**‘’Role of radiological imaging in the diagnosis and characterisation of pancreatic cystic lesions: A systematic review’’**

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**Abstract:**

**Background:** To gather evidence from recent literature on the ability of radiological tests to predict a specific diagnosis in pancreatic cystic lesions and also, assess their aptitude in identifying pathological markers indicative of an aggressive biology.

**Methods:** An electronic literature search was conducted on MEDLINE using the following keywords: ‘’pancrea\*[tiab]’’AND ‘’cyst\*[tiab]’’ and the following terms ‘’computed tomography’’ OR ‘’CT’’ AND ‘’Magnetic resonance imaging’’ OR ‘’MRI’’ OR ‘’MRCP’’ AND ‘’Positron emission tomography’’ OR ‘’PET’’ OR ‘’Positron emission computed tomography’’ OR ‘’PET-CT’’

**Results:** Twenty two papers met the inclusion criteria. The accuracy of CT for reaching a specific diagnosis was 39-61.4 % while its accuracy for differentiating benign from malignant lesions was 61.9-80%. MRI showed a better accuracy in identifying a specific diagnosis of 50-86% while its accuracy in differentiating benign from malignant lesions was 55.6-87%. MRI was superior to CT scan in identifying septations, mural nodules and ductal communication. PET/CT showed a sensitivity of 85.7-100% in diagnosing malignancy with an accuracy of 88-95%.

**Conclusions:** The adequacy of CT imaging in full characterisation of pancreatic cysts is sub-optimal and therefore, a low threshold for supplementary imaging is advised. The use of PET/CT should be considered in high risk patients with equivocal findings.

**Keywords:** Pancreatic cysts, Computed tomography, Magnetic resonance imaging, Positron emission tomography

**Introduction:**

Cystic tumours of the pancreas constitute less than 10% of all pancreatic neoplasms[1]. Their incidental discovery is becoming a frequent source of referral to specialist pancreatic evaluation due to a myriad of reasons a) the wide spread and frequent use of abdominal cross-sectional imaging [2][3] b) the advancements in radiological technologies with improved image resolution[4] c) an increasingly senile population [5]. The identification of these lesions remain a burdensome encounter given the lack of stringent mechanisms to reliably differentiate benign and inflammatory lesions that usually possess a congenial disease course from those with borderline and frankly invasive lesions that usually warrant treatment in fit patients. Moreover, there are financial implications with increased health care costs for patients placed on periodic imaging surveillance.

Pancreatic cystic lesions (PCLs) include a spectrum of disease processes with heterogeneous pathological behaviours ranging from virtually benign lesions such as serous cystadenoma, lymphoepithelial cysts and inflammatory pseudocysts that could be observed safely in contrary to other lesions with inherent malignant potential such as mucinous cystic neoplasms (MCN), main duct/branched type intraductal papillary mucinous neoplasms (IPMN) and solid pseudo-papillary tumours (SPT). The diagnostic dilemma in this clinical entity is further fostered by the wide overlap in the morphological appearances of these cysts on radiological and endoscopic assessment [6][7] with the varied and inconclusive results of cyst fluid biochemical and tumour markers analysis that precludes definitive characterisation into a specific cyst subtype. The ramification of this diagnostic perplexity is reflected in the high incidences of diagnostic inaccuracy reported even among high volume centres with subspecialist pancreatic expertise [8][9].

Radiological assessment plays a pivotal role in the management and risk stratification of pancreatic mucinous cysts as dictated by the Fukuoka and the European experts consensus guidelines [10][11]. These recommendations are based on estimates of the likelihood of malignancy in these tumours based on the presence of high risk stigmata and worrisome features on radiological imaging with suggested management algorithms including the selective use of endoscopic ultrasound (EUS) and proposed timelines of follow up and recommendations of treatment.

The radiological modalities frequently used to image pancreatic cysts include computed tomography (CT), magnetic resonance imaging (MRI) or magnetic resonance cholangiopancreatography (MRCP), Positron emission tomography (PET) which is superseded by fused imaging with computed tomography (PET/CT) and often with a combination of these tests with a view to improve the overall diagnostic accuracy. The aim of this review was to examine the role of radiological imaging tests in the diagnosis and characterisation of PCLs. The reliability of these non-invasive tests in identifying specific morphological features that depict an aggressive tumour biology was also evaluated.

