ORIGINAL ARTICLE

Clinical course and management of extremity frostbite in populations under forced movement in border regions

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ABSTRACT

BACKGROUND: Frostbite is a serious cold injury that can progress to deep tissue damage and even amputation. The increasing number of cases among refugee and migrant populations who are forcibly mobile in border regions necessitates a detailed evaluation of clinical course and risk factors. This study aimed to assess the demographic characteristics, clinical course, laboratory findings, and treatment outcomes of patients presenting with frostbite-related extremity injuries.

METHODS: This retrospective study included a total of 154 patients who presented with a clinically confirmed diagnosis of frostbite. Patients were analyzed according to three predefined classifications: treatment approach (conservative, medical, advanced/interventional), anatomical distribution of frostbite involvement, and time to hospital presentation (≤12 h, 12–24 h, 24–36 h, 36–48 h, and >48 h). Demographic data, clinical findings, laboratory parameters, treatment modalities, and clinical outcomes were evaluated. Statistical analyses were performed using non-parametric tests and Chi-square analysis.

RESULTS: The median age of the patients was 23 years, and 94.2% were foreign nationals. The most common time to presentation was 12–24 h after cold exposure (61%). As the time to hospital admission increased, frostbite grade, number of affected extremities, frequency of hypotension, white blood cell (WBC) levels, and length of hospital stay increased significantly ($p<0.001$). Amputation was performed in 77.3% of patients, and all amputated cases had fourth-grade frostbite. Amputation was significantly associated with delayed presentation, hypotension, elevated WBC levels, larger frostbite area, and longer hospital stay ($p<0.05$).

CONCLUSION: Delayed presentation and severe systemic involvement are the most important determinants of amputation risk. Early diagnosis, rapid and controlled rewarming, appropriate patient transfer, and timely access to advanced treatment options are critical for reducing amputation rates.

Keywords: Amputation; cold injury; frostbite; public health; refugees.

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INTRODUCTION

Cold injuries are complex yet preventable conditions that result from exposure to extremely low temperatures and can lead to tragic outcomes, ranging from cellular-level damage to multi-organ involvement.[1,2] This process begins with superficial vasoconstriction and local heat loss and may progress through the formation of extracellular ice crystals, endothelial injury, microthrombosis, and reperfusion injury, ultimately resulting in deep tissue necrosis, amputation, and death.[3,4] Therefore, frostbite is not merely a localized tissue injury but a complex clinical condition involving systemic inflammatory responses, coagulation disturbances, and metabolic alterations.[5]

Frostbite is most commonly encountered in harsh environmental conditions such as polar regions, high-altitude mountainous areas, military operation zones, conflict regions, and migration routes.[6,7] In recent years, increasing geopolitical instability and forced migration have dramatically raised the incidence of frostbite. Severe frostbite cases reported among migrant populations at European border crossings, along the Balkan route, and at North American borders indicate that this condition represents a global public health problem.[8-10] Key factors increasing the risk of frostbite among migrants and refugees include long-distance walking, lack of appropriate equipment, exposure to wind and moisture, nighttime travel, hypothermia, malnutrition, and trauma.[11,12] These individuals are more vulnerable to the disease not only because of environmental challenges but also due to adverse social and humanitarian conditions.[13]

The epidemiology of frostbite is closely associated with age, sex, occupation, and socioeconomic status. Young adult males, soldiers, mountaineers, homeless individuals, and irregular migrants have been reported to be at particularly high risk.[14,15] Children, on the other hand, are more prone to severe clinical presentations due to rapid heat loss resulting from a higher surface area-to-mass ratio.[16] Time to hospital presentation is one of the most critical determinants of frostbite prognosis. The literature demonstrates that rapid and controlled rewarming within the first 6–12 h significantly reduces tissue loss, whereas delays substantially increase the risk of amputation.[17,18] However, delayed presentation rates are known to be high among migrant populations because of barriers to healthcare access during migration.[19]

In the diagnosis and management of frostbite, imaging modalities such as planar scintigraphy, magnetic resonance imaging (MRI), and angiography play an important role in determining the extent of necrosis and the amount of viable tissue.[20] Laboratory parameters assist in assessing clinical severity by reflecting the grade of inflammation, coagulation status, oxidative stress, and organ function.[21,22] Amputation rates in advanced frostbite cases have been reported to range between 30% and 70%, imposing substantial individual, functional, and psychosocial burdens.[23,24] The presence of amputation is associated with additional consequences, including physical disability, psychological trauma, and difficulties in accessing healthcare services.[25] Moreover, frostbite-related amputations constitute a significant economic burden.

This study aims to comprehensively evaluate the regional epidemiology, pathophysiology, and clinical outcomes of frostbite by analyzing the demographic, clinical, and laboratory characteristics of patients presenting with frostbite in a border region.

MATERIALS AND METHODS

Study Design and Setting

This retrospective, observational study was conducted at a tertiary-level burn center located in a border region with a high volume of forced migration movements. Medical records of patients hospitalized with a diagnosis of frostbite between September 2020 and September 2025 were reviewed retrospectively. The study was approved by the Van Training and Research Hospital Clinical Research Ethics Committee (approval date: August 08, 2025, approval number: 60KAEK/2025-06-01). The study was designed in accordance with the principles of the Declaration of Helsinki.

