Cost-effectiveness targets for multi-detector row CT angiography in the work-up of patients with intermittent claudication
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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
The study investigated the use of multi-detector row computed tomographic angiography (CTA) compared with gadolinium-enhanced magnetic resonance angiography (MRA) in the work-up of patients with intermittent claudication. To reflect clinical practice, the authors evaluated two treatment scenarios after initial imaging work-up. In the first scenario (minimally invasive treatment), percutaneous treatment was performed on patients in whom a lesion suitable for percutaneous treatment had been detected at imaging work-up; otherwise, patients started a supervised exercise programme. In the second scenario (more invasive treatment), bypass surgery was performed in those patients who did not have lesions that were suitable for angiography. Intra-arterial digital subtraction angiography (DSA) would be used in cases where additional work-up was required.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised hypothetical cohorts of 60-year-old men with symptoms of severe unilateral claudication for 1 year, an ankle-brachial index of 0.70, and no history of coronary artery disease. All of the patients had at least one significant stenosis in the suprainguinal or infrainguinal arterial tract. Patients were excluded if they had isolated infrapopliteal disease.

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

Dates to which data relate
The effectiveness data were derived from studies published between 1961 and 2002. The health care use data appears to have been mainly collected from studies published between 1998 and 2000. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from a review of published studies, supplemented with authors' assumptions.

Modelling
The authors used a decision analytic model to evaluate the societal cost-effectiveness of diagnostic imaging strategies for the work-up of patients with intermittent claudication. An embedded Monte Carlo Markov model was used to include data on treatment and follow-up. A total of 100,000 patients were considered for the simulation.
Outcomes assessed in the review
The outcomes assessed were:

the sensitivity of MRA for the detection of stenoses of more than 50%;

the probability that MRA would facilitate recommendation of angioplasty given that the lesion was suitable, the lesion was suitable for bypass surgery, and the lesion was not suitable for invasive treatment;

the probability that MRA would facilitate recommendation of bypass surgery given that the lesion was suitable, the lesion was suitable for angioplasty, and the lesion was not suitable for invasive treatment;

the mortality and morbidity of DSA;

the probability that additional diagnostic work-up is required after MRA;

the health-related quality of life for several health states (i.e. no or mild intermittent claudication, severe intermittent claudication, critical limb ischaemia, amputation below knee, and amputation above knee);

the proportions of suprainguinal and infrainguinal lesions that were suitable for percutaneous treatment; and

the annual rate of critical limb ischaemia in patients with intermittent claudication.

Study designs and other criteria for inclusion in the review
The authors did not report the study designs included in the review. However, they did report that several published meta-analyses were included.

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
Approximately 15 primary studies were included in the review.

Methods of combining primary studies
Not relevant.

Investigation of differences between primary studies
Not relevant.

Results of the review
The sensitivity of MRA for the detection of stenoses of more than 50% was 0.96.
The probabilities that MR would facilitate recommendation of angioplasty given that the lesion was suitable, the lesion was suitable for bypass surgery, and the lesion was not suitable for invasive treatment were, respectively, 0.79, 0.03 and 0.

The probabilities that MR would facilitate recommendation of bypass surgery given that the lesion was suitable, the lesion was suitable for angioplasty, and the lesion was not suitable for invasive treatment were, respectively, 0.97, 0.14 and 0.

The morbidity of DSA was 0.03 and the mortality was 3.3 x10^-4.

The probability that additional diagnostic work-up was required after MRA was 0.07.

The health-related quality of life for the different health states was:

- 0.79 for no or mild intermittent claudication,
- 0.71 for severe intermittent claudication,
- 0.35 for critical limb ischaemia,
- 0.61 for amputation below knee, and
- 0.20 for amputation above knee.

The proportions of suprainguinal and infrainguinal lesions that were suitable for percutaneous treatment were 51% and 18%, respectively.

The annual rate of critical limb ischaemia in patients with intermittent claudication was 0.017 for patients younger than 65 years and 0.036 for patients aged 65 years and older.

