Surgery versus medical follow-up in patients with asymptomatic primary hyperparathyroidism: a decision analysis

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
Five strategies for the treatment of patients with asymptomatic primary hyperparathyroidism were studied. The strategies were bilateral neck exploration (BNE), unilateral neck exploration (UNE), video-assisted parathyroidectomy (VAP), and lifelong medical follow-up shifting for either BNE or UNE in case of disease progression.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of patients with asymptomatic primary hyperparathyroidism. Patients with multiple endocrine neoplasia or parathyroid cancer were excluded.

Setting
The setting was a hospital. The economic study was carried out in France.

Dates to which data relate
The effectiveness data were derived from studies published between 1970 and 2004. Some resource use data came from a source published in 2002. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Modelling
A Markov model with a lifetime horizon and 1-month cycles was constructed to compare the clinical and economic outcomes of the five alternative strategies in a hypothetical cohort of patients with asymptomatic primary hyperparathyroidism. The typical patient was a 55-year-old woman with sporadic primary hyperparathyroidism. The model considered short-term complications and recurrence rates for each approach. No other details of the model were given.

Outcomes assessed in the review
The outcomes estimated from the literature were:
the short-term events (death, haematoma, transient dysphonia, transient hypocalcaemia, and persistent hyperparathyroidism) associated with BNE (both first operation and re-operation), UNE, VAP, and cervicosternotomy;

the long-term events (permanent dysphonia, permanent hypoparathyroidism, recurrent hyperparathyroidism, and scar) associated with BNE (both first operation and re-operation), UNE, VAP, and cervicosternotomy;

the rate of indication for surgical treatment;

the rate of surgery for patients undergoing medical follow-up; and

the mortality rates.

Study designs and other criteria for inclusion in the review
A review of the literature was undertaken to derive the clinical data used in the decision model. Databases were reviewed from 1970 to 2004. Studies were excluded in the following cases:

if the patient series was less than 30;

if they did not report separate results for primary hyperparathyroidism and other hyperparathyroidism;

if the results for patients with multiple endocrine neoplasia or parathyroid cancer could not be excluded; or

if localisation studies had been performed in the same series reporting the results of BNE.

If the same series was published more than once, only data from the latest publication were considered. Details of the designs of the primary studies were not provided.

Sources searched to identify primary studies
MEDLINE was searched. The search was supplemented by manual searches of the bibliographies of selected articles.

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
Fifty-one primary studies provided clinical evidence.

Methods of combining primary studies
When possible, a summary analysis was performed and 95% confidence intervals (CIs) were calculated.

Investigation of differences between primary studies
Not reported.

Results of the review
With first BNE, the rates of short-term events were as follows:
death 0.21%, haematoma 0.37%, transient dysphonia 1.87%, transient hypocalcaemia 9.98%, and persistent hyperparathyroidism 5.28%.

With first BNE, the rates of long-term events were as follows:
permanent dysphonia 0%, permanent hypoparathyroidism 1.75%, recurrent hyperparathyroidism 0.06% per year, and scar 100%.

With second BNE (re-operation), the rates of short-term events were as follows:
death 0.29%, haematoma 3.92%, transient dysphonia 3.49%, transient hypocalcemia 10.40%, and persistent hyperparathyroidism 10.17%.

With second BNE (re-operation), the rates of long-term events were as follows:
permanent dysphonia 0.47%, permanent hypoparathyroidism 5.61%, recurrent hyperparathyroidism 0.70% per year, and scar 100%.

With UNE, the rates of short-term events were as follows:
haematoma 0.59%, transient dysphonia 1.09%, transient hypocalcaemia 6.28%, sestamibi scintigraphy 6.43%, ultrasonography 5.62%, and ultrasonography and sestamibi scintigraphy 3.50%.

With UNE, the rates of long-term events were as follows:
permanent dysphonia 0%, permanent hypoparathyroidism 0%, recurrent hyperparathyroidism 0.34% per year, and scar 100%.

With VAP, the rates of short-term events were as follows:
anaesthesia-related death 0.0054%, conversion into BNE 11.75%, haematoma 0.38%, transient dysphonia 0.64%, transient hypocalcaemia 1.66%, and persistent hyperparathyroidism 1.40%.

With VAP, the rates of long-term events were as follows:
permanent dysphonia 0.38%, permanent hypoparathyroidism 0%, recurrent hyperparathyroidism 0.34% per year, and scar 100%.

With cervicosternotomy, the rates of short-term events were as follows:
death 1.89%, haematoma 2.74%, transient dysphonia 6.85%, transient hypocalcemia 33.95%, and persistent hyperparathyroidism 16.18%.

With cervicosternotomy, the rates of long-term events were as follows:
permanent dysphonia 12.68%, permanent hypoparathyroidism 2.63%, recurrent hyperparathyroidism 0%, and scar 100%.

The rate of surgery for asymptomatic patients during a 10-year medical follow-up was 24.5%.

The mean quality of life weight for each event (in the short and long term) was also reported.

Measure of benefits used in the economic analysis
The summary benefit measure used was the number of quality-adjusted life-years (QALYs). These were estimated by combining the expected survival and utility adjustments. The utility weights were obtained from a survey in an opportunistic sample of 109 volunteers without the disease, using the time trade-off method. An annual discount rate of
3% was applied.