Patient Population

A total of 154 patients who were hospitalized and treated with a diagnosis of extremity frostbite were included in the study. All patients had clinically confirmed frostbite affecting at least one extremity at the time of presentation. Demographic data (age, sex), migration and shelter status, environmental exposure history, clinical findings, laboratory parameters, imaging results, treatments administered, and clinical outcomes were recorded.

Initial Clinical Assessment

At the time of hospital admission, all patients underwent an initial evaluation in accordance with standard trauma and burn management protocols. After stabilization of vital signs, core body temperature, presence of systemic hypothermia, level of consciousness, and accompanying traumatic findings were assessed. Local examination included documentation of frostbite grade, depth of involvement, blister formation, color changes, signs of necrosis, and distal circulation status.

Rewarming Protocol

According to the standard frostbite treatment protocol applied at our center, all patients received controlled local rewarming. Local hydrotherapy was performed using water at 42°C for 15 min every 6 h during the first 72 h. The duration of rewarming was terminated based on clinical findings and perfusion status.

Medical Treatment

To support reperfusion of pre-ischemic tissues and prevent microthrombosis, all patients were initiated on standard medical therapy. This protocol included enoxaparin 1 mg/kg/

day subcutaneously (divided into two doses), acetylsalicylic acid 100 mg/day orally, iloprost 0.5–2 ng/kg/min through intravenous infusion (6 h/day), pentoxifylline 400 mg orally 3 times daily, and amlodipine 5–10 mg/day orally for adult patients. Depending on clinical status, a beta-blocker (metoprolol 25–50 mg/day orally) was added in cases of tachycardia or hypertension, while dexamethasone 4–8 mg/day intravenously was included in patients with marked inflammation and edema. For infection prophylaxis, all adult patients were started on ceftriaxone 2 g/day intravenously at the time of hospitalization. Analgesia was provided with paracetamol 1,000 mg orally or intravenously 3–4 times daily and ibuprofen 400–600 mg orally 3 times daily; in cases where adequate pain control was not achieved, tramadol 50–100 mg orally or intravenously 2–3 times daily was added.

Imaging and Surgical Evaluation

The decision for amputation was not based on a single parameter but on a comprehensive multidisciplinary clinical evaluation involving burn surgeons, orthopedic surgeons, vascular surgeons, and infectious disease specialists. The amputation decision was primarily based on clinical criteria rather than imaging findings.

The following criteria were considered collectively: presence of fourth-degree frostbite with irreversible tissue necrosis or gangrene, absence of distal perfusion despite standardized medical therapy and controlled rewarming, progressive tissue necrosis observed in serial physical examinations, clear demarcation of non-viable tissue, and development of severe infection or systemic complications.

Doppler ultrasonography was routinely used to assess vascular flow and tissue perfusion. Advanced imaging modalities, including scintigraphy, MRI, or angiography, were performed in hemodynamically stable patients when available to support the evaluation of tissue viability. However, due to the retrospective nature of the study and the high proportion of patients presenting at advanced stages, these modalities could not be applied uniformly to all cases.

In all patients, the final surgical decision was guided primarily by clinical assessment of tissue viability and disease progression, with imaging findings serving as supportive tools when obtainable (Fig. 1).

Inclusion and Exclusion Criteria

Inclusion criteria were the presence of a clinically confirmed diagnosis of frostbite, complete medical records, and first-time presentation for frostbite injury.

Exclusion criteria included incomplete medical records; non-freezing cold injuries; electrical or chemical burns; trauma-related tissue loss; and patients with comorbidities affecting circulation, such as peripheral vascular disease, Raynaud phenomenon, or connective tissue disorders. In addition, individuals with chronic alcohol dependence or those from whom a reliable medical history could not be obtained were excluded.

Data Collection

All patient data were systematically recorded using a standardized data collection form. In addition to demographic variables (age, sex, smoking status), the clinical characteristics of frostbite injury were evaluated in detail. The number of affected digits in the right and left hands and feet, percentage of tissue involvement, extent of involvement, and frostbite grade (grades 1–4) were recorded separately.

For analytical purposes, patients were categorized according to the anatomical distribution of frostbite involvement into seven predefined groups: Group 1 (both hands and both feet affected), Group 2 (both hands and one foot affected), Group 3 (one hand and both feet affected), Group 4 (both feet affected), Group 5 (both hands affected), Group 6 (one hand affected), and Group 7 (one foot affected).

In addition, time to clinical presentation was stratified into five categories: Group A (≤12 h), Group B (12–24 h), Group C (24–36 h), Group D (36–48 h), and Group E (>48 h).

Laboratory data obtained at admission were retrieved from the hospital's electronic medical record system and transferred to the study dataset. The analyzed laboratory parameters included complete blood count (hemoglobin, g/dL; white blood cell (WBC) count, ×103/μL; platelet count, ×103/μL), renal function tests (urea, mg/dL; creatinine, mg/dL), liver enzymes (aspartate aminotransferase, U/L; alanine aminotransferase, U/L), electrolytes (sodium, mmol/L; potassium, mmol/L; magnesium, mg/dL; calcium, mg/dL), C-reactive protein (mg/L), international normalized ratio, and albumin levels (g/dL).

Statistical Analysis

Statistical analyses were performed using IBM Statistical Package for the Social Sciences Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). The normality of data distribution was assessed using the Shapiro–Wilk test. As the data did not show normal distribution, nonparametric tests were used (Mann–Whitney U test or Kruskal–Wallis test). The Chi-square test was applied for comparisons of categorical variables. A $p<0.05$ was considered statistically significant.

