Diagnostic performance of imaging modalities in chronic pancreatitis: a systematic review and meta-analysis

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Received: 3 May 2016 / Revised: 20 September 2016 / Accepted: 16 December 2016 / Published online: 27 January 2017

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Abstract

Objectives Obtain summary estimates of sensitivity and specificity for imaging modalities for chronic pancreatitis (CP) assessment.

Methods A systematic search was performed in Cochrane Library, MEDLINE, Embase and CINAHL databases for studies evaluating imaging modalities for the diagnosis of CP up to September 2016. A bivariate random-effects modeling was used to obtain summary estimates of sensitivity and specificity.

Results We included 43 studies evaluating 3460 patients. Sensitivity of endoscopic retrograde cholangiopancreatography (ERCP) (82%; 95%CI: 76%-87%) was significant higher than that of abdominal ultrasonography (US) (67%; 95%CI: 53%-78%; P=0.018). The sensitivity estimates of endoscopic ultrasonography (EUS), magnetic resonance imaging (MRI), and computed tomography (CT) were 81% (95%CI: 70%-89%), 78% (95%CI: 69%-85%), and 75% (95%CI: 66%-83%), respectively, and did not differ significantly from each other. Estimates of specificity were comparable for EUS (90%; 95%CI: 82%-95%), ERCP (94%; 95%CI: 87%-98%), MRI (96%; 95%CI: 90%-98%), and US (98%; 95%CI: 89%-100%).

Conclusions EUS, ERCP, MRI and CT all have comparable high diagnostic accuracy in the initial diagnosis of CP. EUS and ERCP are outperformers and US has the lowest accuracy. The choice of imaging modality can therefore be made based on invasiveness, local availability, experience and costs.

Key Points
- EUS, ERCP, MRI and CT have high diagnostic sensitivity for chronic pancreatitis
- Diagnostic specificity is comparable for all imaging modalities
- EUS and ERCP are outperformers and US has the lowest accuracy
- The choice of imaging can be made based on clinical considerations

Keywords Chronic pancreatitis · Diagnostic imaging · Diagnostic accuracy · Meta-analysis

Introduction

Chronic pancreatitis (CP) is a disabling inflammatory disease of the pancreas characterized by severe recurrent or continuous abdominal pain and considerable impact on the quality of life [1–4]. Patients with CP usually develop endocrine and exocrine insufficiency during the course of the disease as a result of the progressive loss of pancreatic parenchyma.

There is lack of international consensus regarding the initial diagnosis of CP, particularly at its early stages. The diagnosis is often made by a combination of clinical symptoms (e.g. abdominal pain, malabsorption, diabetes mellitus), pancreatic function tests (e.g. fecal elastase-1) and morphological abnormalities seen on imaging (e.g. calcifications, ductal lesions, pseudocysts) [5, 6]. Imaging plays a key role in the diagnosis and therapeutic management of patients with CP. The most frequently used imaging modalities for CP are endoscopic ultrasonography (EUS), endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance imaging (MRI), and computed tomography (CT).
cholangiopancreatography (ERCP), magnetic resonance imaging (MRI), computed tomography (CT) and ultrasonography (US).

The aim of this meta-analysis was to determine the diagnostic accuracy of imaging modalities for the initial diagnostic assessment of CP.

Methods

Search

A search was performed in Cochrane Library, MEDLINE, EMBASE and CINAHL databases, without restrictions for publication date or language up to September 2016. The search included terms for chronic pancreatitis, EUS, ERCP, MR imaging, CT and US. For detailed search details, see Appendix Table 5.

Selection of studies

All search hits were screened on title and abstract and eligible articles on full text by two reviewers independently (YI and MAK). Disagreements were solved through discussion with a third reviewer (MAB). Studies were eligible when EUS, ERCP, MR imaging, CT or US was evaluated in patients with suspected CP. Duplicates, reviews, letters, case reports and book chapters were excluded. The remaining studies were potentially eligible and their full text was retrieved. To identify additional relevant studies, the reference lists of the included studies were checked manually. Studies were included if they met the following criteria: (1) sufficient data was reported to construct 2 × 2 tables (true positive, false positive, true negative and false negative); (2) the imaging technique was compared with a reference standard (e.g. surgery, histology, follow-up). Exclusion criteria were: (1) evaluation of imaging techniques other than the aforementioned (e.g. PET-CT, EUS-FNA, EUS-elastography); (2) imaging techniques used for treatment of patients with CP (e.g. therapeutic ERCP, EUS-guided pseudocyst drainage); (3) in vitro studies; (4) studies that included less than five patients with CP; (5) studies where no separate analysis were done for patients with CP; and (6) full-text articles that were not available or retrievable.

Data extraction and critical appraisal

Data was extracted regarding the imaging characteristics: type of imaging modality, scoring criteria, technical features for each modality, and reported observer experience. Also data on the reference standard was extracted, such as clinical follow-up, surgery and histology.

The methodological quality of the included articles was assessed by the Quality Assessment of Diagnostic Accuracy Studies version 2 (QUADAS-2) tool [7]. The QUADAS-2 tool evaluates the risk of bias in four domains (patient selection, index test, reference standard, flow and timing) and the clinical applicability in the first three domains. Signaling questions were used to help assess the risk of bias and applicability. Possible answers were ‘yes’, ‘no’ or ‘unclear’ in which ‘yes’ indicates no risk of bias. In addition the GRADE scoring system for diagnostic tests was used, which assesses the quality of evidence for each imaging modality [8, 9]. Although the criteria are applicable to diagnostic test accuracy, the methods are less well established compared to interventional studies [10]. Two reviewers independently (YI and MAK) assessed the QUADAS-2 and the GRADE scoring system and all disagreements were resolved by reaching consensus.

![Fig. 1 Flow chart](https://example.com/flowchart.png)
Data analysis

Overall diagnostic accuracy

For each included study we constructed a $2 \times 2$ contingency table for each imaging modality. If diagnostic accuracy was compared between different observers, mean values were calculated. Sensitivity and specificity estimates, the positive predictive value and negative predictive values, and the accuracy were calculated from the reconstructed contingency tables. We used the $I^2$ test with 95% confidence interval (95% CI) to quantify heterogeneity [11]. Mean logit sensitivity and specificity were acquired, and the anti-logit transformation was then obtained to calculate summary estimates of

| Study            | Year | Country      | P/R | OE | Modality          | Reference standard for CP diagnosis |
|------------------|------|--------------|-----|----|-------------------|-------------------------------------|
| Adamek et al     | 2000 | Germany      | P   | No | MRCP/ERCP         | Histology (NA), FU (NA)              |
| Albashir et al   | 2010 | USA          | R   | Yes| EUS               | Histology (all)                      |
| Alcaraz et al    | 2000 | Spain        | P   | Yes| MRCP              | Surgery (4), ERCP (70), PTC (7)      |
| Baci et al       | 2006 | USA and Germany | R   | No | MRCP ePFT         | Surgery (NA), ERCP (NA), FU (NA)     |
| Bolog et al      | 2004 | Romania      | R   | No | MRCP              | Surgery (NA), ERCP (NA), FU (NA)     |
| Brand et al      | 2000 | Germany      | P   | No | EUS               | Histology (all)                      |
| Busca et al      | 1995 | France       | P   | No | US/CT/ERCP/EUS    | Histology (7), morphological changes (i.e. calcifications) and exocrine insufficiency (42) + FU (all) |
| Catalano et al   | 1998 | USA          | P   | No | EUS               | Surgery (all)                        |
| Chong et al      | 2007 | USA          | R   | Yes| ERCP/US           | Surgery (25), FU (50)                |
| Connell et al    | 2007 | USA          | R   | Yes| EUS ePFT          | Surgery (36), ERCP (46)              |
| Drumaix et al    | 1980 | France       | P   | No | US/CT             | Surgery (NA), ERCP (NA)              |
| Fusari et al     | 2010 | Italy        | P   | Yes| CT/MRCP Biopsy (33), histology (7) |
| Gebel et al      | 1985 | Germany      | P   | No | US/ERP            | Obduction (NA), Surgery (NA), FU (NA) |
| Giovannini et al | 1994 | France       | P   | No | EUS               | ERCP (all)                           |
| Glaubrenner et al| 2000 | Germany      | P   | Yes| EUS/ERCP          | Surgery (all)                        |
| Gmelin et al     | 1981 | Germany      | P   | No | US/CT/ERCP        | Surgery (NA)+FU (NA)                 |
| Hellebroff et al | 2002 | Germany      | P   | Yes| MRCP+sMRCP ERCP   | ERCP (35), surgery (4), FU (56)      |
| Imdhah et al     | 1999 | Germany      | P   | Yes| CT                | Histology (42), FU (6)               |
| Kremer et al     | 1977 | Germany      | R   | No | US                | Clinical diagnosis (338), ERCP, surgery, ePFT, angiography (NA) |
| Lammer et al     | 1980 | Germany      | R   | No | ERCP/CT           | Surgery (31), angiography (16), clinical diagnosis (60) |
| Lawson et al     | 1978 | USA          | R   | Yes| ERCP/US           | Surgery (25), FU (50)                |
| Lees et al       | 1979 | UK           | P   | No | US                | Surgery (36), ERCP (46)              |
| Lin et al        | 1989 | Taiwan       | R   | No | US/EUS            | Histology (26), CT (4), surgery+ERCP (3) |
| Nattermann et al | 1993 | Germany      | P   | No | MRCP              | ERCP (94), FU (20)                   |
| Pamos et al      | 1998 | Spain        | P   | Yes| MRCP              | ERCP (all)                           |
| Parsi et al      | 2008 | USA          | R   | Yes| ERCP              | FU (all)                             |
| Pistolesi et al  | 1981 | Italy        | P   | No | CT                | Surgery (all)                        |
| Pungpapong et al | 2007 | USA          | P   | Yes| EUS               | Clinical history, lab data, ERCP/CT/MRI and/or surgical pathology (all) |
| Rudowicz-Pietruszewskia et al | 2002 | Poland       | P   | No | MRCP              | ERCP (48), surgery (9), FU (57)       |
| Sui et al        | 2008 | Japan        | P   | Yes| sMRCP             | ERCP (all)                           |
| Savarino et al   | 1980 | Italy        | R   | No | CT                | Surgery (NA), calcifications (NA), clinical and lab data (NA) |
| Scarabino et al  | 1989 | Italy        | R   | No | ERCP, US, CT      | Combination of CT, US and ERCP (all) |
| Schlaudraff et al| 2008 | USA and Germany | P   | Yes| MRCP+sMRCP        | Clinical history, laboratory, radiology (≥2 methods) (all) |
| Stevens et al    | 2009 | USA          | P   | Yes| ERCP              | History (all)                        |
| Sverko et al     | 2011 | Croatia      | R   | No | MRCP              | Histology (all)                      |
| Swobodnik et al  | 1983 | Germany      | P   | No | US/CT/ERCP        | FU (59), surgery (22)                |
| Tox et al        | 2007 | Germany      | R   | Yes| US                | Surgery (79), FU (92)                |
| Trikudanathan et al | 2016 | USA          | R   | Yes| EUS               | Histology (all)                      |
| Triller et al    | 1975 | Switzerland  | P   | No | ERCP              | Surgery (14), autopsy (1), FU (9)     |
| Wiersema et al   | 1993 | USA          | P   | No | EUS/ERCP          | FU (51), ePFT (16)                   |
| Zhang et al      | 2003 | USA          | R   | No | MRCP              | US (12), CT (11), ERCP (6)           |
| Zuccaro et al    | 2009 | USA          | R   | No | MRCP/sMRCP        | ePFT (all)                           |