**Methods**

**Search strategy & Study selection:**

A systematic search was conducted on MEDLINE database in accordance with the Preferred Reporting Items for Systematic Reviews and Metanalysis (PRISMA) statement using the following keywords: [Pancreatic cysts] and/or [‘’pancrea\*’’AND ‘’cyst\*’’ti.ab] with a combination of the following terms ‘’computed tomography’’ OR ‘’CT’’ and ‘’Magnetic resonance imaging’’ OR ‘’MRI’’ OR ‘’MRCP’’ and ‘’Positron emission tomography’’ OR ‘’PET’’ OR ‘’Positron emission computed tomography’’ OR ‘’PET-CT’’ OR ‘’PET/CT’’. The search was restricted to studies reporting on adult patients in English language over the last 15 years (2002-2017).

The generated studies were assessed independently by two authors (EM and PG) after screening their titles and abstracts, the full text of potential studies were read to ensure relevance to the topic of interest. Included papers were required to report on the diagnostic ability of radiological imaging in diagnosing and characterising PCLs with a minimum series of 30 patients and available pathological/cytological confirmation of the findings as a reference diagnosis in the majority of cases. If there were any discrepancies between the two reviewers for the appropriateness of inclusion that was resolved after mutual discussion. Studies were excluded if they were case reports, review articles, conference proceedings or comments/letters to the author. The references of included papers were screened to identify additional relevant articles not captured on the electronic literature search.

**Data extraction:**

The data extracted from the included studies were logged on a data extraction sheet and included the following: publication year, study period, study design, sample size, pathology results, modalities of radiological imaging used, statistical parameters reported: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, cut off maximum standardised uptake value (SUV*max*) used to define malignant lesions in addition to the number of radiological reviewers. Peculiar imaging parameters pertinent to the identification of pathological predictors of aggressive biology such as the presence of septations, mural nodules and main pancreatic duct (MPD) communication were also retrieved and logged.

**Results:**

There were 22 publications eligible for analysis in this systematic review [12]–[33] (table1). These were of retrospective nature in 16 studies while 6 were prospective. The timeline of the included studies was between the years 1997-2016. The mean and median number of patients included per study were 77 and 59 respectively (range 30-154). Reference diagnosis was based on pathological assessment in 1445 patients (87.3%) and a combination of pathology/follow up in 210 patients (12.7%).

Some of the studies reported outcomes in small pancreatic cysts (diameter ≤3cm ) [24] or an IPMN cohort only [19][25][29], while some studies excluded patients with pancreatitis[24][26][27] and main/mixed type IPMN[14][17]. The majority of studies identified patients from a retrospective screen of a radiological database while two other studies identified patients from an EUS registry [32] and a radiological registry of patients who underwent both CT and MRI as a pre-requisite for inclusion[21].

The prevalence of benign and malignant cysts in the overall cohort was 65.6% *vs* 34.4% respectively with: 459 benign IPMN, 203 benign MCN, 196 SCA, 100 pseudocysts, 35 benign neuroendocrine tumour (NET), 88 other benign cysts while malignant tumours were: 227 malignant IPMN, 81 mucinous cystadenocarcinoma, 107 unspecified malignant mucinous cysts (IPMN/MCN), 55 adenocarcinomas with cystic degeneration (ACCD), 83 SPT, 12 malignant NET, 3 rare pancreatic malignancy subtypes (Table 2)

The majority of the studies reported on two or more radiological modalities with few studies reporting on the role of either CT scan [22][24][27][32] or MRI [12][20][21].

A wide spectrum of end points were evaluated which included the ability of the designated radiological test in reaching a specific diagnosis [13][14][15][17][20][26][27][28], diagnosis of benign *vs* malignant cysts[12][14][16][19][23][24][25][29][30][32][33] , differentiation between aggressive and non-aggressive PCLs [18][21][22][26][27][31], identification of pathological predictors of aggressive biology such as the presence of septations, mural nodules and ductal communication [12][13][15][17][20][21][22][26][31] and the differentiation of IPMN from others [31].

**Studies of Computed Tomography**

There were four studies reporting on the use of CT scan as a sole radiological imaging modality [22][24][27][32] while other papers compared its use with MRI [13][15][16][17][18][23][26][28][31] and/or PET scan [15][19][25][29][30][33]. These studies reported on series of patients within a study timeline between 2000-2016. The imaging analysis was conducted by one to three radiologists blinded to clinical and previous imaging findings. There was a variety in the type and phases of CT scanning used for image acquisition in some studies with the use of either 16 or 64 mutidetector CT [22][30], 4 or 16 multi-slice CT [25] or a single portovenous phase CT [22][26].

