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Original article

Diagnostic value of EUS elastography in differentiation of benign and malignant solid pancreatic masses: A meta-analysis

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ABSTRACT

Background/Aims: EUS elastography is a novel technique that can be used for distinguishing benign from malignant lymph nodes and focal pancreatic masses. However, the studies pertaining to EUS elastography for differential diagnosis of solid pancreatic masses have reported widely varied sensitivities and specificities. A meta-analysis of all relevant articles was performed to estimate the overall diagnostic accuracy of EUS elastography for differentiating benign and malignant solid pancreatic masses.

Methods: The literatures were identified by searching in PubMed and Embase databases. Two reviewers independently extracted the information from the literatures for constructing 2 × 2 table. A random-effect model or a fixed-effect model was used to estimate the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio. A summary receiver operating characteristic curve (SROC) also was constructed. Meta-regression and subgroup analysis were used to explore the sources of heterogeneity.

Results: 13 studies including a total of 1042 patients with solid pancreatic masses were selected for meta-analysis. The pooled sensitivity and specificity of EUS elastography for differentiating benign and malignant solid pancreatic masses were 95% (95% confidence interval [CI], 93%–96%), 69% (95% CI, 63%–75%), respectively. The area under SROC (AUC) was 0.8695. Two significant variables were associated with heterogeneity: color pattern and blinding.

Conclusion: As a less invasive modality, EUS elastography is a promising method for differentiating benign and malignant solid pancreatic masses with a high sensitivity, and it can prove to be a valuable supplement to EUS-FNA.

The etiology of solid pancreatic masses includes focal pancreatitis, pancreatic carcinoma, endocrine tumor, metastasis, lymphoma, and so forth. Differential diagnosis of benign and malignant pancreatic masses is very critical for making clinical decision. However, the differentiation remains a challenge, because clinical and biochemical evidence, including computed tomography (CT), magnetic resonance imaging (MRI), EUS, or tumor markers, can be nonspecific [1–3]. EUS-guided FNA (EUS-FNA) can obtain cytological samples to make pathological diagnosis, but it is an invasive procedure, and can produce a false-negative result up to 17.9%–22% [4–6].

Elastography is a method for the real-time evaluation of tissue stiffness that can be applied during ultrasound examination. Malignant tumor tissues are generally harder than normal tissues, so elastography can be used to distinguish malignant tissues from benign tissues based on the tissue stiffness. Elastography has been employed for analysis of superficial organ lesions, such as thyroid gland [7], breast [8,9], and liver [10,11], with a promising result.

EUS elastography is a novel technique that can produce elastic images of deep tissues during conventional EUS examination. The usefulness in distinguishing benign from malignant lymph nodes [12–14] and focal pancreatic masses [15–27] has been validated. As a less invasive means of diagnosing pancreatic masses, EUS elastography is considered that can reduce the need for EUS-FNA and avoid its associated risks [18,28]. However, the reported accuracy of

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EUS elastography for differential diagnosis of benign and malignant solid pancreatic masses varies widely, with sensitivity ranging from 81% to 100%, and specificity ranging from 20% to 92.9% [15–27]. Therefore, we performed a meta-analysis of studies on this topic to assess the overall accuracy of EUS elastography in differential diagnosis of benign and malignant solid pancreatic masses.

1. Methods

1.1. Study selection

Inclusion criteria: (1) diagnostic clinical trials evaluating the accuracy of EUS elastography in differential diagnosis of benign and malignant solid pancreatic masses; (2) acceptable reference standards included EUS-FNA, surgical exploration, or a clinical follow-up period of at least 6 months; (3) the outcome data available to reconstruct a diagnostic 2 × 2 table (true positive, true negative, false positive, false negative).

Exclusion criteria: (1) complete data unavailable; (2) duplicated or updated data; (3) did not include their own data such as reviews, comments, editorials, letters and congress; (4) case reports.

1.2. Literature search

A systematic search was performed in PubMed and Embase databases up to February 2012. The search terms included medical subject headings "elasticity imaging techniques", "pancreatic neoplasms", and free-text terms "elastography", "sonoelastography", "elastosonoendoscopy", "pancreatic tumor", "pancreatic cancer", "focal pancreatitis", "pancreatic mass" or "pancreatic masses". The reference lists of all articles were screened for potentially relevant articles that were not identified by the initial search. Two reviewers (Pei QS and Zou XP) independently searched and extracted the data according to the defined inclusion and exclusion criteria. Disagreements were resolved by discussion and consensus with a third reviewer (Luo HS). We contacted with the authors for more details if necessary.