RESULTS

Demographic Characteristics

A total of 154 patients were included in the study. The median age was 23 years (range: 16–52 years), and the majority of the patients were male. Most of the patients were foreign nationals presenting with frostbite injuries during irregular migration routes.

Frostbite-Affected Extremities

Frostbite involvement was identified in four extremities in 16 patients (10.4%), three extremities in 45 patients (29.2%), two extremities in 68 patients (44.2%), and a single extremity in 25 patients (16.2%) (Table 1). According to the anatomical

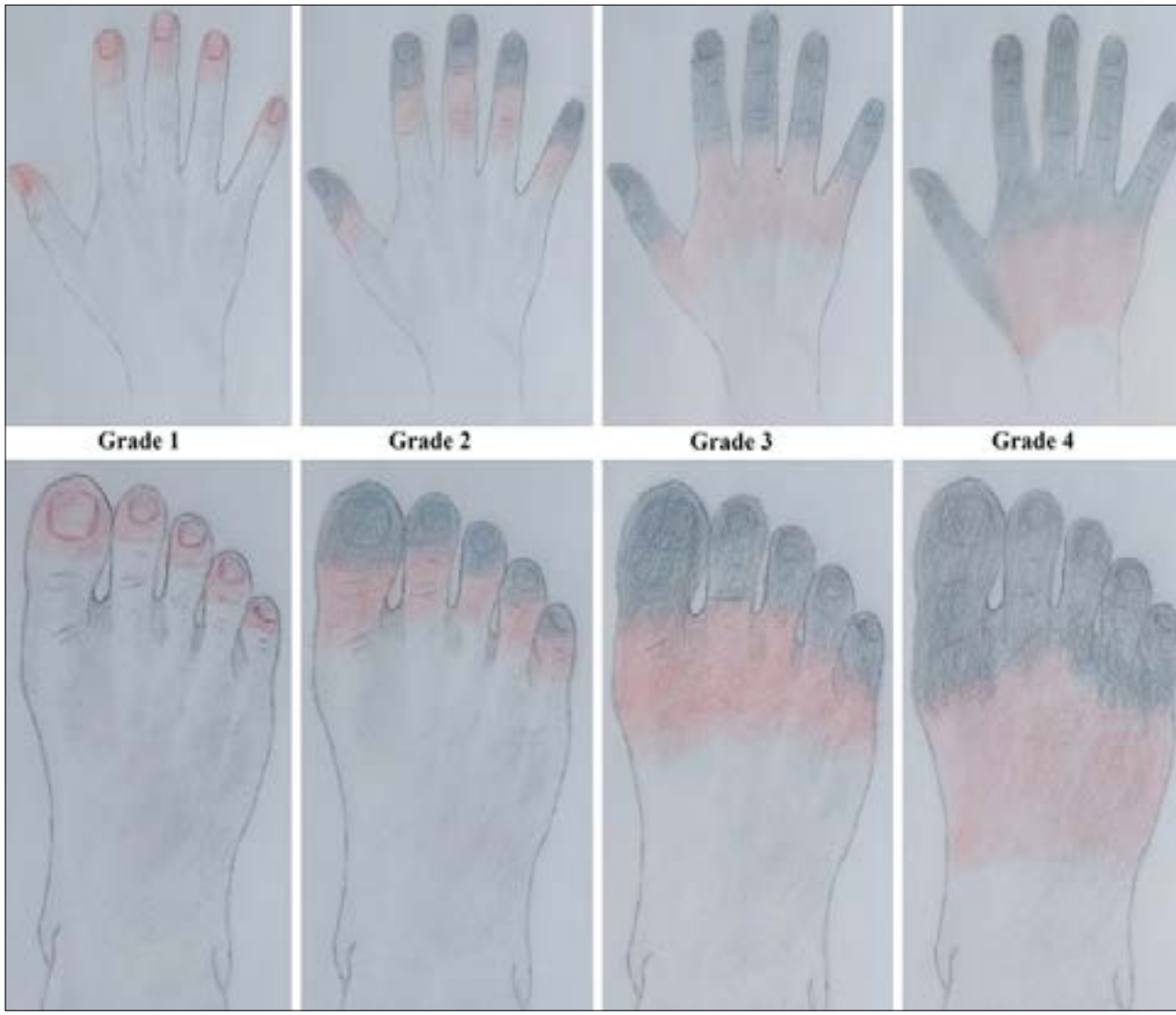


Figure 1. Schematic representation of the clinical grading of frostbite injuries involving the fingers and toes. Grade 1 is characterized by superficial epidermal involvement with erythema and edema. Grade 2 demonstrates deeper dermal injury with blister formation. Grade 3 involves full-thickness skin and subcutaneous tissue damage, often associated with hemorrhagic blisters. Grade 4 represents the most severe form, with involvement of deep structures including muscle, tendon, and bone, resulting in irreversible tissue necrosis and gangrene.

distribution of frostbite involvement, patients were classified into seven groups, the proportional and numerical distributions were as follows: Group 4 (both feet) constituted the largest proportion (31.8%, n=49), followed by Group 2 (both hands and one foot, 16.2%, n=25), Group 3 (one hand and both feet, 13.0%, n=20), Group 5 (both hands, 12.3%, n=19), Group 1 (both hands and both feet, 10.4%, n=16), Group 6 (one hand, 9.2%, n=14), and Group 7 (one foot, 7.1%, n=11) (Table 2).

