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Research paper

Imaging modalities in the diagnosis of pancreatic adenocarcinoma: A systematic review and meta-analysis of sensitivity, specificity and diagnostic accuracy

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ABSTRACT

Background: Pancreatic cancer, primarily pancreatic ductal adenocarcinoma (PDAC), accounts for 2.4% of cancer diagnoses and 5.8% of cancer death annually. Early diagnoses can improve 5-year survival in PDAC. The aim of this systematic review was to determine the sensitivity, specificity and diagnostic accuracy values for MRI, CT, PET & PET/CT, EUS and transabdominal ultrasound (TAUS) in the diagnosis of PDAC.

Methods: A systematic review was undertaken to identify studies reporting sensitivity, specificity and/or diagnostic accuracy for the diagnosis of PDAC with MRI, CT, PET, EUS or TAUS. Proportional meta-analysis was performed for each modality.

Results: A total of 5399 patients, 3567 with PDAC, from 52 studies were included. The sensitivity, specificity and diagnostic accuracy were 93% (95% CI = 88–96), 89% (95% CI = 82–94) and 90% (95% CI = 86–94) for MRI; 90% (95% CI = 87–93), 87% (95% CI = 79–93) and 89% (95% CI = 85–93) for CT; 89% (95% CI = 85–93), 70% (95% CI = 54–84) and 84% (95% CI = 79–89) for PET; 91% (95% CI = 87–94), 86% (95% CI = 81–91) and 89% (95% CI = 87–92) for EUS; and 88% (95% CI = 86–90), 94% (95% CI = 87–98) and 91% (95% C = 87–93) for TAUS.

Conclusion: This review concludes all modalities, except for PET, are equivalent within 95% confidence intervals for the diagnosis of PDAC.

1. Introduction

More than 3000 Australians are estimated to have developed pancreatic cancer in 2015, making it the 10th most commonly diagnosed cancer in Australia [1]. Despite accounting for only 2.4% of all new cancer diagnoses, pancreatic cancer caused an estimated 5.8% of all deaths from cancer in 2015. Further, patients diagnosed with this disease entity can expect 24% and 6% 1- and 5-year survivals respectively; only a modest improvement on the 4% 5-year survival with the same diagnosis in 1982–1986 [1]. As a result of its poor prognosis, pancreatic cancer has an impact out of proportion to its incidence.

The imbalance between incidence and mortality in pancreatic cancer can be partially explained by the fact that these cancers are often clinically silent until advanced stages, often following metastases [2]. Patients who are diagnosed with localized disease have a 26% 5-year survival, while only 2% of patients diagnosed with advanced disease survive at 5 years [3]. Because of this stark survival contrast, any improvement in detection will significantly improve survival in pancreatic cancer through earlier intervention.

Previous reviews of diagnostic imaging modalities used in pancreatic ductal adenocarcinoma (PDAC), the most common form of pancreatic cancer, have been undertaken [4–6]. However these reviews have not taken into account the rapid advancement in imaging technology in their analysis. For example, it is inappropriate to compare modern nuclear imaging techniques such as positron emission tomography

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(PET) to computed tomography (CT) or magnetic resonance imaging (MRI) technology from 20 years earlier.

The American Agency for Healthcare Research and Quality published a report on the diagnosis and staging of PDAC in 2015 in which it highlighted the paucity of high-quality, systematic review literature on the detection of this disease [6]. It is therefore the aim of this systematic review to determine the sensitivity, specificity and diagnostic accuracy of the available imaging modalities for the detection of PDAC.

2. Design and methods

The study protocol for this systematic review was prospectively registered with PROSPERO, international prospective register of systematic reviews, (registration number: CRD42015024862) and may be found on the PROSPERO website (https://www.crd.york.ac.uk/PROSPERO/). The study protocol followed the PRISMA checklist (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [7].

2.1. Inclusion criteria

Full-text English language studies of adult human patients published between January 2004 and June 2015 were considered for this review. Case reports, systematic reviews, meta-analyses, editorials, abstracts, and unpublished articles were excluded.

2.2. Search

A systematic search was applied to PubMed/MEDLINE, EMBASE, Cochrane and CINAHL from January 2004 up to June 2015 in order to identify all publications that reported on the accuracy of MRI, CT, PET, PET/CT, or ultrasound in the diagnosis of pancreatic adenocarcinoma. Search keywords were: 'Pancreas', 'Adenocarcinoma', 'Computed Tomography', 'CT', 'Endoscopic Retrograde Cholangiopancreatography', 'ERCP', 'Magnetic Resonance Cholangiopancreatography', 'MRCP', 'Endoscopic Ultrasound', 'EUS', 'Abdominal Ultrasound', 'Positron Emission Tomography', 'PET', 'Multidetector Computed Tomography', 'MDCT', 'Magnetic Resonance Imaging', 'MRI', and 'Ultrasonography'. Subject headings were adjusted to comply with each database's specific indexing system. All articles were vetted sequentially by title, abstract and full text by two independent reviewers at each step. All disagreements were resolved by consensus after discussion between the reviewers. Reference lists of all included articles were searched manually for further studies also meeting inclusion criteria.

