Cost-effectiveness of accelerated tissue plasminogen activator for acute myocardial infarction

Kellett J

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
Accelerated tissue plasminogen activator (tPA) in the thrombolytic drug treatment of patients with myocardial infarction (MI).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
Patients with confirmed diagnosis of MI.

Setting
Hospital. The economic study was carried out in Ireland.

Dates to which data relate
The effectiveness and cost analysis was based on published reports. The efficacy of tPA compared to streptokinase was based on the results of the GUSTO-I study published in 1993. Probabilities of related cardiovascular events were based on a review of studies published between 1988 and 1995. Hospital costs were based on Irish data from 1988, whereas the other medical care costs referred to 1996. All costs were reported in 1996 prices.

Source of effectiveness data
The effectiveness data were based on a review of previously published studies.

Modelling
A decision tree model was used to integrate various uncertain outcomes from the treatment strategies, and hence, to produce combined estimates of utility and costs.

Outcomes assessed in the review
The following outcomes were assessed in the review:

the probability of death from MI and the reduction of that probability due to the use of tPA relative to use of streptokinase;
the probability of developing and dying from disabling stroke, major bleeding and anaphylaxis;
the increase in the probability of major disabling stroke incurred with tPA compared to other thrombolytics;
the probability of developing congestive heart failure (CHF) and the reduction in risk of CHF due to tPA compared to other thrombolytics.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
The sources were not reported for the probabilities of MI, bleeding, or stroke. For the other chance events, a computer search of the MEDLINE database and consequent manual review of retrieved papers was undertaken.

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
A total of 40 studies was used to derive the parameter values required for the decision tree. The number of sources ranged from a single study to 13 depending on the model parameter.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The following probabilities were used for the base case analysis:

probability of death from MI 2.5%-25%;
reduction of MI death due to use of tPA relative to use of streptokinase 20%;
probability of disabling stroke 1%-2%;
major bleeding 1%-2%;
anaphylaxis 0.2% - 0.6%;
probability of dying from major stroke 50%;
dying from a major bleed 5%-50%;
dying from anaphylaxis 5%;
increase in the probability of major disabling stroke incurred with tPA compared to other thrombolytics 0.3%- 0.4%;

probability of developing CHF 5%-50%;

reduction in risk of CHF due to tPA compared to other thrombolytics 10%.

**Measure of benefits used in the economic analysis**

The benefit measure was quality-adjusted life years gained (QALYs). A Markov process-based model was used to calculate the life expectancy from age specific survival rates adjusted to the excess mortality from stroke and CHF. The utility values for the 4 health states (dead, alive in good health, alive with disabling stroke, alive with CHF) were obtained from previously published studies.

**Direct costs**

Direct costs included hospital costs, medical care for CHF, and nursing home costs after major stroke. In-hospital costs were based on the Irish estimates (1988) for the relevant diagnosis related groups (DRG). An annual estimate of nursing home care costs was based on a telephone survey of 7 establishments within North Tipperary, Ireland in 1996. The general practitioner visits and costs were based on the author's personal communication with the General Medical Services Board. The cost boundary adopted was the health service. Resource quantities were not reported separately from costs. The costs were reported in 1996 prices. Costs were estimated over the remaining life expectancy and discounted at 5%.

**Currency**

Irish pounds (IR). Conversion rates for Swedish Kroner (IR1.00= SEK 9.81) and for US dollars (IR1.00 = US$1.49) were provided based on London market rates at 27 July 1996.

**Sensitivity analysis**

The sensitivity of the outcome with respect to model parameters was analysed using threshold analysis with a threshold of IR10,000 per QALY. Parameters for which the inversion point value was reported were age, time after symptom onset, probabilities of dying from MI (no treatment), of stroke (after tPA), of major bleed (after tPA), and of anaphylaxis (after tPA), incremental cost of tPA over streptokinase, cost of managing non-fatal MI, cost of bleed, cost of anaphylactic shock, cost of long term stroke, cost of long term heart failure, utility of survival with major stroke, utility of survival with CHF, and the discount rates for both costs and benefits.

**Estimated benefits used in the economic analysis**

The incremental QALYs (tPA over streptokinase) gained by a base case patient (an "average" 65-year-old man with definite acute MI presenting 4 hours after the onset of symptoms) over his remaining life time were estimated to be 0.1523. Health benefits were discounted by 5% per annum. The decision tree model takes into account possible side-effects in terms of increased risk of stroke.

**Cost results**

The total incremental cost of tPA compared to streptokinase over the remaining life expectancy of the base case patient was IR940.61, discounted at 5%.

**Synthesis of costs and benefits**

The incremental cost per QALY saved was IR6176.72 and the incremental cost per life-year (i.e.not quality adjusted) gained was IR6290.29. Both costs and benefits were discounted by 5%. Four factors were found to be critical for the cost-effectiveness results (base case value - inversion point value):age (65 - 55.62), probability of dying from stroke without treatment (10.5% - 6.4%), risk of stroke (after tPA) (1.33% - 1.9%), and time after symptom onset (4 hours -
5.05 hours).

Authors' conclusions
The early use of accelerated tPA is cost-effective by the standards of widely used treatments.

CRD COMMENTARY - Selection of comparators
The selection of the comparator was justified since streptokinase is the other main thrombolytic drug, which is indicated to be less effective but also to have fewer side effects and lower cost than the study medication (tissue plasminogen activator). You, as a user of this database, should consider whether this is a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The main efficacy estimate was obtained from one of the major international multi-centre trials and hence can be considered to be valid for the presented modelling purpose. A large quantity of studies was reviewed for the other model parameters, but the reliability of estimates could have been improved by using a more systematic review protocol.

Validity of estimate of costs
Costs and resource quantities were not reported separately. Adequate details were provided of methods used in the cost estimation and no important cost items appear to have been omitted from the analysis.

Other issues
The conclusions reached by the author can be considered well justified. The uncertainty related to the parameter estimates obtained from published literature was addressed by extensive use of sensitivity analysis and, in addition, the analysis was redone using unit costs relevant to UK settings. The results were compared to the relevant study from the USA and were not presented selectively.

Source of funding
None stated

Bibliographic details

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Aged; Aged, 80 and over; Cerebrovascular Disorders /etiology; Comparative Study; Cost-Benefit Analysis; Decision Trees; Drug Costs; Humans; Life Expectancy; Middle Aged; Myocardial Infarction /complications /drug therapy; Plasminogen Activators /therapeutic use; Quality-Adjusted Life Years; Streptokinase /therapeutic use; Tissue Plasminogen Activator /therapeutic use; Treatment Outcome

AccessionNumber
21998008212

Date bibliographic record published
30/11/1999