Long-term follow-up and cost benefit of adrenalectomy in patients with primary hyperaldosteronism

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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
Two treatments for primary hyperaldosteronism (HA), a rare case of hypertension, were examined. The two approaches were medication alone (i.e. antihypertensive drugs) versus surgery (both laparoscopic and open unilateral adrenalectomy) plus medication.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of patients suffering from HA, as diagnosed by an aldosterone-to-renin ratio of greater than 2,500 pmol/L per mg/L/s, who underwent an adrenalectomy. The inclusion and exclusion criteria were not reported.

Setting
The setting was the community. The economic study was carried out in Calgary (AB), Canada.

Dates to which data relate
The effectiveness and resource use data were gathered between January 1992 and September 2001 for adrenalectomy. For lifetime medication treatment the dates were based on the estimated life expectancy of the patient. The price year was 2001.

Source of effectiveness data
The effectiveness evidence came from a single study for the adrenalectomy intervention, and was derived from the authors’ assumptions for lifetime medication.

Link between effectiveness and cost data
The costing was performed retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations to determine the sample size were not reported. Of the 86 patients who underwent adrenalectomy at the study institution over a 9-year period, 24 underwent unilateral adrenalectomy for HA and were included in the study. Their mean age was 52 years and 20 were men. It appears that no patient was excluded from the initial sample
Study design
This was a review of case series. Patients who had undergone adrenalectomy were contacted and recalled to the endocrine surgical clinic for review. The patients were followed for an average (mean value) of 42 months (98% confidence interval: 31 - 53). With the exception of one patient who died after the intervention, no loss to follow-up was reported. No comparison group was used. Data on the efficacy of medication were not estimated.

Analysis of effectiveness
All patients included in the study were accounted for in the clinical analysis. The health outcomes used in the analysis were:

- the success rate, as evaluated from the change in the aldosterone-to-renin ratio;
- perioperative morbidity and mortality;
- the change in supine systolic and diastolic pressure before the operation, at 6 months after the operation, and at the long-term follow-up,
- the change in the use of antihypertensives; and
- patient-perceived blood pressure control after adrenalectomy.

Effectiveness results
Of the 24 unilateral adrenalectomies performed in the study, there were 19 laparoscopic procedures and 5 open procedures.

The aldosterone-to-renin ratio decreased statistically in all but two patients. For these two patients the intervention was considered as a failure. However, the cure rate (patients being normotensive, i.e. blood pressure or less than 140 over 90 mmHg, and on no medication) was only 35%.

No perioperative morbidity was observed and only one death occurred postoperatively.

There was a significant decrease in both the systolic and diastolic blood pressure after surgery (at 6 months and final follow-up) in comparison with the preoperative values.

In terms of the change in antihypertensive use, 8 patients required no medication, 12 patients decreased medication, one had no change and 2 patients increased their dosage.

Twenty-one patients reported that their blood pressure control improved after the intervention, one patient reported no change, and in one the blood pressure was worse.

Clinical conclusions
The effectiveness study showed that adrenalectomy was a safe procedure that reduced the use of medication and improved patient-perceived blood pressure control. The mortality rate was low and the success rate was quite high.

Methods used to derive estimates of effectiveness
The authors made an assumption to evaluate the effectiveness of the medication.

Estimates of effectiveness and key assumptions
It was assumed that lifetime medication was as effective as adrenalectomy plus medication in reducing the symptoms of HA.

**Measure of benefits used in the economic analysis**
No summary benefit measure was used in the economic analysis as the authors assumed that both treatments were equally effective. Thus, a cost-minimisation analysis was conducted.

**Direct costs**
A 3% discount rate was used as the lifetime costs were evaluated. The unit costs were not reported separately from the quantities of resources used. The costs of the surgical services were included in the economic evaluation. For those receiving surgery plus medication, these were the costs of hospital admission plus any ongoing antihypertensive medication for the patient's lifetime. For those receiving medication alone, this was the cost of the drugs only and not the ongoing health service charges. It was estimated by extrapolating the cost of medication taken before surgery for the lifetime of the patient. The cost/resource boundary adopted in the study was that of a fully publicly funded health care system. The costs were estimated from actual data, the Corporate Data Department of Calgary Health Region for hospital costs and the Foothills Hospital outpatient pharmacy for antihypertensive medication. The quantity of medication, which was continued after the surgical intervention, was estimated from the treatment prescribed at final follow-up. The lifetime costs were calculated on the basis of the life expectancy observed in the Calgary region. It was 76.7 years for men and 81.6 years for women. All of the costs were adjusted for inflation. The price year was 2001.

