrome requiring reoperation, anastomosis complications (thrombosis, infection at the surgical site), and venous thromboembolic complications.

After obtaining ethical approval and completing the necessary administrative arrangements, the researcher (a clinical surgical assistant) attended the general operating room, peripheral recovery, vascular surgery department, and intensive care units at Golestan Hospital. Information regarding participants, such as age, gender, and clinical data including risk factors (age, type of injury, compartment syndrome, duration of injury, associated nerve and bone injuries), mortality rates, morbidity rates, and outcomes (limb loss within 30 days' post-surgery, associated nerve injury, postoperative fasciotomy, readmission) was recorded in a data collection form (checklist) that had been approved by three faculty members who are specialized vascular surgeons. The Injury Severity Score (ISS) is a recognized scoring system calculated by summing the squares of the highest values from the Abbreviated Injury Scale (AIS) for the three most severely injured body regions. ISS scores range from zero (representing no injury) to 75 (representing injuries incompatible with life)<sup>6</sup>. The Glasgow Coma Scale (GCS) was used to assess the level of consciousness, with scores ranging from 3 to 15. The first component relates to eye-opening, with a score of 1 to 4. The second component pertains to verbal response, with a score range of 1 to 5, and the third component involves motor response, with a score range of 1 to 6. The collected data were

analyzed using SPSS software version 25. Descriptive quantitative variables were reported using means and standard deviations, while qualitative descriptive variables were reported using frequency and percentages. The independent t-test and chi-square tests were utilized to compare the analytical results between groups. P-value less than 0.05 considered significantly. This research was presented to the Research Ethics Committee and was approved with the number IR.AJUMS.HGOLESTAN.REC.1403.058, ensuring that all participant information remained confidential throughout the study.

## Results

This study included 820 participants, with 26.54% of them experiencing penetrating vascular injuries to the lower extremities. There were no significant differences between genders ( $P = 0.592$ ), initial injury manifestations ( $P = 0.741$ ), age ( $P = 0.194$ ), and injury severity scale ( $P = 0.545$ ) between the two groups. The upper extremity group had a higher frequency of vascular involvement (arterial involvement) ( $P = 0.003$ ), occurrence of compartment syndrome ( $P = 0.014$ ), need for tourniquet application ( $P = 0.006$ ), and associated nerve injury ( $P = 0.005$ ) compared to the lower extremity group. The duration of hospitalization was significantly longer in the lower extremity injuries group than in the upper extremity injuries group ( $P = 0.003$ ) (Table 1). In penetrating arterial injuries, the primary anastomosis technique ( $P=0.006$ ) and arterial ligation ( $P=0.039$ ) were significantly more common in the upper extremity injury group. Venous interposition grafting ( $P=0.032$ ) was significantly more prevalent in the lower extremity injury group (Table 2). For venous injuries, no statistically significant differences in the treatment techniques used between the two groups, such as venous repair ( $P=0.304$ ) and ligation ( $P=0.515$ ). However, the rate of combined fasciotomy ( $P=0.031$ ) was significantly higher in the lower extremity injury group than in the upper extremity injury group (Table 2). The mortality rate within the first thirty days ( $P=0.023$ ), limb loss within the first thirty days ( $P=0.001$ ), need for reoperation ( $P=0.041$ ), and need for therapeutic fasciotomy ( $P=0.001$ ) were significantly higher in the lower extremity injury group. Conversely, the frequency of nerve injury ( $P=0.003$ ) was significantly higher in the upper extremity injury group (Table 3).

Table 1: Demographic and clinical characteristics of participants in the two groups of penetrating vascular upper and lower limb injuries.

