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Catheter-directed thrombolysis for acute limb ischaemia: An audit

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RESEARCH

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ABSTRACT

Background
Acute limb ischaemia (ALI) is commonly managed with surgical intervention but catheter-directed thrombolysis (CDT) is a proven treatment alternative. CDT as a treatment for ALI is not common and is dependent on local practice. All patients receiving urokinase infusions at our institution currently require a bed in the high-dependency unit (HDU). Administering the infusion requires significant nursing time and this can be accommodated in HDU where the nurse-to-patient ratio is higher than it is on general wards.

Aims
To report the outcomes of the initial admission of patients who received CDT to manage ALI, and to give a cost estimate of their care.

Method
A retrospective audit was undertaken of all patients who received CDT with urokinase for the management of ALI over a four-year period. Success of thrombolysis was defined as a patient's survival with no need for any surgical intervention prior to discharge. Outcome measures included the requirement for further vascular procedures in the same admission, the complication rate, and the median urokinase dose and duration. Cost estimates were based on hospital pharmacy and administration data.

Results
Seventy-three patients (median age 66 years, range 27–93 years) were included in the audit. The median urokinase dose was 2.3 million units (range 0.9–5.0 million units) with a median duration of treatment of 26 hours (range 3–96 hours). Fifty-seven patients did not require any further intervention prior to discharge, 14 had further intervention, and two died (one from a brainstem haemorrhage and one who deteriorated despite thrombolysis).

The total cost per CDT case at our institution is currently approximately AUD $4,500 and AUD $6,700 for a patient being treated in HDU for one and two days, respectively. If patients were treated on a general ward, the cost would be approximately AUD $2,600 and AUD $3,000, respectively.

Conclusion
Rates of clinically acceptable clot lysis were high for patients treated with urokinase for ALI. Complication rates were comparable with published studies. Infusions can be required for prolonged periods of time and given the low complication rate, managing patients on a general ward rather than in the HDU is a feasible alternative and would reduce costs substantially.

Key Words
Acute limb ischaemia, Catheter-directed thrombolysis, Urokinase

What this study adds:

1. What is known about this subject?
Catheter-directed thrombolysis (CDT) and surgical intervention are the management options for acute limb ischaemia (ALI), but CDT is not currently widely used in Australian hospitals.

2. What new information is offered in this study?
Managing patients receiving CDT in the high-dependency unit (HDU) setting adds significant costs whereas enabling

ALI patients to be managed on general wards could reduce costs substantially.

3. What are the implications for research, policy, or practice?

In hospitals where CDT is performed, consideration should be given to managing these patients on general wards.

Background

Thrombolytic agents can be administered locally, by catheter-directed thrombolysis (CDT), or systemically. Acute ischaemic stroke[1] and ST-segment-elevation myocardial infarction are frequently managed with thrombolysis,[1,2] but its use in the management of acute limb ischaemia (ALI) is less common given that other treatments are available.[3,4]

Treatment options for ALI are surgery and CDT.[5] A Cochrane review of five randomised trials comparing surgery and thrombolysis for initial management of ALI, reported that there was no clear superiority of either option.[3] The method chosen is decided upon by the treating team and is based on the clinical state of the affected limb (with the presence of sensory and/or motor signs mandating surgical intervention), the preference of the treating team, and the availability of a catheter laboratory. The costs of managing a patient receiving CDT are substantial considering the cost of the urokinase infusion and the nursing care required.

CDT is recommended over systemic thrombolysis for ALI as lower doses of thrombolytic agents can be used, thereby reducing the risk of serious bleeding.[4,6] By inserting a catheter into the affected vascular segment, the thrombolytic agent is delivered directly into the clots. Urokinase is the only feasible thrombolytic agent for peripheral vascular use due to regulatory issues.

The purpose of this audit was to report on CDT in terms of: it achieving clinically acceptable clot lysis; the complication rate; the duration of thrombolysis; and the associated costs and resource implications.

Method

Patients were identified through the Radiology Department's urokinase database. Between January 2009 and February 2013, 109 patients received urokinase at University Hospital Geelong (Geelong, Victoria, Australia). Additional information was obtained from electronic medical records and the picture archiving and communication system (PACS).