**Direct costs**
The analysis of costs took the perspective of the health care system. It included the cost categories of outpatient visits, biological and hormonal measurements, localisation studies, surgical procedures, post-surgical therapies, diagnostic procedures, and medications. A detailed breakdown of the cost items was provided. The unit costs and the quantities of resources used were not presented separately, although costs for each item was presented as first-month costs, first-year costs and following year costs. Inpatient costs were estimated from the cost accounting system of a hospital network of 50 non-profit university hospitals in the Paris region. The hospital costs comprised all personnel costs, supplies, drug and blood products, tests, housekeeping and hospital overheads. The ambulatory costs were derived from the national reimbursement schedule provided by the social security. The drug costs were estimated using average wholesale prices. Resource consumption came from national guidelines and experts’ opinions. Discounting was relevant as the lifetime costs were estimated, and an annual discount rate of 3% was applied. The price year was 2002.

**Statistical analysis of costs**
Statistical analyses of the costs were not carried out.

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

**Currency**
Euros (EUR).

**Sensitivity analysis**
One- and two-way sensitivity analyses were performed to assess the robustness of cost-utility ratios to variations in the clinical and economic inputs used in the decision model. Alternative ranges of values were derived from the literature and 95% CIs or extreme values were used.

**Estimated benefits used in the economic analysis**
The estimated QALYs were 15.7469 with medical follow-up/BNE, 15.7543 with medical follow-up/UNE, 17.0329 with BNE, 17.1181 with UNE, and 17.1221 with VAP.

Thus, VAP was marginally the most effective strategy, resulting in a gain of 0.004 QALYs (1.46 days) compared with the next most effective strategy (UNE).

**Cost results**
The total costs were EUR 2,538 with medical follow-up/BNE, EUR 2,563 with medical follow-up/UNE, EUR 3,537 with BNE, EUR 3,766 with UNE, and EUR 3,835 with VAP.

**Synthesis of costs and benefits**
Incremental cost-utility ratios were calculated to combine the costs and benefits of the alternative strategies.

The incremental analysis showed that medical follow-up/BNE was the reference strategy (less costly and less effective). The incremental cost per QALY gained in comparison with the next less effective strategy was EUR 762 with BNE, EUR 2,688 with UNE, and EUR 17,250 with VAP. Medical follow-up/UNE was eliminated by extended dominance.

The sensitivity analysis showed that the base-case results were quite sensitive to variations in the model inputs, in
particular for the comparison between the three surgical strategies. Some interesting results were as follows:

- when the risk of mortality associated with UNE exceeded 0.88% (base-case 0%), or when the quality of life weight for UNE scarring was less than 0.9885 (base-case: 0.9979), BNE became more effective than (and in some cases dominated) UNE;

- UNE became less costly than BNE when the cost of UNE was decreased by 22%;

- UNE dominated VAP for women older than 71 years of age, or when the risk of mortality associated with VAP exceeded 0.05% (base-case 0.00054%), or when the risk of immediate failure exceeded 3.71% (base-case 1.40%);

- follow-up strategies were less effective but less costly than surgical procedures in 55-year-old women not eligible for surgery.

Other results did not alter the conclusions of the study.

Authors' conclusions
The minimally invasive surgical strategies, namely unilateral neck exploration (UNE) and video-assisted parathyroidectomy (VAP), were cost-effective for patients with asymptomatic primary hyperparathyroidism in comparison with a more invasive surgical procedure, such as bilateral neck exploration (BNE), in France. All surgical options were cost-effective in comparison with medical follow-up strategies.

CRD COMMENTARY - Selection of comparators
The choice of the comparators was intended to include the most widely used approaches for the treatment of patients with asymptomatic primary hyperparathyroidism. Each treatment strategy was satisfactorily described and the reasons for comparing these options were given. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a synthesis of published studies. Some details of the methods and conduct of the review were reported. For example, the search methods and the approach used to combine the primary estimates were provided. However, limited information on the design and characteristics of the primary studies was provided. Thus, it was not possible to assess the validity of the primary studies. The authors stated that much of the data used in the decision model were extrapolated from cohort or observational studies rather than from clinical trials. The issue of uncertainty was extensively addressed in the sensitivity analysis.

Validity of estimate of measure of benefit
The choice of QALYs as the summary benefit measure was appropriate as QALYs capture the impact of the intervention on the two most important dimensions of health, quality of life and survival. Further, QALYs are comparable with the benefits of other health care interventions. Discounting was applied. Some information on the utility adjustments used to calculate the QALYs was provided, and the impact of changing utility values was investigated in the sensitivity analysis.

Validity of estimate of costs
The perspective of the study was clearly reported. A detailed breakdown of the cost items included in the analysis was given, although some costs were presented as macro-categories. However, the unit costs were not presented and information on resource consumption was not provided, which limits the possibility of replicating the analysis in other settings. The sources of the costs were reported for most items. The price year was given, which will facilitate reflation exercises in other time periods. The costs were treated deterministically but the impact of varying some costs was tested in the sensitivity analysis.
Other issues
The authors did not compare their findings with those from other studies. They also did not explicitly address the issue of the generalisability of the study results to other settings. However, the extensive use of sensitivity analyses enhances the external validity of the study. The authors noted some limitations of their study. First, the assumption of no incremental mortality due to lifelong medical follow-up might have biased the analysis in favour of surgical options. Second, patient preference might affect the results of the modelling approach. Third, most data were taken from cohort studies or case-series rather than from randomised controlled trials.

Implications of the study
The study results support the use of VAP or UNE for the treatment of patients with asymptomatic primary hyperparathyroidism. The authors pointed out that locally available facilities and expertise should also guide the choice of the most efficient strategy.

Source of funding
Funded by the Programme National Hospitalier de Recherche Clinique.

Bibliographic details

PubMedID
16322399

DOI
10.1530/eje.1.02029

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Cost-Benefit Analysis; Decision Support Techniques; Female; Follow-Up Studies; Humans; Hyperparathyroidism, Primary /surgery /therapy; Middle Aged; Parathyroidectomy; Quality of Life

AccessionNumber
22006006175

Date bibliographic record published
31/08/2006

Date abstract record published