



Clinical Guide - Thrombolytic Therapy in Peripheral Arterial Disease

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Introduction

Thrombolysis for arterial insufficiency dates back five decades but comparative data with surgery date back one decade only. Systemic fibrinolytic therapy is not effective and has long given way to intra-arterial thrombolysis. Despite this, the role of thrombolytic therapy is still controversial and requires considerable clinical expertise with a team approach usually consisting of an interventional radiologist, a vascular surgeon and/or an internist. The benefit of pharmacological clot lysis must always be weighted against surgical intervention and the risk of bleeding associated with fibrinolysis. All actual intra-arterial lysis protocols result in a certain degree of systemic fibrinolysis, responsible for a real risk of major bleeding comparable to fibrinolysis for myocardial infarction. In particular, intracerebral hemorrhage occurs in up to 1% of treated cases. Although all major vascular centers use fibrinolytic therapy as part of their armamentarium, there is no regulatory agency approving any protocol in Canada at this time.

Indications

Acute arterial embolism

Surgical embolectomy, with a Fogarty catheter for example, is the preferred mode of intervention for proximal acute arterial embolic occlusion. Surgery results in faster restoration of blood flow than fibrinolysis, without the risk of hemorrhage. Local fibrinolysis is occasionally used per- or post-operatively in this context only if there is additional distal clot embolisation difficult to reach surgically and only if there is risk of tissue loss.

Intra-arterial fibrinolysis is a useful means of revascularisation when multiple distal infra-popliteal clots compromise a limb, such as in an acutely ischemic leg resulting from an occluded popliteal aneurysm with no visible run-off on the angiogram.

Acute thrombotic arterial occlusion: native arteries

Although fibrinolysis sometimes results in less extensive surgical interventions (STILE and TOPAS studies, both randomized), major end points such as mortality and amputation-free survival are not significantly different. Nevertheless, timing being the priority, fibrinolysis can precede surgery and vice-versa depending on the immediate availability of these interventions. It is crucial to remember that 8 hours is the time limit to revascularize a profoundly ischemic limb without incurring tissue damage or gangrene. Since intra-arterial fibrinolysis cannot be reliably counted upon to restore adequate flow in 8 hours when there is an underlying atherosclerotic lesion, serious consideration should always be given to surgical revascularisation.

Acute thrombotic arterial occlusion: occluded bypass

It is in this field that intra-arterial fibrinolysis is perhaps the most useful, permitting better planning of the subsequent surgery and resulting in a less extensive procedure. But then again, long term major end points are not necessarily better. It is important to remember that thrombosis of femoro-popliteal or similar bypasses are related to early or late surgical stenosis and atherosclerosis and that restoring flow is usually not sufficient to insure continued patency.

Sub-acute (no immediate muscular or neurologic threat) and chronic peripheral atherosclerotic occlusion

Intra-arterial fibrinolysis can be considered for recently ischemic limbs, ideally if ischemia has been present for less than 14 days. Surgery has been demonstrated superior than thrombolysis for limbs with more than 14 days of sub-acute ischemia.

Occluded dialysis access grafts

Local thrombolysis with a small rapid bolus of a fibrinolytic agent is an interesting procedure to reopen occluded dialysis access grafts.

Intraoperative thrombolysis

Thrombolysis for acute endovascular complications

Local fibrinolysis is a useful adjunctive technique during surgery when there are residual thrombi or new thrombi arising from a complicated procedure. The risk of bleeding must be weighted against the importance of tissue ischemia or graft compromise by poor occluded run-off.

Contraindications

- Absolute:**
1. Stroke or recent TIA, although low dosage regimens might be considered in desperate cases.
 2. Active or recent bleeding
 3. Significant coagulopathy eg Von Willebrands disease, severe thrombocytopenia, HIT etc.
- Relative:**
1. Recent (less than 3 months) neurosurgery or cranial trauma
 2. Resuscitation, surgery or trauma in last 10 days
 3. Uncontrolled HBP (>180 syst. >110 diast.)
 4. Recent puncture of non compressible vessel (i.e. sub-clavian etc)
 5. Intracranial tumor and recent eye surgery
- Minor:**
1. Pregnancy
 2. Endocarditis
 3. Diabetic hemorrhagic retinopathy
 4. Hepatic failure with coagulopathy

Agents and mode of administration

Dosage and methods of administration have not been standardized. Nevertheless sufficient experience has been gained, leading to consensus recommendations by the Society of Vascular & Interventional Radiology: consulting the web site (section on Consensus Documents) is very helpful: <http://www.sirweb.org>

Urokinase (Abbokinase™) has been the agent of choice in the last decade, because of possibly better results than with Streptokinase, although no head to head double blinded prospective comparative study has ever been published. However, Urokinase is presently not available in Canada.

Recombinant t-PA (rtPA or Activase™) has emerged as an alternative to Urokinase and published data show comparable if not somewhat faster revascularisation rates.

Third generation fibrinolytics hold the promise of being more fibrin specific, with more rapid clot lysis, but comparable bleeding risk. Examples are Reteplase (Retavase™) and TNK-tPA. Experience in arterial occlusions is limited compared to rt-PA

References

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