Cost-effectiveness of hemofiltration to prevent contrast nephropathy in patients with chronic kidney disease
Klarenbach S W, Pannu N, Tonelli M A, Manns B 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
The study compared prophylactic haemofiltration (1,000 mL/minute for 4 to 6 hours before the procedure and for 18 to 24 hours after) with intravenous saline (0.5 to 1 mL/kg per hour for 4 to 6 hours before the procedure and 24 hours after) in patients at high risk for contrast nephropathy. Secondary models in this study also incorporated sodium bicarbonate and N-acetylcysteine (600 mg given twice daily for 24 hours before and after the procedure) as the comparators.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of patients at high risk for contrast nephropathy, as defined by an average serum creatinine level of 265 micromol/L, an average age of 70 years and a high prevalence of coronary artery disease.

Setting
The study setting was secondary and tertiary care. The economic study was carried out in Canada.

Dates to which data relate
The effectiveness data were derived from studies published between 1995 and 2004. The resource use data were derived from studies published between 1994 and 2001. The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of published studies.

Modelling
Short-term survival (1-year follow-up) was modelled using a decision model structure. Longer term outcomes for survivors were modelled by a Markov process consisting of health states of chronic kidney disease (CKD) with cardiovascular disease, end-stage renal disease and death. A lifetime horizon was then used.

Outcomes assessed in the review
The outcomes assessed in the review were:
the in-hospital (30-day) mortality in patients with no renal complications, contrast nephropathy, and contrast nephropathy requiring dialysis;

the annual mortality for elderly patients with vascular renal disease and those requiring haemodialysis;

the annual probability of transition to end-stage renal disease (ESRD) in patients with CKD;

the probability of developing contrast nephropathy, contrast nephropathy requiring dialysis, and the fraction who remained dialysis dependent; and

the relative risk of developing contrast nephropathy compared with saline for haemofiltration, sodium bicarbonate and N-acetylcysteine.

Study designs and other criteria for inclusion in the review
The authors reported that the effectiveness data were derived primarily from the randomised study by Marenzi et al. 2003 (see 'Other Publications of Related Interest' below for bibliographic details). Model parameters were also derived from observational studies and meta-analyses.

Sources searched to identify primary studies
The authors reported that a literature search was performed. This involved the use of electronic databases, handsearches of pertinent journals, a review of bibliographies and a search of personal files to obtain model parameters.

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 23 studies were included in the review.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
It was not clear whether the authors investigated any differences between the primary studies.

Results of the review
The results of the review were:

The in-hospital (30-day) mortality was 1.1% (range: 1.1 to 12) in patients with no renal complications, 7.1% (range: 7.1 to 31) in patients with contrast nephropathy, and 35.7% (range: 22.6 to 62) in patients with contrast nephropathy requiring dialysis.

The annual mortality was 17.7% (range: 8.5 to 24.4) for elderly patients with vascular renal disease and 28.9% (range: 24.5 to 43.4) in those requiring haemodialysis;

The annual probability of transition to ESRD in patients with CKD was 3% (range: 1.5 to 22).
The probability of developing contrast nephropathy was 50% (range: 1 to 60), and of developing contrast nephropathy requiring dialysis 50% (range: 7 to 84).

The fraction who remained dialysis dependent was 0% (range: 0 to 27).

The relative risk of developing contrast nephropathy compared with saline was 0.10 (95% confidence interval, CI: 0.03 to 0.32 for haemofiltration, 0.12 (95% CI: 0.02 to 0.95) for sodium bicarbonate, and 0.44 (range: 0.37 to 0.65) for N-acetylcysteine.

**Measure of benefits used in the economic analysis**
The measure of benefits was the quality-adjusted life-years (QALYs). Quality of life estimates for the short- and long-term clinical states were obtained from a published study, where elderly patients after revascularisation for coronary ischaemia were asked to rate their quality of life. The quality of life was 0.84 (range: 0.70 to 0.88) at baseline and 0.62 (range: 0.51 to 0.69) in renal replacement therapy.

**Direct costs**
The direct costs to the third-party payer were included in the analysis. The costs included were chronic care stay in hospital, step-down hospital stay, hospital stay in a ward bed, in-hospital haemodialysis, haemofiltration per 24 hours, capital costs of providing haemofiltration, blood transfusion, sodium bicarbonate, N-acetylcysteine, temporary central venous catheter, tunnelled central venous catheter, and the monthly costs of outpatient haemodialysis. Resource use was derived from four published studies, while the unit costs were derived from published studies and local cost data. Since the costs were incurred during one year, discounting was not necessary and was therefore not performed. The price year was 2003.

**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.

**Currency**
US dollars ($). The conversion rate to Canadian dollars (CAD) and Euros (EUR) was $1 = CAD 1.40 = EUR 0.885.