Patients were included if the indication for the thrombolysis was thrombosis or embolism presenting with ALI. This was confirmed by computed tomography angiography, digital subtraction angiography, or ultrasound. Patients were assessed by the vascular unit at the time of presentation to be in need of urgent surgery or suited for CDT, and thus no specific clinical criteria were required to be eligible for the study. Patients were excluded if urokinase was administered for peripheral embolisation during an endoluminal procedure, deep vein thrombosis, or for arteriovenous fistula/graft thrombosis. The final study population included 73 patients.

All patients in the study received intravenous heparin in the therapeutic range and CDT with urokinase by continuous intra-arterial infusion according to local protocol (bolus urokinase 250,000 units followed by urokinase at 200,000 units/hour for four hours and then 50,000 units/hour maintenance). Treatment at any subsequent admission was not reviewed.

The decision to cease the urokinase infusion was always made in consultation with the Radiology Unit. Hence, the Radiology Unit was informed of any complications that may have been attributable to the thrombolysis. Due to local nursing staff-patient ratio requirements to administer the urokinase infusion, patients receiving CDT were managed in the high-dependency unit (HDU) for the duration of the infusion.

For the purpose of this study, success of thrombolysis was defined as a patient's survival with no need for any surgical intervention prior to discharge. The cost of the urokinase was obtained from the hospital pharmacy department and bed costs from the hospital administration.

Statistical analysis

The indications for thrombolysis, success rates, subsequent intervention rates, and complication rates were calculated as percentages. Median values and ranges have been reported for patient ages, hours of thrombolysis, and doses of urokinase administered.

Results

Seventy-three patients (median age 66 years, range 27–93 years) with peripheral arterial artery occlusions were treated (48 males, 25 females). All were in the lower limb. Table 1 describes the vessel in which the occlusions occurred.

Table 1: Type of vessel involved in lower-limb artery occlusions

Type of vessel	Patients
Native or stented	54 (74%)
Bypass graft	19 (26%)
• Polytetrafluoroethylene	15
• Autologous vein	4

The median urokinase dose was 2.3 million units (range 0.9–5.0 million units) with a median duration of therapy of 26 hours (range 3–96 hours).

Fifty-seven cases (78.1 per cent) were successful. Fourteen patients (19.2 per cent) required at least one further vascular procedure during the same admission as thrombolysis was administered. The number of each definitive intervention performed is listed in Table 2.

Table 2: Subsequent interventions performed post thrombolysis in patients with ALI (n=14)

Procedure	Patients
Amputation	6 (8.2%)
Embolectomy/Thrombectomy	4 (5.5%)
Fasciotomy	2 (2.7%)
Bypass	1 (1.4%)
Endarterectomy	1 (1.4%)

Two patients (2.7 per cent) died—one from a brainstem haemorrhage and one due to the deterioration in their condition despite thrombolysis. One patient had a retroperitoneal bleed requiring endoluminal intervention.

Two patients developed ischaemia in the upper limb (having originally presented with lower-limb ischaemia), secondary to a brachial puncture and required a brachial artery thrombectomy. One patient with a prosthetic profunda to anterior tibial artery bypass graft had significant distal embolisation to the distal third of the anterior tibial artery during the procedure. This resulted in anterior compartment syndrome and subsequent amputation.

Minor complications were encountered in four patients (5.5 per cent): one had possible hematemesis (gastroscopy did not demonstrate any bleeding); two had pseudoaneurysms and one had a thigh haematoma.

All patients receiving urokinase infusions at our institution currently require a bed in the HDU. Administering the infusion requires significant nursing time and this can be accommodated in HDU where the nurse-to-patient ratio is higher than it is on general wards. Based on the median duration of therapy of 26 hours (range 3–96 hours), a patient would occupy a HDU bed for a minimum of one to two days. The cost of a HDU bed at our institution is approximately AUD $2,200/day. The median dose of urokinase was 2.3 million units and 100,000 units of urokinase costs AUD $98.23. Per CDT case, this equates to a total cost of AUD $4,500 and AUD $6,700 for one and two days, respectively.