1.3. Quality assessments

A quality assessment tool for diagnostic accuracy studies, named "QUADAS" checklist, was used to evaluate the study quality [29]. Each item was scored as "yes", "no", or "unclear". We did not incorporate quality scores into the review because their interpretation is problematic and potentially misleading [30]. From the QUADAS checklist we chose 11 items according to the Cochrane Handbook for systematic reviews of diagnostic test accuracy [31].

1.4. Statistical analysis

The sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR) were calculated for each study and then were pooled by using the Mantel–Haenszel fixed effects model [32] without heterogeneity, the DerSimonian–Laird random effects model [33] otherwise.

The Chi-square test and inconsistency index (I-squared, I^2) were used to estimate the heterogeneity [34]. The Chi-square test assessed whether observed differences in results were compatible with chance alone. A P value <0.1 indicated the presence of heterogeneity. An I^2 index was calculated to describe the percentage of the variability that is from heterogeneity rather than chance. $I^2 > 50\%$ was considered significant for heterogeneity. A summary receiver operating characteristic curve (SROC) was constructed by the Moses–Shapiro–Littenberg method [35]. The area under the curve (AUC) was computed by numeric integration of the curve equation by the trapezoidal method. A perfect test has an AUC close to 1, and a poor test has an AUC close to 0.5 [36]. The subgroup analysis and meta-regression analysis were conducted to explore the sources of heterogeneity on the basis of the characteristics of studies [37]. Relative diagnostic odds ratios (RDOR) were expressed in the results of the meta-regression model. RDOR > 1 when studies with a certain characteristic produce a higher diagnostic OR, and vice versa [38]. A P value < 0.05 indicated the presence of heterogeneity in the meta-regression analysis. The characteristics of studies included in the analysis were as follows: (1) diagnostic method (color pattern vs. others); (2) sample size; (3) the prevalence of malignant masses; (4) representative spectrum (yes vs. no); (5) acceptable reference standard (yes vs. no); (6) reference standard results blinded (yes vs. unclear).

The robustness of the meta-analysis to publication bias was assessed by funnel plots and bias indicators, including the Begg–Mazumdar test, and the Harbord–Egger test [39,40]. A P value < 0.05 indicated the presence of publication bias.

The pooled and subgroup sensitivity, specificity, PLR, NLR, DOR, SROC curve, and meta-regression were performed by using Meta-Disc version 1.4 (Meta-Disc, Unit of Clinical Biostatistics, Ramony Cajal Hospital, Madrid, Spain). The assessment of publication bias was performed by using Stata version 11.0 (Stata Corporation, College Station, TX, USA).

2. Results

2.1. Literature search and characteristics of the included studies

A total of 100 studies were initially identified by using the search strategy. 69 studies were excluded by screening the titles and abstracts. Of the 31 studies left, 13 published articles that met the inclusion and exclusion criteria were identified finally. The study selection process is shown in Fig. 1.

A total of 1042 patients were estimated in the meta-analysis, with sample size ranging from 24 to 258 patients (mean $N = 80$). The mean lesion size ranged from 24.7 mm to 39.2 mm. Three diagnostic standards were used, including color pattern, hue histogram, and strain ratio. The malignant pancreatic masses

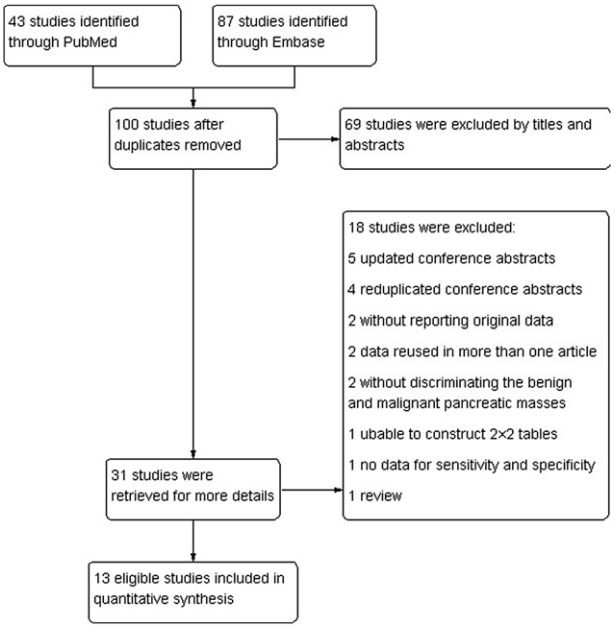

Fig. 1. Flow diagram of the studies identified in the meta-analysis.