Cost-effectiveness analysis of treatment of renal-artery stenoses by medication, angioplasty, stenting and surgery


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
The study compared medication alone (medical), percutaneous transluminal balloon angioplasty (PTA), percutaneous transluminal stent implantation (stent), and renovascular surgery for the management of renal-artery stenoses in hypertensive patients.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was a hypothetical cohort of patients with renal artery stenosis associated with renovascular hypertension or impairment of renal function.

Setting
The setting was secondary care. The economic study was conducted in Germany.

Dates to which data relate
The effectiveness data were derived from studies published between 1989 and April 1999. The cost data were derived from published literature for the year 1998. The price year was 1998.

Source of effectiveness data
The effectiveness data were based on a synthesis/review of the literature and on expert opinion.

Modelling
The authors used a decision-analytic model to assess the clinical and economic outcomes of the four treatment strategies for patients with renal artery stenosis associated with renovascular hypertension.

Outcomes assessed in the review
The outcomes used as input parameters to then model were the probability of the following events: major vascular bleeding, balloon dilation, secondary stent placement, renovascular surgery, haemodialysis, minor stroke, major stroke, death, rehabilitation following revascularisation procedures, hypertension status associated with first-line treatments. The probabilities of the events were assessed for the index hospitalisation, 1st year follow-up, between 1st and 2nd year follow-up, and between 2nd and 3rd year follow-up.
Study designs and other criteria for inclusion in the review
The authors reported that only prospective cohort and controlled trial designs were included in the review and that review articles and case studies were excluded. Studies with less than 20 patients in total or which were published before 1989 were also excluded.

Sources searched to identify primary studies
The authors reported that a comprehensive review of the literature in MEDLINE, EMBASE, SOMED, and the Science Citation Index was undertaken to identify primary studies.

Criteria used to ensure the validity of primary studies
No criteria used to ensure the validity of primary data sources were reported.

Methods used to judge relevance and validity, and for extracting data
No criteria to judge the relevance, validity and extraction of data were reported by the authors.

Number of primary studies included
Eleven primary studies were included in the review.

Methods of combining primary studies
The authors did not report the method used to combine data from primary studies to estimate individual effectiveness parameters.

Investigation of differences between primary studies
The authors reported differences between the primary studies in relation to whether the studies were randomised, the number of patients treated, the type of treatment patients received, the age of patients, and the duration of follow-up of each study. No investigation of the impact of differences between studies on the results of the review was reported.

Results of the review
The results of the outcomes used as input parameters to the model were as follows:

The probability of events during index hospitalisation:

- major vascular bleeding: medical = NA, PTA = 0, stent = 0, surgery = 0.03;
- balloon dilation: medical = NA, PTA = 0, stent = 0, surgery = 0;
- secondary stent placement: medical = 0, PTA = 0, stent = 0, surgery = 0;
- renovascular surgery: medical = NA, PTA = 0.03, stent = 0, surgery = 0.10;
- haemodialysis: medical = NA, PTA = 0.05, stent = 0, surgery = 0;
- minor stroke: medical = NA, PTA = 0, stent = 0, surgery = 0;
- major stroke: medical = NA, PTA = 0, stent = 0, surgery = 0;
- death: medical = NA, PTA = 0, stent = 0, surgery = 0.
The incremental probability of events during 1st year follow-up:

- balloon dilation: medical = 0.27, PTA = 0.17, stent = 0, surgery = 0.17;
- stent placement: medical = 0, PTA = 0, stent = 0.05, surgery = 0;
- renovascular surgery: medical = 0, PTA = 0.17, stent = 0, surgery = 0.7;
- haemodialysis: PTA = 0, stent = 0, surgery = 0;
- minor stroke: medical = 0.07, PTA = 0.01, stent = 0, surgery = 0;
- major stroke: medical = 0.07, PTA = 0.01, stent = 0.03, surgery = 0;
- death: medical = 0.04, PTA = 0.04, stent = 0.02.

The incremental probabilities of events between 1 and 2 years follow-up:

- balloon dilation: stent = 0, surgery = 0;
- stent placement: stent = 0.05;
- renovascular surgery: stent = 0, surgery = 0;
- haemodialysis: stent = 0, surgery = 0;
- minor stroke: stent = 0, surgery = 0;
- major stroke: stent = 0, surgery = 0;
- death: stent = 0.03, surgery = 0.

The incremental probabilities of events between 2 and 3 years follow-up:

- death: stent = 0.06.

The hypertension status associated with first-line treatments:

- hypertension cured: medical = 0, PTA = 0.12, stent = 0.16, surgery = 0.17;
- hypertension improved: medical = 0.7, PTA = 0.71, stent = 0.62, surgery = 0.72;
- hypertension unchanged/worse: medical = 0.3, PTA = 0.17, stent = 0.22, surgery = 0.11.

