The value of frozen section examinations in determining the extent of thyroid surgery in patients with indeterminate fine-needle aspiration cytology

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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 use of intraoperative frozen section examination (FSE) to establish a diagnosis of thyroid cancer in patients undergoing thyroidectomy for nodules with indeterminate cytological results after fine-needle aspiration biopsy (FNAB).

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing thyroidectomy, in whom the indication for surgery was a dominant thyroid nodule with indeterminate FNAB cytological features. Patients in whom the indication for surgery was thyrotoxicosis, local compression due to a benign multinodular goiter, bilateral nodules, or a history of thyroid surgery, were excluded. Also excluded were those who did not undergo an FNAB or intraoperative FSE, and those with benign, malignant, or nondiagnosed FNAB cytological features.

Setting
The setting was a private surgical practice in a medical school-affiliated teaching hospital. The economic study was conducted at the Department of Surgery and Otolaryngology, Long Island Jewish Medical Center-Long Island Campus, Albert Einstein College of Medicine, New York, USA.

Dates to which data relate
The effectiveness and resource use data were gathered between January 1998 and September 2000. No price year was reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was conducted 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. The patients were identified from consecutive
medical records of all patients who underwent thyroid surgery. Of an initial group of 480 medical charts found, 199 cases were eligible and were used for the effectiveness analysis. There were 155 women (78%) with a median age of 47 years (range: 13 - 82), and 44 males (22%) with a median age of 49 years (range: 20 - 71).

Study design
This was a retrospective within-group comparison study based on a review of medical records, as identified from a single centre (the Long Island Jewish Medical Center). A single group of patients who underwent both FNAB and FSE was evaluated. The patients were not followed after the final surgical intervention was performed. All the patients were evaluable at the end of the study.

Analysis of effectiveness
All of the patients included in the initial sample were taken into account in the effectiveness study. The effectiveness analysis compared the diagnostic results obtained with FNAB and FSE. Indeterminate FNAB results were classified as indeterminate, follicular neoplasm (FN), Hurthle cell neoplasm (HCN) and indeterminate with papillary features (IPF). Diagnoses made by FSE were classified as benign, malignant, or deferred for final pathologic examination. Twenty-one patients with indeterminate FNAB results, but whose FNAB results were suggestive of papillary cancer, were considered separately. The findings of FNAB and FSE were confirmed through a final pathologic examination.

Effectiveness results
In the sub-group of 21 patients whose FNAB results were suggestive of papillary cancer, there were 20 cancers (95%). Malignancy was diagnosed by FSE in 14 (67%) patients, the diagnosis was deferred in 6 patients, and in one patient the results were interpreted as malignant (1 false positive result).

In the sample comprising the remaining 178 patients, there were 64 (36%) cases of cancer.

Of these 64 cases, the FNAB results were indeterminate for 30 patients, FN for 14 patients, HCN for 12 patients, and IPF for 8 patients.

Of the same group of 64 cases, FSE identified 30 cases of cancer (47%). Fifty-three per cent (16 out of 30) of these were classified by FNAB as indeterminate, 29% (4 out of 14) as FN, 25% (3 out of 12) as HCN, and 88% (7 out of 8) as IPF.

There was one false-positive result with FNAB, but no false-negative results were observed. Of the 121 FSE that were deferred, 42 (35%) were cancers. The likelihood of making an accurate diagnosis with FSE was related to FNAB category and the final pathological examination results. For each of the FNAB categories (indeterminate, FN, HCN and IPF) FSE identified, respectively:

60% (indeterminate), 27% (FN), 40% (HCN) and 88% (IPF) of patients with papillary cancer;

29% (indeterminate), 0 (FN), 17% (HCN) and 0 (IPF) of patients with Hurthle cell cancer; and

33% (indeterminate), 33% (FN), 0 (HCN) and 0 (IPF) of patients with follicular cancer

Overall, in the overall sample of 178 patients, FSE detected 17% of cancers.

Clinical conclusions
The effectiveness evidence showed that, in patients whose FNAB results were suggestive of papillary cancer, FSE was not useful because FNAB detected almost 100% of the cancers. However, the routine use of FSE was effective in identifying cancer cases, and reduced the number of patients requiring a second surgical procedure.

Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic study. The study was therefore classified as a cost-consequences analysis.

**Direct costs**
Discounting was not relevant since the costs per patients were incurred during a short time. The unit costs were reported separately from the quantities of resources used. The health services included in the economic analysis were operating room, hospital supplies, room and board, hospital stay, anaesthesia, surgeons' fees, FSE, final pathologic examination and preadmission testing. The cost/resource boundary of the study was that of the health service payer. The costs were estimated from actual Medicare reimbursement rates for the New York City/suburban/Long Island region of New York (USA). Data on resource use referred to the same patients as those involved in the effectiveness study. The price year was not reported.

**Statistical analysis of costs**
The costs were treated deterministically. Statistical tests were not conducted on either the costs or quantities.

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

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analyses were performed.

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

**Cost results**
The total costs associated with 178 FSEs were $17,266 ($97 per case).

The total additional costs of 30 thyroidectomies were $13,560 ($452 per case).

The savings due to 30 completion thyroidectomies avoided were $261,870 ($8,729 per case). Thus, the final net savings associated with the routine use of FSE were $231,044 ($1,298 per case).

**Synthesis of costs and benefits**
The costs and benefits were not combined.

**Authors' conclusions**
Intraoperative frozen section examination (FSE) permitted a correct diagnosis of cancer in 17% of those patients undergoing thyroidectomy for nodules with indeterminate cytological results after fine-needle aspiration biopsy (FNAB). Routine FSE was cost-effective because of the high costs of a second (completion) thyroidectomy. However, in patients whose FNAB results were highly suggestive of papillary cancer, FSE did not add any diagnostic information and should not be performed routinely.
CRD COMMENTARY - Selection of comparators
The authors stated that FNAB was the single most useful and common diagnostic tool for the determination of malignancy in patients with thyroid nodules. Usually the results of FNAB are accurate and no further testing is required. However, this study focused on indeterminate FNAB results and the extent to which a thyroidectomy (total or partial) is considered controversial. Thus, the choice of FSE as the comparator appears to have been appropriate, as it may provide the surgeon with the diagnostic information required to perform the most correct surgical intervention. You should decide whether they represent valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used data coming from a review of medical records. A single group of patients underwent both study interventions and their diagnostic value was evaluated in comparison with cytological examination (considered the final test). Thus, this was a within-group comparison study, which avoids the use of an external comparison group. However, details of the outcome assessment were not reported and the design of the study did not exclude the impact of confounding factors and bias on the estimated effectiveness results. The authors did not conduct any statistical tests to compare the outcomes associated with the study interventions. The retrospective design was a further drawback. These issues tend to limit the internal validity of the analysis. The authors conducted a sub-group analysis, which was appropriate due to the difference in the incidence of disease.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis. The study was therefore classified as a cost-consequences analysis.

Validity of estimate of costs
The perspective adopted in the study was not explicitly reported. It appears to have been that of the health service payer because Medicare reimbursement rates were used to estimate the costs. The authors stated that some statistical tests were conducted, but the results of these tests were not presented. Data on resource use came from the sample of patients involved in the effectiveness study. Only the global costs of the procedures were reported and details of the cost categories were not provided. The price year was not reported, thus limiting the possibility of re-flating the estimated costs and replicating the results in other settings. The cost estimates were specific to a suburban region of New York and sensitivity analyses were not conducted. Consequently, the cost analysis should not be generalised to other contexts where the cost data may differ. The authors noted that the risk (and subsequent cost) of a second operation was not considered.

Other issues
The authors made several comparisons of their findings with those from other published studies and found that similar results were reported, in particular for the incidence of malignancy. However, some contrasting results were also found. The issue of the generalisability of the study results was not addressed and sensitivity analyses were not conducted. Thus, there were some limitations to the external validity of the analysis. The study attempted to evaluate the diagnostic accuracy of FSE but standard measures, such as sensitivity and specificity, were not used.

Implications of the study
The study results suggested that FSE may be of diagnostic value for treating patients at risk of thyroid cancer. It may be cost-effective in specific sub-groups of patients when the results of FNAB are indeterminate. However, caution is required when interpreting the results of the study due to the limitations of the analysis and the contrasting results obtained in other studies.

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