| Variable                                 |                                       | Subgroup                                   | Type of injury            |                           | P. Value*  |
|--|---------------------------------------|--|---------------------------|---------------------------|------------|
|  |                                       |  | Lower limb injury (N=445) | Upper limb injury (N=357) |            |
| <b>Gender</b>                            | Men                                   |  | 375 (84.26)               | 319 (82.46)               | 0.592      |
|  | Women                                 |  | 70 (74.15)                | 56 (17.55)                |            |
| <b>Mechanism of Injury</b>               | Stab wounds                           |  | 152 (34.15)               | 154 (41.06)               | 0.648      |
|  | Gunshot and Shotgun                   |  | 118 (26.51)               | 87 (23.20)                |            |
|  | Traffic accidents                     |  | 102 (22.92)               | 100 (26.66)               |            |
|  | Falling down                          |  | 73 (16.42)                | 34 (9.08)                 |            |
| <b>Comorbidities</b>                     | Diabetes                              |  | 45 (10.11)                | 39 (10.40)                | 0.154      |
|  | Blood pressure                        |  | 47 (10.56)                | 38 (10.13)                |            |
|  | Heart disease                         |  | 35 (7.86)                 | 24 (6.40)                 |            |
|  | Other diseases                        |  | 65 (14.60)                | 56 (14.93)                |            |
| <b>Early manifestations of injury</b>    | Hemorrhage                            |  | 342 (76.86)               | 291 (77.60)               | 0.741      |
|  | Ischemia                              |  | 103 (23.14)               | 84 (22.40)                |            |
| <b>Vascular involvement</b>              | Artery                                |  | 142 (31.92)               | 264 (70.40)               | 0.003      |
|  | Venous                                |  | 120 (26.96)               | 37 (9.87)                 |            |
|  | Both (artery and vein)                |  | 183 (41.12)               | 74 (19.73)                |            |
| <b>Involved arteries and veins</b>       | Upper limb                            | Brachial artery                            | 0 (0)                     | 64 (18.93)                | -          |
|  |                                       | Brachial vein                              | 0 (0)                     | 21 (18.91)                | -          |
|  |                                       | Axillary artery                            | 0 (0)                     | 27 (7.98)                 | -          |
|  |                                       | Axillary vein                              | 0 (0)                     | 10 (9.10)                 | -          |
|  |                                       | Subclavian artery                          | 0 (0)                     | 12 (3.57)                 | -          |
|  |                                       | Subclavian vein                            | 0 (0)                     | 6 (5.39)                  | -          |
|  |                                       | Other arteries (radial, ulnar, etc.)       | 0 (0)                     | 235 (69.52)               | -          |
|  | Other veins (cephalic, basilic, etc.) | 0 (0)                                      | 74 (66.66)                | -                         |            |
|  | Lower limb                            | Femoral artery                             | 90 (27.70)                | 0 (0)                     | -          |
|  |                                       | Femoral vein                               | 95 (31.36)                | 0 (0)                     | -          |
|  |                                       | Popliteal artery                           | 102 (31.38)               | 0 (0)                     | -          |
|  |                                       | Popliteal vein                             | 96 (31.98)                | 0 (0)                     | -          |
|  |                                       | Other arteries (tibial and peroneal, etc.) | 133 (40.92)               | 0 (0)                     | -          |
|  |                                       | Other veins (saphenous, etc.)              | 112 (36.96)               | 0 (0)                     | -          |
| <b>Compartment syndrome</b>              |                                       |  | 74 (16.62)                | 32 (8.53)                 | 0.014      |
| <b>Tourniquet closure</b>                |                                       |  | 33 (7.41)                 | 93 (24.80)                | 0.006      |
| <b>Associated nerve damage</b>           |                                       |  | 67 (15.05)                | 104 (27.73)               | 0.005      |
| <b>Quantitative variable</b>             |                                       |  | Mean ± S.D                | Mean ± S.D                | P. Value** |
| <b>Age (years)</b>                       |                                       |  | 39.96 ± 11.10             | 34.80 ± 10.34             | 0.194      |
| <b>ISS: Injury Severity Score (0-75)</b> |                                       |  | 25.31 ± 4.45              | 21.15 ± 4.45              | 0.545      |
| <b>Time of hospitalization (days)</b>    |                                       |  | 17.21 ± 4.13              | 8.31 ± 2.36               | 0.003      |
| <b>GCS (Glasgow Coma Scale)</b>          |                                       |  | 13.87 ± 2.34              | 13.54 ± 1.65              | 0.815      |
| <b>SBP: Systolic Blood Pressure</b>      |                                       |  | 132.17 ± 24.16            | 136.12 ± 19.13            | 0.854      |
| <b>DBP: Diastolic Blood Pressure</b>     |                                       |  | 75.51 ± 11.47             | 71.26 ± 8.23              | 0.154      |
| <b>BMI: Body Mass Index</b>              |                                       |  | 28.18 ± 5.41              | 27.71 ± 5.45              | 0.183      |

