Traditional versus up-front (18F) fluorodeoxyglucose-positron emission tomography staging of non-small-cell lung cancer: a Dutch cooperative randomized study


**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 traditional work-up (TWU) according to international guidelines with early up-front (18F)-fluorodeoxyglucose (18FDG) positron emission tomography (PET). Patients were then followed by histologic or cytologic verification of lesions, or imaging and follow-up. Patients with 18FDG-avid, non-central tumours with suspicion of mediastinal or distant metastases on PET proceeded directly to thoracotomy.

**Type of intervention**
Diagnosis.

**Economic study type**
Cost-effectiveness analysis.

**Study population**
The study population comprised patients with a clinical suspicion of lung cancer that had arisen from history, physical examination and chest X-ray. Additional inclusion criteria were the absence of clinically overt disseminated disease at first presentation, age 18 years or more, and being medically fit for staging and surgery. Pregnant patients or those with diabetes were excluded from the study.

**Setting**
The study setting was inpatient secondary care. The economic study was carried out in the Netherlands.

**Dates to which data relate**
The effectiveness and resource use data were collected from patients enrolled in the study between September 1999 and June 2001. The price year was 2003.

**Link between effectiveness and cost data**
The costing was undertaken prospectively on the same patient sample that provided the effectiveness data.

**Study sample**
The authors reported that a study sample of 465 patients was required to assess if the PET up-front strategy was clinically useful (i.e. it reduced the proportion of patients requiring at least three tests from 50% to 30%). From a total of 2,114 potential patients, 465 (22%) met the inclusion criteria and were enrolled in the study. Of these, 233 were allocated to the TWU group and 232 to the PET group. One patient allocated to TWU declined further investigations after allocation to the group, while two patients allocated to PET declined the intervention. Nine patients allocated to TWU underwent PET.
Study design
The study was a randomised controlled trial (RCT), based on patients being seen at 22 participating hospitals and PET scanning being performed in two centres. Patients were randomly allocated to one of the two groups centrally, by computer, using a permuted block design stratified by institute and performance score. The duration of follow-up ranged from 6 months for those treated with surgery or neoadjuvant therapy to 12 months for those with presumed benign lesions. The authors did not report if there was any loss to follow-up.

Analysis of effectiveness
The primary outcome measures were the number of tests and procedures to finalise staging and to define operability, and the quality of staging. Quality of staging was assessed by comparing the number of correctly clinically staged patients with the final stage as determined at surgery and/or follow-up. The secondary outcome measures included duration of diagnostic process and morbidity due to complications of diagnostic procedures.

At analysis, the patient groups were shown to be comparable in terms of their age, gender, Eastern Cooperative Oncology Group performance scores, weight loss, co-morbidity and history of malignancy.

Effectiveness results
The proportion of patients requiring at least three tests (on top of bronchoscopy, chest X-ray, laboratory measurement, lung function and cardiovascular tests, and thoracotomy) was 52% in the TWU group compared with 51% in the PET group, (p=0.82). The total number of tests necessary to finalise staging was similar between the two groups, (p=0.90).

Agreement between clinical and final stages was similar for the two interventions, (p=0.073). The kappa score was 0.85 (95% confidence interval, CI: 0.80 to 0.90) in the TWU group and 0.78 (95% CI: 0.72 to 0.84) in the PET group.

Morbidity due to staging procedures other than surgery was evenly distributed in the two groups.

Clinical conclusions
The authors concluded that up-front 18FDG-PET in patients with suspected lung cancer did not reduce the overall number of diagnostic tests, but maintained quality of clinical staging.

Measure of benefits used in the economic analysis
The authors did not derive a summary measure of benefit. In effect, a cost-consequences analysis was performed.

Direct costs
The direct costs to the hospital were included in the analysis. Such costs covered the diagnostic tests, therapeutic interventions (e.g. thoracotomy, chemotherapy and radiotherapy), outpatient visits and hospital inpatient care. The unit costs were derived from a micro-costing study approach, which included the costs of personnel, materials, depreciation and overheads. Resource use was derived from patients enrolled into the study between September 1999 and June 2001. Discounting was not relevant, as the costs were incurred during 1 year, and was appropriately not performed. The price year was 2003. The study reported the average costs.

Statistical analysis of costs
The cost data were compared using two-sided Wilcoxon-Mann Whitney tests.

Indirect Costs
Productivity costs were not included.
Currency
US dollars ($). The authors did not report the exchange rate used to convert euros to US dollars.

Sensitivity analysis
The authors did not perform any sensitivity analyses.

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

Cost results
The average total cost of diagnosis and treatment was $11,351 (standard deviation, SD=8,479) in the TWU group compared with $12,581 (SD=9,567) in the PET group, (p=0.14).

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

Authors' conclusions
(18F)-fluorodeoxyglucose (18FDG) positron emission tomography (PET) in patients with suspected lung cancer did not simplify staging nor reduce the costs, but it still provided good-quality clinical staging with the use of less invasive surgery.

CRD COMMENTARY - Selection of comparators
A justification was given for using TWU as the comparator. It represented current practice in the authors' settings. You should decide if the comparator used represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on an RCT. This was appropriate for the study question as well-conducted RCTs are considered to be the 'gold' standard study design when comparing health interventions. The study sample appears to have been representative of the study population. In addition, the patient groups were shown to be comparable at analysis. The authors reported the method of randomisation and length of study. However, they did not report whether blinding took place or the loss to follow-up. Nevertheless, it would appear that the results of the study were internally valid. Power calculations were reported and an appropriate sample size was used.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of benefit. In effect, a cost-consequences analysis was performed. The reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The analysis of the costs was performed from the perspective of the hospital paying for the diagnostic intervention. All the relevant categories of costs, as well as individual costs, appear to have been included in the analysis. The resource use quantities were derived from the same study as that used to derive the effectiveness data. The unit costs were derived from the authors' settings. The price year was reported, which will ease any future inflation exercises. The authors compared costs between the two tests using appropriate statistical techniques. Details of the currency conversion were not reported.

Other issues
The authors reported that their results were difficult to compare with other studies, as their key outcome was substitution rather than the added value of PET. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.
The authors reported a number of further limitations to their study. First, the level of clinical experience with PET was variable among institutions. Second, PET scans were not read in conjunction with computed tomography (CT), which is known to improve the accuracy of either test.

**Implications of the study**
The authors reported that further research should determine whether up-front positioning of PET-CT may be a cost-effective alternative for current practices.

**Source of funding**
Supported by a grant from the ZonMw Program, the Netherlands Organization for Health Research and Development, and the Health Care Efficiency Research Program.

**Bibliographic details**

**PubMedID**
16567772

**DOI**
10.1200/JCO.2005.02.4695

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**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Aged; Carcinoma, Non-Small-Cell Lung /radionuclide imaging /therapy; Female; Fluorodeoxyglucose F18; Health Care Costs; Humans; Lung Neoplasms /radionuclide imaging /therapy; Male; Middle Aged; Neoadjuvant Therapy; Neoplasm Staging /economics /methods /standards; Radiopharmaceuticals; Sensitivity and Specificity; Time Factors

**AccessionNumber**
22007000974

**Date bibliographic record published**
31/12/2007

**Date abstract record published**
31/12/2007