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Review

Positron emission tomography modalities prevent futile radical resection of pancreatic cancer: A meta-analysis

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HIGHLIGHTS

- First attempt to summarize recent articles about the utility of PET modalities in preventing futile resection of PC.
- Subgroup analysis according to different PET modality.

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ABSTRACT

Background: Numerous distant metastases were not detected preoperatively. Positron emission tomography (PET) has been used for oncology diagnosis recently. However, it remains controversial whether PET modality is a more efficient way in detecting unresectable features for radical resection of pancreatic cancer (PC). This meta-analysis aims to validate the efficiency of PET modalities (including PET and PET/CT) in preoperative assessment of PC, and compare them with computed tomography (CT).

Methods: PubMed, EMBASE, Science Citation Index and The Cochrane Library were searched to identify relevant studies. Both PET modality and CT had been performed for all the included patients. A meta-analysis was performed to compare the ability of PET modalities in detecting occult distant metastases and regional lymph nodes invasion with that of CT.

Results: 17 clinical studies that recruited 1343 patients were included. This meta-analysis indicated that PET modalities were more efficient in detecting true positive distant metastases compared with CT (OR = 1.52, 95%CI: 1.23–1.88). In subgroup analysis, when compared with CT alone, PET/CT also showed greater utility in detecting distant metastases (OR = 1.66, 95%CI: 1.31–2.08). There was no definite difference in detecting regional lymph nodes invasion between PET modalities and CT (OR = 0.97, 95%CI: 0.63–1.47).

Conclusion: Compared with CT, PET/CT provides extensive possibility to avoid futile radical resection by detecting occult metastases of PC preoperatively. Surgeons, especially in developing countries, should take PET modalities as a routine preoperative assessment before making operative plan for PC patients.

1. Introduction

Pancreatic cancer (PC) is an especially lethal malignancy, with a mortality rate that almost equals its incidence [1]. It is difficult to diagnose at an early stage and generally has a poor prognosis [2]. Surgical resection is the only potential curative treatment for pancreatic carcinoma. As a result of more optimal patient selection, improvement in surgical techniques, and better postoperative patient care, the outcome of these patients have been improving during the last decades [3,4]. Although China has a lower incidence of pancreatic cancer than western countries, the incidence of this disease in China has increased in recent years. In 2010, 34509 men and 23226 women died from pancreatic cancer in China, with the number of deaths exceeding that in the United State [5].

Early detection and complete surgical resection of the tumor with negative margins offers the only chance of cure for this disease. However, at diagnosis, only 8% of the cancers will be localized, 27% will be locally advanced, and 53% will involve distant metastases [6].Besides arterial invasion, metastasis is also an important contraindication for radical surgery. Indeed, absence of distant metastasis is the first criteria for either “Resectability” or

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"Borderline Resectability" [7]. Selecting optimal candidate for radical resection of PC relies mostly upon these specific features detected by imaging modalities.

Computed tomography (CT) scanning has been the mainstay for assessment primary lesion and resectability of pancreatic tumor. However, based only on morphological features, it is difficult to identify small malignant lesions and to distinguish metastasis lesions from benign tumors. Indeed, numerous missing of small liver metastasis has been reported [8]. Based on the glucose metabolic feature of malignant tumors, positron emission tomography (PET) was introduced in 1976. Since the combination of PET and CT [9], PET/CT has emerged as a promising new imaging modality in the management of patients with malignancy subsequently. Indeed, as a relatively young method, PET/CT was not widely accepted by surgeons as a preoperative assessment, especially in developing countries. Meanwhile, CT is still the most common imaging method for diagnosing and staging PC in China [10].

There were several reviews focus on the utility of PET modalities (including PET and PET/CT) in the diagnosis and prognosis of pancreatic cancer [11–13], but few has focused on the preoperative value of PET modalities and compared them with CT alone. Undoubtedly, saving patient from unnecessary surgical exploration is quite vital for surgeons and patients. In this meta analysis, which include the most recent studies, we focuses on the role of PET modalities in assessing the necessity of radical resection for pancreatic malignancies.

2. Methods

2.1. Inclusion and exclusion criteria

Studies met the following inclusion criteria were included: 1, Clinical trials of pancreatic cancer patients. 2, Published in English. 3, Both PEC/CT and CT were performed before surgery for each patient. 4, All the malignant diagnosis was confirmed by pathology. 5, Enough information for date extraction of the sensitivity of PET modality (PET and PET/CT) and CT in detecting regional lymph nodes invasion and metastases (including liver metastases and other distant metastases).