**Methods used to derive estimates of effectiveness**

It was not possible to derive some of the probability estimates from the literature review, therefore the opinion of 2 of the authors (a vascular surgeon and a nephrologist) was used to supplement the evidence from the literature review.

**Estimates of effectiveness and key assumptions**

The following data were based on expert opinion/authors assumptions.

The incremental probability of events during 1st year follow-up:

- haemodialysis: medical = 0.04.
The incremental of probability of events between 1 and 2 years follow-up:

- balloon dilation: medical = 0.05, PTA = 0.05;
- stent placement: medical = 0.05, PTA = 0.05, surgery = 0.05;
- renovascular surgery: medical = 0.03, PTA = 0.03;
- haemodialysis: medical = 0.01, PTA = 0.01;
- minor stroke: medical = 0, PTA = 0;
- major stroke: medical = 0, PTA = 0;
- death: medical = 0.02, PTA = 0.02.

The incremental probabilities of events between 2 and 3 years follow-up:

- balloon dilation: medical = 0.05, PTA = 0.05, stent = 0.05, surgery = 0.02;
- stent placement: medical = 0.05, PTA = 0.05, stent = 0.01, surgery = 0.05;
- renovascular surgery: medical = 0.03, PTA = 0.03, stent = 0.01, surgery = 0.01;
- haemodialysis: medical = 0.01, PTA = 0.01, stent = 0.01, surgery = 0.01;
- minor stroke: medical = 0, PTA = 0, stent = 0, surgery = 0;
- major stroke: medical = 0, PTA = 0, stent = 0, surgery = 0;
- death: medical = 0.05, PTA = 0.05, surgery = 0.05.

The probability of rehabilitation following revascularisation procedures: medical = NA, PTA = 0.1, stent = 0.1, surgery = 0.6.

The number of rehabilitation days medical: NA, PTA = 28, stent = 28, surgery = 28.

**Measure of benefits used in the economic analysis**
The measure of benefit used in the economic analysis was the percentage of patients with event free survival.

**Direct costs**
The following direct cost items (Eur) were inputs to the model:

- PTA = 3,086;
- stents = Eur 3,086;
- renovascular surgery = Eur 8,791;
- medical management only = Eur 1,063 per year;
- major vascular bleeding = Eur 1,171;
- renovascular surgery (secondary procedure) = Eur 8,791;
PTA (secondary procedure) = Eur 2,210;
haemodialysis = Eur 27,398;
minor stroke = Eur 1,561 per year;
major stroke = Eur 10,714 per year;
death = Eur 2,732;
rehabilitation = Eur 102 per day;

cost of hypertensive medication: hypertension improved = Eur 429 per year, hypertension unchanged/worse = Eur 561 per year,
outpatient follow-up care = Eur 99 per year.

Resource use and costs were reported separately. The authors applied reimbursement values as proxies for unit costs and to reflect the perspective of the analysis. Resource use data were estimated from published literature and expert opinion. Medication costs were valued according to the official German Drug Compendium. Unit cost or price data were derived from published fee schedules. Discounting of costs was undertaken at a rate of 5%. The price year was 1998, and the authors reported an exchange rate of Eur 1.04 = 1 US$.

The treatment strategies were compared for four distinct periods of time: the index hospitalisation period (first 30 days) and after 1, 2, and 3 years of follow-up.

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

**Indirect Costs**
No indirect costs were included in the analysis.

**Currency**
Euros (Eur). An exchange rate of Eur 1.04 = US$1.00 was reported.

**Sensitivity analysis**
The authors reported that extensive one-way sensitivity analyses were conducted to assess the impact of changes in some model parameters. The parameters varied were: the cost of stent implantation, the discount rate, the hospital daily rate for first-line and repeat revascularisation procedures, and the frequency of repeat revascularisation.

**Estimated benefits used in the economic analysis**
The percentage of event free survival's for each of the four treatment strategies were as follows:

end of year 1: medical = 51.0%, PTA = 52.0%, stent = 90.0%, surgery = 61.0%;
end of year 2: medical = 35.8%, PTA = 36.8%, stent = 86.0%, surgery = 56.5%;
end of year 3: medical = 17.6%, PTA = 18.6%, stent = 72.3%, surgery = 47.1%.

The authors reported that the difference at year 3 was statistically significant. The measure of event free survival included the frequency of complications and adverse events that were measured for the analysis.
Cost results
The authors reported the total per patient cost (Eur) for each of the four treatment strategies for the procedure, the initial hospital stay, and at the end of years 1, 2 and 3. The results were as follows:

Procedure: medical = NA, PTA = Eur 2,210, stent = Eur 2,210, surgery = Eur 2,761;
initial hospital stay: medical = NA, PTA = Eur 3,734, stent = Eur 3,118, surgery = Eur 9,917;
end of year 1 cost: medical = Eur 4,758, PTA = Eur 10,454, stent = Eur 5,094, surgery Eur 14,361,
end of year 2: medical = Eur 7,717, PTA = Eur 12,582, stent = Eur 6,690, surgery = Eur 15,594;
end of year 3: medical = Eur 9,121, PTA = Eur 14,670, stent = Eur 8,437, surgery = Eur 17,164.
The costs included the costs of the complications and adverse events specified by the authors.

