

## Cost-effectiveness of Fluorine-18-Fluorodeoxyglucose positron emission tomography in tumours other than lung cancer: A systematic review

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### Abstract

**AIM:** To systematically review published data on the cost-effectiveness of Fluorine-18-Fluorodeoxyglucose positron emission tomography (FDG-PET) or PET/computed tomography (PET/CT) in tumours other than lung cancer.

**METHODS:** A comprehensive literature search of studies published in PubMed/MEDLINE, Scopus and Embase databases through the 10<sup>th</sup> of October in 2013 was carried out. A search algorithm based on a combination of the terms: (1) "PET" or "PET/computed tomography (PET/CT)" or "positron emission tomography"; and (2) "cost-effectiveness" or "cost-utility" or "cost-efficacy" or "technology assessment" or "health technology assessment" was used. Only cost-effectiveness or cost-utility analyses in English language were included. Exclusion criteria were: (1) articles not within the field of interest of this review; (2) review articles, editorials or letters, conference proceedings; and (3) outcome evaluation studies, cost studies or health technology assessment reports. For each included study, information was col-

lected concerning basic study, type of tumours evaluated, perspective/type of study, results, unit and comparison alternatives.

**RESULTS:** Sixteen studies were included. Head and neck tumours were evaluated in 4 articles, lymphoma in 4, colon-rectum tumours in 3 and breast tumours in 2. Only one article was retrieved for melanoma, oesophagus and ovary tumours. Cost-effectiveness results of FDG-PET or PET/CT ranged from dominated to dominant.

**CONCLUSION:** Literature evidence about the cost-effectiveness of FDG-PET or PET/CT in tumours other than lung cancer is still limited. Nevertheless, FDG-PET or PET/CT seems to be cost-effective in selective indications in oncology (staging and restaging of head and neck tumours, staging and treatment evaluation in lymphoma).

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**Key words:** Positron emission tomography; Positron emission tomography/computed tomography; Fluorine-18-Fluorodeoxyglucose; Cost-effectiveness; Oncology

**Core tip:** Evidence based data about the cost-effectiveness of Fluorine-18-Fluorodeoxyglucose positron emission tomography (FDG-PET) or PET/computed tomography (PET/CT) in lung cancer already exist. The aim of our study is to systematically review published data on the cost-effectiveness of FDG-PET or PET/CT in tumours other than lung cancer.

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## INTRODUCTION

Fluorine-18-Fluorodeoxyglucose positron emission tomography (FDG-PET) or PET/computed tomography (PET/CT) is useful imaging techniques to study cellular metabolism. FDG is a glucose analogue which is trapped by cells *via* the glucose transporters; tumour cells usually show increased glucose metabolism and consequently an increased FDG uptake compared to normal cells. This characteristic allows the visualization of tumour cells by using PET imaging<sup>[1]</sup>.

To date, oncology is the most important application of FDG-PET and PET/CT. The role of FDG-PET or PET/CT in oncology is to stage or restage tumours, to evaluate tumour response to treatment, to define patient prognosis, to guide surgery and radiotherapy<sup>[1]</sup>.

FDG-PET and PET/CT have high costs; therefore it is mandatory to combine the effectiveness evaluation of these methods with economic assessment in different oncologic indications, in order to establish the correct usefulness of these methods in different clinical scenarios<sup>[2]</sup>.

Cost-effectiveness analysis is a way to study both efficacy and cost of a medical procedure. These studies use parameters as “life years gained” (LYG) or disability days saved. In cost-utility analysis, measures change with patient preference and authors refer to “quality-adjusted life years” (QALYs). In cost-benefit analyses, monetary units represent the value of the procedure<sup>[3]</sup>. Incremental cost-effectiveness ratio (ICER) and incremental cost-utility ratio (ICUR) are ways to measure the cost of an increasing efficacy (or utility) of a medical procedure. Similarly, net monetary benefit (NMB) is used to correlate cost and efficacy, using an equation including the willingness to pay (WTP) value that represents the maximum cost that a patient would pay for a medical procedure.