The ability of CT scan to reach a specific diagnosis was 17.3% [13],61.4%[14], 53.9%[15], 41%[17] ,39% [27], 40-44% [28] while its accuracy in differentiating benign from malignant lesions was 83.1%[14], 77% [16], 61.9-76.2 [23], 76% -78.8% [24], 80%[33] with a PPV and NPV for identifying malignancy of 86.8%[14], 58.1-73.9 [23], 100% [24], 73% [33] and 63.6%[14], 70.3-76.9 [23],76% [24], 83% [33] respectively .The accuracy for the prediction of aggressive lesions was 48% [18], 75–78% [26], 61% [27], 71%[32] while a single study reported an accuracy of 77% in differentiating benign from malignant IPMN [25].

The sensitivity for diagnosing the presence of septations was 34.6%[13], 54.3%[15] and 73.9% [26] while the accuracy for detection of mural nodules was 5.8%[13], 42.9%[15]. The accuracy in delineation of ductal communication was 85.7%[15] with an area under ROC curve 0.774-0.790 in another study[31]. The inter-observer agreement between reporting radiologists was moderate-good in the diagnosis of benign *vs* malignant PCLs[23][30] and fair in the prediction of markers of aggressiveness[27].

**Studies of Magnetic Resonance imaging**

There were three studies reporting on the use of magnetic resonance techniques as the only radiological imaging modality[12][20][21] while some papers compared its use with CT scan[13][15][16][17][18][23][26][28][30] and PET/CT [16].These studies reported on series of patients in the timeline between 2002-2016 with up to 4 blinded radiologists reporting on MRI images in one study [20].

The accuracy of MRI to reach a specific diagnosis was 20.3%[13], 55.6%[15], 86%[17], 59-63%[20],50% [28], while its accuracy in differentiating benign from malignant lesions was 74.5%[12], 87%[16] and 55.6-76.2% with a PPV 57.1-81.0% and NPV 74.3-78.0% in a separate study[23]. Kim reported a sensitivity and specificity of 94% and 75% respectively for MRI in the prediction of aggressive lesions[21]. Sainani reported an accuracy of 75–78% in the diagnosis of these lesions while Khashab reported an inferior accuracy of only 34% [18]. Song reported a 96.8% sensitivity and 90.8% specificity of MRI in differentiating IPMN from other PCLs [31].

The accuracy for diagnosing the presence of septations was 58.8% [15], 91%[26] while the sensitivity for detection of mural nodules was 57.1%[12], 6.3%[13], 55.6%[15], 9%[17], 33.3%[26], ductal communication was established in 100% of the cases with IPMN in a study [26] which stands in agreement with findings from another study by Song et al with Az value of 0.916 to 0.949 on ROC curve analysis [31].

**Studies of Positron Emission Tomography**

There were 4 studies examining the use of hybrid PET/CT [16][19][25][29], a single study on the use of PET [33] and another study on the utility of PET separately followed by super-imposed CT images (sequential PET/CT) in the same series [30]. The number included per individual study varied between 30 and 64 patients, the studies reported on patients investigated in the period between 1998-2013. The cut off value SUV*max* for diagnosing a malignant lesion was 2.0[19], 2.5[28][32] and 3.6 [16].

The utility of PET was employed to differentiate between benign from malignant cysts[16][30][33] or to differentiate benign from malignant IPMN [19][25][29].

The accuracies for differentiating benign from malignant cysts were 94% for PET/CT [16], 94% for PET[33] with a sensitivity and specificity of 100% ,92% vs 94%,94% respectively. Tann reported inferior results with the use of PET only compared to PET/CT (sensitivity of 57.1%, specificity 65.2%) [30].

The reported accuracies of PET/CT for the differentiation between benign and malignant IPMN were comparable 88%[16],94% [25], 94% [29] with sensitivities and specificities of 88%,100% and 88%,87% respectively [19][25].

**Studies with direct imaging comparison**

Three studies reported a modest improved accuracy in reaching a specific diagnosis with the use of MRI over CT scan: 20.3% *vs* 17.3% [13] , 55.6 % *vs* 53.9 % [15] , 50% *vs* 40-44%[28] while Duconseil et al study showed a clear superior diagnostic accuracy of 86% *vs* 41%[17].