Synthesis of costs and benefits
A synthesis of costs and benefits was carried out by calculating the average cost (Eur) per event free survivor for each of the four treatment strategies. At the end of year 3 the results were:

medical = Eur 51,752 per event free survivor,
PTA = Eur 78,766 per event free survivor,
stent = Eur 11,663 per event free survivor,
surgery = Eur 36,454 per event free survivor.
The benefits were not discounted. The authors did not report incremental cost effectiveness ratios, as one initial treatment strategy, stents, was both more effective and less costly than the other interventions evaluated.

In the sensitivity analyses the authors reported that the model was extremely robust to changes. The author's stated that, for all the variables changed, the average total per patient costs at 3 years and average cost-effectiveness ratio for the stent group, remained superior compared to the other treatment strategies. Only one analysis resulted in the 3-year per patient treatment costs in the stent group being similar to those of an alternative intervention (PTA). This occurred if the actual cost of a stent were added to the reimbursement level allowed for the stent procedure. The authors reported that, overall, the main variable affecting the cost results was the hospital daily rate.

Authors' conclusions
The authors concluded that angioplasty with stent implantation is more cost-effective than balloon dilation alone (PTA), renovascular surgery, or medication alone. The authors stated that renal artery stent implantation simultaneously maximises the event-free survival and minimises costs per event free survivor.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of comparators used, namely that they represented practice in the treatment of renal-artery stenosis and that there was uncertainty about the relative cost-effectiveness of the alternative treatment strategies. You, as a user of this database, should decide if any of the comparators are widely used health technologies in your own setting.

Validity of estimate of measure of effectiveness
The authors reported that a comprehensive search of the medical literature was undertaken in MEDLINE, EMBASE,
SOMED and the Science Citation Index. The authors reported the inclusion and exclusion criteria used to select primary data sources for the review and reported information about the studies included, but did not report the methods used to judge the validity of included studies or data, or the methods used to combine data from more than 1 source to estimate individual effectiveness parameters. They appeared to use data from the available studies selectively. In particular, the authors included 7 studies that evaluated stents in the review, but only used data from 3 of these to estimate effectiveness parameters. The authors did not report any formal investigation of the impact of differences between the primary sources. Lack of data from primary sources meant that the authors had to use expert opinion to supplement the evidence from the review. These factors mean that it is difficult to assess the validity and credibility of the estimates of effectiveness, which were used as inputs to the decision analytic model.

**Validity of estimate of measure of benefit**

The estimation of benefits was proxied by an effectiveness measure of event free survival. This measure assigns an equal weight to each of the events of: minor stroke, major stroke, haemodialysis, and repeat procedures. If there were differences between these events in terms of impact on health status and patient utility, then the analysis might be biased. This is particularly important if one comparator is associated with a high incidence of events that have a major impact on health, such as major stroke, whilst the other comparators are associated with a high incidence of events with less impact on health. Event free survival was estimated with a decision analytic model the structure of which was clearly described, but the authors did not report the methods used to validate the structure of the model in terms of the range of events included and the sequence of those events. The authors noted that they restricted the time frame of the model to 3 years because of a lack of long term data. The robustness of the model to changes in parameter estimates based on expert opinion was not tested by sensitivity analysis.

**Validity of estimate of costs**

All categories of cost relevant to the perspective adopted appear to have been included in the analysis. The perspective adopted meant that costs of social support, informal care and patients were omitted from the analysis. This omission could mean that the costs of the initial interventions and associated complications were underestimated and could affect the conclusions of the analysis. The costs were estimated from reimbursement data, review of the literature and expert opinion. No statistical analysis of costs was conducted. One-way sensitivity analyses of selected cost variables (the cost of stents and cost per day of hospital stay) and the discount rate were conducted. The robustness of the results to uncertainty in the value of other cost parameters was not tested. The authors reported an exchange rate of Eur1.04 = US$1.00. Discounting was undertaken at a rate of 5% per annum.

**Other issues**

The authors made appropriate comparisons of their findings with those from other studies, and addressed the issue of generalisability to other settings. The authors reported that the results of the study could not easily be applied to countries other than Germany. The authors stated that the longer length of hospital stay and the substantial use of institutional rehabilitation prevented extrapolation of their data. The main limitation reported by the authors in relation to the study was the short-term time horizon of the prospective studies used as references. The authors stated that only a few sources provided the required data on adverse events and complication rates for the third year after the beginning of treatment.

**Implications of the study**

The authors conclude that angioplasty with stent implantation is more cost-effective than balloon dilation alone (PTA), renovascular surgery, or medication alone. The authors state that renal artery stent implantation simultaneously maximises the event-free survival and minimises costs per event free survivor.

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