**Sensitivity analysis**
The authors conducted a series of one-way sensitivity analyses over plausible ranges. Some parameters were evaluated in greater detail, such as the relative benefit of haemofiltration compared with intravenous saline, the average baseline risk of developing contrast nephropathy, and the probability of the need for temporary and permanent dialysis should contrast nephropathy occur. Using Markov processes, the authors extended the timeframe over the lifetime of the patient and then discounted the benefits and costs at a rate of 3%. The authors also examined the scenario in which saline administration was performed in the ward setting as opposed to a step-down unit.

**Estimated benefits used in the economic analysis**
The authors did not report the actual number of QALYs gained with each of the interventions being compared.

**Cost results**
The authors reported that the estimated cost of providing haemofiltration was $4,480 per patient.
The estimated cost for haemofiltration over 4 years for 40 high-risk patients treated in this manner was $720,000 per institution.

The incremental costs of this treatment would be $285,000 when compared with saline in the step-down-unit setting, or $539,200 in comparison with saline in a ward setting.

**Synthesis of costs and benefits**

The costs and benefits were combined using an incremental cost-utility ratio (i.e. the additional cost per QALY gained). When haemofiltration was compared with saline, the additional cost per QALY was $3,900. Extending the timeframe to the lifetime of the patient reduced this to $1,400 per QALY gained. The results of the one-way sensitivity analysis showed that varying each of the model parameters did not lead to a cost-effectiveness ratio exceeding $50,000 per QALY for any parameter examined.

When haemofiltration was compared with sodium bicarbonate infusion, the additional cost per QALY was in excess of $1,000,000. When compared with N-acetylcysteine, the incremental cost-utility ratio was $50,100 per QALY gained.

**Authors' conclusions**

The use of prophylactic haemofiltration in patients at high risk for contrast nephropathy could be potentially cost-effective only if certain conditions were satisfied and if its attractiveness was materially diminished in comparison with other strategies.

**CRD COMMENTARY - Selection of comparators**

A justification was given for using intravenous saline, sodium bicarbonate and N-acetylcysteine, namely because they represented the standard care. You should decide if these are widely used health technologies in your own setting.

**Validity of estimate of measure of effectiveness**

The authors reported that a thorough literature search had been undertaken to identify relevant research. They did not, however, describe in detail the methodology used in their review of the literature. For example, the authors did not report the search strategy used, the dates to which the search related, or any other inclusion criteria. However, extensive sensitivity analyses were performed to test the effects of varying the parameter estimates over plausible ranges obtained from the literature.

**Validity of estimate of measure of benefit**

The estimation of benefits was modelled. In the base-case the authors only estimated 1-year outcomes, whereas in the sensitivity analysis, longer term outcomes were derived from their model. The authors validated their model by comparing model-predicted mortality for a given probability of developing contrast nephropathy with randomised trial data.

**Validity of estimate of costs**

All the categories of cost relevant to the perspective of the third-party payer were included in the analysis. Further, it would appear that all the major relevant costs were included in the analysis. The costs and resource use were reported separately and the costs were reported by category, which will enhance the generalisability of the authors' results. The authors, however, did not report the costs or effects for many of the interventions under study, and only reported the incremental cost-utility ratio. The unit costs and resource use were derived from published sources. Appropriate sensitivity analyses of the costs were performed. As all costs in the base-case were incurred during one year, the costs were left undiscounted. The date to which the prices related was appropriately reported, which will aid any possible inflation exercises.
Other issues
The authors reported that the potential scope of prophylactic haemofiltration was unclear because of the uncertainty about implications for resource use and its true effectiveness. However, in the present study, the health benefits and total costs of haemofiltration and its comparators were not fully reported, only the synthesis of the costs and benefits was reported. Again, such lack of detail will limit the understanding of the authors’ results. The issue of generalisability to other settings was addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis, although the authors should have emphasised that in comparison with sodium bicarbonate, haemofiltration was very poorly cost-effective.

The authors reported several further limitations. First, the relative risk of contrast nephropathy with haemofiltration was based on only one randomised trial, and two other trials have not demonstrated any benefit. Second, the data on resource use and costs were obtained from the literature rather than direct measurements. Finally, the potential impact on patients who are currently denied procedures involving contrast because they are deemed to be too high risk but who may have an acceptable risk with effective therapy was not examined in this study.

Implications of the study
The authors reported that before considering the implementation of haemofiltration, it is crucial to confirm the clinical effectiveness and resource use consequences in relation to current standards of care.

Source of funding
Supported in part by the Alberta Kidney Disease Network and the Institute of Health Economics, Edmonton, Canada.

Bibliographic details

PubMedID
16484907

DOI
10.1097/01.CCM.0000206287.22318.C3

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Chronic Disease; Contrast Media /adverse effects; Cost-Benefit Analysis; Hemofiltration /economics; Humans; Kidney Diseases /complications; Renal Insufficiency /chemically induced /prevention & control

AccessionNumber
22006000789