Evidence based data about the cost-effectiveness of FDG-PET and PET/CT in lung cancer already exist. PET is cost-effective in staging of non-small cell lung carcinoma (NSCLC) and seems to be cost-effective for diagnosing solitary pulmonary nodules (SPN)<sup>[4]</sup>. Then, PET cost is appropriate in staging of lung cancer and diagnosis of indeterminate SPNs<sup>[5]</sup>.

Cost-effectiveness studies have been published about the use of FDG-PET or PET/CT in tumours other than lung cancer. The aim of our study is to systematically review published data on the cost-effectiveness of FDG-PET and PET/CT in this setting.

## MATERIALS AND METHODS

A comprehensive computer literature search of the PubMed/MEDLINE, Scopus and Embase databases was carried out to find relevant peer reviewed articles on the

cost-effectiveness of PET or PET/CT in patients with either histologically proven or suspected tumours other than lung cancer.

A search algorithm based on a combination of the terms: (1) “PET” or “PET/CT” or “positron emission tomography”; and (2) “cost-effectiveness” or “cost-utility” or “cost-efficacy” or “technology assessment” or “health technology assessment (HTA)” was used. No beginning date limit was used and the search was updated until October 10<sup>th</sup>, 2013. To expand our search, references of the retrieved articles were also screened for additional studies. Only English studies were included.

All studies or subsets in studies investigating the cost-effectiveness of FDG-PET or PET/CT in patients with suspected tumours other than lung cancer were eligible for inclusion.

The exclusion criteria were: (1) articles not within the field of interest of this review; (2) review articles, editorials or letters, comments, conference proceedings; and (3) outcome evaluation studies, cost studies or health technology assessment reports.

Three researchers (GT, SA and CC) independently reviewed the titles and the abstracts of the retrieved articles, applying the inclusion and exclusion criteria mentioned above. The same three researchers then independently reviewed the full-text version of the articles to confirm their eligibility for inclusion. Disagreements were resolved in a consensus meeting.

For each included study, information was collected concerning basic study (author names, journal, year of publication, country of origin), type of tumours evaluated, perspective/type of study, results, unit and comparison alternatives.

## RESULTS

The comprehensive computer literature search revealed 874 articles. Reviewing titles and abstracts, 841 articles were excluded applying the criteria mentioned above. Thirty-three articles were selected and retrieved in full-text version (Figure 1). One study was found screening the references<sup>[6]</sup> and 18 articles were subsequently excluded<sup>[7-24]</sup>. Finally, 16 studies were included<sup>[6,25-39]</sup>. The characteristics of the included studies (Table 1) and a list of excluded studies on economic evaluation assessment, with reasons for exclusion (Table 2) are provided.

Head and neck tumours were evaluated in 4 articles, lymphoma in 4, colon-rectum tumours in 3 and breast tumours in 2. Only one article was retrieved for melanoma, oesophageal and ovary tumours.

### Cost-effectiveness of FDG-PET or PET/CT in head and neck tumours

Hollenbeak *et al.*<sup>[25]</sup> compared PET with CT scan strategy in patients with N0 head and neck squamous cell carcinoma (HNSCC). A cost-effectiveness analysis was undertaken using a decision tree model approach and the perspective was that of the hospital. The ICER for the PET strategy was \$8718 per year of life saved, or \$2505