P prospective, R retrospective, OE observer experience reported, PTC percutaneous transhepatic cholangiogram, ePFT endoscopic pancreatic function test, FU follow-up, NA not available
sensitivity and specificity with 95% CIs. Forest plots were made to visualize the sensitivity and specificity with the 95% CIs. Summary estimates of sensitivity and specificity, including 95% CI, were obtained by using a random-effects model [12]. In cases where a negative covariance between the logit sensitivity and logit specificity was obtained, summary receiver operating characteristic curve (sROC) were generated for each separate imaging modality. We used the $z$ test to

| Study                  | Nr pts | Age | Male (%) | Nr pts CP | Patient selection                                                                 |
|------------------------|--------|-----|----------|-----------|-----------------------------------------------------------------------------------|
| Adamek et al           | 124    | 55  | 61%      | 57        | Suspected pancreatic mass (clinical presentation, lab, US)                        |
| Albashir et al         | 23     | 43* | 57%      | 19        | Suspected chronic pancreatitis (clinical presentation)                            |
| Alcaraz et al          | 81     | 65**| 31%      | 8         | Suspected pancreatobiliary disease (clinical presentation, US)                    |
| Balci et al            | 30     | 48* | 17%      | 11        | Suspected early CP (clinical presentation)                                         |
| Bolog et al            | 103    | 57* | 43%      | 15        | Suspected pancreatobiliary disease (US/CT or clinical presentation)               |
| Brand et al            | 115    | 61* | 59%      | 24        | Suspected focal pancreatic lesion (US/CT/ERCP or lab/tumour markers)             |
| Buscaif et al          | 62     | 50* | 79%      | 44        | Suspected chronic pancreatitis (clinical presentation, lab, imaging)             |
| Catalano et al         | 80     | 51* | 40%      | 38        | Non-alcoholic recurrent acute pancreatitis (3–11 episodes)                       |
| Chong et al            | 71     | 45* | 46%      | 64        | Suspected chronic pancreatitis (clinical presentation)                            |
| Conwell et al          | 56     | 44* | 45%      | 38        | Suspected chronic pancreatitis (clinical presentation)                            |
| Dramaix et al          | 50     | 52* | 66%      | 18        | Suspected pancreatic disease (clinical presentation)                              |
| Fusari et al           | 40     | 62* | 55%      | 8         | Suspected pancreatic mass (clinical presentation and US)                         |
| Gebel et al            | US: 56, ERP: 45 | NA | NA      | 44        | Suspected pancreatic disease (clinical presentation)                              |
| Giovannini et al       | 26     | NA  | NA       | 17        | Suspected pancreatobiliary disease (clinical presentation, imaging/lab)           |
| Glassbrenner et al     | 85     | NA  | NA       | 41        | Suspected pancreatic mass (clinical presentation, US/CT)                         |
| Ginelin et al          | 41     | 54* | 68%      | 19        | Suspected pancreatic disease (clinical presentation)                              |
| Helferhoff et al       | 95     | NA  | NA       | 26        | Suspected pancreatic disease (clinical presentation)                              |
| Imdhahl et al          | 48     | 58* | 60%      | 12        | Suspected pancreatic disease (clinical presentation)                              |
| Kremer et al           | 446    | NA  | NA       | 61        | Suspected pancreatic disease (clinical presentation)                              |
| Lammer et al           | 107    | NA  | NA       | 39        | Suspected pancreatic disease (clinical presentation)                              |
| Lawson et al           | 75     | NA  | NA       | 26        | Suspected pancreatic disease (clinical presentation)                              |
| Lees et al             | 98     | NA  | NA       | 20        | Suspected pancreatic disease (clinical presentation)                              |
| Lin et al              | 33     | 47* | 58%      | 7         | Suspected pancreatic disease (clinical presentation)                              |
| Nattermann et al       | 114    | 53* | 67%      | 51        | Suspected pancreatic disease (clinical presentation)                              |
| Pamos et al            | 41     | 64* | 59%      | 5         | Suspected pancreatobiliary disease (clinical presentation)                        |
| Parsi et al            | 35     | 46**| 46%      | 24        | Suspected chronic pancreatitis (clinical presentation)                            |
| Pistolesi et al        | 100    | NA  | NA       | 31        | Suspected pancreatic disease (clinical presentation)                              |
| Pungnapong et al       | 79     | 50**| 35%      | 38        | Suspected chronic pancreatitis (clinical presentation)                            |
| Pungnapong et al       | 99     | 55**| 41%      | 40        | Suspected chronic pancreatitis (clinical presentation)                            |
| Rudowicz-Pietruszewska et al | 88     | 52* | 64%      | 9         | Suspected pancreatobiliary disease (clinical presentation, lab, US/CT)            |
| Sai et al              | 28     | 36* | NA       | 16        | Mild chronic pancreatitis (ERCP)                                                 |
| Savario et al          | 108    | 47**| 67%      | 59        | Suspected pancreatic disease (clinical presentation)                              |
| Scabarino et al        | 63     | 44**| 63%      | 12        | Suspected of bilipancreatic disease (clinical presentation)                       |
| Schlaudraff et al      | 62     | NA  | NA       | 9         | Suspected chronic pancreatitis (clinical presentation)                            |
| Stevens et al          | 100    | NA  | NA       | 38%      | Suspected chronic pancreatitis (clinical presentation)                            |
| Sverko et al           | 29     | 44**| 52%      | 14        | Suspected pancreatic disease (clinical presentation)                              |
| Swobodnik et al        | 81     | 49* | 52%      | 27        | Suspected pancreatic disease (clinical presentation)                              |
| Tox et al              | 171    | 61* | NA       | 65        | Suspected pancreatic disease (clinical presentation)                              |
| Trikudanathan et al    | 68     | 39* | 18%      | 56        | Total pancreatectomy for non-calcific chronic pancreatitis                         |
| Triller et al          | 24     | 52* | 83%      | 11        | Suspected pancreatobiliary disease (clinical presentation)                        |
| Wiersema et al         | 67     | 45* | 20%      | 30        | Suspected pancreatobiliary disease (clinical presentation)                        |
| Zhang et al            | 44     | 50* | 30%      | 24        | Suspected early or mild chronic pancreatitis (clinical presentation, US/CT/ERCP) |
| Zuccaro et al          | 69     | 43* | 35%      | 28        | Suspected chronic pancreatitis (clinical presentation)                            |

NA not available

*Mean

**Median
evaluate differences in sensitivity and specificity between the five imaging modalities. A p value of less than 0.05 indicated a statistically significant difference.

Heterogeneity exploration

The following factors were incorporated in the bivariate model and we evaluated the effect on the sensitivity and specificity, and cause of heterogeneity for all imaging modalities according to the QUADAS-2 tool: clear description of criteria for bias (low bias versus high bias or unclear) for (a) patient selection, (b) criteria for the index test used, (c) sufficient description and verification with the reference standard, and (d) the flow and timing.

Head to head comparison

A head to head comparison was performed in studies that compared the diagnostic accuracy of two or more imaging modalities. Heterogeneity was quantified by $I^2$ test, with 95% CI. The random-effects ($I^2 > 25\%$) and fixed effects ($I^2 \leq 25\%$) models were used to obtain summary estimates of sensitivity and specificity, and compared with one another by a paired $z$ test.

For data analysis, Review Manager (RevMan, version 5.3. Copenhagen: The Cochrane Collaboration, 2014) and SAS (version 9.3; SAS Institute, Cary, NC) were used. We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [13].

Table 3 Estimated overall sensitivity, specificity and heterogeneity according to imaging modality

| Modality | N studies | N patients | Sensitivity (95% CI) | Specificity (95% CI) | Heterogeneity ($I^2$) |
|----------|-----------|------------|---------------------|----------------------|---------------------|
| EUS      | 16        | 1249       | 81% (70–89%)        | 90% (82–95%)         | 82%-73%             |
| ERCP     | 11        | 742        | 82% (76–87%)        | 94% (87–98%)         | 39%-67%             |
| MRCP     | 14        | 933        | 78% (69–85%)        | 96% (90–98%)         | 59%-65%             |
| CT       | 10        | 700        | 75% (66–83%)        | 91% (81–96%)         | 50%-71%             |
| US       | 10        | 1005       | 67% (53–78%)        | 98% (89–100%)        | 40%-93%             |

Random effects model

Results

Study selection

The initial search resulted in 11,111 hits, of which 2988 duplicates were removed, resulting in a total of 8123 titles and abstracts that were screened for eligibility. The full text of 277 articles was retrieved; 43 of these articles fulfilled the inclusion criteria. See Appendix Table 6 for the excluded articles. Figure 1 shows the flow chart of the search.

Study and patient characteristics

Study characteristics, including the reference standard for the diagnosis of CP for each included study, are listed in Table 1. The 43 included studies were published between 1975 and 2016; 26 studies were prospective and 23 studies were published after the year 2000. A total of 3460 patients were evaluated, of which 1242 patients were diagnosed with CP [14–56]. The age of the patients ranged from 36 to 65 years, with a median of 50% male. Criteria for selection of patients were those with suspected pancreatic disease or patients with suspected CP. Patient characteristics are depicted in Table 2.

The risk of bias, assessed by QUADAS-2, was low in 28% of the studies and high in 19% of the studies. The concerns about applicability were low in 30% of the studies and high in 40% of the studies. The QUADAS-2 characteristics for each domain are depicted in Fig. 2 and outlined for each study in Appendix Table 7. The quality of evidence for all five imaging modalities according to the GRADE scoring system was very
Fig. 3 Forest plot for sensitivity and specificity.
low. The GRADE scores for each imaging modality and characteristics for each study are outlined in Appendix Tables 8 and 9.

EUS was the most frequently evaluated imaging modality; 16 studies including 1249 patients [15, 19–23, 27, 28, 36, 37, 41, 42, 48, 51, 53, 56]. ERCP was studied in 11 studies including 742 patients [14, 20, 26, 28, 29, 33, 34, 39, 46, 50, 52]; MRCP, including secretin-enhanced MRCP, was evaluated in 14 studies including 933 patients [14, 16–18, 25, 30, 38, 42–44, 47, 49, 54, 55]; CT in 10 studies including 700 patients [20, 24, 25, 29, 31, 33, 40, 45, 46, 50] and abdominal US in 10 studies which included 1005 patients [20, 24, 26, 29, 32, 34–36, 46, 50]. The imaging characteristics for each study and modality in an individual study are listed in Appendix Table 11. Three of the 43 articles reported about complications of the imaging modality used; these were complications related to ERCP (being post-ERCP pancreatitis) with a mean complication rate of 4% [14, 20, 28].

