Response to Comments on “The Use of tPA in the Treatment of Frostbite: A Systematic Review”

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We appreciate the analysis and response to our article.¹ In the design of our systemic review, our intent was to pool the relevant findings. Unfortunately, the inherent potential for bias in the study designs used did not logically permit the combining of the results. Most of the papers were case reports or case series, and it is not proper to pool data from these types of studies. The 2 other papers found by our colleagues at Albany Medical College fall into this category and do not change our conclusions. The results of the 3 cohort studies could not be aggregated due to wide variations in their experimental designs, including different selection criteria, differing doses, routes of administration, type, timing, and duration of antithrombotic therapy, differences in adjuvant therapy, varying outcome measures, and the lack of matched control groups.² The absence of well-matched control groups is a major concern when trying to decide the clinical value of tissue plasminogen activator (tPA) based on scientific criteria. Conclusions regarding causation should not be derived from descriptive protocols such as case reports or series, and the heterogeneity of the cohort studies makes their interpretation difficult.³ Only one randomized, controlled study was found. This study did not find a clear benefit to treatment with tPA.

Based on the studies that we reviewed and the 2 additional studies, we agree that the use of tPA for the treatment of frostbite shows promise. Hopefully, well-designed experimental studies will better define the role of tPA and other modalities in the care of patients with frostbite.

Ethical Approval

This study was approved by our institutional review board.

Statement of Human and Animal Rights

This article does not contain any studies with human or animal subjects.

Statement of Informed Consent

Informed consent was obtained when necessary.

Declaration of Conflicting Interests

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