Table 1 Characteristics of included studies

Ref.	Year	Country	Tumour (histology)	Indication	Perspective, type of study	Results, unit and comparison alternatives
Hollenbeak <i>et al</i> <sup>[25]</sup>	2001	United States	Neck (various)	Staging	Hospital, decision tree	ICER (US\$/LYG (US\$/QALY)): 8718 (2505) (CT + PET <i>vs</i> CT)
Yen <i>et al</i> <sup>[26]</sup>	2009	Taiwan	Head/neck (nasopharyngeal carcinoma)	Restaging	Hospital, decision tree	ICUR (US\$/QALY): 462 (PET + MRI <i>vs</i> MRI)
Sher <i>et al</i> <sup>[27]</sup>	2010	United States	Head/neck (squamous cell carcinoma)	Restaging	Public payer (medicare), markov model	ICER (US\$/QALY): 1500 (PET-CT <i>vs</i> CT in RD after chemotherapy)
Rabalais <i>et al</i> <sup>[28]</sup>	2012	United States	Head/Neck (various)	Restaging	Public payer (medicare), decision tree	ICER (US \$): 3854397 (PET-CT <i>vs</i> neck dissection)
Sloka <i>et al</i> <sup>[29]</sup>	2005	Canada	Breast (various)	Staging	Hospital, meta-analysis, decision tree	PET + ALND dominating ALND [cost savings (US \$): 695, increase in life expectancy: 7.4 d]
Meng <i>et al</i> <sup>[30]</sup>	2011	United Kingdom	Breast (various)	Staging	Health care system, decision tree	NMB (UK£ 30000 per QALY): 1085 (replace SLNB with PET)
Klose <i>et al</i> <sup>[31]</sup>	2000	Germany	Lymphoma (various)	Staging	Hospital, micro-costing approach	ICER (€): 3133 (FDG-PET <i>vs</i> CT)
Bradbury <i>et al</i> <sup>[6]</sup>	2002	United Kingdom	Lymphoma (HL)	Restaging	Health care system, decision tree and Markov model	WTP (£/LYG): 1000 (PET after positive CT <i>vs</i> CT + PET)
Cerci <i>et al</i> <sup>[32]</sup>	2010	Brazil	Lymphoma (HL)	Post-treat	Hospital, decision tree	ICER (\$): 3268 (CT + PET + biopsy <i>vs</i> CT + biopsy)
Cerci <i>et al</i> <sup>[33]</sup>	2011	Brazil	Lymphoma (HL)	Staging	Hospital, micro-costing approach	ICER (\$): 16215 (PET/CT <i>vs</i> CT and biopsy)
Park <i>et al</i> <sup>[34]</sup>	2001	United States	Colon-rectum (various)	Restaging	Public payer (medicare), decision tree	ICER (US\$/LYG): 16437 (CT + PET <i>vs</i> PET)
Lejeune <i>et al</i> <sup>[35]</sup>	2005	France	Colon-rectum (metastases)	Staging	Health care system, decision tree	ICER: dominated (CT <i>vs</i> CT + PET)
Wiering <i>et al</i> <sup>[36]</sup>	2010	Netherlands	Colon-rectum (metastases)	Restaging	Health care system, randomized clinical trial	NMB (€): 11060 (CWU <i>vs</i> CWU + FDG-PET)
Krug <i>et al</i> <sup>[37]</sup>	2010	Belgium	Melanoma (metastases)	Restaging	Health care system, Markov model	ICER: dominated (PET-TC <i>vs</i> CT). NMB (€):1048, gain of 0.2 LMG
Wallace <i>et al</i> <sup>[38]</sup>	2002	United States	Esophagus (various)	Staging	Public payer (medicare), decision tree	Marginal ICER (\$/QALY): 60544 (PET + EUS-FNA <i>vs</i> CT + EUS-FNA)
Mansueto <i>et al</i> <sup>[39]</sup>	2009	Italy	Ovary (various)	Restaging	Health care system, decision tree	ICER (€/SA): 226.77 (PET/CT for All)

CT: Computerized tomography; ICER: Incremental cost-effectiveness ratio; ICUR: Incremental cost-utility ratio; LYG: Life-year gained; MRI: Magnetic resonance imaging; RD: Residual disease; PET: Positron emission tomography; QALY: Quality-adjusted life-year; NMB: Net monetary benefit; ALND: Axillary lymph node dissection; HL: Hodgkin lymphoma; NHL: Non-Hodgkin lymphoma; CWU: Conventional diagnostic work-up; WTP: Willingness to pay; EUS-FNA: Endoscopic ultrasound with fine-needle aspiration biopsy; SLNB: Sentinel lymph node biopsy; SA: Surgery avoided; UK: United Kingdom; US: United States.

per QALY. Authors also evaluated life expectancy and costs. The PET strategy resulted in a life expectancy of 10.1 years, marginally higher than the 9.9 years expected from the No PET strategy. The PET strategy also resulted in 9.8 QALYs versus 9.4 QALYs for the No PET strategy.