Time to Clinical Presentation

All patients were transferred to the emergency department within the first 3 days following exposure. Time to clinical presentation was analyzed in five groups. Of the patients, 26.6% (Group A, 41 cases) presented within the first 12 h, 61.0% (Group B, 94 cases) between 12 and 24 h, 9.2% (Group C, 14 cases) between 24 and 36 h, 0.6% (Group D, 1 case) between 36 and 48 h, and 2.6% (Group E, 4 cases) after 48 h. Increasing delay in emergency department presentation was associated with a higher number of affected extremities ($p<0.001$). Prolonged time to presentation was also associated with increased frostbite severity ($p<0.001$) and a higher frequency of hypotensive cases ($p<0.001$) (Table 2). Longer time to presentation was associated with increased length of hospital stay ($p<0.001$) and higher WBC levels ($p=0.042$) (Table 3).

Amputation Frequency

Amputation was performed in 77.3% of patients (119 cases: 115 foreign nationals and 4 Turkish nationals). Neither the

type (hand vs. foot) nor the number of affected extremities was associated with amputation frequency (p>0.05). All patients who underwent amputation had fourth-grade frostbite and presented later to the emergency department (p<0.001). Amputation was more frequently performed in hypotensive patients (p<0.001). While no association was found between

Table 1. Distribution of the number of affected fingers or toes according to the study groups (Kruskal-Wallis Test)

Parameters	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	Group 7	p
Number of fingers affected on the right hand	2 (2–5)	3 (2–4)	1 (0–4)	0	3 (1–4)	0 (0–4)	0	<0.001
Number of fingers affected on the left hand	3 (1–5)	2 (1–4)	1 (0–4)	0	3 (1–5)	3 (0–4)	0	<0.001
Number of toes affected on the right foot	3 (2–5)	0 (0–4)	3 (2–5)	3 (2–5)	0	0	0 (0–4)	<0.001
Number of toes affected on the left foot	3 (2–5)	3 (0–4)	3 (2–5)	3 (1–5)	0	0	3 (0–4)	<0.001
Total number of fingers/ toes affected	12 (9–19)[a,b,c,d,e,f]	8 (6–11)[c,d,e,f]	9 (7–14)[c,d,e,f]	6 (4–10)[e,f]	6 (3–9)[e,f]	3 (2–4)	4 (3–4)	<0.001
Freezing percentage (%)	9.50 (6–15)[a,b,c,d,e,f]	7 (4–10)[c,d,e,f]	7 (5–12)[c,d,e,f]	5 (3–10)[e,f]	5 (2–8)[e,f]	2.50 (2–3)	3 (2–3)	<0.001

Group 1 (n=16): Patients with 2 hands and 2 feet affected, Group 2 (n=25): Patients with 2 hands and 1 foot affected, Group 3 (n=20): Patients with 1 hand and 2 feet affected, Group 4 (n=49): Patients with 2 feet affected, Group 5 (n=19): Patients with 2 hands affected, Group 6 (n=14): Patients with 1 hand affected, Group 7 (n=11): Patients with 1 foot affected. aComparison to group 2, bComparison to group 3, cComparison to group 4, dComparison to group 5, eComparison to group 6, fComparison to group 7, p<0.05. Bold "p" values indicate statistically significant parameters. Since the parameters did not follow a normal distribution, the data in the table were presented as median (minimum–maximum).

Table 2. Evaluation of the categorical variables according to the hospital access time (Chi-square test)

Parameters	Analysis	Group A (%)	Group B (%)	Group C (%)	Group D (%)	Group E (%)	Total (%)	p
Number of limbs affected	Four limbs	5 (31.3)	6 (37.5)	1 (6.2)	1 (6.2)	3 (18.8)	16 (10.4)	0.001
	Three limbs	11 (24.5)	28 (62.2)	6 (13.3)	0 (0)	0 (0)	45 (29.2)	
	Two limbs	15 (22.1)	46 (67.6	6 (8.8)	0 (0	1 (1.5)	68 (44.2)	
	One limb	10 (40)	14 (56)	1 (4)	0 (0)	0 (0)	25 (16.2)	
Study groups	Group 1	5 (31.3)	6 (37.5)	1 (6.2)	1 (6.2)	3 (18.8)	16 (10.4)	0.020
	Group 2	7 (28)	15 (60)	3 (12)	0 (0)	0 (0)	25 (16.2)	
	Group 3	4 (20)	13 (65)	3 (15)	0 (0)	0 (0)	20 (13	
	Group 4	11 (22.5)	32 (65.3)	5 (10.2)	0 (0)	1 (2)	49 (31.8)	
	Group 5	4 (21.1)	14 (73.6)	1 (5.3)	0 (0)	0 (0)	19 (12.3)	
	Group 6	8 (57.2)	5 (35.7)	1 (7.1)	0 (0)	0 (0)	14 (9.2)	
	Group 7	2 (18.2)	9 (81.8)	0 (0)	0 (0)	0 (0)	11 (7.1)	
Freezing grade	Second-grade	7 (70)	3 (30)	0 (0)	0 (0	0 (0)	10 (6.5)	<0.001
	Third-grade	14 (56)	11 (44)	0 (0)	0 (0)	0 (0)	25 (16.2)	
	Fourth-grade	20 (16.8)	80 (67.2)	14 (11.8)	1 (0.8)	4 (3.4)	119 (77.3)	
Blood pressure	Hypotensive	6 (6.8)	64 (71.9)	14 (15.7)	1 (1.1)	4 (4.5)	89 (57.8)	<0.001
	Normotensive	28 (49.1)	29 (50.9)	0 (0)	0 (0)	0 (0)	57 (37)	
	Hypertensive	7 (87.5)	1 (12.5)	0 (0)	0 (0)	0 (0)	8 (5.2)	