Discussion

European[7] and United States[8] registries report that surgery is used three to five times more frequently than thrombolysis for ALI. This is despite the 2005 ACC/AHA guidelines on peripheral artery disease[5] and the 2012 American College of Chest Physician guidelines on antithrombotic therapy for peripheral artery disease,[6] concluding that CDT is effective and beneficial and is indicated in a subgroup of patients with ALI—patients in whom the signs do not dictate urgent time-critical intervention to avert immediate limb death. These recommendations were based on two randomised trials, the STILE[9] and TOPAS[10] trials, which compared thrombolysis and surgery.

In our audit, 78.1 per cent of patients survived and did not require any further vascular interventions before discharge from hospital. This is much higher than the 23 per cent reported by the TOPAS investigators.[10] Our results are similar to the studies by Swischuk et al.[11] and Wongwanit et al.[12] who reported success rates of 86 per cent and 86.5 per cent, respectively. These studies administered intra-arterial recombinant tissue-type plasminogen activator infusions. The first study included patients with occluded bypass grafts or native arteries while the second only included patients with occlusions in native arteries.

In the TOPAS[10] and STILE[9] trials, the rates of amputation at six months were 17.6 per cent and 11.8 per cent, respectively, and the death rates, 16 per cent and 6.5 per cent, respectively. These trials were extended over six months to compare CDT with surgery. The purpose of this audit was to analyse the efficacy of CDT in achieving clinically acceptable clot lysis (such that the patient could be discharged, their presenting symptoms/signs having been alleviated) versus adverse outcomes (including lack of success). The other studies quoted looked at the longitudinal outcomes of people with peripheral vascular disease, extending well beyond the initial hospital episode and including subsequent treatments with their own attendant risks.

Our audit was specifically directed at the efficacy and costs associated with CDT in relieving the presenting acute episode such that discharge was possible and should not in any way be interpreted as a form of comparison with thrombectomy.

Thrombolysis has the benefit of being less invasive than surgery. The STILE[13] and TOPAS[10] trials reported that in patients who had received thrombolysis and later required surgical intervention, the magnitude and complexity of the procedure was often less than in those who had not received prior thrombolytic therapy. Thrombolysis is also a potentially attractive alternative to surgery because the culprit lesion can be identified and treated during the procedure with balloon angioplasty or stent placement.

A concern with thrombolysis is the risk of major haemorrhage.[3] Surgery has its own potential serious complications and therefore the specific risks for each patient need to be assessed.[3] In our audit, the stroke/intracerebral haemorrhage rate and other major haemorrhage rates were both 1.4 per cent. In the Cochrane review,[3] the stroke/intracerebral haemorrhage rate was 1.3 per cent, but the major haemorrhage rate of 8.8 per cent was much higher than in our audit.

Although two patients developed brachial artery thrombi as a consequence of the brachial artery puncture for the CDT, this complication is not specific to thrombolysis but rather to brachial artery access in general. Furthermore, the retroperitoneal haemorrhage was likely a complication of the original angiographic approach causing trauma to the external iliac artery. The resultant retroperitoneal bleed was exacerbated by the thrombolytic therapy, but treatment with an endovascular graft resolved the issue.

Given the complication rate, many patients requiring thrombolysis could be appropriately managed on general wards (bed cost approximately AUD $350 per day) if there were suitably trained staff. This would substantially reduce costs to approximately AUD $2,600 and AUD $3,000, respectively.

These results are of a single tertiary centre, which services a very large population and hence the study group is likely to be representative of the general population.

The purpose of this audit was to report on CDT as management for ALI during a patient's initial admission. Any major complications from the urokinase would have declared themselves at the time of therapy. Future studies could follow up patients treated with CDT and report on longer-term outcomes.

Conclusion

This single centre audit of all thrombolysis cases performed to manage ALI over a four-year period, demonstrated high rates of clinically acceptable clot lysis, with complication rates comparable to previously published studies. Infusions can be required for prolonged periods of time and given the low complication rate, managing patients on a general ward rather than in the HDU is a feasible alternative. This has the potential to reduce treatment costs substantially.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

ETHICS COMMITTEE APPROVAL

Barwon Health Human Research Ethics Committee.
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