Yen *et al*<sup>[26]</sup> defined as the baseline case a 46-year-old male patient who was suspected of having recurrent nasopharyngeal carcinoma (NPC) during his post-treatment follow-up. The analysis for cost-utility is based on the decision-tree model for three different strategies: (1) magnetic resonance imaging (MRI)-only; (2) PET-only; and (3) MRI-PET (performing PET if MRI result is uncertain). The additional cost per additional QALYs for strategy 2 relative to strategy 1 was calculated to be United States \$1389 (United States \$750/0.54) and that for strategy 3 relative to strategy 1 is calculated to be United States \$462 (United States \$550/1.19). Strategy 3 dominates over strategy 2 because strategy 3 costs less and yields more QALYs than strategy 2.

Sher *et al*<sup>[27]</sup> analysed the cost-effectiveness of CT and PET/CT as predictors of the need for adjuvant neck dissection (AND) compared with ND for all patients with node-positive HNSCC. Authors designed a Markov model to simulate the clinical history of a 50-year-old man with node-positive stage IVA squamous cell carcinoma of the oropharynx. Three strategies were evaluated: carrying out NDs on all patients; NDs only for patients with residual disease (RD) on CT; NDs on patients with RD on PET/CT. With a few exceptions, the PET/CT strategy dominated the other two strategies (ICER of 1500 United States \$/QALY for PET-CT versus CT in RD after chemotherapy).

Rabalais *et al*<sup>[28]</sup> considered a patient with an oropharyngeal cancer with pre-treatment N2 disease having a complete response. Standardized costs were obtained using national databases. Four different strategies were analysed: PET/CT only; ND and physical examination (PE); ND + PE + CT; ND + PE + PET/CT. The ICER was of 3854397 United States \$ for PET-CT versus neck

**Table 2** Characteristics of excluded studies

Ref.	Year	Country	Tumors (histology)	Reason for exclusion
Bongers <i>et al</i> <sup>[7]</sup>	2002	Netherlands	Neck (laryngeal cancer)	Cost study
van Hooren <i>et al</i> <sup>[8]</sup>	2009	Netherlands	Neck (laryngeal carcinoma)	Cost study
Uly-de Groot <i>et al</i> <sup>[9]</sup>	2010	Netherlands	Head/neck (metastases)	Cost study
Kurien <i>et al</i> <sup>[10]</sup>	2011	United States	Head/neck (various)	Cost study
Schergerin <i>et al</i> <sup>[11]</sup>	2009	United States	Breast (various)	No PET comparison
Auguste <i>et al</i> <sup>[12]</sup>	2011	United Kingdom	Breast (various)	Review
Cooper <i>et al</i> <sup>[13]</sup>	2011	United Kingdom	Breast (various)	Review
Strobel <i>et al</i> <sup>[14]</sup>	2007	Switzerland	Lymphoma (various)	Cost study
Moulin-Romsee <i>et al</i> <sup>[15]</sup>	2008	Belgium	Lymphoma (NHL)	Cost study
Brush <i>et al</i> <sup>[16]</sup>	2011	United Kingdom	Colon-rectum (various)	Review
von Schulthess <i>et al</i> <sup>[17]</sup>	1998	Switzerland	Melanoma (various)	Cost study
Bastiaannet <i>et al</i> <sup>[18]</sup>	2012	Netherlands	Melanoma (various)	Cost study
Heinzel <i>et al</i> <sup>[19]</sup>	2012	Germany	Brain (glioma)	Aminoacid PET
Heinzel <i>et al</i> <sup>[20]</sup>	2012	Germany	Brain (glioma)	Aminoacid PET
Hetzel <i>et al</i> <sup>[21]</sup>	2003	Germany	Bone (metastases)	F18-Fluoride PET
Tateishi <i>et al</i> <sup>[22]</sup>	2010	Japan	Bone (metastases)	F18-Fluoride PET
Heinrich <i>et al</i> <sup>[23]</sup>	2005	Austria	Pancreas (various)	Cost study
Rondina <i>et al</i> <sup>[24]</sup>	2012	United States	Occult (various)	Cost study

