Cost-effectiveness of emergency intraarterial intracerebral thrombolysis: a pilot study

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
Emergency intraarterial intracerebral thrombolysis as a treatment strategy for thromboembolic intracerebral events. Treatment with intraarterial urokinase, was compared with standard treatment without intraarterial urokinase.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with symptoms suggestive of middle cerebral artery occlusion aged between 19 and 80.

Setting
Hospital. All patients in the effectiveness study were treated at the University Hospitals of Cleveland Ohio, USA.

Dates to which data relate
The effectiveness data was collected between October 1993 and September 1994. Hospital costs related to the same period but projected costs of extended care in a nursing home were derived from US government census data from 1985, adjusted for inflation at 3% pa for 10 years.

Source of effectiveness data
Evidence was based on a single study.

Link between effectiveness and cost data
Direct costs were based on the same patient sample as the effectiveness study but the costs of long term care were derived from government data.

Study sample
More than 60 patients were entered into a treatment protocol for the use of intraarterial urokinase in the study period (October 1993 to September 1994), in the University Hospitals of Cleveland, Ohio. Patients or relatives gave consent but the number of refusals, if any, was not stated. The selection criteria for inclusion in the study included:

a) clinical examination suggesting a large cerebral vessel occlusion;

b) computed tomography of the brain that failed to show evidence of haemorrhage or infarction;
c) cerebral angiogram demonstration of vessel occlusion compatible with the patient's clinical symptoms;

and d) less than 6 hours of elapsed time since the initial symptoms.

Only patients with ischemic symptoms referable to the middle cerebral artery territory were included in the study. From the 60 entered into the protocol 34 were eventually proved to have middle cerebral artery thromboembolic disease and 8 of these had been treated with intraarterial urokinase. The remaining 26 were used as a control for comparison. There was no randomisation. The majority of the control group were excluded from intraarterial urokinase treatment because a period of more than 6 hours from the time of ictus to the time of angiography had elapsed. No power calculations were given.

**Study design**
Nonrandomised trial with concurrent controls. Effectiveness was measured over 24 hours from initial assessment.

**Analysis of effectiveness**
It is not stated whether analysis was based on intention to treat but the short time scale involved in measurement of effectiveness may make this irrelevant. The primary health outcome used in the analysis was the improvement in points on the National Institute of Health (NIH) stroke scale, over a 24 hour period. An initial neurologic examination was performed on admission and the patient's condition rated using the 15 criteria, 42 point scale. This method has been previously validated and is in widespread use. The patient's condition was rerated after 24 hours. A 4 point improvement was considered a significantly positive result.

**Effectiveness results**
The mean change in NIH stroke score after 24 hours was -0.5 in the control group and 5.125 in the treated group. This was tested for significance using an unpaired t-test. The P value was 0.0088, no confidence interval stated.

A small matched control group was chosen from the larger control: matching for severity of initial symptoms with the treated group. The mean change in score in the small control group was still -0.5 but the numbers were considered too small to perform a valid statistical paired t-test.

**Clinical conclusions**
There was successful angiographically confirmed clot lysis in all 8 patients treated by intraarterial urokinase. One of these patients deteriorated clinically in 24 hours and the other 7 improved. The improvement relative to those not treated was statistically significant.

**Measure of benefits used in the economic analysis**
The outcome measure used was the change in score on the NIH stroke scale after 24 hours. Two studies were quoted in support of the statement that a 4 point increase in score over this timescale is clinically significant: Haley EC et al (1992) and Barnwell (1994).

**Direct costs**
Costs of the initial stay in hospital plus treatment were directly measured and used in cost effectiveness calculations. Quantities and costs were not given separately. Length of stay in days was given but this did not correlate directly with stated costs. Treatment with intraarterial urokinase was offered on a compassionate use basis but it was not stated whether the hospital costs quoted are otherwise charges made for hospital stay and treatment or costs to the hospital. Projected nursing home costs were calculated but were not used in cost effectiveness calculations. 1995 prices were used. Costs were relfated at 3%.
Indirect Costs
These were discussed extensively but were not used in the cost-effectiveness calculations.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
The mean change in NIH score after 24 hours was -0.5 in the control group and 5.125 in the treated group. This was tested for significance using an unpaired t-test. The P value was 0.0088, no confidence interval stated. The difference between the two, 5.125 -(-0.5) = 5.625, was used in the economic analysis.

Cost results
The mean cost for the treated population is $15,202.38 and the mean cost for the untreated population is $13,478. These costs cover treatment and initial stay in hospital.

Synthesis of costs and benefits
The incremental cost-effectiveness ratio is given as the (15,202-13,478)/5.125-(-0.5) = 307. This was $307 per point on the stroke scale gained.

Authors’ conclusions
Aggressive treatment of stroke was cost effective. Stroke should be regarded as an acute medical event. Comparative studies are required to evaluate emergency therapy for acute stroke. A more detailed model of indirect costs of stroke is needed. Sample bias may be present in this study because exclusion criteria for the majority of the 34 controls was a period greater than 6 hours from the time of ictus to the time of angiography. The smaller matched study was too small to show statistical significance but the change in score between the smaller control and the larger control was the same suggesting that sample bias may not have significantly affected results.

CRD Commentary
It was not made sufficiently clear how costs of hospitalisation and treatment were arrived at and because quantities and prices are not quoted it was impossible to generalise results to other health care settings such as the UK.

The sample bias was also an issue: there may be other differences than just stroke severity which could cause bias. Unexplored differences which led to the control group being excluded from treatment may explain all the differences in results.

Bibliographic details

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Other publications of related interest


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Aged; Brain Ischemia /drug therapy /economics; Cerebral Infarction /drug therapy /economics; Cost-Benefit Analysis; Costs and Cost Analysis; Emergencies; Female; Fibrinolytic Agents /administration & dosage /adverse effects /economics; Follow-Up Studies; Humans; Intracranial Embolism and Thrombosis /drug therapy /economics; Length of Stay /economics; Male; Middle Aged; Neurologic Examination /drug effects; Pilot Projects; Skilled Nursing Facilities /economics; Thrombolytic Therapy /economics; Treatment Outcome; Urokinase-Type Plasminogen Activator /administration & dosage /adverse effects /economics

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