Frostbite

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KEYWORDS

• Frostbite • Rewarming • Thrombolysis • Prostacyclin • rTPA • Gangrene
• Amputation • Telemedicine

KEY POINTS

- Frostbite is associated with significant morbidity, and prevention is key.
- Freeze-thaw-freeze cycles must be avoided.
- New therapies, such as parenteral iloprost or thrombolytics, offer significant promise in the management of deep frostbite injury.
- Expert opinion is now readily available via telemedicine.

INTRODUCTION

Frostbite injury can result in debilitating long-term irreversible morbidity. Despite this, frostbite management strategies remained constant and unchanged until recent years, when novel therapies have led to promising, tissue-saving, outcomes. This article gives a background understanding of frostbite and its pathophysiology and reviews the current evidence and latest frostbite management strategies to educate clinicians to maximize the outcomes of their patients.

Epidemiology

The first physical evidence of frostbite injury is in a 5000-year-old pre-Columbian mummy discovered in the Andes.[1] In military medicine, cold injuries, including frostbite, have long been recognized as a significant cause of mortality and morbidity. Examples of this include Hannibal crossing the Alps in 218 BC, when only 19,000 survived out of 38,000, or the American War of Independence, in which cold casualty rates in George Washington's army were described as being as high as 10%.[2,3] Napoleon

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Bonaparte's Surgeon in Chief, Dominique Jean Larrey,[4] during the failed invasion of Russia in the winter of 1812 to 1813, wrote the first authoritative report on frostbite and cold injury. Frostbite continues to afflict modern militaries.[5–7]

Within the civilian environment, frostbite can affect a myriad of individuals. One civilian subgroup is that of mountaineers. A cross-sectional questionnaire found a mean incidence of 366 per 1000 population per year.[8] The British Antarctic Survey found an incidence for cold injury of 65.6 per 1000 per year; 95% of this was for frostbite, with recreation being a risk factor.[9] On Denali, frostbite was found to be the most common (18.1%) individual diagnosis made at the medical facilities.[10] An epidemiologic review of the first 10 years of the so-called Everest ER (emergency room) found that cold exposure accounted for 18.4% of all trauma visits, of which 83.7% were attributable to frostbite.[11]

In the nonadventurer civilian population, there are certain recognized risk factors for frostbite injury. These risk factors include alcohol consumption, smoking, vagrancy, psychiatric disturbance, unplanned exposure to cold with inadequate protection, previous cold injury, several medications (eg, β-blockers), and working with equipment that uses NO_2 or CO_2.[12–17] Alongside the aforementioned, there seem to be important genetic risk factors that include African American ethnicity and O group blood typing.[6,18] Possession of the angiotensin-converting enzyme DD allele may also increase risk.[19]

Pathophysiology

Frostbite is a freezing cold thermal injury that occurs when tissues are exposed to temperatures below their freezing point. Pathologic changes can be divided into direct cellular injury and indirect cellular injury, also referred to as progressive dermal ischemia.

Direct cellular injury

Direct cellular injury occurs because of a variety of mechanisms. These mechanisms can be summarized as ice crystal formation (intracellular and extracellular), cell dehydration and shrinkage, electrolyte disturbances, denaturation of lipid-protein complexes, and thermal shock.[20] These mechanisms result in cell injury and death.

Indirect cellular injury (progressive dermal ischemia)

Indirect cellular injury is secondary to progressive microvascular insult and is more severe than the direct cellular effect.[20,21] Following thawing, microvascular thrombosis occurs, resulting in continued cell injury and death.[22] Endothelial damage, intravascular sludging, increased levels of inflammatory mediators and free radicals, reperfusion injury, and thrombosis all play a role in contributing to progressive dermal ischemia and positively reinforce each other.[22–30]

Classification

There have been several proposed classifications for frostbite and historically the degrees classification has been favored. This system divided frostbite into frostnip, first-degree, second-degree, third-degree, and fourth-degree frostbite depending on depth of injury. Others clinicians have opted for a simpler classification of superficial (first-degree and second-degree) and deep (third-degree and fourth-degree).[22] Because bone loss is always distal to the observed extent of frostbite, these classifications often fail to predict likely amputation levels, which only become apparent at subsequent mummification.

Over recent years there has been an effort to formulate a reproducible and prognostic classification system rather than the established observational systems. Cauchy and colleagues[31] proposed a classification system of 4 grades for frostbite of the hand or foot based on the appearance of the lesion after rapid rewarming, appearance at day 2, and radioisotope uptake on bone scan at day 2. The advantage of this classification is that it gives an early prognostic indicator of bone and tissue loss and the likely

anatomic level of loss. This grading system relies on isotope bone scanning. In the field, Cauchy and colleagues[32] suggest the use of portable Doppler or the clinical stigmata of soft tissue cyanosis as surrogate markers for amputation risk.

PREHOSPITAL MANAGEMENT

Prevention

Prevention of frostbite enables effective and safe functioning within a cold environment and is the responsibility of individuals, team leaders, and companies/employers who place individuals in at-risk areas. The following are areas of prevention to consider; however, it is not an exhaustive list and an individualized risk assessment and plan formation must be taken for every cold exposure.