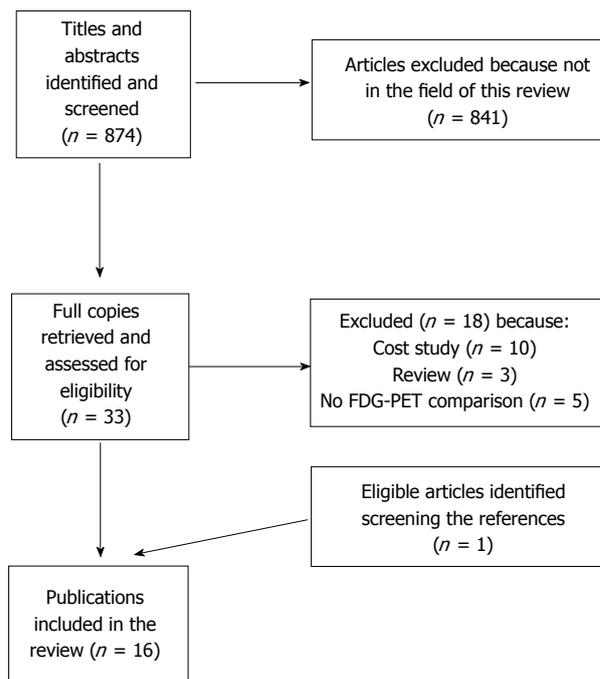
PET: Positron emission tomography.

dissection. The most cost-effective strategy was PET/CT scans on all patients following treatment, and proceed with neck dissections on those with positive scans.

#### Cost-effectiveness of FDG-PET or PET/CT in lymphoma

Klose *et al*<sup>[31]</sup> measured the ICER of FDG-PET versus CT as diagnostic procedures in the primary staging of malignant lymphomas. ICER were €478 per correctly staged patient for CT versus “no diagnostics” and €3133 for FDG-PET versus CT. Direct costs of the diagnostic procedures were calculated based on the cost accounting system of the University Hospital in Ulm using a micro-costing approach.

Bradbury *et al*<sup>[6]</sup> studied patients who have a partial or complete response to induction therapy. They compared five strategies: all for surveillance; all for consolidation; CT only; PET after positive CT; CT + PET. Perspective was that of health care system. Strategies 4 and 5 were cost-effective, provided WTP exceeded £1000/LYG, and for almost all input values considered, provided WTP ex-



**Figure 1** Flowchart of the systematic review. FDG-PET: Fluorine-18-Fluoro-deoxyglucose positron emission tomography.

ceeded £5000/LYG.

In two studies, Cerci *et al*<sup>[32]</sup> calculated the cost-effectiveness of PET in hodgkin lymphoma (HL). In both studies, perspective was that of the hospital. In the first one<sup>[32]</sup>, they assessed the cost effectiveness of FDG-PET in patients with HL with unconfirmed complete remission (CRu) or partial remission (PR) after first-line treatment. The ICER comparing the restaging strategy of CT, PET, and biopsy with the restaging strategy of only CT and biopsy (without PET) would be \$3268 per true case detected.

In the second study<sup>[33]</sup>, staging costs were studied in more strategies: conventional strategy (strategy I) including physical examination, laboratory tests, bone marrow biopsy (BMB), and CT scans (cervical, thoracic, abdominal, and pelvic); strategy II (with CT + PET) including physical examination, laboratory tests, bilateral BMB, CT scans, and PET scans; strategy III (with PET/CT) including physical examination, laboratory tests, bilateral BMB, and PET-CT scans with diagnostic CT using contrast agent. The ICER of PET/CT strategy was \$16215 per patient with modified treatment. PET/CT costs at the beginning and end of treatment would increase total costs of HL staging and first-line treatment by only 2%.

