

Single Shot TNK for Severe Frostbite

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Disclosure

- Alexandra Lacey, MD has no conflicts to report

Background

- Severe frostbite is a rare disease process but causes extensive morbidity due to multiple amputations
- Frostbite can occur to anybody when the temperature drops below 40 degrees Fahrenheit
- A recent study from the Armed Forces in 2018-2019 showed the rate of severe frostbite was 36.5 per 100,000 which is one of the highest publicly available military rates in the world¹

Pathophysiology

- Systemic cooling shunts blood from the extremities to the core
- Ice crystals begin to form extracellularly causing dehydration and damage to the tissues
- Intracellular crystals develop next cause cell lysis
- Endothelial cells rupture triggering clot formation in the microvasculature
- Dying cells release prothrombotic factors worsening tissue ischemia²

Frostbite Diagnosis

- Physical exam
 - Cauchy grading scale³
- Doppler exam
- Advanced imaging techniques

Grading severity of frostbite after rewarming			
Absence of cyanosis	Cyanosis on distal phalanx	Cyanosis up to MP joint	Cyanosis proximal to MP joint
			
			
Grade 1 No amputation of bone	Grade 2 Moderate risk of amputation	Grade 3 High risk of amputation	Grade 4 Risk of amputation 100%

Physical Exam



Rewarmed



24 hours



10 days



Advanced Diagnostics



Physical Exam (24 hours)



Formal Angiography (24 hours)

Current Standards

- All patients who present frozen are first treated with rapid rewarming
- Tissue is then assessed for perfusion
 - Grade 3-4 receives thrombolytic therapy if no contraindications to treatment
 - All tissue affected is scored as “At Risk” using Hennepin Frostbite Score⁴
- Thrombolytic therapy delivered within 6 hours of rapid rewarming⁵
- >80% salvage rate of affected frostbitten tissue

Thrombolytic Treatments

Tissue Plasminogen Activator (tPA)

- Naturally occurring compound in human tissues
- Predominant treatment for the last 30 years
- Frostbite treatment algorithms based upon stroke literature from the 1980s
- 0.15 mg/kg bolus followed by infusion for 6 hours

Tenecteplase (TNK)

- Variant of tPA with 3 amino acid substitutions resulting in increased affinity for and degradation of fibrin
- More resistant to natural de-activation in the body (longer half-life)
- Improved outcomes in stroke literature with lower complication rates than tPA (AcT, TRACE-2, and ATTEST-2)⁶⁻⁸
- Delivered as a single 0.25 mg/kg injection one time

Tenecteplase (TNK) as a Novel Treatment

- Promising data in stroke literature
- Easier delivery
 - Lyophilized powder stored at room temp
 - Quickly reconstituted
 - Delivered in a single injection
- Cheaper cost per dose by approximately \$3000

Treatment Process Change

Former Standard

- Patient evaluated after rapid rewarming completed
- Grade 3-4 frostbite diagnosed
- Transfer to burn unit
- Start infusion of tPA x 6 hours

New Standard

- Patient evaluated after rapid rewarming completed
- Grade 3-4 frostbite diagnosed
- Deliver single dose of TNK in Emergency Department

Data Collection

- December 2025 – March 2026
- 14 doses of TNK delivered to 13 patients
- Demographics
 - Middle aged (median 49 years)
 - White (61.5%)
 - Male (69%)

Results

- Time to thrombolytic delivery rapidly improved
 - Previous years varied from 6-12 hours from rewarming
 - New time to thrombolytics averaged 2.48 hours
 - Two patients received TNK prior to transfer from remote hospitals

Results

- Eight of thirteen patients required some degree of amputation
- Median salvage score was 90%
 - Two patients lost all affected tissue
 - Five patients had 100% of tissue salvaged

Complications

- No cases of angioedema or other serious adverse reactions were seen
- One patient developed a flank hematoma necessitating cessation of therapeutic enoxaparin
 - No blood transfusion required

Conclusions

- Tenecteplase is a safe treatment for severe frostbite
- Ease of use dramatically decreased our time from rewarming to thrombolytic delivery
- Tissue salvage rates were improved from prior years data

Upcoming Investigations

- Upcoming research will utilize thromboelastography (TEG) to determine optimal dosing of TNK
- Larger populations needed to determine true salvage rates and risks with this medication given small sample size (N=14)

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