

Free-Flap Salvage by Thrombolytic Agents? An Evidence-Based Systemic Analysis

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INTRODUCTION:

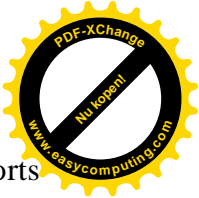
Despite the advances in microsurgery and the experience gained in clinical practice, failures caused by thrombosis at the site of microanastomosis remains a challenge to plastic surgeons. The failure rate of approximately 5% of all free-flap surgeries clinically suggested that there may be a place for pharmacological intervention at the time of threatened flap failure. But there was no consensus on the role of thrombolytic agents in free-flap salvage.

METHODS:

We performed a systemic literature review by searching the PubMed database from January 1980 to December 2010. We used the following key words: thrombolytic agents, streptokinase, urokinase, recombinant tissue plasminogen activator, free flap, free tissue transfer, and thrombosis. We excluded the non-English articles, and studies in experiment animals, and digit or limb replantations. Two reviewers independently extracted data in two steps: titles and abstracts, and then full text articles. This search was supplemented by a review of reference lists of potentially eligible studies. Relevant studies were assigned a level of evidence according to the American Society of Plastic Surgeons Evidence Rating Scale for Therapy.

RESULTS:

Through our electronic and reference search we identified 22 citations. There was neither



randomized controlled trial nor meta-analysis meets our study topic. There were fifteen case reports (Level V Evidence), three case series (Level IV Evidence), and four retrospective comparative studies (Level III Evidence). In the four retrospective comparative studies (Table 1), only one used uniform thrombolytic agent (recombinant tissue plasminogen activator, rTPA) with a standard dose of 2.5 mg, and had clearly-defined indication of thrombolysis and its additive dose.¹ In this study, though with a higher salvage rate by using the rTPA, there was no statistic significance between the treatment and control groups ($p = 0.17$). Indication for thrombolysis varied from 'established extensive clot in either the arterial or the venous system'², 'no sufficient restoration of blood flow after blood clot evacuation'¹, to 'failure to reestablish venous outflow after establishing good arterial inflow'³. The salvage rate of the treatment groups ranged from 30% to 75% and the control groups shared similar results with the salvage rate ranged from 29% to 67%.

CONCLUSIONS:

The literature on the clinical efficacy of thrombolytic agents in the free-flap salvage has not been well documented. All of the findings come from the four retrospective comparative studies and the equivocal results suggest that it is not possible to draw clear conclusions about the role of thrombolytic agents in free-flap salvage. Further studies are needed regarding their indications, dose, routes of administration, efficacy, safety, and patient randomization. Intensive flap monitoring at a specialized microsurgical intensive care unit by well-trained staffs and urgent re-exploration remain critical for free-flap salvage.



Reference:

1. Rinker, B. D., Stewart, D.H., Pu, L. L., et al. Role of recombinant tissue plasminogen activator in free flap salvage. *J. Reconstr. Microsurg.* 23: 69, 2007.
2. Bui, D. T., Cordeiro, P. G., Hu, Q. Y., et al. Free flap reexploration: indications, treatment, and outcomes in 1193 free flaps. *Plast. Reconstr. Surgery.* 119: 2092, 2007.
3. Panchapakesan, V., Addison, P., Beausang, E., et al. Role of thrombolysis in free-flap salvage. *J. Reconstr. Microsurg.* 19: 523, 2003.
4. Yui, N. W., Evans, G. R., Miller, M. J., et al. Thrombolytic therapy: what is its role in free flap salvage? *Ann. Plast. Surg.* 46: 601, 2001.

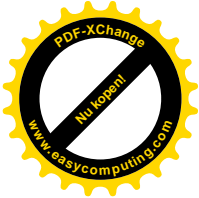
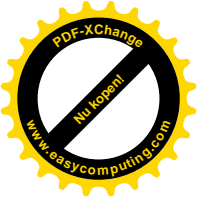


Table 1. The four retrospective comparative studies

Author, Year	Flap No.	Thrombolytic agents, doses, and case numbers	Salvaged Cases (%)
Yii, 2001 ⁴	41	UK (mean, 100,000 units) : 7 cases; rTPA (15 mg) : 1 case	6 (75%)
		Control: 33 cases	22 (67%)
Panchapakesan, 2003 ³	44	SK or UK (250,000 units): 20 cases	6 (30%)
		Control: 24 cases	13 (54%)
Rinker, 2007 ¹	22	rTPA (2.5mg to 5 mg): 15 cases	10 (67%)
		Control: 7 cases	2 (29%)
Bui, 2007 ²	38	SK (50,000 to 250,000 units) or rTPA (5 to 20 mg): 20 cases	13 (65%)
		Control: 18 cases	11 (61%)

Abbreviation: UK, urokinase; rTPA, recombinant tissue plasminogen activator; SK, streptokinase.