Overall diagnostic accuracy

Analyses for summary estimates of sensitivity and specificity were done for EUS, ERCP, MRI, CT and US (Table 3). Figures 3 and 4 show sensitivity and specificity of individual studies in forest plots and in receiver operator curves (ROC), respectively. A negative covariance between the logit sensitivity and logit specificity was not obtained; therefore, no sROC for MRI and US could be drawn. The summary estimate of sensitivity for EUS, ERCP, MRCP, CT and US was 81%, 82%, 78%, 75% and 67%, respectively. The summary estimate of specificity for EUS, ERCP, MRCP, CT and US was 90%, 94%, 96%, 91% and 98%, respectively. Sensitivity of ERCP was significant higher than sensitivity of US (p = 0.018). Other pairwise comparisons of sensitivity between imaging modalities revealed no significant difference. Specificity did not differ significantly among all modalities (Table 3). Sensitivity and specificity values for each study are listed in Appendix Table 10.

Heterogeneity exploration

The bivariate model for heterogeneity exploration showed that the factor ‘flow and timing’ was significantly associated with a higher sensitivity of US (p = 0.01). ‘Description and verification with the reference standard’ was significantly associated with a higher specificity for MRCP (p = 0.0002).

Head to head comparison

Six head to head comparisons were performed (Table 4). The specificity of ERCP and EUS, and the sensitivity of ERCP, EUS and CT in the summary estimates of the head to head studies were significantly higher as compared with US.

The head to head comparison of US versus ERCP comparison yields a sensitivity of 57% (49–65%) versus 78% (71–85%) (p < 0.001); and a specificity of 94% (74–99%) versus...
98% (89–100%) \( (p = 0.003) \), respectively [20, 26, 29, 34, 46, 50]. The comparison between US and CT yields a sensitivity of 58% (49–66%) and 77% (68–83%) \( (p = 0.002) \), respectively [20, 24, 29, 46, 50]. And finally, the comparison of EUS versus US comparison yields a sensitivity of 90% (82–98%) versus 63% (49–76%) \( (p = 0.001) \); and a specificity of 100% versus 91% (82–99%) \( (p = 0.04) \), respectively [20, 36]. There were no significant differences in the sensitivity and specificity estimates between ERCP and EUS [20, 28, 53], MRCP and sMRCP [30, 47, 55] or ERCP and CT [20, 29, 33, 46, 50]. The heterogeneity \( (I^2) \) between US and ERCP \((>25\%)\) was higher \((>25\%)\) than in the other comparisons \((I^2 \leq 25\%)\).

### Discussion

EUS, ERCP, MRI and CT all have comparable high diagnostic accuracy in the initial diagnosis of chronic pancreatitis. EUS and ERCP are outperformers and US has the lowest accuracy. The choice of imaging modality can therefore be made on the basis of invasiveness, local availability, experience and costs.

Several recent guidelines [57–59] advocate the use of EUS, MRCP or CT for the diagnosis of CP, although summary estimates of their accuracy, thus far, were lacking. There is one guideline from Germany on CP that has reported sensitivity and specificity regarding EUS, ERCP, MRCP and US, although not for CT [60]. In this guideline 14 studies were selected, reporting ranges rather than pooling the data on sensitivity and specificity estimates. This method resulted in results slightly different from those in the present meta-analyses. For example the guideline reports a sensitivity of 70–80% for ERCP and 88% for MRI versus summary estimates of 82% and 78%, respectively, in the present meta-analyses. The European Society of Radiology (ESR) is developing the ESR iGuide, a clinical decision support system for European imaging referral guidelines, covering various clinical scenarios, indications and recommendations (www.esriguide.org) [61–63]. The results from the present systematic review may be useful to incorporate in that system.

We excluded three studies where sensitivity and specificity data were provided, but it was not possible to extract sufficient data to produce \(2 \times 2\) tables and calculate the diagnostic accuracy values, because only the sensitivity and specificity estimates were given [64–66]. In the study by Wang et al., estimates of sensitivity and specificity for EUS, ERCP and US were in line with the present results; the sensitivity of MR imaging and CT, however, were much lower (66% and 61%) [66]. The studies by Clave et al. and Orti et al. showed a lower sensitivity of ERCP (62% and 70%, respectively) compared to present results (82%) [64, 65].

The risk of missing important studies was minimized by performing a search in four major databases by two reviewers independently, without setting any restrictions for language and publication date. However, this systematic review has some limitations. The heterogeneity of the pooled studies was moderate to high in all analyses (between 39% and 93%). However, in the head to head comparison analyses, the heterogeneity was low in most comparisons \((<25\%)\). Furthermore, the heterogeneity of the reference standards used in the studies could have influenced individual study results. Surgery, histology and long-term follow-up of patients are reliable methods. Some reference standards, such as the use of endoscopic pancreatic function test (ePFT) for establishing the diagnosis of CP, could have resulted in under- or

| Comparison | \( N \) studies | \( N \) patients | Modality | Sensitivity (95% CI) | Specificity (95% CI) |
|------------|----------------|----------------|----------|---------------------|---------------------|
| US vs ERCP\(^a\) | 6 | 423 | US | 57% (49–65%) | 94% (74–99%) |
| | | | ERCP | 78% (71–85%) | 98% (89–100%) |
| US vs CT\(^b\) | 5 | 297 | US | 58% (49–66%) | 77% (71–83%) |
| | | | CT | 77% (68–83%) | 82% (74–88%) |
| CT vs ERCP\(^b\) | 5 | 354 | CT | 75% (67–82%) | 86% (81–90%) |
| | | | ERCP | 84% (77–89%) | 90% (85–93%) |
| EUS vs ERCP\(^b\) | 3 | 214 | EUS | 88% (80–93%) | 85% (76–91%) |
| | | | ERCP | 86% (78–91%) | 92% (85–96%) |
| MRCP vs sMRCP\(^b\) | 3 | 226 | MRCP | 62% (49–73%) | 94% (89–97%) |
| | | | sMRCP | 68% (56–79%) | 91% (85–94%) |
| EUS vs US\(^b\) | 2 | 95 | EUS | 90% (82–98%) | 100% |
| | | | US | 63% (49–76%) | 91% (82–99%) |

Sensitivity: US vs ERCP \((p < 0.001)\), US vs CT \((p = 0.002)\), EUS vs US \((p = 0.001)\)

Specificity: US vs ERCP \((p = 0.003)\), EUS vs US \((p = 0.04)\)

\(^a\) Random effects model

\(^b\) Fixed effects model
overestimation of the sensitivity and specificity. In addition, the diagnosis of CP and the criteria used are different in different stages of the disease (e.g. absence of calcifications in the early phase of the disease). Another limitation was that our analyses included imaging studies and imaging protocols performed over the last 40 years in different centres with inherent variations in techniques and equipment. Especially in the last decade the quality of some imaging modalities (e.g. MRCP and CT) has improved considerably. Also there were concerns about the quality of the available evidence, as assessed by QUADAS-2 and the GRADE scoring system.

The highest scores for accuracy in the diagnosis of CP were found for EUS and ERCP, but these are invasive techniques. ERCP has a relatively high risk of complications, such as post-ERCP pancreatitis (1.6–15.7%, mean complication rate of 4%) and is nowadays only used for therapeutic purposes (e.g. stenting of pancreatic duct) [67–69]. To date, diagnostic ERCP is largely replaced by EUS and the cross-sectional imaging modalities CT and MRCP.

It has been suggested that CT is better in detecting parenchymal calcifications and intraductal calcifications compared to MRCP [70–73]. On the other hand, MRCP is more often able to detect significant abnormalities of the pancreatic duct (e.g. PD dilatation and strictures) and slight changes of the pancreatic parenchyma and side branches, which can be attributed to early signs CP (i.e. atrophy, side branch ectasia) compared to CT [74]. Early diagnosis can also lead to a timely start of treatment, which has been associated with improved long-term outcome [75]. Nevertheless, for very early CP this association needs to be established in further research, such as the ESCAPE trial, evaluating the effect of early intervention in patients with CP [76]. As diagnostic sensitivity of CT and MRCP is not significantly lower than that of ERCP and EUS, and specificity is comparable, non-invasive modalities except for US are a likely first choice in patients with suspected pancreatic disease including chronic pancreatitis.

**Acknowledgements** The scientific guarantor of this publication is M.A. Boermeester. The authors of this manuscript declare relationships with the following companies: Baxter, Acelity/KCI, Ipsen, Mylan, Johnson & Johnson, Bard. The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article. The authors state that this work has not received any funding. Two of the authors have significant statistical expertise (SB, MAB). Institutional review board approval was not required because of the nature of the study (a systematic review).

**APPENDIX**

**Table 5** Search terms

| MeSH terms                          | All Fields                                      |
|-------------------------------------|------------------------------------------------|
| Chronic pancreatitis                | Chronic pancreatitis [All Fields]              |
| AND EUS OR ERCP                     | EUS [All Fields]                               |
| OR MRCP                             | Magnetic resonance imaging [All Fields]        |
| OR sMRCP                            | Magnetic Resonance Imaging [All Fields]        |
| OR CT                               | Tomography, X-Ray Computed [MeSH]             |
| OR US                               | Ultrasonography [MeSH]                         |

