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Review

Diagnostic performance of Fluorine-18-Fluorodeoxyglucose positron emission tomography in the assessment of pleural abnormalities in cancer patients: A systematic review and a meta-analysis

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ABSTRACT

Objective: To systematically review and meta-analyze published data about the diagnostic performance of Fluorine-18-Fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) and PET/computed tomography (PET/CT) in the assessment of pleural abnormalities in cancer patients.
Methods: A comprehensive literature search of studies published through June 2013 regarding the role of ^{18}F-FDG-PET and PET/CT in evaluating pleural abnormalities in cancer patients was performed. All retrieved studies were reviewed and qualitatively analyzed. Pooled sensitivity, specificity, positive and negative likelihood ratio (LR+ and LR−) and diagnostic odd ratio (DOR) of ^{18}F-FDG-PET or PET/CT on a per patient-based analysis were calculated. The area under the summary ROC curve (AUC) was calculated to measure the accuracy of these methods in the assessment of pleural abnormalities. Sub-analyses considering ^{18}F-FDG-PET/CT and patients with lung cancer only were carried out.
Results: Eight studies comprising 360 cancer patients (323 with lung cancer) were included. The meta-analysis of these selected studies provided the following results: sensitivity 86% [95% confidence interval (95%CI): 80–91%], specificity 80% [95%CI: 73–85%], LR+ 3.7 [95%CI: 2.8–4.9], LR− 0.18 [95%CI: 0.09–0.34], DOR 27 [95%CI: 13–56]. The AUC was 0.907. No significant improvement considering PET/CT studies only and patients with lung cancer was found.
Conclusions: ^{18}F-FDG-PET and PET/CT demonstrated to be useful diagnostic imaging methods in the assessment of pleural abnormalities in cancer patients, nevertheless possible sources of false-negative and false-positive results should be kept in mind. The literature focusing on the use of ^{18}F-FDG-PET and PET/CT in this setting remains still limited and prospective studies are needed.

1. Introduction

Pleural abnormalities are quite common in cancer patients, particularly in those with lung cancer [1]. Malignant pleural abnormalities in patients with known tumors may be caused by the local extension of a lung cancer or by metastatic disease, nevertheless some pleural abnormalities in these patients may be benign [2,3].

In cancer patients, differentiating between benign and malignant pleural abnormalities is crucial and may influence treatment strategy and prognosis. In fact, in cancer patients with malignant pleural lesions the prognosis is extremely worse when compared to benign pleural abnormalities and surgery is often contraindicated [2–5].

Several diagnostic tests have been used in this setting, including computed tomography (CT), magnetic resonance imaging (MRI), thoracocentesis, biochemical parameters, pleural biopsy, and thoracoscopy. However, these tests have some limitations being sometimes inaccurate or invasive [2–5].

Fluorine-18-Fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) and PET/CT have been proposed as non-invasive imaging methods to assess the disease extent in cancer patients

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[6]. Since ^{18}F-FDG is a glucose analog, this radiopharmaceutical may be very useful in detecting malignant lesions which usually present high glucose metabolism [6]. Hybrid PET/CT device allows enhanced detection and characterization of neoplastic lesions, by combining the functional data obtained by PET with morphological data obtained by CT [6].

Several studies have evaluated the diagnostic performance of ^{18}F-FDG-PET or PET/CT in the differential diagnosis between malignant and benign pleural abnormalities, reporting different values of sensitivity and specificity [7]. The purpose of our study is to systematically review and meta-analyze published data on the diagnostic performance of ^{18}F-FDG-PET or PET/CT in the assessment of pleural abnormalities in cancer patients only, in order to provide more evidence based data and to address further studies in this setting.

2. Methods

This systematic review and meta-analysis was performed according to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) statement which describes an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses [8].

2.1. Search strategy

A comprehensive computer literature search of the PubMed/MEDLINE and Scopus databases was conducted to find relevant published articles on the diagnostic performance of ^{18}F-FDG-PET or PET/CT in the assessment of pleural abnormalities in cancer patients. We used a search algorithm that was based on a combination of the terms: (a) "PET" OR "positron emission tomography" AND (b) "pleural" or "pleura". No beginning date limit was used; the search was updated until June 30th, 2013. No language restriction was used. To expand our search, references of the retrieved articles were also screened for additional studies.