- Adequate calorie and fluid intake
- Appropriate clothing for environment, using a layering system
- Avoid sweating by reducing exercise intensity if necessary
- Avoid constricting items
- Mittens are preferable to finger gloves and should be attached to the person; spares should be carried
- Appropriate boots for environment/task that fit correctly
- Do not climb in adverse weather conditions
- Daily foot care
- Buddy-buddy check system
- Avoid alcohol and smoking
- Be aware of the risks associated with increased altitude
- Be aware wind-chill effect
- Avoid prolonged immobility
- Avoid fatigue
- Be careful when removing gloves to perform tasks; never directly touch metal in extreme cold or in moderate cold if wet
- Leaders/commanders must ensure all are fit, trained, and capable of operating in proposed location/climate; this should take into account comorbidities and current medications
- A thorough evacuation and medical plan must be in place before departure; this must include communications

Patient Evaluation Overview

Early recognition

Early recognition is vital; paresthesia may be the first symptom and, if present, measures should be taken to prevent any further damage. Recognition of frostnip, hypothermia, and subsequently taking appropriate action to avoid further cold exposure is important for preventing further damage. Note that it may take several hours for an individual to rewarm after excessive cold and reexposure to the cold too soon risks rapid deterioration. If an individual incurs a cold injury, all other team members must be assessed.

Clinical presentation

Complaint of feeling cold, numb, and/or clumsy. Appearance is variable and can be misleading. The affected area may appear a yellow-white color or be a mottled blue. Clinically it may be insensate or obviously frozen. Note that the characteristic edema and blistering does not occur until after rewarming.

Once frostbite has occurred, evaluation and management depend on several factors, including location, accessibility of definitive care, and severity.

Fig. 1 shows grade 2 and 3 frostbite at various time points.
Consider before evaluation:

1. Once boots are removed swelling may occur, preventing redonning of boots.
2. Freeze-thaw-freeze cycles must be avoided; therefore, only consider rewarming if this can be avoided.
3. Is there a better, more sheltered, area to perform evaluation?
4. Will the patient need to walk out? If yes, consider whether removal of boots and potential rewarming is going to prevent this. It may be better to walk out on a frozen foot.

TREATMENT

Hurley[33] described frostbite in a similar manner to how ischemic cerebrovascular events are now described,[34] with some tissue cells killed, some unaffected, and a

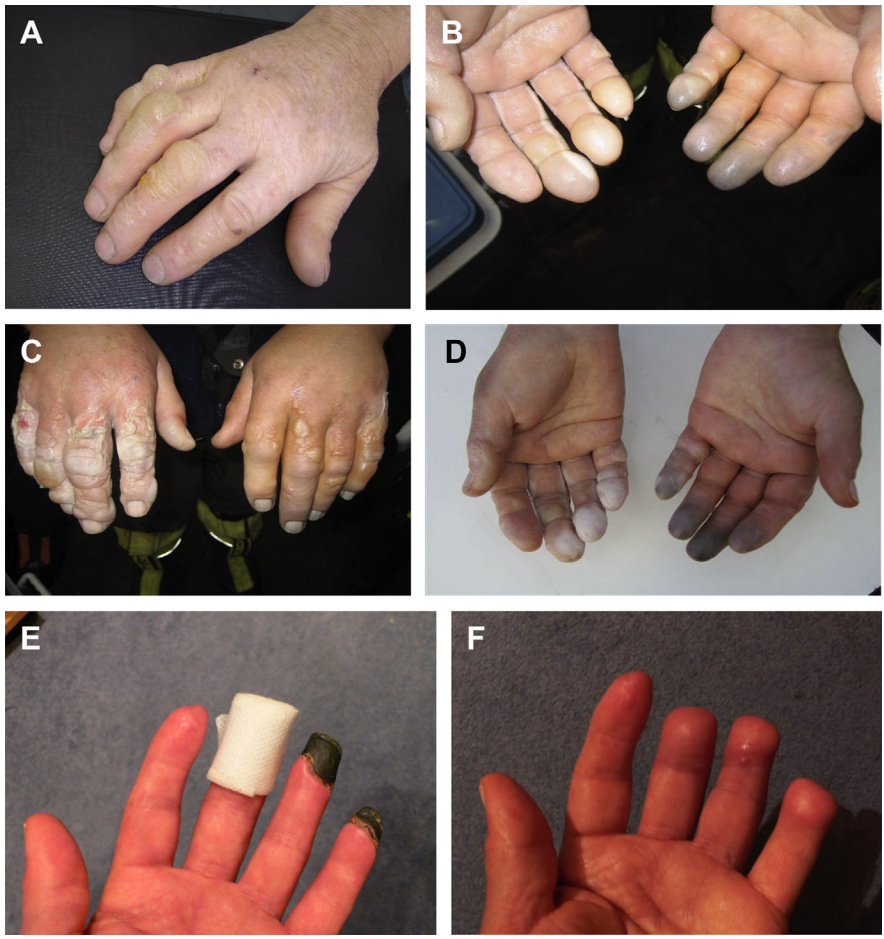

Fig. 1. (*A*) Twenty-four hours following grade 2 frostbite injury with blister formation. (*B*) Grade 2 right hand and grade 3 left hand at 36 hours. (*C*) Grade 2 right hand and grade 3 left hand at 36 hours following soaks in povidone iodine. (*D*) Grade 2 right hand and grade 3 left hand at 5 days. (*E*) Grade 3 at 3 months; note the mummification. (*F*) Grade 3 at 4 months.

large number injured but potentially salvageable with optimum treatment. Treatment is therefore designed to prevent the injured cells from dying, thus minimizing tissue loss.