*MeSH Medical Subject Headings*
| Author          | Year | Journal                          | Reason for exclusion     |
|-----------------|------|----------------------------------|--------------------------|
| Borsukov et al  | 2001 | Ross Gastroenterol Zh            | Article not available    |
| Diad'kin et al  | 2013 | Vestnik rentgenologii i radiologii | Article not available    |
| Dotsenko et al  | 1985 | Vrach Delo                       | Article not available    |
| Rosch et al     | 1989 | Z Gastroenterologie              | Article not available    |
| Suzdalev et al  | 1992 | Likars'ka sprava                 | Article not available    |
| Agarwal et al   | 2008 | GIE                              | Exclusive patient group  |
| Brailski et al  | 1989 | Vutr Boles                       | Exclusive patient group  |
| Brailski et al  | 1984 | Vutr Boles                       | Exclusive patient group  |
| Brimiene et al  | 2011 | Medicina                         | Exclusive patient group  |
| Carlucci et al  | 1989 | HPB Surgery                      | Exclusive patient group  |
| Chowdhury et al | 2005 | Pancreas                         | Exclusive patient group  |
| Cotton et al    | 1980 | Radiology                        | Exclusive patient group  |
| Dell’Maschio et al | 1991 | Radiology                        | Exclusive patient group  |
| Erturk et al    | 2006 | Ann J Gastroenterol              | Exclusive patient group  |
| Frick et al     | 1982 | Gastrointest Rad                 | Exclusive patient group  |
| Gheonea et al   | 2013 | BMC Gastroenterology             | Exclusive patient group  |
| Goodale et al   | 1981 | Ann Surg                         | Exclusive patient group  |
| Haminen et al   | 2002 | Radiology                        | Exclusive patient group  |
| Hatano et al    | 1998 | Nippon rinsho J                  | Exclusive patient group  |
| Hocke et al     | 2008 | Dtsch Med Wochenschr             | Exclusive patient group  |
| Hocke et al     | 2006 | WJG                              | Exclusive patient group  |
| Hocke et al     | 2012 | Z Gastroenterologie              | Exclusive patient group  |
| Huang et al     | 2011 | J Dig dis                        | Exclusive patient group  |
| Imbriaco et al  | 2006 | Radiol Med                       | Exclusive patient group  |
| Kawai et al     | 2012 | Eur J Rad                        | Exclusive patient group  |
| Kim et al       | 2007 | J MRI                            | Exclusive patient group  |
| Kursawa et al   | 1991 | Radiol Diagn                     | Exclusive patient group  |
| Lu et al        | 2013 | Acad J Sec Mil Med University    | Exclusive patient group  |
| Lutz et al      | 1975 | Klin Wschr                       | Exclusive patient group  |
| Morris-Stiff et al | 2009 | J Pancreas                       | Exclusive patient group  |
| Papp et al      | 1978 | Wiener klin Wochenschr           | Exclusive patient group  |
| Pomerri et al   | 1991 | Radiologia Med                   | Exclusive patient group  |
| Rosch et al     | 2000 | Ann J Gastroenterol              | Exclusive patient group  |
| Sandrasegaran et al | 2013 | AJR                              | Exclusive patient group  |
| Sendler et al   | 2000 | World J Surg                     | Exclusive patient group  |
| Sugumar et al   | 2011 | Gut                              | Exclusive patient group  |
| Testoni et al   | 1981 | Acta Endoscopica                 | Exclusive patient group  |
| Tuishin et al   | 2003 | Voprosy onkologii                | Exclusive patient group  |
| Varadaraju et al| 2007 | GIE                              | Exclusive patient group  |
| Viceconte et al | 1980 | Ann ital chir                    | Exclusive patient group  |
| Yamada et al    | 2010 | Abdom Imaging                    | Exclusive patient group  |
| Zhu et al       | 2013 | PLOS one                         | Exclusive patient group  |
| Bhutani et al   | 2009 | Pancreas                         | In vitro                 |
| Akisik et al    | 2013 | AJR                              | No diagnostic values for CP |
| Alempijević et al | 2005 | Vojnosanit Pregl                | No diagnostic values for CP |
| Alpern et al    | 1985 | Radiology                        | No diagnostic values for CP |
| Ardelean et al  | 2014 | Med Ultrason                     | No diagnostic values for CP |
| Ardengh et al   | 2011 | GIE                              | No diagnostic values for CP |
| Ascunce et al   | 2010 | Surg End                         | No diagnostic values for CP |
| Baert et al     | 1977 | Radiologie                       | No diagnostic values for CP |
| Balci et al     | 2010 | J MRI                            | No diagnostic values for CP |
| Beliao et al    | 2012 | Eur J Rad                        | No diagnostic values for CP |
| Bender et al    | 1999 | Invest Rad                       | No diagnostic values for CP |
| Bhatt et al     | 2005 | Indian J Rad Imag Ass            | No diagnostic values for CP |
| Bonanno et al   | 1994 | Giorn Ital End Dig               | No diagnostic values for CP |
| Brunhmann et al | 1976 | RoFo                             | No diagnostic values for CP |
| Caletti et al   | 1982 | British j Surgery                | No diagnostic values for CP |
| Cao             | 1989 | Zhonghua yi xue za zhi           | No diagnostic values for CP |
| Cappeliez et al | 2000 | Radiology                        | No diagnostic values for CP |
| Chang et al     | 2010 | GIE                              | No diagnostic values for CP |
| Author           | Year | Journal                          | Reason for exclusion |
|------------------|------|----------------------------------|----------------------|
| Cohen et al      | 2014 | Dig Dis Sci                      | No diagnostic values for CP |
| Concia et al     | 2014 | Invest Rad                       | No diagnostic values for CP |
| Dale et al       | 1979 | Electromedica                    | No diagnostic values for CP |
| Das et al        | 2008 | GIE                              | No diagnostic values for CP |
| Delbeke et al    | 1999 | J Nucl Med                       | No diagnostic values for CP |
| Dite et al       | 1982 | Vnitrni Lekarstvi                | No diagnostic values for CP |
| Dronamraju et al | 2016 | Ann Gastroenterol                | No diagnostic values for CP |
| D’Souza et al    | 2015 | Dig Dis Sci                      | No diagnostic values for CP |
| Ettner et al     | 1979 | Dtsch Zeitschr Verdaauungs- und Stoffwechselkrankheiten | No diagnostic values for CP |
| Eloubeidi et al  | 2013 | Pancreas                         | No diagnostic values for CP |
| Ergul et al      | 2014 | Rev Esp Med Nucl Im Mol          | No diagnostic values for CP |
| Ferrucci et al   | 1979 | Radiology                        | No diagnostic values for CP |
| Foley et al      | 1980 | Gastrointest Rad                 | No diagnostic values for CP |
| Fontana et al    | 1976 | Gut                              | No diagnostic values for CP |
| Foster et al     | 1984 | BMJ                              | No diagnostic values for CP |
| Gardner et al    | 2014 | Pancreas                         | No diagnostic values for CP |
| Gincul et al     | 2014 | Endoscopy                        | No diagnostic values for CP |
| Gowland et al    | 1981 | Lancet                           | No diagnostic values for CP |
| Grant et al      | 1981 | J Am Osteopathic Ass             | No diagnostic values for CP |
| Harada et al     | 1977 | Gastroenterologica Jap           | No diagnostic values for CP |
| He et al         | 2014 | Pancreas                         | No diagnostic values for CP |
| Hoki et al       | 2009 | J Gastroenterol                  | No diagnostic values for CP |
| Hollerbach et al | 1994 | Med Klinik                       | No diagnostic values for CP |
| Horii et al      | 1982 | Jap J Gastroenterol              | No diagnostic values for CP |
| Johnson et al    | 1999 | Radiology                        | No diagnostic values for CP |
| Jones et al      | 1988 | Clin Radiol                      | No diagnostic values for CP |
| Kamisawa et al   | 2007 | J Gastroenterol                  | No diagnostic values for CP |
| Kersting et al   | 2009 | Gastroenterology                 | No diagnostic values for CP |
| Kitano et al     | 2004 | Gut                              | No diagnostic values for CP |
| Laghi et al      | 1998 | Chirurgia                        | No diagnostic values for CP |
| Leblanc et al    | 2014 | Pancreas                         | No diagnostic values for CP |
| Leblanc et al    | 2014 | Pancreas                         | No diagnostic values for CP |
| Li et al         | 2001 | Zhongguo yi xue ke xue           | No diagnostic values for CP |
| Loginov et al    | 1976 | Sovetskaya Meditsina             | No diagnostic values for CP |
| Lopez et al      | 2002 | Radiology                        | No diagnostic values for CP |
| Manfredi         | 2000 | Radiology                        | No diagnostic values for CP |
| Modder et al     | 1979 | RoFo                             | No diagnostic values for CP |
| Montori et al    | 1979 | Min Diet Gastroent               | No diagnostic values for CP |
| Napoleon et al   | 2010 | Endoscopy                        | No diagnostic values for CP |
| Novis et al      | 1976 | S Afr Med J                      | No diagnostic values for CP |
| Ohtsubo et al    | 2008 | Gastroenterolog Endoscopy        | No diagnostic values for CP |
| Orlikov et al    | 2007 | Ter Arkh                         | No diagnostic values for CP |
| Park et al       | 2008 | The Korean J Gastroenter         | No diagnostic values for CP |
| Petersein et al  | 2002 | RoFo                             | No diagnostic values for CP |
| Pezzelli et al   | 2013 | Pancreas                         | No diagnostic values for CP |
| Pomerrit et al   | 1997 | Radiologia Med                   | No diagnostic values for CP |
| Rickes et al     | 2002 | Scand J Gastroenterol            | No diagnostic values for CP |
| Rosenberg et al  | 1979 | MMW                              | No diagnostic values for CP |
| Russell et al    | 1978 | Gut                              | No diagnostic values for CP |
| Sahai et al      | 1998 | GIE                              | No diagnostic values for CP |
| Sainani et al    | 2009 | AJG                              | No diagnostic values for CP |
| Sica et al       | 2002 | J MRI                            | No diagnostic values for CP |
| Sica et al       | 1999 | Radiology                        | No diagnostic values for CP |
| Songur et al     | 2000 | Digest Endoscopy                 | No diagnostic values for CP |
| Stevens et al    | 2010 | WJG                             | No diagnostic values for CP |
| Struve et al     | 1982 | Diagnostik & Intensivtherapie     | No diagnostic values for CP |
| Sun et al        | 2010 | Acad J Sec Mil Med University    | No diagnostic values for CP |
| Tamura et al     | 2006 | Radiology                        | No diagnostic values for CP |
| Tellez-Avila et al | 2014 | WJG                             | No diagnostic values for CP |
| Author              | Year | Journal                          | Reason for exclusion         |
|---------------------|------|----------------------------------|------------------------------|
| Tirkes et al        | 2016 | J MRI                            | No diagnostic values for CP  |
| Trikudanathan et al | 2015 | Am J Gastroenterol               | No diagnostic values for CP  |
| Tripathi et al      | 2002 | Indian J Gastroenterol           | No diagnostic values for CP  |
| Tymper et al        | 1979 | Leber Magen Darm                 | No diagnostic values for CP  |
| Tymper et al        | 1977 | Verhand Dtschen Gesellschaft fur Innere Medizin | No diagnostic values for CP |
| Uskudar et al       | 2009 | Pancreas                         | No diagnostic values for CP  |
| Valentini et al     | 1981 | Endoscopy                        | No diagnostic values for CP  |
| Varghese et al      | 2002 | Clin Radiol                      | No diagnostic values for CP  |
| Wang et al          | 2013 | WJG                              | No diagnostic values for CP  |
| Wierzbicka-Paczos et al | 1998 | Gastroenterologia Polska         | No diagnostic values for CP  |
| Ho et al            | 2006 | Clin Gastroenterol Hep           | No reference standard        |
| Kalmar et al        | 1984 | Southern Medical J               | No reference standard        |
| Kalmin et al        | 2011 | Can J Gastroenterol              | No reference standard        |
| Kaufman et al       | 1989 | GIE                              | No reference standard        |
| Kunon et al         | 2012 | GIE                              | No reference standard        |
| Manfredi et al      | 1998 | La Rad Medica                    | No reference standard        |
| Novotny et al       | 2000 | Bratisl Lek Listy                | No reference standard        |
| Ponette et al       | 1976 | Acta Gastro-Enterol Belgica      | No reference standard        |
| Sanyal et al        | 2012 | AJR                              | No reference standard        |
| Yoshimoto et al     | 1980 | Jap J Gastroenterol              | No reference standard        |
| Grossjohann et al   | 2010 | Scand J Gastroenterol            | Not enough patients          |
| Sood et al          | 1992 | Indian J Gastroenterol           | Not enough patients          |
| Zhi et al           | 2002 | Chin J Digestive Dis             | Not enough patients          |
| Zhong et al         | 2003 | WJG                              | Not enough patients          |
| Ainsworth et al     | 2003 | Endoscopy                        | Only sensitivity reported    |
| Bastid et al        | 1995 | J d’Echographie et de Med par Ultrasons | Only sensitivity reported    |
| Campisi et al       | 2009 | Clin Radiol                      | Only sensitivity reported    |
| Dancygier et al     | 1986 | Scand J Gastroenterol            | Only sensitivity reported    |
| Giday et al         | 2011 | J Gastroenterol                  | Only sensitivity reported    |
| Guarita et al       | 1982 | AMB                              | Only sensitivity reported    |
| Guo et al           | 2003 | Chin J Digestive Dis             | Only sensitivity reported    |
| Kahl et al          | 2002 | GIE                              | Only sensitivity reported    |
| Kim et al           | 2001 | AJR                              | Only sensitivity reported    |
| Kolmannskog et al   | 1981 | Acta Radiologica                 | Only sensitivity reported    |
| Lackner et al       | 1980 | RoFo                             | Only sensitivity reported    |
| Lawson              | 1978 | Radiology                        | Only sensitivity reported    |
| Manfredi            | 2002 | Radiology                        | Only sensitivity reported    |
| Mao et al           | 2011 | WCJD                             | Only sensitivity reported    |
| Nakashio            | 1992 | Acta medica                      | Only sensitivity reported    |
| Noguchi et al       | 1985 | Gastroenterolog Endoscopy        | Only sensitivity reported    |
| Prupp               | 2011 | Vestnik kihurjig imeni           | Only sensitivity reported    |
| Rossi et al         | 1996 | Giorn Ital End Dig               | Only sensitivity reported    |
| Sahel et al         | 1976 | Acta Endoscopica                 | Only sensitivity reported    |
| Seicean et al       | 2010 | Ultraschall Med                  | Only sensitivity reported    |
| Sildiroglu          | 1985 | Rontgenpraxis                    | Only sensitivity reported    |
| Singh et al         | 1993 | Indian J Rad Imag                | Only sensitivity reported    |
| Sivak et al         | 1986 | Scand J Gastroenterol            | Only sensitivity reported    |
| Stabile Ianora et al| 2013 | Recenti Prog Med                 | Only sensitivity reported    |
| Stevens et al       | 2008 | Dig Dis Sci                      | Only sensitivity reported    |
| Author          | Year | Journal                           | Reason for exclusion                  |
|-----------------|------|-----------------------------------|---------------------------------------|
| Stevens et al   | 2010 | Dig Dis Sci                       | Only sensitivity reported             |
| Triller et al   | 1983 | Computertomographie               | Only sensitivity reported             |
| Uchida et al    | 1997 | Jap J Clin Radiology              | Only sensitivity reported             |
| Vitale et al    | 2009 | The Am Surgeon                    | Only sensitivity reported             |
| Wang et al      | 2009 | J Gastro Hep                      | Only sensitivity reported             |
| Wu et al        | 2006 | World Chin J Dig                  | Only sensitivity reported             |
| Yanling et al   | 2001 | Chinese J Gastroenterol           | Only sensitivity reported             |
| Zhou et al      | 1993 | Zhonghua nei ke za zhi            | Only sensitivity reported             |
| Arthale et al   | 2002 | GIE                               | Other disease                         |
| Doust et al     | 1976 | Radiology                         | Other disease                         |
| Engjom et al    | 2015 | Scan J Gastroenterol              | Other disease                         |
| Huang et al     | 2009 | Acad J See Mil Med University     | Other disease                         |
| Kushnir et al   | 2011 | GIE                               | Other disease                         |
| Lai et al       | 2004 | Endoscopy                         | Other disease                         |
| Leblanc et al   | 2014 | Pancreas                          | Other disease                         |
| Matos et al     | 2001 | GIE                               | Other disease                         |
| Mosler et al    | 2012 | Dig Dis Sci                       | Other disease                         |
| Novis et al     | 2010 | Rev Colegio Brasileiro Cirurg     | Other disease                         |
| Rana et al      | 2012 | J Gastro Hep                      | Other disease                         |
| Ranney et al    | 2012 | GIE                               | Other disease                         |
| Sainani et al   | 2015 | Pancreas                          | Other disease                         |
| Soto et al      | 2005 | Radiology                         | Other disease                         |
| Aksik et al     | 2009 | Radiology                         | Other imaging modality                |
| Cherian et al   | 2010 | HPB Surgery                       | Other imaging modality                |
| Glaser et al    | 1994 | Int J Pancreatology               | Other imaging modality                |
| Glaser et al    | 1989 | Scand J Gastroenterol             | Other imaging modality                |
| Glaser et al    | 1985 | Ultraschall Med                   | Other imaging modality                |
| Hocke et al     | 2007 | Pancreas                          | Other imaging modality                |
| Kurnon et al    | 2010 | GIE                               | Other imaging modality                |
| Safoui et al    | 2008 | GIE                               | Other imaging modality                |
| Sreenarasinghiah| 2008 | J Clin Gastroenterol              | Other imaging modality                |
| Tummula et al   | 2013 | Clin Transl Gastroenterol         | Other imaging modality                |
| Uehara et al    | 2011 | J Gastro Hep                      | Other imaging modality                |
| Abdalla et al   | 2012 | Gastroenterology                  | Other type of article                 |
| Arsat et al     | 1981 | Med Chirurgie Digest              | Other type of article                 |
| Ashida et al    | 2011 | J Gastro Hep                      | Other type of article                 |
| Chvatalova et al| 2012 | Pancreatology                     | Other type of article                 |
| Czako et al     | 2007 | J Gastroenterol                   | Other type of article                 |
| Gupta et al     | 2013 | JIMSA                             | Other type of article                 |
| Heverhagen et al| 2007 | RoFo                              | Other type of article                 |
| Kasugai et al   | 1982 | Stomach and intestine             | Other type of article                 |
| Kent et al      | 2008 | Pancreas                          | Other type of article                 |
| Markwardt et al | 1980 | Radiologia Diagn                  | Other type of article                 |
| Munoz et al     | 2010 | Rev Med de Chile                  | Other type of article                 |
| Musunuri et al  | 2015 | Ind J Gastroenterol               | Other type of article                 |
| Quinn et al     | 2012 | Gut                               | Other type of article                 |
| Romagnuolo et al| 2012 | GIE                               | Other type of article                 |
| Sherman et al   | 2012 | GIE                               | Other type of article                 |
| Shibukawa et al | 2015 | Dig Endos                         | Other type of article                 |
| Stevens et al   | 2008 | Pancreas                          | Other type of article                 |
| Takahashi et al | 2014 | AJR                               | Other type of article                 |
| Trus et al      | 1998 | Probl Gen Surg                    | Other type of article                 |
| Vadrot et al    | 1981 | Med Chirurgie Digest              | Other type of article                 |
| Zaruba et al    | 2012 | Pancreatology                     | Other type of article                 |
| Zhang et al     | 2011 | J Gastro Hep                      | Other type of article                 |
Table 7 QUADAS-2 characteristics for each study