2.3. Study Selection

Selection criteria were predefined and applied to results of the search strategy. Original studies reporting sensitivity and/or specificity for MRI, CT, PET/CT, and/or ultrasound for diagnosis of PDAC were included in this systematic review. Further, only studies reporting on > 20 patients with surgical or histological confirmation of adenocarcinoma and clinical follow up to rule out false negative initial imaging were included. Studies that did not explicitly state how final diagnoses were made were excluded.

2.4. Data extraction

Study design; patient numbers and demographics; imaging modalities investigated; reference tests; diagnosis verification; tumor size; reported specificity, sensitivity and diagnostic accuracy were extracted by two independent reviewers. Where sensitivity and/or specificity values were reported for variations on the same modality (for example contrast enhanced versus non contrast enhanced ultrasound) the values with the highest combined sensitivity and specificity were used. Extracted data was then compared and discrepancies were resolved between the reviewers.

2.5. Outcomes

Primary outcome measures were proportionally-weighted sensitivity, specificity and diagnostic accuracy stratified by imaging modality for the diagnosis of PDAC.

2.6. Statistical analysis

Freeman-Tukey transformations were used to obtain proportional meta-analyses of sensitivity, specificity and diagnostic accuracy for each imaging modality (MRI, CT, PET, EUS, TAUS) [8,9]. Diagnostic accuracy was determined from the sensitivity and specificity values and was only calculated from studies that reported both a sensitivity and specificity for the same population. Cumulative data were expressed with 95% confidence intervals using a more conservative random effects model. Data analysis was performed using MedCalc for Windows, version 15.8 (Ostend, Belgium).

3. Results

The search strategy returned 1347 original articles, of which 135 were selected for full-text review with 52 of these meeting all inclusion criteria for final analysis (Fig. 1). These 52 studies represent 5399 patients, of whom 3567 had PDAC (Table 1). Eleven of these studies report data for MRI (349/586 patients with PDAC) [10–20], 15 for CT/MDCT (815/1338 with PDAC) [14,17,18,20–31], 10 report on PET/CT (567/829 with PDAC) [11,14,29,32–38], and 29 report data on ultrasound (2574/3732 patients with PDAC). These ultrasound studies were split between endoscopic ultrasound (EUS) [11,26,28,30,39–56] and trans-abdominal ultrasound (TAUS) [24,27,57–61], with patient numbers similar between modalities (1857 for conventional and 1875 for EUS) (Table 1).

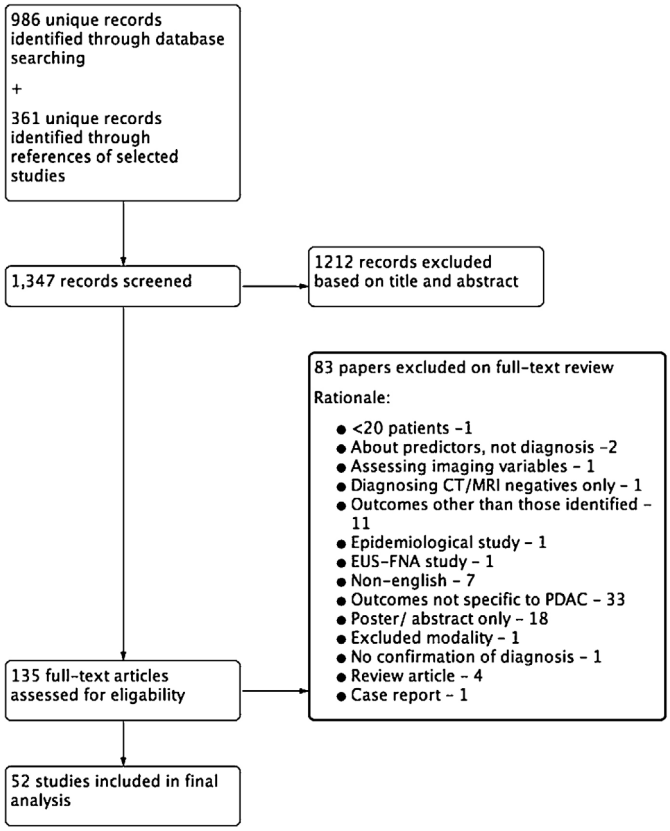

Fig. 1. Flow diagram depicting acquisition of reviewed articles.