Nonpharmacologic Options

Open field

Consider turning back, and seek shelter from the elements.[35,36] There is a risk that the casualty may have concurrent hypothermia and if 1 member of a party has cold injury, others are at risk of cold injury so all should be assessed and removed from the elements.

Removal of clothing and jewelry

Ideally, socks and gloves should be replaced for dry pairs and boots removed. Foot swelling may prevent redonning boots, precluding the individual walking any further, so removal should only occur in a stable, sheltered location with the possibility of evacuation. Rings or similar items should be removed because with subsequent swelling this may not be possible.

Rehydration

Adequate hydration with oral (ideally warmed) fluids are warranted; intravenous (IV) fluids are an alternative.

Rewarming

- Hillside:
  - Warming by placing in another person/s armpit or groin can be attempted for up to 10 minutes. With return of sensation, the person can continue with additional improved protective measures, if they have frostnip.[35] If not, the individual needs to get to the nearest warm shelter and seek medical treatment, and a diagnosis of frostbite can be given.
  - Avoid applying dry heat (heat pads) directly on frozen tissue or rubbing, which cause tissue damage via burning and mechanical disruption respectively.
  - Ideally, a frostbitten foot should not be walked on, although this may be required practically for evacuation from remote, cold areas. Efforts should be made with splints and pads to minimize movement if walking is required.[37,38]
  - During transport, there is a risk for partial rewarming and refreezing, and individuals should be protected from indirect heat sources such as engines. The Alaska State Guidelines advocate short transport times (<2 hours) to secondary care sites, because "the risks posed by improper rewarming or refreezing outweigh the risks of delaying treatment for deep frostbite."[36] If transport time is greater than 2 hours, treatment of hypothermia takes precedence, with limb rewarming an unavoidable side effect. However, protecting the limb from refreezing is vital.
- Prehospital medical facility (ie, base camp medical center):
  - Immerse the affected part in water at 37°C to 39°C.[39] The affected limb will have impaired temperature sensation, thus if a thermometer is not available the unaffected limb should be placed in first for at least 30 seconds to ensure that the water is not too hot, which would risk injury.[38]

Once rewarmed, it is highly important that the limb is not refrozen.

Dressing and blisters

- Following rewarming, the limb should be allowed to air dry. Do not rub at any point.
- Apply aloe vera to the area and cover with a dry dressing (avoid circumferential dressings because of risk of continued swelling).

- Blisters indicate thawing[36] and should be left intact, especially if hemorrhagic. Elevation reduces blister size. Blisters are not typically aspirated/deroofed in the field.[38]
- Elevate to minimize swelling.
- Antibacterial daily or twice-daily baths are recommended and redressing every 12 to 24 hours should be performed.[38]
- Splinting and bulky dressings may offer protection to the affected area; attempt to dress between digits.

Smoking
Smoking must be avoided.

Portable recompression bag (Gamow bag)
Hyperbaric pressure bags are widely available and provide a rapid simulated reduction in altitude. Although not practical to rewarm the frostbitten area while in the bag, for 2 reasons it may be beneficial to spend periods of time in the bag following rewarming. First, while in the bag there is increased Spo_2 (peripheral capillary oxygen saturation), and second it is thought that a reduction in altitude helps to minimize cold-induced peripheral vasoconstriction and combat hypothermia.[32,40] This theory requires further evidence; however, as long as it does not interrupt rewarming or delay evacuation it may be a useful in-field adjunct.

Pharmacologic Treatment

Further details on the evidence and mechanism of action for each point discussed here is provided later in the article.

Analgesia
Rewarming can be a painful process and parenteral opioid treatment may be required for adequate analgesia; if given in the prehospital setting, start at a low dose and slowly titrate to pain, and ideally have naloxone available.

Antiinflammatory medications
All patients should be started on ibuprofen because of its dual effect as an analgesic and antiinflammatory (unless contraindicated) at a dose of 12 mg/kg twice a day up to a maximum of 2400 mg/d; 400 mg twice a day is often a practical dose.[41] Aspirin is an alternative; however, it theoretically blocks prostaglandins, which are beneficial to healing, thus ibuprofen is preferred.[42]

Oxygen
Supplementary oxygen to increase Spo_2 theoretically increases oxygen delivery to the tissues; however, this may be limited by peripheral vasoconstriction and/or microthrombi. Nevertheless it is thought that, at high altitude, oxygen may be beneficial.[32] Oxygen supplementation at lower altitudes, such as 4000 to 6000 m, is debated, although maintaining saturations greater than 90% is recommended.[38]

Tetanus
Frostbite wounds are not tetanus-prone wounds and thus standard tetanus toxoid guidelines should be followed.