The respective sensitivities of CT and MRI scan in the distinction between benign and malignant cysts were comparable in two studies 83% *vs* 83%[16] and 57.7-69.2% *vs* 65.4-76.9% [23] while Kauhanen et al reported better accuracy with the use of MRI 87% *vs* 77%[16]. MRI showed better ability than CT scan in the diagnosis of septations with sensitivities of 46.9% *vs* 34.6%[13] , 58.8% *vs* 54.3%[15] and 91% *vs* 73.9% [26].

MRI had better sensitivity for identifying mural nodules in comparison to CT in two studies: 9% *vs* nil [17] and 55.6% *vs* 42.9% [15]. MRI showed higher sensitivity in establishing ductal communication 100% *vs* 85.7% [26] and also in the distinction of IPMN from others with a sensitivity of 96.8% *vs* 80.6% [31] and better interobserver agreement in comparison to CT scan [31].

There were four studies comparing the use of PET technology in the diagnosis of malignant cysts with two of the publications from the same institution [29][33]. The accuracy of PET/CT was superior to MRI and CT scan in identifying malignant cysts 94% *vs* 87% *vs* 77% respectively[16] while in another study PET/CT had accuracy of 94% vs 77% for that of CT scan [25]. Sperti et al reported better outcomes with PET/CT over cross sectional imaging in a cohort of patients imaged with a mix of CT and MRI of 95% vs 72% respectively [29].

**Discussion:**

The wide spread availability and short scanning time has made CT scan the preferred modality for abdominal imaging in routine clinical practice. This is reflected in the number of studies included in this review reporting on its use in the characterisation of PCLs. The accuracy of CT performance in establishing a specific diagnosis was low with a diagnostic accuracy ranging between 39-61.4%. Duconseil et al concluded that CT use is not adequate for full characterisation and should be supplemented by the use of either MRI or EUS [17]. This view is supported by the findings from Khashab et al as the use of EUS-fine needle aspiration (FNA) in their study had an incremental value of 36% in helping to reach the correct diagnosis after imaging with CT scan [18]. Of note, two of the included studies with direct comparison between CT and MRI in the same cohort didn’t not show a substantial benefit with the use of MRI over CT scan in establishing a specific diagnosis with accuracies of 55.6% *vs* 53.9%[15] and 50% *vs* 40-44% [28] respectively while a third study showed a clear advantage with an accuracy of 86% *vs* 41% [17].

In addition, CT studies has shown wide-ranged results in its ability differentiation between benign and malignant cysts with sensitivities of 36.3-94% and specificities of 73-100%. This disparity is likely to be induced by the difference in the selection criteria and case mix in the included studies as well as the type and phase of scanning used. Sainani et al showed a better sensitivity with the use of a focused pancreatic protocol in comparison with the use of a single phase examination in the elucidation of morphological features although the difference did not reach statistical significance (*p*-value=0.09)[26].

Previous reports on a large cohort of patients has shown a prevalence of 1.2-2.6% for incidental PCLs with the use of CT [2][34] while that of MRI was shown to be of 19.6% in another study [35]. This discrepancy demonstrates the superiority of MRI in the detection of pancreatic cysts. The use of MRI is considered to be advantageous given its higher image resolution that result in better delineation of cyst morphology, multiplicity, communication with the MPD which is of utmost importance in the differential diagnosis of mucinous lesions [36][37]. The use of MRI also negates the potential risks with repeated radiation exposure in cases where long term pancreatic surveillance is indicated. The accuracy of MRI to predict a specific diagnosis in the included studies varied between 50-86% and its ability to identify markers of aggressive behaviour was superior to CT scan [15][17][26]. Sainani et al showed sensitivities of 100% and 73% with the use of MRI in the detection of ductal communication and septations respectively [26].

Song et al found better sensitivity with MRI over CT in differentiating IPMN from others 96.8% vs 80.6%[31]. A clear advantage is demonstrated in the sensitivity of MRI in identifying septations, mural nodules and ductal communication[17][26] , this support its use whenever there is a high index of suspicion of a mucinous lesion and in cases where confirmation of diagnosis by surgical resection is not advised. The main draw-back with MRI imaging is its low spatial resolution and inadequacy in overall disease staging in comparison to triple phase CT.