| Study                          | Bias Patient selection | Bias Index test | Bias Reference standard | Flow and timing | Applicability Patient selection | Applicability Index test | Applicability Reference standard |
|-------------------------------|------------------------|-----------------|-------------------------|-----------------|---------------------------------|--------------------------|----------------------------------|
| Adamek et al                  | Low                    | Low             | Low                     | Low             | Unclear                         | Unclear                  | Low                               |
| Albashir et al                | Low                    | Low             | Low                     | Low             | Low                             | Low                      | Low                               |
| Alcaraz et al                 | Low                    | Low             | Low                     | Low             | Unclear                         | Low                      | Low                               |
| Balcì et al                   | Low                    | Low             | Unclear                 | Low             | Low                             | Low                      | Unclear                          |
| Bolog et al                   | Low                    | Unclear         | Low                     | Low             | High                            | Unclear                  | Low                               |
| Brand et al                   | Low                    | Low             | Low                     | High            | Low                             | Low                      | Low                               |
| Buscail et al                 | Low                    | Unclear         | Low                     | Low             | High                            | Unclear                  | Low                               |
| Catalano et al                | Unclear                | Low             | Unclear                 | Low             | Low                             | Low                      | Low                               |
| Chong et al                   | Low                    | Low             | Low                     | Low             | Low                             | Low                      | Low                               |
| Conwell et al                 | Low                    | Low             | High                    | Low             | Low                             | Low                      | Unclear                          |
| Dramaix et al                 | Low                    | Low             | Low                     | Low             | Low                             | Low                      | Unclear                          |
| Fusari et al                  | Unclear                | Low             | Low                     | Low             | High                            | Low                      | Low                               |
| Gebel et al                   | Low                    | Low             | Low                     | High            | Low                             | Unclear                  | Low                               |
| Giovannini et al              | Unclear                | Unclear         | Low                     | Low             | High                            | Unclear                  | Unclear                          |
| Glasbrenner et al             | Low                    | Low             | Low                     | Low             | High                            | Low                      | Low                               |
| GMelin et al                  | Low                    | Low             | Low                     | Low             | High                            | Low                      | Unclear                          |
| Hellerhoff et al              | Low                    | Low             | Low                     | Low             | Low                             | Low                      | Low                               |
| Im Dahl et al                 | Low                    | Low             | Unclear                 | Low             | Low                             | Unclear                  | Low                               |
| Kremmer et al                 | High                   | Unclear         | Low                     | Low             | High                            | Unclear                  | Low                               |
| Lammer et al                  | Low                    | Low             | Unclear                 | Low             | Low                             | Unclear                  | Unclear                          |
| Lawson et al                  | Low                    | Low             | Unclear                 | Low             | Low                             | Low                      | Unclear                          |
| Lees et al                    | Low                    | Low             | Low                     | High            | Low                             | Low                      | Low                               |
| Lin et al                     | High                   | Unclear         | Low                     | Low             | Low                             | Unclear                  | Low                               |
| Nattermann et al              | Unclear                | Low             | Low                     | Low             | High                            | Unclear                  | Low                               |
| Pamos et al                   | Low                    | Low             | Low                     | Low             | High                            | Unclear                  | Low                               |
| Parsi et al                   | Low                    | Low             | Low                     | Low             | Low                             | Unclear                  | Low                               |
| Pistolesi et al               | Unclear                | Low             | Low                     | Low             | Low                             | Low                      | Low                               |
| Pungpapong et al              | Low                    | Low             | Low                     | Low             | Low                             | Low                      | Low                               |
| Pungpapong et al              | Low                    | Unclear         | Unclear                 | Low             | Low                             | Low                      | Low                               |
| Rudowicz Pietr-uszewska et al | Low                    | Unclear         | Low                     | Low             | High                            | Unclear                  | Unclear                          |
| Sai et al                     | High                   | Low             | Low                     | Low             | Low                             | Low                      | Low                               |
| Savarino et al                | Unclear                | Low             | Low                     | Low             | Low                             | Low                      | Low                               |
| Scarabino et al               | Low                    | Unclear         | Unclear                 | Low             | High                            | Unclear                  | Low                               |
| Schlaudraff et al             | Low                    | Unclear         | Low                     | Low             | Low                             | Low                      | Low                               |
| Stevens et al                 | Low                    | Low             | Low                     | Low             | Low                             | Low                      | Unclear                          |
| Sverko et al                  | Unclear                | Unclear         | Low                     | Low             | Low                             | Unclear                  | Low                               |
| Swobodnik et al               | Low                    | Low             | Low                     | Low             | Low                             | Low                      | Low                               |
| Tox et al                     | Low                    | Unclear         | Unclear                 | Low             | Low                             | Low                      | Low                               |
| Trikudanathan et al           | Unclear                | Low             | Unclear                 | Low             | High                            | Low                      | Low                               |
| Triller et al                 | Unclear                | Low             | Unclear                 | Low             | Unclear                         | Low                      | Unclear                          |
| Wiersema et al                | Unclear                | Low             | Unclear                 | Low             | High                            | Unclear                  | Unclear                          |
| Zhang et al                   | High                   | Unclear         | High                    | Low             | Low                             | Unclear                  | High                             |
| Zuccaro et al                 | Unclear                | Low             | Unclear                 | Low             | Low                             | Low                      | Unclear                          |
## Table 8  GRADE scoring system