Antibiotics
This area is controversial and prophylactic antibiotics have not been shown to reduce amputation[38]; however, they are often used on clinical judgment in cases of severe/extensive frostbite. If evacuation times are long and signs of infection develop, antibiotic therapy should be started, ideally with swabs taken.

Prehospital novel agents

The in-hospital use of iloprost or thrombolytics (most notable recombinant tissue plasminogen activator [rTPA]) has resulted in reduced amputation rates; however, their use seems to be time dependent, with prolonged evacuation timelines precluding usage.[41] For this reason some clinicians have advocated initiating treatment in the prehospital setting, similar to that of prehospital thrombolysis of myocardial infarction. Supporting this viewpoint is the recent publication of 2 successful case studies describing thrombolysis at K2 basecamp, and iloprost has been used in community hospitals in Canada.[32,43] However, the considerable, potentially life-threatening, side effect/complication profile associated with thrombolysis must be remembered, particularly in patients with trauma. However, iloprost, which has a safer side effect profile, is not licensed for IV usage in the United States. The authors think that the early usage of thrombolysis/iloprost is a positive forward step in frostbite management; however, we advise extreme caution because it is better to have a limb-threatening injury than a life-threatening complication. Practitioners must ensure that they are competent and have the capability to use these medications.

Sympathetic blockade

Current evidence has not shown a positive effect in frostbite management and therefore this is not advised in current guidelines.[38] However, a recent case report describes prehospital blockade to good effect so perhaps early prehospital blockade needs further exploration, but it cannot currently be advised.[44]

Telemedicine

This facilitates access to expert opinion when in austere locations or if evacuation times are long, and it has been successfully used in the past.[45] Details of how to access this can be found later in the article.

HOSPITAL MANAGEMENT

Patient Evaluation Overview

Systematic approach

All patients should be assessed using the <C>ABCDE (Catastrophic bleeding, airway, circulation, disability and exposure) paradigm and injuries treated according to priority. This approach may mean initially ignoring a frostbitten limb.

Hypothermia and frostbite frequently accompany each other. If there is moderate/severe hypothermia, a core temperature of more than 35°C must be achieved before treatment of frostbite commences.[38,46]

Detailed patient history

Areas of specific questioning include time of injury (<24 hours or >24 hours ago), mechanism of injury, climatic conditions at time of injury, freeze-thaw-freeze events, and in-field treatment.

Clinical photography

Undertake on admission and repeat throughout treatment. This photography documents the appearance and prevents the need for repeated dressing removal, which can be painful, damage tissue, and increase infection risk.

Imaging

Bone scanning, magnetic resonance angiography (MRA), and angiography all offer prognostic information and guide management.

Technecium^{99} (^{99}Tc) triple-phase bone scanning when used at day 2 postinjury offers prognostic information, accurately predicting amputation level in 84% of cases.[31,47,48] MRA is often easier to access and an attractive alternative. Importantly MRA has been shown to estimate the level of tissue loss and some clinicians suggest that it is advantageous compared with ^{99}Tc triple-phase bone scanning because it allows direct visualization of occluded vessels and surrounding tissue and may show a clearer demarcation of ischemic tissues.[49,50] This argument has yet to be confirmed in larger studies. **Fig. 2** shows an example of ^{99}Tc triple-phase bone scanning in frostbite injury.

Digital subtraction angiography clearly visualizes vessel patency and should be performed on all who are being considered for thrombolysis.[41]

Nonpharmacologic Management

Prevent constriction

Jewelry and other potentially constricting items must be removed because swelling will occur on thawing.

Fluids

Dehydration may have occurred because of cold diuresis, altitude, or extreme activity. Oral hydration is preferred; however, if the patient is hypothermic or severely dehydrated, warmed IV fluids should be used.

Rewarming

Rapid rewarming should be commenced in the presence of fully or partially frozen tissue.[51] A whirlpool bath should be used with the temperature set at 37°C to 39°C and either povidone iodine or chlorhexidine added for antiseptic qualities.[38,39] Rewarming should continue until a red/purple color appears and the extremity tissue becomes pliable; this typically takes up to 30 minutes but may require longer.[38,52] Active motion is encouraged; however, the affected tissue should not touch the side of the bath.

Rewarming may be painful and parenteral analgesia may be required; note that return of sensation is a favorable sign.

Blister management

Blisters can be clear or hemorrhagic and give an indication to the depth of injury. Hemorrhagic blisters indicate injury into the reticular dermis.

Guidelines produced by the Wilderness Medical Society advise selective drainage of clear/cloudy blisters and to leave hemorrhagic blisters alone.[38] However, there is

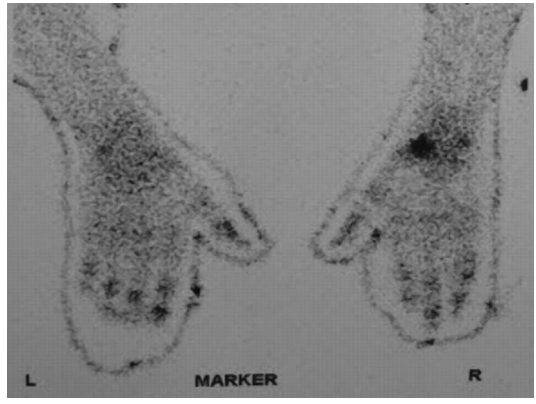

Fig. 2. ^{99}Tc triple-phase bone scan in frostbite injury. Note the terminal digits have reduced signal, most markedly in the left hand, suggesting that substantial tissue necrosis has occurred.

a limited evidence for this. The authors advocate the drainage and debridement of all blisters when in the hospital setting. This process should be performed in a sterile manner and may require a general anesthetic. The authors believe that this ultimately aids wound care and tissue healing.

