Cost-effectiveness of patient selection using penumbral-based MRI for intravenous thrombolysis

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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.

CRD summary
This study investigated the cost-effectiveness of the selection of patients, for intravenous recombinant tissue plasminogen activator, using penumbral-based magnetic resonance imaging (MRI) as well as the usual practice, for patients presenting with acute ischaemic stroke symptoms. The authors concluded that including penumbral-based MRI in the selection process was highly cost-effective. Despite some limitations, the methods appear to have been appropriate, the results were adequately reported, and the conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The aim was to assess the potential cost-effectiveness of selecting patients for intravenous recombinant tissue plasminogen activator (tPA) treatment based on penumbral-based magnetic resonance imaging (MRI) as well as the usual practice. A hypothetical cohort of patients presenting to the emergency department with acute ischaemic stroke symptoms, was assessed. The average age was 68 years and the average weight was 70kg.

Interventions
The addition of penumbral-based MRI to the usual care was compared with usual care alone, which consisted of computed tomography (CT), in selecting patients for intravenous tPA. The selection for thrombolysis was carried out up to six hours after symptom onset for the MRI plus CT, while that for CT alone was carried out within three hours.

Location/setting
USA/acute hospital care.

Methods
Analytical approach:
A decision-analytic model was used to synthesise the data from published clinical studies, clinical trials, claims databases, and expert opinion. The analysis was carried out over the lifetime of the patients and the authors did not state the perspective.

Effectiveness data:
The clinical efficacy, for the two strategies, was measured using the modified Rankin Scale (mRS) at day 90 and the data were from a pooled analysis of the major intravenous tPA clinical trials. The treatment with intravenous tPA was time dependent and the time from the onset of stroke symptoms to treatment was from the Genentech Stroke Presentation Survey and a published study. Two clinical trials provided the data to calculate the percentage of patients with each mRS score at day 90, the percentage selected by MRI within three hours versus after three hours from the onset of stroke, and the occurrence of symptomatic intracerebral haemorrhage. Patient mortality was from the US National Vital Statistics Reports, and was adjusted to stroke survivors, using data from a published study.

Monetary benefit and utility valuations:
The utility values, for each mRS score, were from a published study on stroke patients. Data from several published studies, which measured the utilities for mRS scores, were used in the sensitivity analysis.
Measure of benefit:
The measures of benefit were life-years saved, quality-adjusted life-years (QALYs), and avoided major disabilities, which were defined as a mRS score of four or more. Discounting was applied at an annual rate of 3%.

Cost data:
Published literature was used to estimate the costs for hospitalisation and after hospitalisation, for patients with each mRS score. The study used to estimate the hospitalisation costs was conducted in community hospitals and it was assumed that it did not include the costs of MRI. The MRI costs were from standard US costing sources, using procedural costs, and Medicare reimbursement schedules. The additional costs incurred by patients who experienced symptomatic intracerebral haemorrhages were estimated using an approach similar to that of a published study. The intravenous tPA costs were from the wholesale acquisition price and an assumed dose of 0.9mg per kg. The costs of administration and physician time to monitor administration were from the Resource-Based Relative Value Scale. The costs were discounted at 3% per year and reported in US dollars ($) for the year 2007.

Analysis of uncertainty:
The model parameters and assumptions were examined in one-way sensitivity analyses, using 95% confidence intervals, where available, or varying by ±20%. A probabilistic sensitivity analysis with 10,000 Monte Carlo simulations was performed. These results were presented in a tornado diagram and a scatter plot on the cost-effectiveness plane.

Results
Over the patients’ remaining lifetime, the total discounted costs for patient selection were $85,505 with CT and $85,607 with penumbral-based MRI and CT. The discounted QALYs were 6.84 with CT and 6.94 with MRI. The increment cost with MRI versus without was $1,840 per life-year gained, $1,004 per QALY gained, and $12,861 per major disability avoided.

The sensitivity analysis showed that the incremental cost per QALY gained was relatively insensitive to changes in the parameters. The tornado diagram showed that the results were most sensitive to changes in the odds of achieving a favourable outcome. With the utility values from other published sources, there was minimal impact on the incremental cost per QALY. Varying the model parameters simultaneously in the probabilistic sensitivity analysis showed that the mean incremental cost per QALY was $50,000 or less in 99.7% of simulations and in 22.7% of simulations the MRI selection cost less and had higher QALYs than CT alone.

Authors’ conclusions
The authors concluded that including penumbral-based MRI in the selection of ischaemic stroke patients for intravenous tPA treatment was highly cost-effective.

CRD commentary
Interventions:
The interventions were adequately described and current practice was included. The patient cohort characteristics were clearly stated and the generalisability of the intervention can be assessed. Penumbral-based MRI might be feasible in other settings.

Effectiveness/benefits:
The effectiveness of penumbral MRI for stroke patients was from a pooled analysis of clinical trial data, which appear to have been of good quality, but it was unclear if a systematic review was undertaken to ensure the best available evidence was used. The utility values were directly from studies of patients with stroke, but the valuation methods were not reported, making it difficult to assess the quality of the estimates. The outcome measures were appropriately discounted.

Costs:
The perspective was not stated, but appears to have been that of the health provider, as the analysis was based on the direct medical resources. Resource use was from national sources, patient-level hospital data, and an expert's opinion for MRI processing. The authors acknowledged that they made some assumptions for the logistical challenges and resource implications of MRI diagnostics in different settings.
Analysis and results:
The analytic approach was satisfactorily reported, and the results were reported clearly. The sensitivity analyses appear to have been appropriate for this type of analysis. The authors acknowledged some limitations of their study including assumptions for the proportion of patients treated within the three-hour window, the definition of mismatch, and the lack of randomised controlled trial data for the key efficacy estimate. The authors' acknowledged the limits in the generalisability of their findings, such as the lack of MRI facilities in rural hospitals and the additional implementation costs.

Concluding remarks:
There were limitations, with the availability of data for some model estimates, but the methods appear to have been appropriate and the results were adequately reported. The conclusions reached by the authors appear to be appropriate.

Funding
Supported by GE Healthcare.

Bibliographic details

PubMedID
19286581

DOI
10.1161/STROKEAHA.108.540138

Original Paper URL
http://stroke.ahajournals.org/cgi/content/abstract/40/5/1710

Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Algorithms; Cerebral Hemorrhage /pathology; Cost-Benefit Analysis; Decision Support Techniques; Female; Fibrinolytic Agents /administration & dosage /economics /therapeutic use; Humans; Image Processing, Computer-Assisted; Infusions, Intravenous; Magnetic Resonance Imaging /economics; Male; Patient Selection; Proportional Hazards Models; Quality-Adjusted Life Years; Stroke /economics /pathology /therapy; Thrombolytic Therapy /economics; Tomography, X-Ray Computed /economics; Treatment Outcome

AccessionNumber
22009101901

Date bibliographic record published
02/12/2009

Date abstract record published
09/02/2011