Is thrombolysis of lower extremity acute arterial occlusion cost-effective?
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Thrombolysis was compared with peripheral artery surgery for the treatment of acute lower extremity ischaemia.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis

Study population
The study population was described as patients with acute lower extremity ischaemia. The study sample comprised 544 patients with thrombotic or embolic events of less than 14 days' duration. The patients were randomised to either surgery or thrombolysis. Patients with both native arterial and bypass graft occlusions were included.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were obtained from a trial published in 1998 (see Other Publications of Related Interest). The resource use and cost data were taken from studies published between 1995 and 1998. The price year used was 1997.

Source of effectiveness data
The effectiveness data were derived from a review of published studies.

Modelling
A decision-analytical Markov model was used to determine the cost-effectiveness of thrombolysis, relative to surgery, for a hypothetical cohort of patients with acute lower extremity arterial occlusion.

Outcomes assessed in the review
The following outcomes were assessed in the review: mortality, amputation, rate of intracranial haemorrhage, and the number of additional interventions required following the initial procedure.

Study designs and other criteria for inclusion in the review
The data were obtained from a large randomised controlled trial of thrombolysis and surgery (the TOPAS trial, see Other Publications of Related Interest), in addition to other published studies of surgery and US mortality reports. The
authors reported that the TOPAS trial was the largest study to date that compared thrombolysis with surgery. However, this trial did not consider the costs associated with the two interventions.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
Six primary studies were included in the review.

**Methods of combining primary studies**
Not reported.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The following probabilities were assessed in the review:

- mortality was 20% for the thrombolysis group and 17% for the surgery group;
- the amputation rate was 15% for the thrombolysis group and 13.1% for the surgery group;
- the rate of intracranial haemorrhage was 1.1% for the thrombolysis group and 0% for the surgery group; and
- the number of additional interventions required following the initial procedure was 544 for the thrombolysis group and 439 for the surgery group.

**Measure of benefits used in the economic analysis**
The summary measure of benefit was the number of quality-adjusted life-years (QALYs) gained. The authors assigned quality-adjustment weights of 1 for no morbidity, 0 for death, 0.40 for people who survive stroke, and 0.80 for people having amputation. The values for stroke and amputation were derived from two published studies. The authors did not report the methods used in the primary studies to generate the quality-adjustment factors.

**Direct costs**
The resource use and unit costs were not reported separately. The authors stated that the costs, and not charges or reimbursement fees, were used. The hospital costs were estimated from the cost accounting system at the New York Presbyterian Hospital, and from the literature. The costs of thrombolysis were derived from the average cost incurred by 25 patients, admitted to New York Presbyterian Hospital over a 6-month period, who received thrombolysis and no adjunctive open surgical procedure. The open surgical procedures were divided into major, moderate and minor. A major procedure was defined as the insertion of a new bypass graft, replacement of an existing graft, or excision or
repair of an aneurysm. A moderate procedure was defined as a graft revision, endarterectomy, profundaplasty, exploratory vascular procedure, or a transmetatarsal amputation. A minor procedure was defined as thromboembolectomy or embolectomy, amputation of digits, or fasciotomy.

The direct costs were as follows:

the cost of thrombolysis was $21,918;

the cost of patients assigned thrombolysis, who could not receive the therapy, was $1,358;

the cost of a major surgical procedure was $20,271;

the cost of a moderate surgical procedure was $12,596;

the cost of a minor surgical procedure was $5,938;

the cost of a percutaneous catheter-based procedure was $11,020;

the cost of major amputation was $32,191;

the estimated cost of the first year after a stroke was $51,150;

the annual cost of stroke for subsequent years was $26,880; and

the annual cost of amputation was $39,735.

All the costs were converted to 1997 US dollars using the medical care component of the Consumer Price Index for All Urban Consumers. The costs were discounted at a rate of 3% per year.

Statistical analysis of costs
No statistical analysis of costs was reported.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($). No currency conversions were reported.

Sensitivity analysis
A one-way sensitivity analysis was conducted by changing the values of mortality, amputation rate, and the cost of thrombolysis. A two-way sensitivity analysis was carried out by simultaneously changing the 1-year amputation and mortality rates. A three-way sensitivity analysis was conducted by simultaneously changing the mortality rate, amputation rate and cost of thrombolysis.