**Methods used to derive estimates of effectiveness**

The authors supplemented the results obtained from the review of the literature with their own assumptions.

**Estimates of effectiveness and key assumptions**

The authors assumed the following.

- The sensitivity of DSA for the detection of stenoses of more than 50% was 1.

- The probabilities that DSA would facilitate recommendation of angioplasty given that the lesion was suitable, the lesion was suitable for bypass surgery, and the lesion was not suitable for invasive treatment were, respectively, 1, 0 and 0.

- The probabilities that DSA would facilitate recommendation of bypass surgery given that the lesion was suitable, the lesion was suitable for angioplasty, and the lesion was not suitable for invasive treatment were, respectively, 1, 0 and 0.

- The mortality and morbidity-related risk associated with angiography were assumed to be, respectively, 0 and 0. The respective values associated with CTA were assumed to be 9.0 x10^-6 and 3.1 x10^-4.

- The probabilities of each given treatment being recommended on the basis of CTA findings were assumed to be the same as those for MRA.

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

The summary measure of benefits used was the number of quality-adjusted life-years (QALYs). Estimated health values were obtained from the review. The estimated health values for patients with intermittent claudication were available from a study performed with participants from the Netherlands, which derived values from responses to the NHS Economic Evaluation Database (NHS EED) produced by the Centre for Reviews and Dissemination. Copyright © 2019 University of York.
EuroQol-5D and converted them to time trade-off values. The estimated health values for patients with critical limb ischaemia and amputation were derived from a study conducted among the general public. The estimated health benefits were discounted at a rate of 3%.

**Direct costs**
The direct costs considered were those of the health care system. These included the costs of MRA and DSA, surgery, amputation, one year of supervised exercise, and the costs of planned but not performed angioplasty (e.g. the inefficient use of personnel, room and equipment). The unit costs of MRA, DSA and amputations were derived from Medicare reimbursement rates. All of the other unit costs were derived from the literature. In addition, the authors made several assumptions in the estimation of health care resource use. Resource use and the costs were not reported separately. Discounting was relevant, as the costs were incurred through the lifetime of the patient, and was appropriately applied at a rate of 3% per annum. The study reported the average costs. All of the costs were converted to 1998 prices using the Consumer Price Index.

**Statistical analysis of costs**
The costs were treated as point estimates (i.e. the data were deterministic).

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

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were performed. In these analyses:

the thresholds (i.e. the willingness-to-pay for an extra QALY) were varied;

two different patient cohorts (40-year-old men with characteristics similar to those in the base-case and 70-year-old men with a history of coronary artery disease and other characteristics similar to those in the base-case) were considered;

quality of life with no or mild intermittent claudication was varied; and

the costs of revascularisation were varied (by 50% and 150% of the baseline estimates).

**Estimated benefits used in the economic analysis**
In the minimally invasive treatment scenario, MRA yielded 6.1487 QALYs and CTA yielded 6.1490 QALYs.

In the more invasive treatment scenario, MRA yielded 6.2137 QALYs and CTA yielded 6.2151 QALYs.

**Cost results**
In the minimally invasive treatment scenario, MRA cost $21,942 and CTA cost $21,965.

In the more invasive treatment scenario, MRA cost $48,965 and CTA cost $49,102.

**Synthesis of costs and benefits**
In the minimally invasive treatment scenario, using a societal willingness-to-pay of $100,000 per QALY, CTA was
equivalent to MRA in terms of cost-effectiveness if the cost of the modality was $420, the sensitivity for the detection of significant stenoses was 90%, and 20% of the patients required additional work-up because of equivocal CTA results.

In the more invasive treatment scenario, using a societal willingness-to-pay of $100,000 per QALY, CTA was equivalent to MRA in terms of cost-effectiveness if the cost of the modality was $673, the sensitivity for the detection of significant stenoses was 95%, and 20% of the patients required additional work-up because of equivocal CTA results.