Group 1 (n=16): Patients with 2 hands and 2 feet affected, Group 2 (n=25): Patients with 2 hands and 1 foot affected, Group 3 (n=20): Patients with 1 hand and 2 feet affected, Group 4 (n=49): Patients with 2 feet affected, Group 5 (n=19): Patients with 2 hands affected, Group 6 (n=14): Patients with 1 hand affected, Group 7 (n=11): Patients with 1 foot affected, Group A (n=41): Patients that arrive at the hospital within the first 12 h, Group B (n=94): Patients that arrive at the hospital between 12 and 24 h, Group C (n=14): Patients that arrive at the hospital between 24 and 36 h, Group D (n=1): Patients that arrive at the hospital between 36 and 48 h, Group E (n=4): Patients that arrive at the hospital after 48 h. Bold "p" values indicate statistically significant parameters.

Table 3. Comparison of the parameters according to the hospital access time (Kruskal-Wallis Test)

Parameters	Group A	Group B	Group C	Group D	Group E	p
Total number of fingers/ toes affected	7 (2–16)	6 (3–14)	8 (4–13)	14 (14–14)	12.50 (5–19)	0.058
Freezing per-centage (%)	5 (2–12)	5 (2–12)	6 (3–12)	11 (11–11)	10.50 (4–15)	0.072
Length of hospital stay (day)	11 (4–24)	13 (6–29)	16 (9–27)	40 (40–40)	35.50 (26–43)	<0.001
pH	7.36 (7.29–7.43)	7.35 (7.25–7.43)	7.36 (7.30–7.44)	7.41 (7.41–7.41)	7.37 (7.23–7.39)	0.580
PaO_2 (mmHg)	86 (77–95)	84 (75–96)	84 (76–93)	84 (84–84)	87.50 (83–91)	0.097
$PaCO_2$ (mmHg)	43 (37–47)	42 (30–52)	42 (38–48)	41 (41–41)	41 (40–42)	0.550
Glucose (mg/dL)	91 (75–115)	92.50 (68–132)	96 (75–131)	91 (91–91)	76 (62–81)	0.054
WBC (10^3/uL)	8.90 (4.70–19.80)	9.65 (3.50–19.10)	9.95 (7.20–16.80)	17.20 (17.20–17.20)	16.75 (10–19.10)	0.042
Hgb (g/dL)	13.60 (10.50–16.50)	13.70 (10.30–16.80)	13.30 (10.60–16.80)	15.60 (15.60–15.60)	16.30 (10.80–17)	0.435
INR	1 (0.50–1.40)	1 (0.60–1.50)	0.90 (0.80–1.20)	1 (1–1)	0.80 (0.60–0.80)	0.054
ALT (U/L)	55 (33–78)	59 (35–80)	66.50 (40–80)	67 (67–67)	59 (36–79)	0.757
AST (U/L)	50 (32–70)	53.50 (29–70)	53 (33–68)	59 (59–59)	58.50 (31–82)	0.971
Creatinine (mg/dL)	0.90 (0.50–1.40)	0.90 (0.50–1.60)	0.90 (0.60–1.30)	1.20 (1.20–1.20)	1 (0.90–1.40)	0.509
Na (mEq/L)	139 (132–145)	139 (131–147)	139.50 (135–146)	139 (139–139)	137 (132–141)	0.823
K (mEq/L)	3.90 (3.10–4.90)	4 (3.10–5.30)	3.95 (3.10–5)	4.60 (4.60–4.60)	4 (3.10–4.80)	0.438
Mg (mg/dL)	1.90 (1.50–2.20)	1.90 (1.40–2.30)	1.80 (1.60–2.20)	1.80 (1.80–1.80)	1.85 (1.20–2)	0.977
Ca (mg/dL)	8.50 (7.10–9.90)	8.45 (7.10–9.90)	8.60 (7.30–9.90)	7.10 (7.10–7.10)	8.25 (7.80–9.70)	0.557
Albumin (g/dL)	3.20 (1.80–5.20)	3.50 (1.80–5.20)	4.10 (1.70–5.10)	1.60 (1.60–1.60)	2.30 (1.60–5.10)	0.247

Group A (n=41): Patients that arrive at the hospital within the first 12 h, Group B (n=94): Patients that arrive at the hospital between 12 and 24 h, Group C (n=14): Patients that arrive at the hospital between 24 and 36 h, Group D (n=1): Patients that arrive at the hospital between 36 and 48 h, Group E (n=4): Patients that arrive at the hospital after 48 h. Bold "p" values indicate statistically significant parameters. pH: Blood acidity level; PaO2: Partial arterial oxygen pressure; PaCO2: Partial arterial carbon dioxide pressure; WBC: White blood cell count; Hgb: Hemoglobin; INR: International normalized ratio; ALT: Alanine aminotransferase, AST: Aspartate aminotransferase; Na: sodium; K: Potassium; Mg: Magnesium; Ca: calcium.



Figure 2. Clinical presentation of frostbite injuries involving the hand and fingers at varying degrees of severity.

amputation frequency and smoking status (p=0.488), a significant association was observed with alcohol use (p=0.007), with alcohol consumption associated with a reduced risk of amputation (Table 4). Patients who underwent amputation had a significantly higher percentage of frostbite involvement (p=0.037) and longer hospital stays (p<0.001) (Table 5). In addition, WBC levels were significantly higher in patients who underwent amputation (p=0.009) (Table 5; Figs. 2 and 3).