2.2. Study selection

Studies or subsets in studies investigating the diagnostic performance of ^{18}F-FDG-PET or PET/CT in the assessment of pleural abnormalities in cancer patients were eligible for inclusion. The exclusion criteria were: (a) articles not within the field of interest of this review, (b) articles evaluating the performance of ^{18}F-FDG-PET or PET/CT in assessing pleural lesions in patients without cancer history, (c) review articles, editorials or letters, comments, conference proceedings, and (d) case reports or small case series.

Three researchers (GT, RS and SA) independently reviewed the titles and abstracts of the retrieved articles, applying the inclusion and exclusion criteria mentioned above. Articles were rejected if they were clearly ineligible. The same three researchers then independently reviewed the full-text version of the remaining articles to determine their eligibility for inclusion. Disagreements were resolved in a consensus meeting.

2.3. Data extraction

For each included study, information was collected concerning basic study (authors, journals and year of publication, country of origin, study design), patient characteristics (mean age, gender, number of patients evaluated and type of primary tumor), technical aspects (device used, radiopharmaceutical injected dose, time between ^{18}F-FDG injection and image acquisition, image analysis, applied reference standard). For each study the number of true positive, false positive, true negative and false negative findings for ^{18}F-FDG-PET or PET/CT was recorded on a per patient-based analysis considering the qualitative PET analysis (visual analysis) performed by the authors.

2.4. Quality assessment

The 2011 Oxford Center for Evidence-Based Medicine checklist for diagnostic studies was used for quality assessment of the included studies [9]. This checklist has 5 major parts as follows: representative spectrum of the patients, consecutive patient recruitment, ascertainment of the gold standard regardless of the index test results, independent blind comparison between the gold standard and index test results, enough explanation of the test to permit replication.

2.5. Statistical analysis

Sensitivity, specificity, accuracy, positive and negative predictive value, positive and negative likelihood ratio (LR+ and LR−) and diagnostic odd ratio (DOR) of ^{18}F-FDG-PET or PET/CT in the assessment of pleural abnormalities in cancer patients were obtained from individual studies on a per patient-based analysis. A random effects model was used for statistical pooling of the data. Pooled data were presented with 95% confidence intervals (95%CI). An I-square index was used to test for heterogeneity between studies. The area under the summary ROC curve (AUC) was calculated to measure the accuracy of ^{18}F-FDG-PET or PET/CT. For publication bias evaluation, funnel plots, Egger's regression intercept [10], and Duval and Tweedie's method [11] were used. Spearman correlation coefficient between false positive rate (1-specificity) and true positive rate (sensitivity) of the included studies was used for evaluation of the threshold effect and p-value < 0.05 was considered statistically significant.

Statistical analyses were performed using Meta-DiSc statistical software version 1.4 (Unit of Clinical Biostatistics, Ramón y Cajal Hospital, Madrid, Spain) [12] and Comprehensive Meta-Analysis (CMA) software version 2 (Biostat, Englewood, NJ, USA).

3. Results

3.1. Literature search

The comprehensive computer literature search from PubMed/MEDLINE and Scopus databases revealed 540 articles. Reviewing titles and abstracts, 532 articles were excluded: 464 because not in the field of interest of this review, 18 because evaluating the performance of ^{18}F-FDG-PET or PET/CT in assessing pleural lesions in patients without cancer history, 35 as reviews or editorials, 15 as case reports. Finally, eight articles (including 360 cancer patients) were selected and were eligible for the systematic review and meta-analysis [13–20]; no additional studies were found screening the references of these articles. The characteristics of the included studies are presented in Tables 1–4.

3.2. Qualitative analysis (systematic review)

Using the database search, 8 original articles written over the past 13 years were selected [13–20]; all except one [14] were retrospective studies. Most of the patients evaluated had lung cancer (323 out of 360), with a preponderance of the male gender (Table 1).

Five studies used hybrid PET/CT [16–20] whereas three studies used PET only [13–15]. Heterogeneous technical aspects between the included studies were found (Table 2).

The PET image analysis was performed by using qualitative criteria (visual analysis) in all the included studies [13–20] and semi-quantitative criteria (based on the calculation of the standardized uptake value [SUV]) in 5 out of 8 articles [16–20].