#### Cost-effectiveness of FDG-PET or PET/CT in colon-rectum tumours

Park *et al*<sup>[34]</sup> studied patients with an increase in carcino-embryonic antigen levels of more than 5 ng/mL during follow-up testing after the resection of their primary colorectal cancer. The CT + FDG-PET strategy was higher in mean cost by \$429 per patient, but resulted in an increase in the mean life expectancy of 9.527 d per

patient. Their perspective was that of public payer (Medicare) and they used a model approach (decision tree).

Lejeune *et al.*<sup>[35]</sup> compared CT and CT + PET to assess the cost-effectiveness of FDG-PET in the management of metachronous liver metastases of colorectal cancer. CT was a dominated strategy, presenting an extra cost of €2671 (\$3213) and a similar expected effectiveness-per-patient compared with CT + PET (1.88 years life expectancy per patient).

Wiering *et al.*<sup>[36]</sup> evaluated the clinical effectiveness, impact on health care resources and cost-effectiveness of adding FDG-PET to the diagnostic algorithm, during a randomized clinical trial from a health care perspective. Both health-related quality of life and QALYs showed no significant difference between the conventional diagnostic work-up (CDW) and PET groups. NMB ranged from €1004 to €11060 depending on the monetary value given to a QALY. A bootstrap procedure was performed to provide an estimate of the uncertainty surrounding ICER.

#### Cost-effectiveness of FDG-PET or PET/CT in breast cancer

Sloka *et al.*<sup>[29]</sup> conducted a meta-analysis of studies for the accuracy of PET in staging breast cancer. The representative population is a 55-year-old woman presenting with stage I or II breast cancer. Authors compared PET and axillary lymph node dissection (ALND) in selected patients with ALND in all patients. A cost savings of \$695 per person is expected for the PET strategy, with an increase in life expectancy (7.4 d), when compared with the non-PET strategy. This cost savings remained in favour of the PET strategy when subjected to a sensitivity analysis. ICER was not calculated.

Meng *et al.*<sup>[30]</sup> evaluated the cost-effectiveness of MRI and PET compared with sentinel lymph node biopsy (SLNB) for assessment of axillary lymph node metastases in newly-diagnosed early stage breast cancer patients in the United Kingdom. The perspective was that of the health care system. MRI and PET are assessed firstly as a replacement for SLNB and secondly as an additional test prior to SLNB. The baseline SLNB strategy is dominated by the strategies of replacing SLNB with PET, with a NMB of 1085 (measured in United Kingdom £30000 per QALY).

#### Cost-effectiveness of FDG-PET or PET/CT in melanoma

Krug *et al.*<sup>[37]</sup> performed a cost-effectiveness analysis, using a Markov model over a 10-year-period, to compare two different surveillance programs, either PET/CT or whole-body CT, in patients with suspected pulmonary metastasized melanoma. The Belgian health care payer perspective was adopted. The PET/CT strategy was dominant with a net saving of €1048 and a gain of 0.2 life-months gained.

#### Cost-effectiveness of PET or PET/CT in oesophageal cancer

Wallace *et al.*<sup>[38]</sup> compared the health care costs and ef-

fectiveness of multiple staging options for patients with oesophageal cancer. A decision-analysis model was constructed to compare different staging strategies: CT scan, endoscopic ultrasound with fine-needle aspiration biopsy (EUS-FNA), PET, thoracoscopy/laparoscopy, and combinations of these. The marginal cost-effectiveness ratio for PET + EUS-FNA was \$60544 per QALY.