DISCUSSION

This study evaluated the epidemiological and clinical characteristics of patients hospitalized for frostbite injuries and demonstrated that frostbite is not merely a clinical condition resulting from environmental exposure, but also a significant public health problem closely associated with forced migration, sociopolitical conditions, and delayed access to health-

Table 4. Evaluation of the categorical variables according to the presence or absence of amputation (Chi-square test)

Parameters	Analysis	Absence (n=35) (%)	Presence (n=119) (%)	Total (%)	p
Number of limbs affected	Four limbs	2 (12.5)	14 (87.5)	16 (10.4)	0.259
	Three limbs	7 (15.6)	38 (84.4)	45 (29.2)	
	Two limbs	20 (29.4)	48 (70.6)	68 (44.2)	
	One limb	6 (24)	19 (76)	25 (16.2)	
Study groups	Group 1	2 (12.5)	14 (87.5)	16 (10.4)	0.241
	Group 2	3 (12)	22 (88)	25 (16.2)	
	Group 3	4 (20)	16 (80)	20 (13)	
	Group 4	16 (32.7)	33 (67.3)	49 (31.8)	
	Group 5	4 (21.1)	15 (78.9)	19 (12.3)	
	Group 6	5 (35.7)	9 (64.3)	14 (9.2)	
	Group 7	1 (9.1)	10 (90.9)	11 (7.1)	
Freezing grade	Second-grade	10 (100)	0 (0)	10 (6.5)	<0.001
	Third-grade	25 (100)	0 (0)	25 (16.2)	
	Fourth-grade	0 (0)	119 (100)	119 (77.3)	
Hospital access time	Group A	21 (51.2)	20 (48.8)	41 (26.6)	<0.001
	Group B	14 (14.9)	80 (85.1)	94 (61)	
	Group C	0 (0)	14 (100)	14 (9.2)	
	Group D	0 (0)	1 (100)	1 (0.6)	
	Group E	0 (0)	4 (100)	4 (2.6)	
Blood pressure	Hypotensive	6 (6.7)	83 (93.3)	89 (57.8)	<0.001
	Normotensive	24 (42.1)	33 (57.9)	57 (37)	
	Hypertensive	5 (62.5)	3 (37.5)	8 (5.2)	
Smoking	No	27 (21.6)	98 (78.4)	125 (81.2)	0.488
	Yes	8 (27.6)	21 (72.4)	29 (18.8)	
Alcohol use	No	27 (19.4)	112 (80.6)	139 (90.3)	0.007
	Yes	8 (53.3)	7 (46.7)	15 (9.7)	

Group 1 (n=16): Patients with 2 hands and 2 feet affected, Group 2 (n=25): Patients with 2 hands and 1 foot affected, Group 3 (n=20): Patients with 1 hand and 2 feet affected, Group 4 (n=49): Patients with 2 feet affected, Group 5 (n=19): Patients with 2 hands affected, Group 6 (n=14): Patients with 1 hand affected, Group 7 (n=11): Patients with 1 foot affected, Group A: Patients that arrive at the hospital within the first 12 h, Group B: Patients that arrive at the hospital between 12 and 24 h, Group C: Patients that arrive at the hospital between 24 and 36 h, Group D: Patients that arrive at the hospital between 36 and 48 h, Group E: Patients that arrive at the hospital after 48 h. Bold "p" values indicate statistically significant parameters.



Figure 3. Clinical images demonstrating advanced frostbite injuries (Grade 3–4) affecting the foot and toes.

Table 5. Comparison of the parameters according to the presence or absence of amputation (Mann-Whitney U Test).

Parameters	Analysis	Absence (n=35)	Presence (n=119)	p
Clinical findings	Total number of fingers/toes affected	6 (3–11)	7 (2–19)	0.110
	Freezing percentage (%)	5 (3–8)	6 (2–15)	0.037
	Length of hospital stay (day)	9 (4–15)	14 (8–43)	<0.001
Laboratory findings	pH	7.35 (7.29–7.43)	7.36 (7.23–7.44)	0.807
	PaO_2 (mmHg)	85 (80–95)	84 (75–96)	0.201
	$PaCO_2$ (mmHg)	42 (36–50)	42 (30–52)	0.755
	Glucose (mg/dL)	90 (75–115)	93 (62–132)	0.359
	WBC (10^3/uL)	7.90 (3.50–17.60)	10.10 (3.60–19.80)	0.009
	Hgb (g/dL)	13.30 (10.50–16.80)	13.90 (10.30–17)	0.235
	INR	1 (0.80–1.20)	1 (0.50–1.50)	0.757
	ALT (U/L)	53 (33–80)	61 (35–80)	0.325
	AST (U/L)	53 (31–70)	53 (29–82)	0.458
	Creatinine (mg/dL)	0.90 (0.50–1.60)	0.90 (0.50–1.40)	0.454
	Na (mEq/L)	138 (132–145)	139 (131–147)	0.545
	K (mEq/L)	3.90 (3.10–5)	4 (3.10–5.30)	0.223
	Mg (mg/dL)	1.90 (1.50–2.20)	1.80 (1.20–2.30)	0.119
	Ca (mg/dL)	8.60 (7.10–9.90)	8.40 (7.10–9.90)	0.666
	Albumin (g/dL)	3.30 (1.80–5.20)	3.40 (1.60–5.20)	0.612