Estimated benefits used in the economic analysis
The authors reported that initial surgery resulted in an average life expectancy of 5.04 years, and initial thrombolysis resulted in an average life expectancy of 4.75 years. The authors also reported in the 'Methods' section that long-term survival was estimated in terms of the QALYs. This implied that the results reported were QALYs rather than life-years, although this was not clearly stated in the paper.
Cost results
The average life-time costs were $76,326 for thrombolysis and $57,429 for surgery. These included the costs of secondary procedures and the long-term costs of stroke and amputation.

Synthesis of costs and benefits
The thrombolysis strategy provided an average life expectancy of 4.75 years at a lifetime cost of $76,326. The surgery strategy provided an average life expectancy of 5.04 years at a lifetime cost of $57,429.

The authors reported that a cost-effectiveness ratio was not determined since the strategy of initial surgery was both less costly and extended life. The authors’ decision was appropriate.

The sensitivity analysis showed that thrombolysis became cost-effective under three circumstances:
if the 1-year mortality rate for thrombolysis was lowered from 20 to 10.7%,
if the amputation rate for thrombolysis was decreased from 15 to 3.9%, or
if the 1-year cost of thrombolysis could be reduced to a level below $13,000.

Authors’ conclusions
The authors concluded that the initial surgery strategy provided the most efficient and economical utilisation of resources for acute lower extremity arterial occlusion. They suggested that it is the high cost of thrombolysis, the need for secondary interventions and the long-term costs of amputations that make thrombolysis economically unfavourable.

CRD COMMENTARY - Selection of comparators
The comparator was justified on the grounds that it represented current practice in the authors’ setting. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness was estimated from a review of published studies, and using short-term data from one large randomised clinical trial of thrombolysis and surgery (see Other Publications of Related Interest). The authors reported that this trial indicated that the mortality and amputation rates at 1 year were considered statistically equivalent. The results of this trial were extrapolated over the lifetime of a hypothetical 65-year-old cohort, using national mortality data and data from other published studies to estimate the consequences of stroke and amputation. No information was provided on how these studies were identified, or the criteria on which they were selected and assessed. In addition, the methods used to extract the data were not reported.

Validity of estimate of measure of benefit
The summary measure of benefit was the number of QALYs gained. However, it was unclear whether the life-years or QALYs were reported in the paper. The health benefits were modelled in order to extrapolate the clinical trial data at 1 year over the lifetime of a hypothetical cohort of 65-year-old patients. The authors noted that the assumptions they made to extrapolate the data were a limitation of their study. In particular, they assumed that after 1 year, no further strokes or amputations occurred and that no additional procedures were conducted. This could bias the analysis if there are differences between the intervention and comparator in terms of the long-term rates of these events. The authors did not report the methods used in the primary studies to derive the utility values for the estimation of QALYs.

Validity of estimate of costs
The authors did not report the perspective of the study. Thus, it was not possible to assess whether the relevant range of costs was considered. No indirect costs were included. You should decide if any relevant costs were omitted, and
whether these are likely to affect the authors' conclusions when applied to your own setting. The authors reported that the costs were used, rather than the charges. These costs were derived from local accounting data and published literature. The costs and prices were not reported separately. The authors used one-, two- and three-way sensitivity analyses to test the robustness of the results to a wide variation in the parameters. The results of the analysis were sensitive to the mortality, amputation and costs of thrombolysis.

**Other issues**
The authors compared their results with those from other studies and explored the differences between them. In addition, they discussed the possible reasons why thrombolysis was more expensive and less beneficial than the results of the clinical trial would suggest. The factors that needed to vary for thrombolysis to become cost-effective were reported. This discussion was useful in assessing the relevance of the results to other settings and populations. The authors also noted that the randomised trial, which was used as the primary source of the short-term data, was criticised for including a heterogeneous population. This may have reduced the internal validity of the results, but increased the generalisability or external validity of the data. However, the generalisability of the study was limited by the selective reporting of the data used in the model.

The authors reported further limitations to their study:

- they did not adjust their analysis to account for the patient's preference for either thrombolysis or surgery;
- the follow-up from TOPAS was only 1-year, even though the long-term fate of a large randomised group of patients treated with thrombolysis or surgery is unknown; and
- they assumed that there were no additional costs incurred by patients in either group after one year.

**Implications of the study**
The authors concluded that there are no data to support the use of thrombolysis. In addition, further research is required to assess the long-term consequences of thrombolysis and surgery. In the meantime, the heterogeneous nature of the patient population means that the treatment should be individualised, with attention paid to both the outcomes and the costs.

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**Other publications of related interest**

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