#### Cost-effectiveness of FDG-PET or PET/CT in ovary tumours

Mansueto *et al.*<sup>[39]</sup> evaluated the economic impact of the introduction of PET/CT in the early detection of recurrent ovarian cancer through a cost-effectiveness analysis of different diagnostic strategies: (1) CT only or baseline strategy; (2) PET/CT for negative CT or strategy A; and (3) PET/CT for all or strategy B. Strategy A is dominated by strategy B, which is more expensive (€2909 *vs* €2958), but also more effective (3 cases of surgery avoided) and presented an ICER of €226.77 per surgery avoided (range: €49.50-€433.00).

## DISCUSSION

PET and PET/CT have high costs: in Germany<sup>[40]</sup>, costs per examination range between €600 (\$885) and €1000 (\$1474); in United States, a median reimbursement is of \$952.83; in Great Britain<sup>[41]</sup>, costs may vary between £635-£1300 (\$1030-\$2109). Reimbursement amount may vary in different country.

Three types of economic evaluation of a medical procedure may be performed: cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA)<sup>[42]</sup>. Authors performing CEA analyse medical procedure including costs and LYG. ICER quantifies costs of a medical procedure, considering procedure efficacy. Acceptable ICER limit may vary in different country. CUA analyses costs and efficacy considering QALYs to quantify quality of life, too. CBA counts in monetary units (NMB) advantages of an imaging technique<sup>[40]</sup>. WTP value represents the maximum cost acceptable for a medical procedure.

Many groups have studied cost-effectiveness of PET/CT. Evidence based data about the cost-effectiveness of FDG-PET and PET/CT in lung cancer already exist. Cost-effectiveness of PET/CT has been studied in staging of NSCLC<sup>[43]</sup>, in diagnosis of a SPN<sup>[44]</sup> and follow-up of NSCLC<sup>[45]</sup>. Currently, best PET/CT cost-effectiveness values are in staging NSCLC. German health care system has confirmed cost-effectiveness of FDG-PET/CT in staging and restaging of NSCLC<sup>[46]</sup>.

Many authors made reviews<sup>[4,40]</sup> or health technology HTA reports<sup>[47,48]</sup> about the cost-effectiveness of PET in oncology. No systematic reviews about cost-effectiveness of FDG-PET in tumours other than lung cancer have been done until now.

In this study, cost-effectiveness of FDG-PET in staging of head and neck tumours has been analysed in one study. Hollenbeak *et al.*<sup>[25]</sup> concluded that FDG-PET is

cost-effective in staging and treating a N0 carcinoma, but prospective studies are needed to validate these results. Cost-effectiveness of FDG-PET in restaging head and neck tumours is controversial. Yen *et al.*<sup>[26]</sup> analysed that PET-only strategy will become the most cost-effective for recurrent NPC in patients in the near future as the cost of PET will decrease. Rabalais *et al.*<sup>[28]</sup> assessed that PET/CT is the most cost-effective strategy for surveillance of the patient with pre-treatment N2 disease, a controlled primary tumour, and a clinically negative neck after completion of chemo-radiotherapy (CRT). Sher *et al.*<sup>[27]</sup> showed that PET/CT is the dominant, cost-effective strategy after CRT for N2-N3 head and neck squamous cell cancer, determining the necessity for adjuvant ND. Finally, FDG-PET seems to be cost-effective in staging and restaging in patients with head and neck tumours.

Cost-effectiveness of FDG-PET in staging of breast cancer is not clear. Sloka *et al.*<sup>[29]</sup> found that PET strategy allows cost savings and that the use of this strategy for the staging of breast cancer was economically viable in Canada. Meng *et al.*<sup>[30]</sup> demonstrated that MRI is more cost-effective than SLNB in diagnosis of axillary metastases. In fact, sensitivity of MRI was higher than PET, with lower costs. In conclusion, more studies are needed to evaluate cost-effectiveness of FDG-PET in patients with breast cancer.