There is a paucity in the number of studies reporting on the role of PET imaging in the assessment of PCLs. The results of these studies report on findings from single institutional series with a limited number of patients. The majority of these studies has shown better sensitivities and diagnostic accuracies in comparison to CT scan .The use of fused PET images with CT scan results in a better anatomic precision to the areas of avid FDG uptake and helps in better staging. The findings from Tann et al [30] has shown an inferiority of PET in comparison to PET/CT which stipulate that PET should always be combined with CT to improve the diagnostic outcome which is currently the incorporated technique in new generation scanners. A previous metanalysis of three studies reporting on the malignant potential of IPMN (n=106) has shown a pooled sensitivity and specificity of 0.968 (95% CI 0.900–0.995) and 0.911 (95% CI 0.815–0.998) for PET/CT which was higher to pooled sensitivity and specificity for a comparable number of patients imaged with CT/MRI which was 0.809 (95% CI 0.714–0.883) and 0.762 (95% CI 0.654–0.851) respectively [38].

The limitations with the use of PET/CT are induced by the false positive results with increased FDG uptake in inflammatory lesions [39]–[41] and the fear of false negatives in hypometabolic tumours. The advent of dual phase PET/CT in the absence of cancer specific radiotracers might provide the solution for this drawback as benign lesions show decreased FDG uptake in the delayed phase while the SUV*max* increases further secondary to up-regulation of glucose consumption and transport in malignant lesions[19]

Despite the overall encouraging results with the use of PET technology in these studies there is insufficient evidence to recommend its routine use in the absence of high quality studies. The benefits of PET/CT in the management of patients with suspected pancreatic cancer have been investigated by our group in a multicentre diagnostic accuracy trial which contained a subset of patients with pancreatic cysts (The PET-PANC trial). It showed an improved clinical staging over CT based diagnostic work-up and prevented futile laparotomies in 20% of patients scheduled for surgery and influenced the management plans of 45% of the cases included in the trial [42], the full results and recommendations are still awaited and hopefully will explore the future utility of PET/CT in this group .

There were a number of limitations in the evidence obtained from studies included in this systematic review. The majority of the included studies were retrospective case series from single institutions with an evident selection bias. Some of the series excluded patients with pancreatitis or IPMN[17][24][26][27], Kim et al reported on a subset of patients who underwent both CT and MRI as a mandatory requirement for inclusion [21]. Gerke et al identified patients from a retrospective review of EUS registry [32] while the series published by Sperti et al[33] included a third of patients with suspected IPMN which are a subset with a higher malignant potential at baseline. The outcomes of patients who did not proceed with operative intervention following initial diagnosis and were followed up was not reported and therefore it’s difficult to speculate the ultimate fate of these lesions.

The experience and interobserver agreement of radiologists varied in the published series, although the blinding effect to clinical and previous imaging findings in the study design was prudent in eliminating reader’s bias in image interpretation but it is likely to have impacted the overall diagnostic accuracy. The optimal cut off for SUV*max* in diagnosing malignancywas inconsistent among studies reporting on PET scans. Sperti et al considered an SUV*max* of 2.5 positive in his two reports [29][33] , Saito et al used an SUV*max* 2.0 to diagnose malignancy [19] while Kauhanen et al identified an SUV*max* of 3.6 to have the best discriminative value between benign and malignant lesions[16]. These limitations along with the heterogeneity of the studies prevents sensible pooling of the existing data to draw any valid conclusions from the included studies.

The use of EUS has become increasingly popular as an adjunctive tool to radiological imaging to aid in further characterisation of PCLs. Its ability to differentiate between benign and malignant lesions based on morphological features alone is sub-optimal in the absence of classical appearances for a particular cyst subtype but its diagnostic accuracy is further improved by cyst fluid analysis via EUS-FNA [43][44][45]. The role of EUS has not been addressed formally in this review as it’s an adjunct to radiological imaging rather than a primary imaging tool and therefore its role is currently dictated by the experts guidelines recommendations[10][11]

With the increasing rate of PCLs diagnosis and the feared morbidities and mortalities associated with pancreatic resections, a robust and stringent mechanism in full characterisation of PCLs is required. The evidence required to validate which radiological modality is superior in which particular subset would necessitate a standardised comparison of the diagnostic yield for each modality separately and in conjunction. The included patients should have a sufficient longitudinal follow up given the slow growth rate for the majority of these tumours. In addition, the technological innovation over the course of time together with the progression in identifying novel molecular biomarkers, will hopefully continue to add on to the existing diagnostic accuracies of these imaging techniques.