| EUS  | Outcome | № of studies (№ of patients) | Study design | Factors that may decrease quality of evidence | Effect per 1000 patients tested pre-test probability of 47.2% | Quality of evidence |
|------|---------|------------------------------|--------------|-----------------------------------------------|-------------------------------------------------------------|--------------------|
|      | True positives | 16 (1249) | Cohort & case-control | Serious<sup>a</sup> Serious<sup>b</sup> Very serious<sup>c</sup> Very serious<sup>d</sup> NA | 387 (335 to 425) 85 (47 to 137) | ⚫⚫⚫⚫ VERY LOW |
|      | False negatives | 16 (1249) | Cohort & case-control | Serious<sup>a</sup> Serious<sup>b</sup> Serious<sup>c</sup> Serious<sup>d</sup> NA | 480 (438 to 502) 48 (26 to 90) | ⚫⚫⚫⚫ VERY LOW |
| ERCPOutcome | True positives | 11 (742) | Cohort & case-control | Not serious<sup>e</sup> Serious<sup>f</sup> Serious<sup>g</sup> Serious<sup>h</sup> NA | 349 (324 to 371) 77 (55 to 102) | ⚫⚫⚫⚫ VERY LOW |
|      | False negatives | 11 (742) | Cohort & case-control | Not serious<sup>e</sup> Serious<sup>f</sup> Serious<sup>g</sup> Serious<sup>h</sup> NA | 540 (499 to 563) 34 (11 to 75) | ⚫⚫⚫⚫ VERY LOW |
| MRCPOutcome | True positives | 14 (933) | Cohort & case-control-type studies | Serious<sup>i</sup> Serious<sup>j</sup> Serious<sup>k</sup> Very serious<sup>l</sup> NA | 225 (199 to 246) 64 (43 to 90) | ⚫⚫⚫⚫ VERY LOW |
|      | False negatives | 14 (933) | Cohort & case-control-type studies | Serious<sup>i</sup> Serious<sup>j</sup> Serious<sup>k</sup> Not serious<sup>l</sup> NA | 683 (640 to 697) 28 (14 to 71) | ⚫⚫⚫⚫ VERY LOW |
| CTOutcome | True positives | 10 (700) | Cohort & case-control | Serious<sup>m</sup> Serious<sup>n</sup> Serious<sup>o</sup> Very serious<sup>p</sup> NA | 288 (253 to 319) 96 (65 to 131) | ⚫⚫⚫⚫ VERY LOW |
|      | False negatives | 10 (700) | Cohort & case-control | Serious<sup>m</sup> Serious<sup>n</sup> Serious<sup>o</sup> Serious<sup>p</sup> NA | 561 (499 to 591) 55 (25 to 117) | ⚫⚫⚫⚫ VERY LOW |
| USOutcome | True positives | 10 (700) | Cohort & case-control | Serious<sup>m</sup> Serious<sup>n</sup> Serious<sup>o</sup> Very serious<sup>p</sup> NA | 288 (253 to 319) 96 (65 to 131) | ⚫⚫⚫⚫ VERY LOW |
|      | False negatives | 10 (700) | Cohort & case-control | Serious<sup>m</sup> Serious<sup>n</sup> Serious<sup>o</sup> Serious<sup>p</sup> NA | 561 (499 to 591) 55 (25 to 117) | ⚫⚫⚫⚫ VERY LOW |

Notes:
- <sup>a</sup> Risk of bias
- <sup>b</sup> Indirectness
- <sup>c</sup> Inconsistency
- <sup>d</sup> Imprecision
- <sup>e</sup> Publication bias
- <sup>f</sup> Pre-test probability of 47.2%

Eur Radiol (2017) 27:3820–3844
Table 8 (continued)

|                | 10 (1005) | Cohort & case-control | Serious | Serious | Serious | Very serious | NA       | 172 (136 to 200) |
|----------------|-----------|-----------------------|---------|---------|---------|-------------|---------|------------------|
| True positives | 10 (1005) | Cohort & case-control | Serious | Serious | Serious | Very serious | NA       | 172 (136 to 200) |
| False negatives| 85 (57 to 121) | Very low                |         |         |         |             |         | Very low         |
| True negatives | 728 (661 to 743) | Very low                |         |         |         |             |         | Very low         |
| False positives| 15 (0 to 82) | Very low                |         |         |         |             |         | Very low         |

NA not available

a Risk of bias: based on QUADAS-2 risk of bias; 7 studies not serious, 9 studies serious
b Indirectness: based on QUADAS-2 applicability; 7 studies not serious, 9 studies serious
c Inconsistency: based on heterogeneity and visual inspection CIs
d Imprecision: based on study numbers and CIs of summary estimate (CIs 0–10 = not serious, 11–15 = serious, more than 15 = very serious)
e Based on QUADAS-2 risk of bias: 8 studies not serious, 3 studies serious
f Based on QUADAS-2 applicability: 6 studies not serious, 5 studies serious
g Based on heterogeneity and visual inspection CIs
h Based on study numbers and CIs of summary estimate (CIs 0–10 = not serious, 11–15 = serious, more than 15 = very serious)
i Risk of bias: based on QUADAS-2 risk of bias; 7 studies not serious, 5 studies serious, 1 study very serious
j Indirectness: based on QUADAS-2 applicability; 6 studies not serious, 8 studies serious
k Inconsistency: based on heterogeneity and visual inspection CIs
l Imprecision: based on study numbers and CIs of summary estimate (CIs 0–10 = not serious, 11–15 = serious, more than 15 = very serious)
m Risk of bias: based on QUADAS-2 risk of bias; 5 studies not serious, 5 studies serious
n Indirectness: based on QUADAS-2 applicability; 6 studies not serious, 4 studies serious
o Inconsistency: based on heterogeneity and visual inspection CIs
p Imprecision: based on study numbers and CIs of summary estimate (CIs 0–10 = not serious, 11–15 = serious, more than 15 = very serious)
q Risk of bias: based on QUADAS-2 risk of bias; 6 studies not serious, 3 studies serious, 1 study very serious
r Indirectness: based on QUADAS-2 applicability; 5 studies not serious, 5 studies serious
s Inconsistency: based on heterogeneity and visual inspection CIs
t Imprecision: based on study numbers and CIs of summary estimate (CIs 0–10 = not serious, 11–15 = serious, more than 15 = very serious)
Table 9  GRADE characteristics for each study

| Modality | Name first author | Risk of bias | Indirectness | Inconsistency | Imprecision | Publication bias |
|----------|------------------|--------------|--------------|--------------|-------------|-----------------|
| EUS      | Albashir et al   | Low          | Low          | Sensitivity: very serious | Sensitivity: very serious | Not assessed     |
|          | Brand et al      | Serious      | Serious      | Specificity: serious | Specificity: serious |                 |
|          | Buscail et al    | Low          | Low          |              |             |                 |
|          | Catalano et al   | Low          | Low          |              |             |                 |
|          | Chong et al      | Low          | Low          |              |             |                 |
|          | Conwell et al    | Serious      | Serious      |              |             |                 |
|          | Giovannini et al | Serious      | Serious      |              |             |                 |
|          | Glasbrenner et al| Low          | Low          |              |             |                 |
|          | Lin et al        | Serious      | Serious      |              |             |                 |
|          | Nattermann et al | Low          | Serious      |              |             |                 |
|          | Pangpapong et al | Low          | Low          |              |             |                 |
|          | Pangpapong et al | Low          | Low          |              |             |                 |
|          | Stevens et al    | Serious      | Serious      |              |             |                 |
|          | Tox et al        | Serious      | Low          |              |             |                 |
|          | Trikudanathan et al | Serious | Serious      |              |             |                 |
|          | Wiersema et al   | Serious      | Serious      |              |             |                 |
| ERCP     | Adamek et al     | Low          | Low          | Sensitivity: serious | Sensitivity: serious | Not assessed     |
|          | Buscail et al    | Low          | Serious      | Specificity: serious | Specificity: serious |                 |
|          | Gehel et al      | Low          | Low          |              |             |                 |
|          | Glasbrenner et al| Low          | Low          |              |             |                 |
|          | Gmelin et al     | Low          | Low          |              |             |                 |
|          | Lammer et al     | Serious      | Serious      |              |             |                 |
|          | Lawson et al     | Low          | Low          |              |             |                 |
|          | Parsi et al      | Low          | Low          |              |             |                 |
|          | Scarabino et al  | Serious      | Serious      |              |             |                 |
|          | Swobodnik et al  | Low          | Low          |              |             |                 |
|          | Triller et al    | Serious      | Serious      |              |             |                 |
| MRCP     | Adamek et al     | Low          | Low          | Sensitivity: serious | Sensitivity: very serious | Not assessed     |
|          | Alcaraz et al    | Low          | Serious      | Specificity: serious | Specificity: not serious |                 |
|          | Balci et al      | Low          | Serious      |              |             |                 |
|          | Bolog et al      | Serious      | Serious      |              |             |                 |
|          | Fusari et al     | Low          | Low          |              |             |                 |
|          | Hellerhoff et al | Low          | Low          |              |             |                 |
|          | Pamos et al      | Low          | Low          |              |             |                 |
|          | Pangpapong et al | Low          | Low          |              |             |                 |
|          | Rudowicz-Pietruszewska | Low | Serious      |              |             |                 |
|          | Sai et al        | Serious      | Low          |              |             |                 |
|          | Schlaudraff et al| Low          | Low          |              |             |                 |
|          | Sverko et al     | Serious      | Serious      |              |             |                 |
|          | Zhang et al      | Very serious | Serious      |              |             |                 |
|          | Zucarco et al    | Serious      | Serious      |              |             |                 |
| CT       | Buscail et al    | Low          | Low          | Sensitivity: serious | Sensitivity: very serious | Not assessed     |
|          | Dramaix et al    | Low          | Low          | Specificity: serious | Specificity: serious |                 |
|          | Fusari et al     | Low          | Low          |              |             |                 |
|          | Gmelin et al     | Low          | Low          |              |             |                 |
|          | Imdahl et al     | Low          | Low          |              |             |                 |
|          | Lammer et al     | Serious      | Serious      |              |             |                 |
|          | Pistolesi et al  | Low          | Low          |              |             |                 |
|          | Savarino et al   | Serious      | Low          |              |             |                 |
|          | Scarabino et al  | Serious      | Serious      |              |             |                 |
|          | Swobodnik et al  | Low          | Low          |              |             |                 |
| CT       | Buscail et al    | Low          | Low          | Sensitivity: serious | Sensitivity: very serious | Not assessed     |
|          | Dramaix et al    | Low          | Low          | Specificity: very serious | Specificity: serious |                 |
|          | Gehel et al      | Low          | Low          |              |             |                 |
|          | Gmelin et al     | Low          | Low          |              |             |                 |
|          | Kremer et al     | Very serious | Serious      |              |             |                 |
|          | Lawson et al     | Low          | Low          |              |             |                 |
|          | Lees et al       | Serious      | Low          |              |             |                 |
|          | Lin et al        | Serious      | Serious      |              |             |                 |
|          | Scarabino et al  | Serious      | Serious      |              |             |                 |