Tissue protection and dressings

Protection and prevention of further tissue insult is paramount throughout the patient journey.

Affected areas should be splinted, elevated, and dressed in a loose protective dressing with padding between digits. Topical aloe vera cream/gel (an antiprostaglandin) should be applied to thawed tissue under the dressing.[38]

Later during the demarcation period, tissue protection consists of bespoke protective footwear.

Nutrition

All patients require high-protein, high-calorie, individually tailored diets.[53]

Pharmacologic Options

Analgesia

Rewarming can be intensely painful. Analgesia must be titrated to pain; parenteral opiates may be required.

All patients (unless contraindication) should be commenced on a nonsteroidal anti-inflammatory drug such as ibuprofen[38] because of its dual affect as an analgesic and antiinflammatory. Oral ibuprofen at a dose of 12 mg/kg twice a day provides systemic antiprostaglandin activity that limits the cascade of inflammatory damage.[54] This dosage can be increased to a maximum of 2400 mg/day if the patient is experiencing pain, and can be continued until wounds are healed or amputation occurs. A dose of 400 mg twice a day is a practical regimen on which to start most patients, and this can then be increased to 600 mg 4 times a day as pain dictates. Gut protection, such as a proton pump inhibitor, should be considered.

Aspirin is an alternative to ibuprofen. However, aspirin theoretically blocks some prostaglandins that are beneficial to wound healing.[55] Although aspirin has been shown to be beneficial in a rabbit ear model, even that article advocated ibuprofen rather than aspirin.[42]

Antibiotics

Infection can increase tissue loss and decrease patient outcome, thus systemic antibiotics must be commenced in proven infection and guided by skin swab results. Prophylactic antibiotics are controversial; a retrospective study showed no reduction in amputation with prophylactic antibiotic use.[56] However, some clinicians advocate prophylactic antibiotic use in the presence of edematous tissue, malnutrition, immunosuppression, or severe frostbite over a large surface area. This recommendation is not evidence based.

Tetanus toxoid

Frostbite wounds are not tetanus-prone wounds and thus standard tetanus toxoid guidelines should be followed.

Thrombolytic therapy

The aim is to reverse microvascular thrombosis, restoring blood flow. Endovascular delivery of a thrombolytic agent such as rTPA is used.

In 2005, Twomey and colleagues[57] published their results of an open-labeled study analyzing the effects of tissue plasminogen activator (TPA) in severe frostbite (confirmed

by ^{99}Tc triple-phase bone scanning). In cases with no freeze-thaw cycles, cold exposure for less than 24 hours or a warm ischemia time of more than 6 hours TPA resulted in a reduction in expected amputations.[57] In 2007, Bruen and colleagues[17] further added to the literature base with a retrospective comparative study showing that TPA within 24 hours of injury reduced the amputation rate from 41% to 10%. Gonzaga and colleagues[58] undertook a retrospective cohort study within their unit and found that, following thrombolysis, there was an amputation rate of 31.4% for 472 at-risk digits.

Cauchy and colleagues[59] undertook a randomized controlled trial of 44 patients in which 1 arm received rTPA with iloprost and aspirin. The other 2 arms received either aspirin with buflomedil or aspirin with iloprost. rTPA was beneficial (3.1% of digits amputated) compared with the buflomedil arm (39.6%); however, this benefit was inferior to that in the iloprost arm (0%). Individual case reports have also shown positive results with thrombolytic therapy.[46,60,61]

Before delivery of thrombolytic therapy, clinicians must be sure of patient factors, unit ability, and mechanism/technique of delivery, including monitoring.

- The injury must be severe with potential tissue loss and have occurred within the last 24 hours with no freeze-thaw cycles.[57] There must be no contraindications to thrombolysis, including, but not limited to, recent trauma or surgery, bleeding diathesis, and neurologic impairment.
- The unit's staff must be competent in their ability to delivery thrombolysis, which usually requires regular monitoring, blood tests, and imaging, be able to manage complications. Critical care is often required.
- Thrombolysis can be delivered via IV or intra-arterial (IA) routes.[41] IA is our preferred route. A vasodilator such as papaverine may be added to reduce vasospasm. Heparin should be used as an adjunctive therapy in the case of thrombolytic therapy to minimize new clot formation or enlargement of existing clots, and equally heparin should be continued for a period after thrombolytic treatment has concluded.[38,41]
- Monitoring is required to assess efficacy of treatment. This monitoring must include regular patient observations, including assessment of affected area, thromboplastin must be checked (this guides heparin infusion rate), and angiographs repeated as appropriate.