Chi-square test, \*\* Independent t-test

Table 2: Themes, subthemes, and sub-subthemes from analysis of data

| Variable           | Type of Injury  | Method of Surgery             | Type of injury            |                           | P. Value* |
|--------------------|-----------------|-------------------------------|---------------------------|---------------------------|-----------|
|                    |                 |                               | Lower limb injury (N=325) | Upper limb injury (N=338) |           |
| Penetrating Injury | Arterial Injury | Arterial repair               | 37 (11.38)                | 40 (11.83)                | 0.413     |
|                    |                 | Primary anastomosis           | 8 (2.40)                  | 96 (28.40)                | 0.006     |
|                    |                 | Venous interposition grafting | 203 (62.46)               | 78 (23.07)                | 0.032     |
|                    |                 | Arterial ligation             | 76 (23.38)                | 101 (29.88)               | 0.039     |
|                    |                 | Shunt use                     | 4 (1.23)                  | 8 (2.38)                  | 0.614     |
|                    |                 | Combined fasciotomy           | 109 (33.53)               | 78 (23.07)                | 0.174     |
|                    | Venous Injury   | -                             | Type of injury            |                           | P. Value* |
|                    |                 |                               | Lower limb injury (N=303) | Upper limb (N=111)injury  |           |
|                    |                 | Venous repair                 | 58 (7.59)                 | 5 (4.50)                  | 0.304     |
|                    |                 | Primary anastomosis           | 0 (0)                     | 0 (0)                     | -         |
|                    |                 | Venous interposition grafting | 0 (0)                     | 0 (0)                     | -         |
|                    |                 | Venous ligation               | 280 (92.40)               | 106 (95.49)               | 0.515     |
|                    |                 | Shunt use                     | 0 (0)                     | 0 (0)                     | -         |
|                    |                 | Combined fasciotomy           | 79 (26.07)                | 23 (20.72)                | 0.031     |

\*Chi-square test

Table 3: Comparison of the therapeutic outcomes of penetrating injury of the upper limb with those of the lower limb.

| Variable                             | Type of injury            |                           | P.Value* |
|--------------------------------------|---------------------------|---------------------------|----------|
|                                      | Lower limb injury (N=445) | Upper limb injury (N=375) |          |
| Mortality in the first thirty days   | 49 (11.01)                | 14 (3.73)                 | 0.0230   |
| Limb loss in the first thirty days   | 34 (64.7)                 | 9 (40.2)                  | 0.001    |
| Reoperation                          | 44 (9.88)                 | 16 (4.26)                 | 0.041    |
| Rehospitalization within thirty days | 26 (5.84)                 | 22 (5.86)                 | 0.451    |
| Nerve damage                         | 23 (5.16)                 | 56 (14.93)                | 0.003    |
| Therapeutic fasciotomy               | 54 (12.13)                | 7 (1.86)                  | 0.001    |

\*Chi-square test

## Discussion

Vascular penetrating trauma to the limbs typically presents with complex patterns of injury, which can result in significant complications and prolonged disability. The incidence of these injuries is on the rise<sup>5</sup>. Due to potential differences in injury patterns and clinical outcomes between patients with penetrating trauma to the upper extremities and those with trauma to the lower extremities, previous research has only focused on each group separately without comparing them simultaneously. To address this gap, the present

study directly compared the characteristics, surgical approaches, and treatment outcomes of patients with vascular penetrating trauma to the upper and lower extremities.

The results revealed that the majority of participants in both the upper and lower extremity injury groups were male and aged between 30 and 40, consistent with previous studies by Kim et al.<sup>14</sup>, Gallo et al.<sup>15</sup>, and Tan et al.<sup>16</sup>. This age group, consisting mainly of younger and middle-aged men, is more susceptible to trauma-related injuries due to increased exposure to risk factors.

Therefore, it is crucial to pay close attention to this demographic.

The results of the present study indicated that the mortality rate in the lower extremity injury group was significantly higher than that in the upper extremity injury group ( $P=0.023$ ). This finding is consistent with studies by Kim et al.<sup>14</sup> and Tan et al.<sup>16</sup>, but contradicts the results of Gallo et al.<sup>15</sup>. The higher mortality rate in lower extremity injuries may be due to the greater severity and extent of vascular injuries in the lower limbs, longer hospital stays, a higher association with dangerous bony injuries (especially pelvis and femur fractures), an increased occurrence of compartment syndrome and amputations, as well as a greater need for reoperation. All of these factors individually contribute to a higher mortality risk.

Furthermore, according to reference texts<sup>17,18</sup>, the vessels of the lower extremities supply a larger body volume than those of the upper extremities (36% vs. 18%). Disruption of their vascular integrity can result in ischemia in larger body areas, more rapid progression to hemorrhagic shock, and consequently higher mortality rates. Therefore, it is essential to pay attention to this issue.