3836 Eur Radiol (2017) 27:3820–3844
| Study               | Sensitivity | Specificity | Accuracy | PPV    | NPV    | TP     | TN     | FP     | FN     |
|---------------------|-------------|-------------|----------|--------|--------|--------|--------|--------|--------|
| Adamek et al        | MRCP: 88%,  | MRCP: 94%,  | MRCP:    | MRCP:  | MRCP:  | MRCP:  | MRCP:  | MRCP:  | MRCP:  |
|                     | ERCP: 90%   | ERCP: 91%   | ERCP: 93%, | 0%     | 91%    | 50%    | 51%    | 4%     | 0%     |
| Albashir et al      | 84%         | 100%        | 87%      | 100%   | 57%    | 16     | 4      | 2      | 3      |
| Alcaraz et al       | 50%         | 99%         | 94%      | 80%    | 95%    | 4      | 72     | 1      | 4      |
| Balcí et al         | 82%         | 63%         | 70%      | 56%    | 9      | 12     | 7      | 2      |
| Bolog et al         | 90%         | 98%         | 95%      | 90%    | 98%    | 14     | 86     | 2      | 1      |
| Brand et al         | 42%         | 96%         | 84%      | 71%    | 86%    | 10     | 87     | 4      | 14     |
| Buscali et al       | US: 58%, CT: 75%, ERCP: 74%, EUS: 88% | US: 75%, CT: 95%, ERCP: 100%, EUS: 100% | US: 65%, CT: 81%, ERCP: 82%, EUS: 92% | US: 87%, CT: 97%, ERCP: 100%, EUS: 100% | US: 44%, CT: 61%, ERCP: 62%, EUS: 78% | US: 26, CT: 33, ERCP: 33, EUS: 39 | US: 14, CT: 17, ERCP: 18, EUS: 18 | US: 4, CT: 1, ERCP: 0, EUS: 0 | US: 18, CT: 11, ERCP: 11, EUS: 5 |
| Catalano et al      | 84%         | 98%         | 91%      | 97%    | 87%    | 32     | 41     | 1      | 6      |
| Chong et al         | 83%         | 80%         | 83%      | 98%    | 69%    | 53     | 1      | 1      |
| Conwell et al       | 26%         | 100%        | 50%      | 100%   | 39%    | 10     | 18     | 0      | 28     |
| Dramaix et al       | CT: 60%, US: 60%, MRI: 88% | CT: 100%, US: 95% | CT: 86% US: 82% | CT: 100%, US: 90% | CT: 76% US: 76% | CT: 11 US: 11 | MRE: 17, US: 32 | US: 9, US: 2 | US: 7 |
| Fusari et al        | US: 82%, ERCP: 56%, MRI: 100%, EUS: 97%, ERCP: 97% | US: 91%, ERCP: 82%, MRI: 97% | US: 95% ERCP: 90% | US: 89% ERCP: 80% | US: 18, ERCP: 9 | US: 3, ERCP: 28 | US: 1, ERCP: 10 | US: 4, ERCP: 7 |
| Gebel et al         | US: 82%, ERP: 94%, MRI: 100%, EUS: 97%, ERCP: 97% | US: 91%, ERP: 82%, MRI: 97% | US: 95%, ERP: 90% | US: 89%, ERP: 80% | US: 18, ERP: 9 | US: 3, ERCP: 28 | US: 1, ERP: 0 | US: 4, ERP: 7 |
| Giovannini et al    | 88%         | 94%         | 95%      | 85%    | 95%    | 32     | 41     | 1      | 6      |
| Glusmbrenner et al  | US: 93%, ERCP: 85%, MRI: 100%, EUS: 97%, ERCP: 97% | US: 91%, ERCP: 82%, MRI: 97% | US: 95%, ERCP: 90% | US: 89%, ERCP: 80% | US: 18, ERCP: 9 | US: 3, ERCP: 28 | US: 1, ERP: 0 | US: 4, ERP: 7 |
| Gmelin et al        | US: 82%, CT: 95%, ERCP: 91% | US: 91%, CT: 89%, ERCP: 89% | US: 95%, CT: 90%, ERCP: 90% | US: 89%, CT: 87%, ERCP: 89% | US: 18, ERCP: 9 | US: 3, ERCP: 28 | US: 1, ERP: 0 | US: 4, ERP: 7 |
| Hellehookh et al    | MRI: 77%, sMRI: 89% | MRI: 100%, sMRI: 100% | MRI: 94% sMRI: 97% | MRI: 92% sMRI: 96% | MRI: 20, sMRI: 23 | MRI: 6, sMRI: 3 |
| Imdieh et al        | 58%         | 91%         | 83%      | 70%    | 85%    | 7       | 33     | 3      | 5      |
| Klement et al       | 64%         | 99%         | 94%      | 89%    | 95%    | 42     | 378    | 5      | 21     |
| Kallmenn et al      | ERP: 85%, CT: 64% | ERP: 97%, CT: 93% | ERP: 94%, CT: 81% | ERP: 92%, CT: 79% | ERP: 33, CT: 25 | ERP: 66, CT: 48 | ERP: 2, ERP: 14 | ERP: 6, CT: 10 |
| Lawson et al        | US: 38%, ERP: 73% | US: 100%, ERP: 98% | US: 99%, ERP: 98% | US: 75%, ERP: 87% | US: 10, ERP: 19 | US: 49, ERP: 48 | US: 0, ERP: 10 | US: 16, ERP: 7 |
| Lees et al          | 100%        | 97%         | 98%      | 91%    | 100%   | 20     | 76     | 2      | 0      |
| Lin et al           | US: 86%, EUS: 100% | US: 100%, EUS: 100% | US: 97%, EUS: 100% | US: 96%, EUS: 100% | US: 6, EUS: 7 | US: 26, EUS: 26 | US: 0, EUS: 0 | US: 1, EUS: 0 |
| Nattermann et al    | 98%         | 57%         | 75%      | 65%    | 97%    | 50     | 36     | 27     | 1      |
| Pamos et al         | 80%         | 100%        | 98%      | 97%    | 97%    | 4      | 36     | 0      | 1      |
| Parsi et al         | 71%         | 91%         | 77%      | 94%    | 59%    | 17     | 10     | 1      | 7      |
| Pistolesi et al     | 58%         | 81%         | 74%      | 58%    | 81%    | 18     | 56     | 13     | 13     |
| Punngpang et al     | 71%         | 88%         | 80%      | 84%    | 77%    | 27     | 36     | 5      | 11     |
| Punngpang et al     | EUS: 93%, MRCP: 65% | EUS: 93%, MRCP: 90% | EUS: 93%, MRCP: 80% | EUS: 90%, MRCP: 81% | EUS: 95%, MRCP: 79% | EUS: 37, MRCP: 26 | MRCP: 53 | MRCP: 6 |
| Rudowicz-Pietruszewski et al | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% |
| Sai et al           | 60%         | 79%         | 68%      | 77%    | 60%    | 10     | 9      | 3      | 6      |
| Savarino et al      | 90%         | 59%         | 76%      | 73%    | 83%    | 53     | 29     | 20     | 6      |
| Scarabino et al     | ERP: 83%, CT: 42%, ERCP: 70% | ERP: 67%, US: 34% | ERP: 70%, US: 35% | ERP: 37%, US: 13% | ERP: 94%, US: 71% | ERP: 10, US: 5, ERCP: 10, US: 34, CT: 15 | ERP: 17, ERCP: 2, US: 7, ERP: 10, US: 15 | ERP: 17, ERCP: 2, US: 7, ERP: 10, US: 15 |
Table 10 (continued)

| Study          | Sensitivity | Specificity | Accuracy | PPV    | NPV    | TP  | TN  | FP  | FN  |
|----------------|-------------|-------------|----------|--------|--------|-----|-----|-----|-----|
| Schlaudraff et al | MRCP: 67%, sMRCP: 73% | MRCP: 93%, sMRCP: 96% | MRCP: 89%, sMRCP: 93% | MRCP: 63%, sMRCP: 78% | MRCP: 95%, sMRCP: 95% | TP  | TN  | FP  | FN  |
| Stevens et al   | Radial: 68%, Linear: 44% | Radial: 95% | Linear: 95% | Radial: 84% | Linear: 74% | Radial: 90%, Linear: 86% | Radial: 81%, Linear: 71% | TP  | TN  | FP  | FN  |
| Sverko et al    | 79%         | 93%         | 86%      | 92%    | 82%    | 11  | 14  | 3   | 1   |
| Swobodnik et al | US: 52%, CT: 74%, ERCP: 93% | US: 100%, CT: 98%, ERCP: 100% | US: 100%, CT: 95%, ERCP: 100% | US: 100%, CT: 95%, ERCP: 100% | US: 100%, CT: 95%, ERCP: 100% | US: 100%, CT: 95%, ERCP: 100% | TP  | TN  | FP  | FN  |
| Tox et al       | 77%         | 75%         | 76%      | 66%    | 84%    | 50  | 80  | 26  | 15  |
| Trikudanathan et al | 61%      | 75%         | 63%      | 92%    | 29%    | 34  | 9   | 3   | 22  |
| Triller et al   | 82%         | 85%         | 83%      | 82%    | 85%    | 9   | 11  | 2   | 5   |
| Wiersema et al  | 80%         | 86%         | 84%      | 83%    | 84%    | 24  | 32  | 5   | 6   |
| Zhang et al     | 92%         | 75%         | 84%      | 81%    | 88%    | 22  | 15  | 5   | 2   |
| Zuccaro et al   | MRCP: 46%, sMRCP: 46% | MRCP: 85%, sMRCP: 59% | MRCP: 70%, sMRCP: 59% | MRCP: 68%, sMRCP: 50% | MRCP: 70%, sMRCP: 65% | MRCP: 13, sMRCP: 13 | MRCP: 35, sMRCP: 28 | MRCP: 6, sMRCP: 15 | MRCP: 3, sMRCP: 2 |

PPV positive predictive value, NPV negative predictive value, TP true positive, TN true negative, FP false positive, FN false negative

Table 11 Imaging characteristics for each study

Magnetic resonance imaging (MRI)

| Study          | Year | Magnetic field | Coil type | Contrast | Secretin enhancement | Sequence | Scoring criteria                                                                 |
|----------------|------|----------------|-----------|----------|----------------------|----------|----------------------------------------------------------------------------------|
| Adamek et al   | 2000 | 1.0 T          | Body coil | No       | No                   | T2       | Size of common bile and pancreatic duct, the nature and degree of pancreatic duct obstruction, and accuracy in diagnosing pathological findings |
| Akanz et al    | 2000 | 1.5 T          | NA        | No       | No                   | T2 (HASTE & RARE) | NA increased arterial enhancement pattern, normal gland size and normal ductal morphology (Cambridge classification) |
| Baki et al     | 2006 | 1.5 T          | Four-element quadrature phased-array surface coil | No IV | No | T1, T2 | Increased arterial enhancement pattern, normal gland size and normal ductal morphology (Cambridge classification) |
| Bolog et al    | 2004 | 1.0 T          | Synergy body coil | No | NA  | T1, T2 | 1-5 score to identify pancreatic masses (definite benign = 1, probably benign = 2 etc.) |
| Fusani et al   | 2010 | 1.5 T          | Phased-array synergy body coil | Oral | No | T2 | Cambridge classification |
| Hellerhoff et al | 2002 | 1.5 T          | Phased-array synergy surface coil | Oral | No | T2 | Presence of 1 or more of the following features: main pancreatic duct dilatation in absence of structural obstruction, dilated side branches, intraductal stones, |
| Pamos et al    | 1998 | 1.5 T          | Body coil | NA | No | T2 | Presence of 1 or more of the following features: main pancreatic duct dilatation in absence of structural obstruction, dilated side branches, intraductal stones, |
| Pungnapong et al | 2007 | 1.5 T          | Phased-array surface coil | IV/Oral | No | T1, T2, (HASTE) | Presence of 1 or more of the following features: main pancreatic duct dilatation in absence of structural obstruction, dilated side branches, intraductal stones, |
Table 11  (continued)