Thrombolysis can be challenging for clinicians with minimal previous exposure to frostbite injury. A recent publication gave a simple stepwise approach for rTPA administration (**Fig. 3**). Nevertheless, contacting a specialist practitioner may be required (discussed later).[41]

Iloprost

Iloprost is a prostacyclin analogue with vasodilatory properties. It also reduces capillary permeability, suppresses platelet aggregation, and activates fibrinolysis.[20] IV iloprost is unavailable in the United States.

Groechenig[62] published his experience of treating severe frostbite with iloprost in 1994 and the results were promising with no amputations. Focus returned to iloprost following a randomized controlled trial published by Cauchy and colleagues[59] that showed a reduced amputation rate among 407 digits that were at risk (47 patients). All received identical initial treatment before being randomized into 1 of 3 arms: buflomedil, iloprost, or iloprost and IV rTPA. The iloprost arm had no amputations.[59] Two recent case reports also showed excellent results in grade 3 frostbite.[43]

Iloprost is administered as an IV infusion at a set rate in a monitored environment; it can be given peripherally or centrally. The infusion should be delivered at an

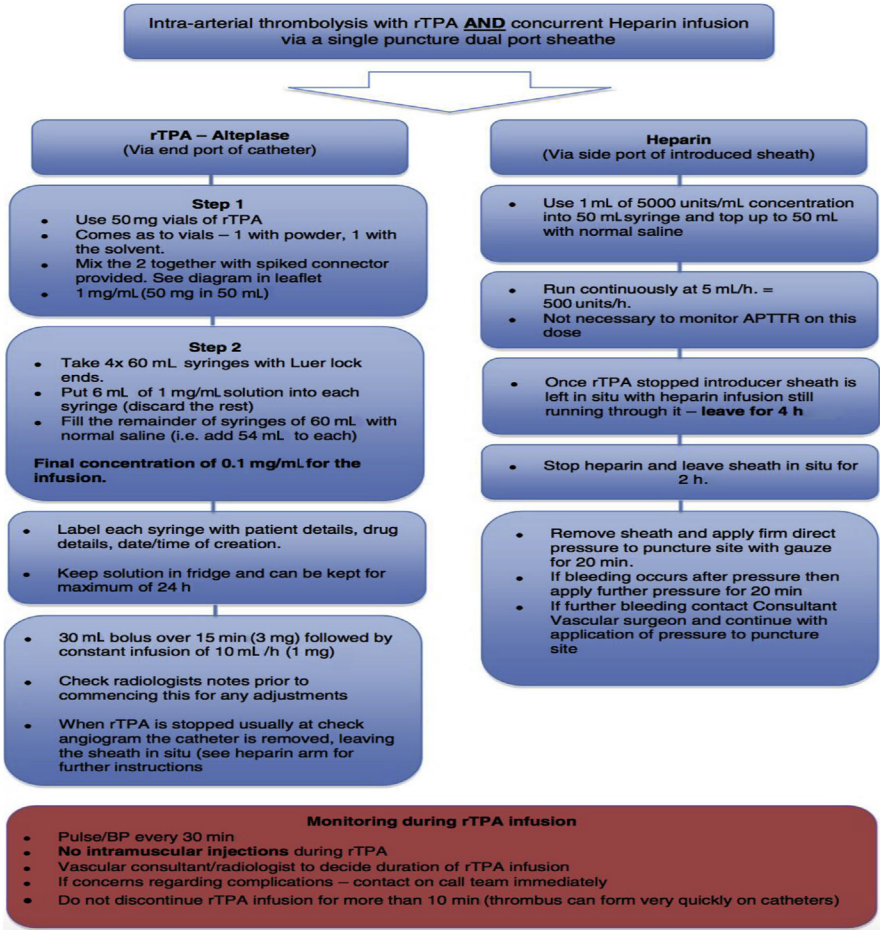

Fig. 3. A stepwise approach to IA thrombolysis and concurrent heparin infusion. APTTR, activated partial thromboplastin time ratio. (*From* Handford C, Buxton P, Russell K, et al. Frostbite: a practical approach to hospital management. Extrem Physiol Med 2014;3:7.)

accurate rate, usually achieved with a syringe driver. Clinicians should start at a rate of 0.5 ng/kg/min and escalate via increments of 0.5 ng/kg/min to a maximum dose of 2 ng/kg/min.[59] Escalation of delivered dose is performed until intolerable side effects develop, such as facial flushing and headache. The dose regimen is usually 6 hours daily for a total of 5 to 8 days.[43,59] A practical guide to aid clinicians in the administration of iloprost was recently published (**Fig. 4**).[41] **Fig. 5** shows a patient following a 5-day course of iloprost.

Iloprost has key advantages compared with rTPA. It does not require radiological intervention for use, can be administered on a general monitored ward, can be used more than 24 hours after injury, and is not contraindicated in trauma.

Surgical Treatment Options

Fasciotomy

On rewarming there is a risk of compartment syndrome if significant swelling occurs on reperfusion. In such a case rapid fasciotomy is indicated.