These target values did not change substantially when the societal willingness-to-pay was varied. For the younger cohort the target criterion for the cost of CTA was more lenient, whereas for the older cohort the target criterion was stricter.

There was an inverse relationship between health-related quality of life and the estimated costs of CTA.

**Authors' conclusions**

Multi-detector row computed tomographic angiography (CTA), compared with currently used imaging modalities such as magnetic resonance angiography (MRA), has the potential to be cost-effective in the evaluation of patients with intermittent claudication.

**CRD COMMENTARY - Selection of comparators**

Gadolinium-enhanced MRA was used as the comparator as it represented current practice in the authors' settings. You should decide if this is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**

The authors did not state that a systematic review of the literature had been undertaken to identify relevant research and minimise biases. The authors also failed to describe much of the methodology used in their review, such as the sources searched, the study designs for inclusion, and the methods used to judge the validity of the studies. The authors also supplemented the results from the review of the literature with their own assumptions. The authors did not report if these had been derived from expert opinion, or were based on the literature. However, they did perform sensitivity analyses on the effectiveness parameters used in the model.

**Validity of estimate of measure of benefit**

The estimation of benefits was modelled using a decision analytic model, which appears to have been appropriate for the research question posed. The fact that QALYs were used as the summary measure of benefit enables comparisons with the findings from other interventions. The benefits were discounted at a rate of 3%. However, there is controversy in the health economics literature about the discounting of health benefits.

**Validity of estimate of costs**

Although the authors reported that the costs were estimated from a societal perspective, the indirect costs were not included. It was also unclear whether all the relevant costs were included in the analysis, as the authors did not report what resources were included for each treatment modality. The costs and the quantities were not reported separately, which will limit the transferability of the authors' results to other settings. The costs were derived from Medicare reimbursement rates and from published sources. Appropriate sensitivity analyses of the costs, using ranges that appear to have been appropriate, were performed. Although all of the costs were converted to 1998 prices using the Consumer Price Index, it would have been more appropriate had these been converted using the health section of the Consumer Price Index as, generally, health care cost inflation is higher than for the economy in general. Medicare reimbursement rates were used to proxy prices, consequently these cost estimates might not represent the actual costs of the treatment provided. The price year was reported, which will aid any possible inflation exercises.
Other issues
The authors did not make appropriate comparisons of their findings with those from other studies, although they did point out that the cost of a contrast material-enhanced CTA examination was estimated to be $237, which was below the target cost they found. The issue of generalisability to other settings was partially addressed in the sensitivity analysis since different age groups were evaluated. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.

The authors reported a number of further limitations. First, they used several data sources and made a number of assumptions to keep the model tractable. Second, they assumed that MRA and CTA were clinically interchangeable, an assumption that may not be realistic. Third, the model did not consider regional health care circumstances such as the expertise of the radiologists and the availability of the equipment. Fourth, to determine the cost-effectiveness of CTA it might have been better had these comparisons been made through a randomised controlled trial. Finally, the authors based the societal willingness-to-pay for one additional QALY on an assumption.

Implications of the study
The authors reported that the role of new imaging modalities that have shown fairly good preliminary results could be assessed by performing a pragmatic randomised controlled trial in which the new modality is compared with the imaging modality currently in use.

Source of funding
Supported in part by the Netherlands Organization for Scientific Research.

Bibliographic details

PubMedID
12773672

DOI
10.1148/radiol.2273020441

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Angiography, Digital Subtraction /economics /methods; Contrast Media; Cost-Benefit Analysis; Costs and Cost Analysis; Decision Trees; Gadolinium; Humans; Intermittent Claudication /economics /radiography /therapy; Magnetic Resonance Angiography /economics; Quality-Adjusted Life Years; Sensitivity and Specificity; Tomography, X-Ray Computed /economics /methods
AccessionNumber
22003009457

Date bibliographic record published
30/09/2005

Date abstract record published
30/09/2005