Randomized prospective evaluation of frozen-section analysis for follicular neoplasms of the thyroid

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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 frozen-section analysis to establish a precise diagnosis of malignancy on patients with a dominant thyroid nodule, which was demonstrated by fine-needle aspiration (FNA) to be a follicular or Hurthle cell neoplasm of the thyroid. Patients had thyroid lobectomy and isthmusectomy. A surgeon and a pathologist examined the specimen. In the case of a diagnosed malignancy, a total thyroidectomy was performed during the initial exploration.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of patients with a dominant thyroid nodule, which FNA had shown to be a follicular or Hurthle cell neoplasm of the thyroid. Patients were excluded from the study if they had contralateral nodular thyroid disease, had received radiation to the head or neck in childhood, had familial thyroid cancer, or had evidence of local extension of metastases. They were also excluded if they had FNA specimens clearly diagnostic of either a benign or malignant tumour or suggestive of papillary, medullary, or the follicular variant of papillary carcinoma of the thyroid.

Setting
The setting was secondary care. The economic study was conducted in the USA.

Dates to which data relate
The dates during which the effectiveness and resource evidence was collected were not given. The price year was not given.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used for the effectiveness data.

Study sample
No power calculations to determine the sample size were reported. All patients who met the inclusion criteria at the time of surgical exploration were included in the study. An overall sample of 68 patients was considered, but 7 patients
were excluded because they were not eligible. Two patients were excluded for preoperative demonstration of bilateral disease, 1 patient for nodal metastasis, and 4 patients for modification of the initial FNA diagnosis after review of outside cytologic material. The study sample comprised 29 patients in the frozen-section group and 32 patients in the non frozen-section group. One patient in the non frozen-section group was excluded because of a conscious protocol violation, leaving 31 patients in the group. The mean age in the frozen-section group was 40 (+/- 2) years, and 79% of the patients were women. The mean age in the non frozen-section group was 43 (+/- 2) years, and 69% were women.

Study design
This was a randomised controlled trial carried out in a single centre (the Johns Hopkins Medical Institutions, Baltimore, Maryland, USA). The patients were allocated between the two groups, either to have frozen section or not. Randomisation was carried out at the time of surgical exploration using a random number code kept in individual sealed envelopes in the operating room. Apart from the frozen section, both groups of patients underwent the same investigation. The surgical treatment was then determined by the results of the investigations. The patients were followed up until discharge.

Analysis of effectiveness
The basis for the analysis of the clinical study was not stated, but appears to have been intention to treat. The primary health outcome assessed was the presence of malignancy. The secondary health outcomes were surgical time, anaesthesia time, and length of hospital stay. The groups were shown to be similar in terms of the age, gender composition and size of tumour.

Effectiveness results
In the frozen-section group, frozen-section analysis showed malignancy only in 1 patient (3.4%), while permanent histological analysis showed well-differentiated thyroid carcinoma in a further 6 (21%) patients. The remaining 29 nodules were all benign.

In the non frozen-section group, permanent histology found 3 patients (10%) to have cancer, while the remaining 28 nodules were benign.

The surgical time was 109 (+/- 7.5) minutes in the frozen-section group and 113 (+/- 7) minutes in the non frozen-section group.

The anaesthesia time was 147 (+/- 7.3) minutes in the frozen-section group and 155 (+/- 8) minutes in the non frozen-section group.

The length of hospital stay was 1 day in both groups.

The differences in terms of the secondary outcomes were not statistically significant.

Clinical conclusions
Two of the 61 patients benefited from frozen section, one in the frozen-section group and one in the non frozen-section group. The reason for the latter was that the tumour appeared suspicious. Hence, a directed frozen section was performed. Frozen-section analysis is not a useful tool as a routine procedure but should be used when there is a suspicious case.

Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic analysis. A cost-consequences analysis was therefore carried out.
Direct costs
Discounting was not carried out as it was irrelevant, due to the short time horizon of the analysis. The quantities measured for each patient were surgical time, anaesthesia time, length of hospital stay, and the time of an intraoperative pathological consultation based on frozen-section analysis. The cost/resource boundary adopted was that of the hospital. The unit costs and the quantities of resources were not reported. The total hospital charges for each patient were calculated, as was the mean charge per frozen section. The quantities and costs were estimated using actual data from the hospital. No price year was given.

Statistical analysis of costs
Statistical analyses of the total costs were performed to test for statistical significance of the results.

Indirect Costs
The indirect costs were irrelevant since the study was conducted from the perspective of the hospital.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
No measure of benefit was calculated. See the ‘Effectiveness Results’ section.

Cost results
The total hospital charges (+/- standard error of the mean) were $4,156 (+/- 139) for a patient in the frozen-section group and $4,216 (+/- 176) for a patient in the non frozen-section group. No statistically significant difference in the costs was found. The mean charge per frozen section was $430. The mean charge for informative frozen section was $12,470, since 29 frozen sections were performed and only one was informative.

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

Authors' conclusions
Routine frozen-section analysis did not aid the diagnosis for patients with follicular neoplasms of the thyroid. There was no cost argument for or against routine frozen section.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was justified as it often represents current practice. The aim of the study was to see whether frozen section could be justified. You should assess whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis used a randomised controlled trial, which enhanced the internal validity of the analysis. The method of randomisation was reported. The study sample was representative of the study population, and the patient groups were shown to be comparable at analysis. However, the authors did not calculate a measure of the diagnostic...
accuracy of frozen-section analysis combined with histological tests, to compare with a diagnosis based on histological tests alone. There was an implicit assumption that the ultimate diagnosis would be the same in both groups of patients, and that the only difference between the groups would, therefore, be one of the costs. The authors did not discuss the speed of diagnosis as a variable, which would vary with the method of diagnosis. The speed of diagnosis could then affect the health outcomes for the patients.

Validity of estimate of measure of benefit
The authors implied that there was no difference in diagnosis between the two groups of patients. Hence, there was no difference in the outcomes. The authors stated that they did not assess the contribution of speed of diagnosis to the benefit of the diagnostic method.

Validity of estimate of costs
The data on resource use and hospital charges were valid as they were taken from the single study. It appears that all the categories of costs relevant to the perspective adopted were included in the analysis. However, the charges rather than costs were used in the economic analyses. In addition, the unit costs and the quantities of resources were not reported separately. The cost data should have given the price year of the hospital charges. The cost estimates appear to have been specific to the study setting.

Other issues
The authors compared their results with the findings from other studies. However, they did not address the issue of generalisability to other settings. A population of patients with a dominant thyroid nodule was enrolled into the study, and this was reflected in the conclusions. The study findings, however, should be limited to the specific study population considered in the analysis. The authors reported the study results selectively.

Implications of the study
The authors recommend abandoning the routine use of frozen-section analysis, and only using frozen section after a review of the specimen suggests gross evidence of invasive tumour growth. However, the authors did not address the fact that if the costs are no higher for the routine frozen-section group and, if it sometimes leads to a speedier diagnosis (even if rare) and quicker treatment, then that is a good argument in its favour.

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None stated.

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Other publications of related interest

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