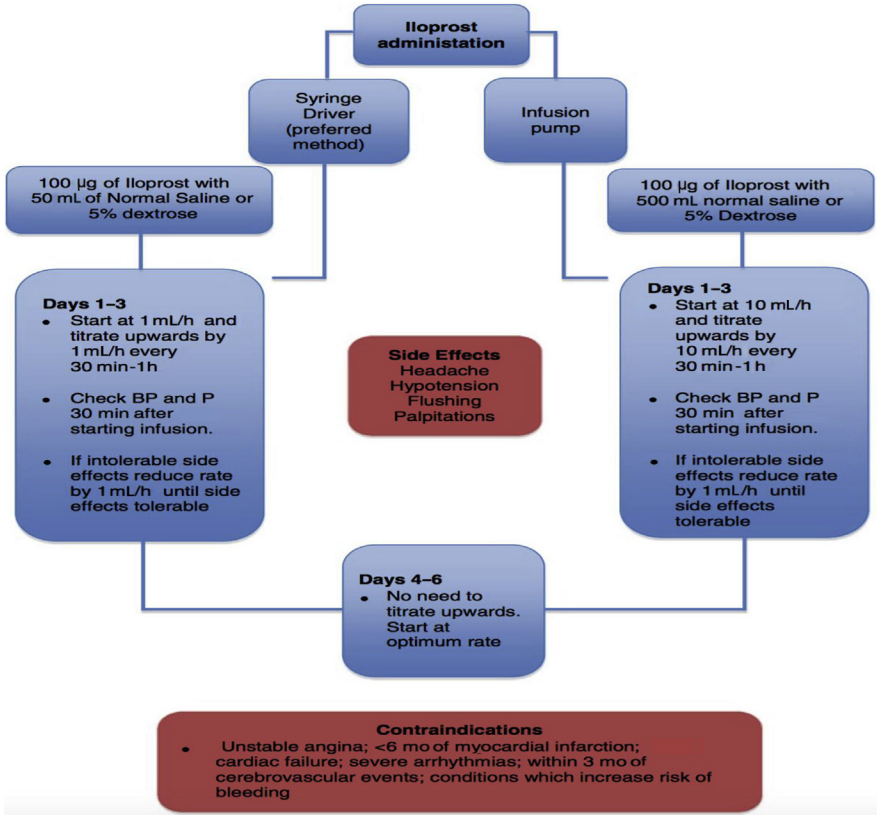

Fig. 4. A stepwise approach to iloprost administration. BP, blood pressure; P, pulse. (*From* Handford C, Buxton P, Russell K, et al. Frostbite: a practical approach to hospital management. Extrem Physiol Med 2014;3:7.)

Amputation

Immediate or early amputation should be avoided and autoamputation/demarcation awaited.

Amputation must be planned to maximize functional outcome. Early amputation may be unavoidable in cases of wet gangrene, liquefaction, overwhelming infection, or spreading sepsis.[63,64] In such cases, planning is still key and using MRA/^{99}Tc triple-phase bone scanning is useful.

Topical negative pressure dressings and tissue reconstruction

Following injury good-quality tissue is wanted after healing. This tissue is key at load-bearing sites and functionally significant areas. Little is published on the best way to achieve this and healing via secondary intention is the usual course of action. Topical negative pressure facilitates wound healing via secondary intention and may be considered as an adjunct to healing.[65–68]

An alternative to healing via secondary intention is skin coverage. An experimental study by Delgado-Martínez and colleagues[69] argues that, in structurally significant areas such as the hands or feet, or areas with a poor vascular bed, which is the case in most significant frostbite injuries, flap coverage should be used. In their

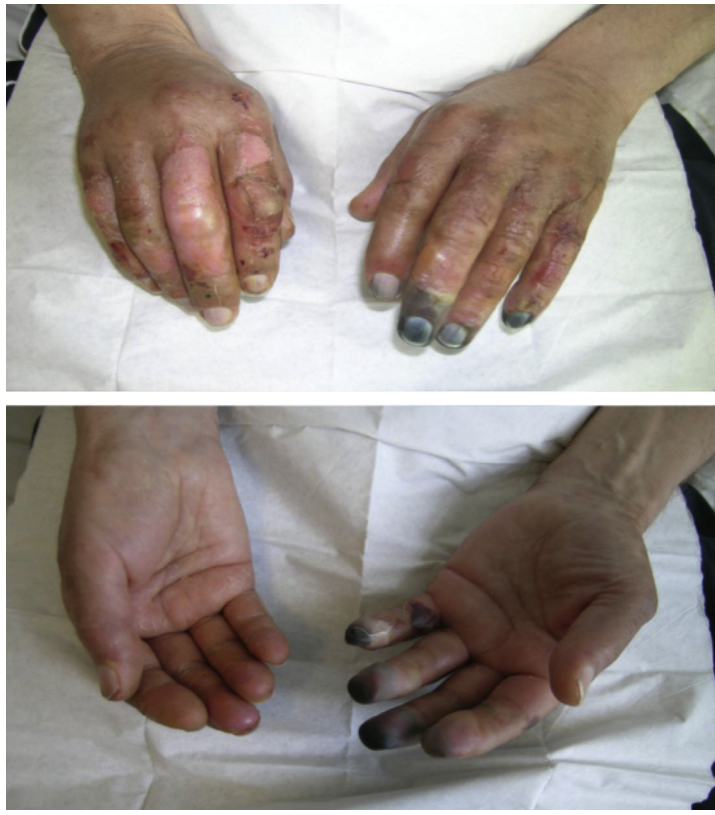

Fig. 5. Appearance following a 5-day iloprost infusion, showing the close correlation between the initial ^{99}Tc triple-phase bone scan (see Fig. 2) and the subsequent clinical appearance (day 10 following iloprost).