**Statistical analysis of costs**
The costs were reported as means and 95% confidence intervals (CIs). Standard statistical analyses were conducted to test the statistical significance of the differences in the total costs.

**Indirect Costs**
The indirect costs were not included.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
Sensitivity analyses were not conducted.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The estimated lifetime costs per patient were Can$19,960 (95% CI: 4,361 - 116,839) for adrenalectomy plus ongoing antihypertensive medication and Can$39,080 (95% CI: 27,493 - 50,667) for lifetime medication alone. The difference reached statistical significance, (p=0.014).

The estimated cost-savings per patient for adrenalectomy were Can$31,132 (95% CI: -7,886 - 100,265).

**Synthesis of costs and benefits**
Not relevant as a cost-minimisation analysis was conducted.
Authors' conclusions
Adrenalectomy for hyperaldosteronism (HA) resulted in a significant long-term reduction in blood pressure.

CRD COMMENTARY - Selection of comparators
The authors stated that surgery and medication represented two alternative approaches for the treatment of patients with HA. In particular, adrenalectomy was considered as the best approach for patients with solitary aldosterone-producing adenoma, while antihypertensive medication represented the most common approach for idiopathic hyperplasia of the adrenal gland. The improvements in medical therapies make them more and more effective for the treatment of both HA diseases. You should decide whether they represent widely used approaches in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a series of patients who were analysed retrospectively. This design was not appropriate for the study question due to its retrospective nature. In addition, the lack of an explicit control group, with which to ascertain efficacy evidence for patients receiving medication alone, means that the equality of the effectiveness data was based solely on the authors' assumptions. There was little to back up this major assumption and, as such, this raises doubt over the validity of the results. Confounding and bias cannot be ruled out. The sample size was small and power calculations were not performed. These issues tend to limit the internal validity of the analysis.

Validity of estimate of measure of benefit
No summary benefit measure was used in the economic analysis as the authors assumed that medication was as effective as surgery. The analysis was therefore categorised as a cost-minimisation study.

Validity of estimate of costs
The authors stated that the economic evaluation was carried out from the perspective of a fully publicly funded health care system. A detailed breakdown of the costs was not reported, as only the main cost categories were mentioned. The unit costs and the quantities of resources used were not reported separately, and this may hinder the reproducibility of the study to other settings. The price year was reported, thus facilitating reflation exercises in other settings. The costs were appropriately reflated. The source of the cost data was reported. Resource use was estimated on the basis of standard drug usage. The cost estimates were specific to the study settings and no sensitivity analyses were conducted. The authors stated that the estimated costs were likely to have been higher due to the overestimated life expectancy among the patients involved in the study. The authors also admitted that some categories of costs that would have been relevant, such as productivity losses, were not included in the analysis.

Other issues
The authors compared their findings with those from published studies and found similar results in their series of data. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not conducted. Thus, the external validity of the analysis was low. The study involved patients with HA and this was reflected in the conclusions of the analysis. The authors noted many of the drawbacks of their analysis.

Implications of the study
The study results suggest that surgery for patients with HA was cheaper than lifetime medication, even under pessimistic scenarios. However, it has to be noted that the effectiveness results (similar success of the two interventions) were based on a weak design.

Source of funding
Part supported by a Mary-Jo Reeve Traveling Fellowship and the Division of Surgical Oncology at the University of Calgary.
Bibliographic details

PubMedID
12445071

DOI
10.1046/j.1365-2168.2002.02261.x

Indexing Status
Subject indexing assigned by NLM

MeSH
Adrenalectomy /economics /methods; Aldosterone /blood; Antihypertensive Agents /economics /therapeutic use; Blood Pressure /physiology; Cost-Benefit Analysis; Female; Follow-Up Studies; Humans; Hyperaldosteronism /economics /physiopathology /surgery; Hypertension /prevention & control; Long-Term Care; Male; Middle Aged; Renin /blood

AccessionNumber
22003000027

Date bibliographic record published
30/11/2003

Date abstract record published
30/11/2003