Bold "p" values indicate statistically significant parameters. pH: Blood acidity level; PaO2: Partial arterial oxygen pressure; PaCO2: Partial arterial carbon dioxide pressure; WBC: White blood cell count; Hgb: Hemoglobin; INR: İnternational normalized ratio; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; Na: Sodium; K: Potassium; Mg: Magnesium; Ca: Calcium; PaO2: Partial arterial oxygen pressure; PaCO2: Partial arterial carbon dioxide pressure; Glucose: Blood glucose level; Creatinine: Serum creatinine level; Albumin: Serum albumin level; Length of hospital stay: Duration of hospitalization; Freezing percentage: Percentage of body surface affected by freezing.

care services.[3,8,10] The predominance of refugee and migrant individuals in the study population is consistent with trends reported in previous studies,[14,15] indicating that, in border regions, the primary determinant of frostbite severity is not cold exposure alone but rather migration-related delayed presentation and structural vulnerabilities.[11-13]

In hospital-based series from Europe and North America, the proportion of migrant or homeless individuals among patients with severe frostbite has been reported to range between 35% and 62%.[8-10] In contrast, the remarkably high proportion of foreign nationals in our cohort (94.2%) highlights a substantially increased burden of frostbite-related vulnerability among populations affected by forced migration in border regions. Similarly, while previous studies have reported median ages ranging from 30 to 45 years,[15,16] the median age in our study was 23 years, suggesting that frostbite in this setting disproportionately affects younger adults. Notably, in their comprehensive clinical review, Handford et al.[17] emphasized that frostbite occurs most frequently among young men, particularly migrants, individuals with inadequate shelter conditions, and those compelled to work outdoors.

The near-exclusive male predominance in our cohort (98.1%) is consistent with the demographic distributions reported by Ervasti et al.[26] and Cauchy et al.,[19] both of whom identified frostbite as most prevalent among males aged 20–40 years. These findings further support the notion that frostbite is driven less by biological susceptibility and more by exposure duration, environmental risk factors, and adverse socioeconomic conditions.

The extent of extremity involvement represents another notable finding of this study. In our cohort, 83.8% of patients had involvement of two or more extremities, a proportion substantially higher than the approximately 52% reported by Ervasti et al.[26] in Finland and the 48% reported by Cauchy et al.[19] in Alpine Mountaineering Series. This discrepancy is likely attributable to prolonged cold exposure, inadequate protective clothing, and restricted mobility during irregular border crossings. Handford et al.[17] similarly reported that multi-extremity involvement reflects prolonged and severe cold exposure and is associated with poorer functional outcomes.

Delayed hospital presentation emerged as one of the most critical findings of our study. The pathophysiology of frostbite is classically described as a biphasic process consisting

of freezing and reperfusion phases.[3,4] During the freezing phase, extracellular ice crystal formation, capillary leakage, endothelial injury, and microthrombosis impair early tissue perfusion, whereas during the reperfusion phase, reactive oxygen species, inflammatory cytokines, and complement activation further exacerbate tissue damage.[5,21] In our cohort, only 26.6% of patients presented within the first 12 h, which likely facilitated the progression of these pathophysiological mechanisms.

Consistent with the findings of Cauchy et al.[19] and Regli et al.,[4] who reported that presentation beyond 24 h increases the risk of tissue loss by two- to fourfold, our data demonstrated a statistically significant association between prolonged presentation time and both frostbite severity ($p<0.001$) and the need for amputation ($p<0.001$). More than 70% of our patients presented after the first 12 h, in marked contrast to early presentation rates exceeding 50% as reported by tertiary care centers outside border regions.[26,27]

The high amputation rate observed in our study (77.3%) is considerably greater than that reported in most civilian series.[24-27] Wibbenmeyer et al.[2] reported an amputation rate of 28% in a multicenter U.S. cohort, while Regli et al.[4] reported an approximate rate of 31% in their meta-analysis. In contrast, Cauchy et al.[19] demonstrated that amputation rates in fourth-degree frostbite may reach 60–80%. The fact that all amputated patients in our series had fourth-degree frostbite is consistent with these observations.

The significantly elevated WBC levels observed in patients undergoing amputation support the role of an intense systemic inflammatory response in severe frostbite.[21,22] Although elevated WBC counts have previously been described as markers of tissue necrosis and secondary infection,[22] clinical evidence quantifying the relationship between WBC levels and amputation risk remains limited. In this context, our findings provide additional support for incorporating inflammatory markers into early prognostic assessment models.

From a therapeutic perspective, early intervention is of critical importance. Controlled rewarming, adequate analgesia, hydration, and trauma management constitute the foundation of standard care.[17,18] In advanced frostbite, thrombolytic therapy with tissue plasminogen activator, particularly when administered within the first 24 h, has been shown to significantly reduce amputation rates.[27-30] In the landmark studies by Bruen et al.,[27] Limb salvage rates of 60–80% were reported following thrombolytic therapy. However, in our study, the predominance of delayed presentation severely limited the applicability of thrombolytic treatment.