The results showed that the rate of limb loss (amputation) in the lower extremity group was higher than that in the upper extremity group, which is consistent with the findings of studies by Gallo et al.<sup>15</sup>; Kim et al.<sup>14</sup>, and Tan et al.<sup>16</sup>. According to the information available in reference texts, this may be due to a higher incidence of compartment syndrome in the lower extremities, insufficient collateral circulation in the lower limbs (compared to the upper limbs), a greater likelihood of bony injuries, and the severity of injuries sustained in the lower extremities.

The results also indicated that the need for reoperation, the occurrence of compartment syndrome, and the requirement for therapeutic fasciotomy were significantly higher in the lower extremity group than in the upper extremity group. This results aligns with the results of studies by Kim et al.<sup>14</sup>, Gallo et al.<sup>15</sup>, and Tan et al.<sup>16</sup>, as well as references<sup>17,18</sup>. This can be due to a higher likelihood of thrombosis formation, fewer collateral arteries in the lower extremities compared to the upper extremities, a greater incidence of post-operative compartment syndrome in lower extremity injuries, and an increased risk of ischemia in the lower limbs compared to upper limb injuries. Therefore,

attention to this issue is considered essential.

The results indicated that the incidence of nerve injury was significantly higher in the upper extremity group compared to the lower extremity group, which is consistent with the findings of studies by Kim et al.<sup>14</sup>, Gallo et al.<sup>15</sup>, Tan et al.<sup>16</sup>, and Ratnayake et al.<sup>19</sup>, who reported that the frequency of nerve injuries resulting from penetrating trauma to the upper extremities ranged from 40% to 86%. This is likely due to the proximity of blood vessels and nerves in the upper extremities compared to the lower extremities, which aligns with the findings in reference texts<sup>17,18</sup> (subclavian and axillary artery injuries are typically associated with brachial plexus injuries, and brachial artery injuries are usually associated with median and ulnar nerve injuries). Therefore, the anatomy of the upper extremities has a greater potential for accompanying nerve injuries. Moreover, the occurrence of these nerve injuries imposes greater long-term disabilities on individuals. Thus, thorough attention to nerve injuries before and during surgery for upper extremity injuries seems essential.

The results also showed that the length of hospital stay in the lower extremity injury group was significantly longer, which is consistent with the findings of studies by Kim et al.<sup>14</sup> and Gallo et al.<sup>15</sup>. This can be attributed to the greater severity of lower extremity injuries and the complexity of the subsequent surgical procedures.

In the treatment of penetrating arterial injuries, the use of primary anastomosis in the lower extremities was significantly lower. In comparison, the use of venous interposition grafts was higher, consistent with the results of the study by Gallo et al.<sup>15</sup>. This difference is likely due to the extent and severity of injuries in the lower extremities, as the saphenous vein must be used in a reversed manner, given the length of the injury.

The limitations of the present study include being conducted at a single center, a lack of similar studies comparing treatment outcomes between the upper and lower extremities in the region, and limited access to some participant information. Future research is recommended to be multicentric and include meta-analyses.

## Conclusion

In summary, the results of the present study show statistically significant differences between the initial manifestations, management, surgery, and outcomes of

penetrating injuries to the upper and lower extremities. Specifically, the mortality rate, amputation, compartment syndrome, and re-fasciotomy were higher in lower extremity penetrating trauma, while the occurrence of associated nerve injuries was greater in upper extremity penetrating trauma. Therefore, attention to these factors in penetrating injuries is essential to prevent increased mortality and morbidity.

### Acknowledgments

The authors would like to thank the patients and personnel of Golestan Hospital for their cooperation in performing the present study.

### Conflict of Interest Disclosures

The authors declare that they have no competing interests.

### Funding Sources

This paper is adapted from a proposal with the same name, which was financially supported by Jundishapur University of Medical Sciences.

### Authors' Contributions

M. M. and H.GH. conceived of the present idea. H. GH. And M.Z developed the idea and obtained written informed consent from the patients. H. G. and I.N wrote the manuscript. H. M. helped to conduct the literature review, verified the analytical methods, and wrote the manuscript. H. G. and Z.F also helped to conduct the literature review. M. M. performed the experiments, whereas H. G. contributed to the analysis and wrote the manuscript. A. GH. And H.GH helped with the analyses and wrote the manuscript. All authors reviewed the results and approved the final version of the manuscript.

### Ethical Statement

The study protocol was consistent with the ethical principles of Helsinki Declaration. It was approved by Research Ethics Committee of Jundishapur University of Medical Sciences with the Ethical ID IR.AJUMS.HGOLESTAN.REC.1399.087.

### Declaration of Generative AI and AI-assisted technologies

Not cleared.

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