Magnetic resonance imaging (MRI)

| Study                        | Year | Magnetic field | Coil type                  | Contrast | Secretin enhancement | Sequence | Scoring criteria                                                                 |
|------------------------------|------|----------------|----------------------------|----------|----------------------|----------|--------------------------------------------------------------------------------|
| Radowicz-Pietrzewska et al   | 2002 | 0.5 T          | Body coil                  | NA       | No                   | T2       | ductal irregularity, reduced T1 signal intensity, atrophy of pancreatic parenchyma and reduced secretory response to secretin administration |
| Schlaudraff et al            | 2008 | 1.0 T          | Dedicated quadrature torso phased-array coil | NA       | No                   | T2, T2 (HASTE) | Pancreatic duct stenosis/dilatation, side branch stenosis/dilatation, pseudocysts, extrapancreatic abscess. Based on observers' judgement |
| Sverko et al                 | 2011 | 1.0 T          | NA                         | IV       | No                   | T1, T2 (HASTE) | NA |
| Zhang et al                  | 2003 | 1.5 T          | NA                         | IV       | No                   | T1       | Signal intensity by gadolinium (presence of SIR less than 1.73 in the arterial phase) |
| Zuccaro et al                | 2009 | NA             | Phased-array-torso coil    | IV       | No                   | T1, T2, T2 (HASTE) | Mild CP: secretin-induced T2 intensity significantly reduced; side branch ectasia, mild ductal dilatation. Moderate CP: abnormal enhancement pattern on T1 after gadolinium administration. Severe CP: atrophy or diffuse/local enlargement of the gland, calcification, chronic pseudocysts |

Secretin-enhanced magnetic resonance imaging (sMRI)

| Study                        | Year | Magnetic field | Coil type                  | Contrast | Secretin enhancement | Sequence | Scoring criteria                                                                 |
|------------------------------|------|----------------|----------------------------|----------|----------------------|----------|--------------------------------------------------------------------------------|
| Hellerhoff et al             | 2002 | 1.5 T          | Synergy phased-array surface coil | IV       | Yes                  | T2       | Cambridge classification                                                        |
| Sai et al                    | 2008 | 1.5 T          | Phased-array multi coil     | IV       | Yes                  | NA       | Cambridge classification                                                        |
| Schlaudraff et al            | 2008 | 1.0 T          | Dedicated quadrature phased-array torso coil | NA       | Yes                  | T2, T2 (HASTE) | Pancreatic duct stenosis/dilatation, side branch stenosis/dilatation, pseudocysts, extrapancreatic abscess. Based on observers' judgement |
| Zuccaro et al                | 2009 | NA             | Phased-array torso coil     | IV       | Yes                  | T1, T2, T2 (HASTE) | Mild CP: secretin-induced T2 intensity significantly reduced; side branch ectasia, mild ductal dilatation. Moderate CP: abnormal enhancement pattern on T1 after gadolinium administration. Severe CP: atrophy or diffuse/local enlargement of the gland, calcification, chronic pseudocysts |

Ultrasonography (US)

| Study                        | Year | Transducer     | Scoring criteria                                      |
|------------------------------|------|----------------|--------------------------------------------------------|
| Buscali et al                | 1995 | NA             | NA                                                     |
| Danmaix et al                | 1980 | Unist/ Kretz combination 200 | NA                                                     |
| Gebel et al                  | 1985 | ADR 2130 Imager 2380 Sonoline 8000 | Duct abnormalities                                      |
| Gmelin et al                 | 1981 | Sono fluoroskop 1, unistad model 849 | Criteria for PC, CP and normal pancreas were extracted from literature |
| Kremer et al                 | 1977 | NA             | Rettammersayer specified examination technique        |
| Lawson et al                 | 1978 | 13 mm diameter 3.5 MHz/13 or 19 mm diameter 2.25 MHz | Identification of a mass, pseudocyst or generalized glandular enlargement with abnormal parenchymal echogenicity |
### Magnetic resonance imaging (MRI)

| Study                  | Year | Magnetic field | Coil type                  | Contrast                  | Secretin enhancement | Sequence                  | Scoring criteria                                                                 |
|------------------------|------|----------------|----------------------------|---------------------------|----------------------|---------------------------|----------------------------------------------------------------------------------|
| Lees et al             | 1979 | 2.5 MHz        | Appearance of pancreatic parenchyma and duct system/size and shape of the pancreas and from previous reports |
| Lin et al              | 1989 | SAL-90A 3.75 MHz | NA                         |                           |                      |                           |                                                                                  |
| Scarabino et al        | 1989 | NA             | NA                         |                           |                      |                           |                                                                                  |
| Swobodnik et al        | 1983 | Siemens imager 2300 linear array | Organ enlarged or atrophic dense structure, areas of scars or calcification (more echogenic), sonolucent areas only during acute inflammation, dilatation of the pancreatic duct system, symmetric contours, no smooth outlines |

### Computed tomography (CT)

| Study                  | Year | Scanner                  | Contrast | Scoring criteria |
|------------------------|------|--------------------------|----------|------------------|
| Buscail et al          | 1995 | NA                       | NA       |                  |
| Dramaix et al          | 1980 | OHIO nuclear - Delta Scan 50S | Oral      |                  |
| Fusari et al           | 2010 | Marcon MX8000 (four-detector row) | IV | 1-5 score to identify pancreatic masses (definitive benign = 1, probably benign = 2 etc.) |
| Gmelin et al           | 1981 | NA                       | NA       | Criteria for PC, CP and normal pancreas were extracted from literature |
| Indahl et al           | 1999 | Somatom Plus 4 helical scanner | IV |                  |
| Lammer et al           | 1980 | EM1-5005                 | Oral     | 3 stadia typical for CP |
| Pistolesi et al        | 1981 | Ohio-Nuclear Delta 50 scanner | NA | Overall enlargement of the pancreas or calcifications |
| Savarino et al         | 1980 | EM1-5005                 | Oral     | Parenchymal atrophy, pancreatic calcifications, pseudocysts or abscesses |
| Scarabino et al        | 1989 | NA                       | NA       | Atrophy of the organ (during acute inflammation: segmental enlargement) during acute phase; segments without clear outlines, cysts or calcifications and dense structure |
| Swobodnik et al        | 1983 | General Electric CT-T8000 | Oral/IV  |                  |

### Endoscopic ultrasonography (EUS)

| Study                  | Year | Scanner                  | Transducer | MHZ | Scoring criteria |
|------------------------|------|--------------------------|------------|-----|------------------|
| Albashir et al         | 2010 | NA                       | Radial     | NA  | 9 features; >4 diagnostic for CP |
| Brand et al            | 2000 | Olympus GF-UM 3GF-UM 2GF-UM | Radial     | NA  | Own criteria (increased parenchymal lobulations, calcification and/or ductal changes or focal lesion) |
| Buscail et al          | 1995 | Olympus EU-M3            | NA         | 7.5/12 |                  |
| Catalano et al         | 1998 | Olympus EU-M/EU-M20      | NA         | 7.5/12 | Wiersema criteria (11 features), own classification system |
| Chong et al            | 2007 | Olympus EU-M20/GF-UM130/GF-UM160/GF-UC30P/GF-UC140P/GF-UC140 | Radial     | NA  | 9 features; >3 diagnostic for CP |
| Conwell et al          | 2007 | NA                       | NA         | 9 features; >3 diagnostic for CP |
| Giovannini et al       | 1994 | Pentax FG-32-UA          | Linear     | NA  | Wiersema criteria (11 features) |
| Globrenner et al       | 1990 | Olympus EU-M20          | Radial     | 7.5/12 |                  |
| Lin et al              | 1989 | Olympus GF-EUM 2/GF-UM2  | Radial     | 7.5 MHz | NA                 |
| Nattermann et al       | 1993 | Olympus GF-UM-3/EU-M3   | NA         | 7.5/12 |                  |
| Pangraspong et al      | 2007 | Olympus GF-U160-AL5/GF-U140P | Radial & linear | NA  | MST criteria; >4 features diagnostic for CP |
| Pangraspong et al      | 2007 | Olympus GF-U140P/ UCT140-AL5 | Linear     | 7.5 MHz | MST criteria; >4 features diagnostic for CP |
Table 11  (continued)

Magnetic resonance imaging (MRI)

| Study            | Year | Magnetic field | Coil type | Contrast | Secretin enhancement | Sequence | Scoring criteria                        |
|------------------|------|----------------|-----------|----------|----------------------|----------|-----------------------------------------|
| Stevens et al    | 2009 | Olympus GF-UM-130/GF-UE-160/GF-UC-160P-OL5 | Radial & linear | NA       | 9 features; >4 diagnostic for CP |
| Tox et al        | 2007 | Olympus GF-UM20, Pentax EG-3620-UR/EG-3830-UT | NA       | NA       | Own criteria          |
| Trikudanathan    | 2016 | Olympus         | Linear    | 7.5 MHz  | Wiersema criteria (11 features) >4 is CP |
| Wiersema et al   | 1993 | Olympus EU-M3/EU-M20 | NA       | NA       | Wiersema criteria (11 features) >3 is CP |

Endoscopic retrograde cholangiopancreatography (ERCP)

| Study            | Year | Technical features | Scoring criteria                        |
|------------------|------|--------------------|-----------------------------------------|
| Adamek et al     | 2000 | NA                 | Own criteria                           |
| Buscail et al    | 1995 | NA                 | Own criteria (normal/moderate changes (3 abnormal side branches and normal main duct)/marked changes (side and main duct abnormalities)) |
| Gebel et al      | 1995 | NA                 | Deyhe criteria                         |
| Glasbrenner et al| 2000 | Olympus            | Cambridge classification               |
| Glmeln et al     | 1981 | NA                 | Criteria according to references       |
| Lamber et al     | 1980 | Olympus JFB        | Loffler criteria                       |
| Lawson et al     | 1978 | NA                 | Criteria according to references       |
| Parsi et al      | 2008 | NA                 | Cambridge classification               |
| Scarabino et al  | 1989 | NA                 | Own criteria (variation in diameter of the main duct in the whole organ (exception: segmental pancreatitis), cystic dilatation of side branches, kinking of the duct stones in canalicular structures, distension of the main duct) |
| Swobodnik et al  | 1983 | Olympus JFB-2/3    | NA                                     |
| Triller et al    | 1975 | NA                 | NA                                     |

NA not available
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