Advanced imaging modalities play an important role in assessing tissue viability in frostbite injuries. Nevertheless, in clinical practice, particularly among patients presenting at advanced stages, the decision for amputation is often based primarily on multidisciplinary clinical assessment rather than imaging findings.[20] In our cohort, surgical decision-making was guided by criteria including clinical progression of tissue necrosis, distal perfusion status, signs of infection, and tissue demarcation. Limited systematic access to advanced imaging and the high proportion of late-stage presentations resulted in surgical decisions being predominantly clinically driven. These findings indicate that the applicability of imaging-based algorithms is closely linked to both institutional resources and timing of presentation. Accordingly, clinical algorithms for frostbite management in border regions should be addressed through a multilayered public health approach that integrates not only medical care but also migrant health policies, early access to care, and effective referral systems.

Limitations of the Study

The primary limitation of this study is its retrospective, single-center design, which limits the generalizability of the findings and precludes causal inferences. The predominance of high-risk migrant and refugee individuals in the study population may result in findings that reflect a specific patient group rather than the general population.

The fact that a substantial proportion of patients presented late limited the evaluation of the effectiveness of advanced early-stage treatment options. In addition, certain variables, such as duration of environmental exposure and use of protective equipment, could not be objectively verified because they were based on patient history.

The inability to apply advanced imaging modalities uniformly to all patients and the lack of assessment of long-term functional and psychosocial outcomes represent additional limitations of this study.

CONCLUSION

This study provides clinical evidence that delayed hospital admission and higher frostbite grade at presentation are independent and strong predictors of amputation risk in patients with frostbite injuries.

In addition, hypotension at admission and elevated WBC levels were identified as significant biological markers associated with poor limb outcomes.

Our findings quantitatively demonstrate the protective role of early, controlled rewarming and timely medical intervention in limiting tissue necrosis and preserving limb integrity.

By analyzing a unique patient population from a border region, this study contributes novel data on the clinical course, treatment response, and prognostic factors of severe frostbite in real-world settings.

Compared with previous cohorts, our study reports one of the highest documented amputation rates, highlighting the critical impact of delayed access to care on clinical outcomes.

These results refine current understanding of frostbite pathophysiology and progression, support early risk stratification

based on presentation characteristics, and may assist clinicians in identifying high-risk patients who require aggressive monitoring and intervention.

Furthermore, our data suggest that incorporating simple clinical variables (time to presentation, blood pressure, WBC levels, and frostbite grade) into early decision-making algorithms may improve prognostic accuracy and guide resource allocation in emergency settings.

Furthermore, the study adds to the limited body of literature on predictors of amputation in frostbite and provides evidence-based parameters that can be incorporated into future clinical algorithms and management guidelines.

Multicenter observational studies using standardized data collection protocols are needed to validate these findings and clarify the impact of early thrombolytic therapy and advanced imaging on clinical outcomes.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Sınır bölgelerinde zorunlu hareket halindeki popülasyonlarda ekstremite donmalarının klinik seyri ve tedavisi

AMAÇ: Donma, derin doku hasarı ve amputasyona kadar ilerleyebilen ciddi bir soğuk yaralanmasıdır. Sınır bölgelerinde zorunlu hareket halinde bulunan mülteci ve göçmen popülasyonlarında vaka sayılarındaki artış, klinik seyir ve risk faktörlerinin ayrıntılı olarak değerlendirilmesini gerekli kılmaktadır. Bu çalışma, donmaya bağlı ekstremite yaralanmaları ile başvuran hastaların demografik özelliklerini, klinik seyirlerini, laboratuvar bulgularını ve tedavi sonuçlarını değerlendirmeyi amaçlamıştır.

GEREÇ VE YÖNTEM: Bu retrospektif çalışmaya, klinik olarak doğrulanmış donma ile başvuran toplam 154 hasta dahil edilmiştir. Hastalar üç önceden tanımlanmış sınıflandırmaya göre analiz edildi: tedavi yaklaşımı (konservatif, medikal ve ileri/girişimsel), donma yaralanmasının anatomik dağılımı ve hastaneye başvuru süresi (≤12 saat, 12–24 saat, 24–36 saat, 36–48 saat ve >48 saat). Demografik veriler, klinik bulgular, laboratuvar parametreleri, uygulanan tedavi yöntemleri ve klinik sonuçlar değerlendirildi. İstatistiksel analizler nonparametrik testler ve ki-kare analizi kullanılarak gerçekleştirildi.

BULGULAR: Hastaların ortanca yaşı 23 yıl olup, %94.2'si yabancı uyrukluydu. En sık hastaneye başvuru zamanı, soğuğa maruziyetten sonraki 12–24 saatler arasında (%61) idi. Hastaneye başvuru süresi uzadıkça, donma derecesi, etkilenen ekstremite sayısı, hipotansiyon sıklığı, beyaz kan hücresi (WBC) düzeyleri ve hastanede yatış süresi anlamlı olarak arttı ($p<0.001$). Hastaların %77.3'üne amputasyon uygulandı ve amputasyon yapılan tüm olgularda dördüncü derece donma mevcuttu. Amputasyon, gecikmiş başvuru, hipotansiyon, yüksek WBC düzeyleri, daha geniş donma alanı ve daha uzun hastanede yatış süresi ile anlamlı şekilde ilişkili bulundu ($p<0.05$).

SONUÇ: Gecikmiş başvuru ve ağır sistemik tutulum amputasyon riskini belirleyen en önemli faktörlerdir. Erken tanı, hızlı ve kontrollü yeniden ısıtma, uygun hasta transferi ve ileri tedavi seçeneklerine zamanında erişim, amputasyon oranlarının azaltılmasında kritik öneme sahiptir.

Anahtar sözcükler: Amputasyon; donma; halk sağlığı; mülteciler; soğuk yaralanması.

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