Studies were excluded as follows: 1, Sample size was less than 20.2, abstracts, reviews, case reports and comments, 3, Absence of date about regional lymph node and metastasis. 4, Absence of any information about surgery.

2.2. Searching strategies and study selection

PubMed, EMBASE, Science Citation Index and The Cochrane Library were searched to identify relevant studies. The following search algorithm was used: "positron emission tomography" OR "positron-emission tomography" OR "PET"; "computed tomography" OR "CT"; "metastasis" OR "metastases" OR "neoplasma metastasis"; "pancreatic cancer" OR "pancreatic ductal adenocarcinoma" OR "PDAC" OR "pancreatic neoplasmas". The references lists of selected studies were also searched to ensure that no potential studies were neglected. Two investigators (L.W. and P.D.) independently read the title and abstract of potential eligible studies. The full texts of all eligible articles were then screened for detailed evaluation. Differences of opinion in the selection process were resolved by consensus. If failed to reach an agreement, the final decision would be made by a third investigator (B.-L.T.).

2.3. End points measures

The primary end point was the presence of PET/CT or CT finding of metastases which were followed by cancel of radical resection. The secondary end points were the presence of PET/CT or CT findings of regional lymph nodes invasion and other parameters.

2.4. Data extraction and quality assessment

Two researchers (L.W. and W.-G. W.) independently extracted following data from all selected articles: first author, country, study period, study design, characteristic of enrolled patients, CT and PET/CT findings preoperatively, and the basic surgical information. The quality of the extracted data was then adjudicated by a third researcher (B.-L.T.). The Newcastle-Ottawa scale (NOS) was conducted to evaluate the quality of the included studies [14]. The maximum "stars" obtained for "Selection", "Comparability" and "Outcome" categories were 4, 2 and 3 respectively. Studies which got at least 6 "stars" were considered high in quality.

2.5. Statistical analysis

Meta-analysis was carried out using STATA 14.0 software. Odds Ratio (OR) was chosen as summary statistic to dichotomous variables. Pooled OR and the corresponding 95% CI was shown by forest plot. Heterogeneity was measured with I^2, and low heterogeneity was defined as an $I^2 < 33\%$ [15]. $P < 0.05$ was considered of significant significance. Publication bias was identified using funnel plot analysis.

3. Results

3.1. Literature search and study selection

Initially, a total of 1308 articles were identified in PubMed, EMBASE, Science Citation Index and The Cochrane Library. We excluded 1188 articles after screening titles and abstracts, in which 437 were duplicated and 751 were irrelevant. The remaining 120 articles were retrieved for more detailed evaluation. Among these articles, 35 studies were excluded for absence of CT data. 19 studies were excluded for absence of eligible data about distant metastasis. 49 articles were excluded for absence of surgical information and other reasons as shown in the flow diagram (Fig. 1). Finally, 17 appropriate studies were included for further analysis [10,16–31].

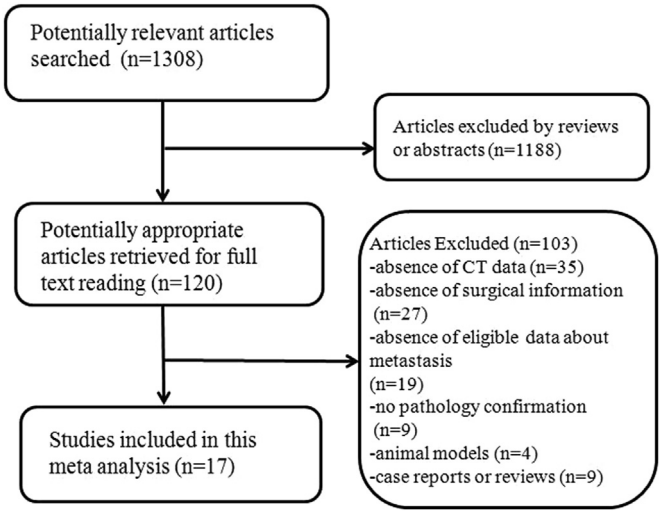

Fig. 1. Flow diagram of study selection.