Cost-effectiveness of FDG-PET in restaging HL is discussed. In his first study, Cerci *et al.*<sup>[32]</sup> showed that for patients with HL presenting in CRu/PR with suspicious residual masses after first-line therapy, restaging FDG-PET was cost effective, producing 1% cost savings to Brazil public health care system. Bradbury *et al.*<sup>[6]</sup> found that PET seemed to be cost-effective after CT in patients who have had a response to induction therapy. About cost-effectiveness of FDG-PET in staging lymphoma, in his second study, Cerci *et al.*<sup>[33]</sup> concluded that PET/CT ICER (\$16215) in the initial staging and end treatment of patients with HL was acceptable for health system. Klose *et al.*<sup>[31]</sup> demonstrated that the use of PET could produce cost savings but more studies are needed to confirm the long-term cost-effectiveness of this procedure. Finally, FDG-PET seems to be cost-effective in staging and treatment evaluation in patients with lymphoma.

About cost-effectiveness of FDG-PET in restaging colon-rectum cancer, Wiering *et al.*<sup>[36]</sup> concluded that FDG-PET in patients with resectable colorectal liver metastases resulted in better patient selection with potential cost savings. Park *et al.*<sup>[34]</sup> showed the relative cost-effectiveness of using a CT and FDG-PET for managing patients candidates for surgical hepatic resection. Lejeune *et al.*<sup>[35]</sup> demonstrated the economic value of CT and PET, with the consequence of decreasing the number of inappropriate surgical acts. In conclusion, further studies are needed to conclude that FDG-PET in patients with colon-rectum cancer is cost-effective.

Few evidences are available about cost-effectiveness in other tumours. Krug *et al.*<sup>[37]</sup> showed that PET/CT strategy

was cost-effective in restaging of patients with suspected pulmonary metastases of melanoma. Wallace *et al.*<sup>[38]</sup> demonstrated that initial PET and EUS-FNA staging were more effective but also more expensive than other imaging strategies in oesophagus cancer. Mansueto *et al.*<sup>[39]</sup> concluded that PET/CT in patients with suspected ovarian cancer recurrence was more cost-effective than CT only. So, there could be potentially cost-savings for the Italian National and Regional Healthcare System. In these tumours, cost-effectiveness of FDG-PET is not clear.

This study has several limitations. The review included studies with different economic model and perspective, produced in different country. Acceptable cost-effectiveness parameters (ICER, ICUR, LYG and NMB) may vary in different groups and health system. Authors often considered PET included in a complex diagnostic strategy, with the consequence of a not focused PET analysis. Many studies analysed PET scan and not hybrid PET/CT scan. In near future, PET/CT may be more accurate and then more cost-effective than PET scan alone. Only English language and FDG-PET studies have been included.

Finally, literature evidence about the cost-effectiveness of FDG-PET or PET/CT in tumours other than lung cancer is still limited. Not enough studies have been published about ovary cancer, oesophageal carcinoma and melanoma to assess cost-effectiveness of this strategy in medical management. More studies are available about cost-effectiveness of FDG-PET in staging and restaging colon-rectum cancer and staging breast cancer, but without clear economic parameters in favour of PET strategy. FDG-PET or PET/CT seems to be cost-effective in selective indications in oncology (staging and restaging of head and neck tumours, staging and treatment evaluation in lymphoma). Although more studies are needed to assess cost-effectiveness of FDG-PET, application of PET/CT will probably improve efficacy and economic outcome in these indications, in the near future.

## COMMENTS

### Background

Fluorine-18-Fluorodeoxyglucose positron emission tomography (FDG-PET) or PET/computed tomography (PET/CT) are useful imaging techniques to study cellular metabolism.

### Research frontiers

Cost-effectiveness analysis is a way to study both efficacy and cost of a medical procedure. These studies use parameters as "life years gained" or disability days saved. In cost-utility analysis, measures change with patient preference and authors refer to "quality-adjusted life years".

### Innovations and breakthroughs

In this study, cost-effectiveness of FDG-PET in staging of head and neck tumours has been analysed in one study.

### Applications

Although more studies are needed to assess cost-effectiveness of FDG-PET, application of PET/CT will probably improve efficacy and economic outcome in these indications, in the near future.

### Peer review

This study is well designed and well done. The authors also realized and pointed out that the literature is limited on the cancer types studies in this article.

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