practice these investigators advocate the use of axial flaps. Skin grafts have a role in areas with limited structural importance; however, their limitations consist of variable take rates, contraction, rigidity, lack of padding, and poor reinnervation, all of which could result in functional problems.[69]

Potential Adjunctive Therapies

The following have been described in case reports and/or animal studies. However, there is insufficient evidence at this time to advocate their use on a routine basis.

Hyperbaric oxygen therapy

Hyperbaric oxygen therapy (HBOT) has been used to aid wound healing.[70] HBOT increases oxygen tension within the blood and thus increases oxygen delivery and may increase the deformability of erythrocytes and decrease bacterial load.[38] However, for the frostbitten tissues to experience increased oxygen tension, there must be a patent microvasculature.

Case reports describe HBOT use in frostbite injury in both immediate and delayed presentations, with no amputations reported.[71,72] Animal studies are contradictory.[73–75] Further investigation is warranted.

Sympathectomy

Surgical or chemical sympathectomy results in reflex vasodilation and increased blood flow but reported outcomes are mixed.[76,77] For this reason, sympathectomy in acute frostbite management is not recommended.[38]

Sympathectomy may have a role in the management of chronic complications such as vasospasm and hyperhidrosis; however, surgical sympathectomy is both invasive and irreversible and further research is warranted.[78,79]

Topical agents

Aloe vera has long been accepted as a topical treatment of frostbite injury. Investigations into other agents, such as poly-l-arginine contained in lotion and ganoderma triterpenids, and nanogel delivery methods have been attempted.[80–82] Trials are limited, small scale, and on animal models, therefore until further data are accumulated these cannot be recommended.

Complications

Functional loss and rehabilitation

Functional loss is variable depending on extent and area affected. All patients with significant injury should be managed by a multidisciplinary team consisting of physicians, occupational therapists, specialist nurses, physiotherapist, and (if needed) a prosthetist/orthotist. Mental health input may also be prudent. The aim should be to return the individual to the optimal function and independence. Many patients will continue to pursue outdoor endeavors and their future risk of cold injury must be discussed with them.

Cold sensitivity

Taylor[78] found that 53% of patients with significant frostbite injury showed subsequent cold hypersensitivity, 40% numbness of the digits, and 33% had reduced sensitivity to touch. Taylor[78] postulated that these may be secondary to a thermophysiologic response with an increased tendency to vasospasm, and others have supported these findings.[83]

Chronic pain

Chronic pain is common and can be troublesome to treat, and early use of chronic pain specialists should be sought. Medications such as amitriptyline or gabapentin may be beneficial.

In major trauma and burns, early commencement of neuropathic pain medication to reduce the risk of chronic neuropathic pain is becoming standard practice.[84,85] Although no trials have been performed in frostbite, the authors advocate consideration of a neuropathy agent as early as possible.

Chronic ulceration

Subsequent poor tissue quality and/or altered biomechanics and pressure areas following lower limb amputations can lead to chronic ulceration in previously frostbitten skin. As is the case in burns, malignant transformation can occur in such areas and must be monitored for.[86]

Arthritis

Arthritis following frostbite is well reported.[87–89] Localized osteoporosis and subchondral bone loss can be seen after injury and likely reflects vascular insult. In the skeletally immature, damage to the epiphysis may occur, leading to growth arrest/deformity.[88,90]

TELEMEDICINE

Increased availability of and reliance on telecommunications, photographic sharing, and video communications have led to a growth in telemedicine, which facilitates access to and use of subject matter experts, optimizing patient outcome.[45,91] Telemedicine can be accessed by those who are in an isolated austere environment, aiding initial management decisions and advising on expedition continuation. Medical practitioners with limited experience or knowledge regarding frostbite can also seek guidance and advice via telemedicine.

Further information can be found on the British Mountaineering Council Web site (https://www.thebmc.co.uk/how-to-get-expert-frostbite-advice). At the time of writing, the University of Utah Health Care Burn Center also provides a frostbite telemedicine service (http://healthcare.utah.edu/burncenter/frostbite.php).

SUMMARY

Management of frostbite is undermined by poor evidence; this is caused by low patient numbers and therefore little economic incentive for drug company/large institutional input. To further progress the understanding and management, large, likely multicenter, trials are warranted. An international patient register would be a positive starting point.

Despite these limitations, new management options in deep frostbite injury offer promise in minimizing the morbidity associated with this significant injury. This article highlights simple and effective treatment steps that all clinicians can perform through every echelon of care. The more complex and specialist treatments, most notably thrombolysis or iloprost infusion, should always be considered and, via telemedicine, expert opinion can be sought, ultimately optimizing patient outcome.

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