**Conclusions:**

The management of pancreatic cysts identified on CT scan should be interpreted in light of available clinical and biochemical findings at presentation. The treatment course of cysts that are definitively characterised at this stage should be modelled according to the natural history peculiar to the cyst subtype. Lesions with suspicious or inconclusive features warrant further evaluation with either MRI or EUS to characterise them further. The use of PET/CT should be considered in cases which remain equivocal and in high risk patients whenever active treatment is contemplated.

**Conflicts of Interest**

CMH received grants from Cancer Research UK and the Royal College of Surgeons, the rest of the authors declare no conflicts of interest.

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**Appendix:**

Figures and Tables

Records identified through database searching
(n =1530)

## Identification

Records after duplicates removed (n=28)

N

Records excluded based on title/abstract

(n=1449)

N

Records screened for potential inclusion

(n=1502)

N

## Screening

Full-text articles excluded
(n=31)

-Irrelevant findings (n=25)

-Pathological confirmation of diagnosis in <50% of the cases (n=2)

-Study cohort <30 patients (n=4)

Full-text articles assessed for eligibility
(n = 53)

## Eligibility

Studies included in the systematic review

(n= 22)

## Included

 **Figure1:** Flow diagram of study selection

## Included

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| ***Author*** | ***Country*** | ***Year Published*** | ***Study period*** | ***Study Type*** | ***No of patients*** | ***Radiological Imaging***  |
|  |  |  |  |  |  |  |
| **Hwang et al** | Korea | 2017 | 2010-2013 | Retrospective | 55 | MRI |
| **Du et al** | China | 2017 | 2015-2016 | Prospective | 68 | CT, MRI |
| **Jang et al** | South Korea | 2015 | 1998-2011 | Retrospective | 318 | CT |
| **Lu et al** | China | 2015 | 2011-2013 | Prospective | 31 | CT, MRI, PET/CT |
| **Kauhanen et al** | Finland | 2015 | 2005-2011 | Prospective | 148 | CT, MRI |
| **Duconseil et al** | France | 2013 | 2006-2010 | Retrospective | 154 | CT,MRI |
| **Khashab et al** | USA | 2013 | 2004-2012 | Retrospective | 48 | PET/CT |
| **Saito et al** | Japan | 2012 | 2007-2010 | Prospective | 62 | MRI |
| **De Jong et al** | Netherland | 2012 | 2006-2009 | Retrospective | 51 | MRI |
| **Kim et al** | Korea | 2011 | 2006-2009 | Prospective | 114 | CT |
| **Sahani et al** | USA | 2011 | 2001-2008 | Retrospective | 63 | CT, MRI |
| **Lee et al** | Korea | 2011 | 2004-2009 | Retrospective | 33 | CT |
| **Pongpornsub et al** | Thailand | 2010 | 2005-2009 | Retrospective | 31 | CT, PET/CT |
| **Hong et al** | Korea | 2009 | 2000-2007 | Retrospective | 30 | CT, MRI |
| **Sainani et al** | USA | 2008 | 2004-2007 | Retrospective | 48 | CT |
| **Fisher et al** | USA | 2008 | 1997-2003 | Retrospective | 70 | CT, MRI |
| **Visser et al** | USA | 2007 | 1998-2005 | Prospective | 64 | PET/CT |
| **Sperti et al** | Italy | 2007 | 2002-2004 | Retrospective | 30 | CT, PET/;CT |
| **Tann et al** | USA | 2007 | 2002-2006 | Retrospective | 53 | CT, MRI |
| **Song et al** | Korea | 2006 | 1998-2003 | Retrospective | 66 | CT |
| **Gerke et al** | USA | 2005 | 2000-2003 | Prospective | 50 | CT, PET |
| **Sperti et al** | Italy | 2005 | 2000-2003 | Prospective | 50 | CT, PET |

**Table 1:** Studies included in the systematic review

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **total no** |  |  |  |  |  |  |  |  |  |  |  |  |
|  | **Benign/Pre malignant** |  | **Malignant (including high grade dysplasia)** |  |
|  |  | ***IPMN*** | ***MCN*** | ***SCA*** | ***Pseudocyst*** | ***NET*** | ***other*** |  | ***IPMN*** | ***MCA*** | ***ACCD*** | ***SPT*** | ***NET*** | ***Other*** |
|  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |
| **Hwang** | 55ὰ | 35(63.6%) | 6(11%) | - | - | - | - |   | 12(21.8%) | 2(3.6%) | - | - | - | - |
| **Du** | 68 | 6(8.8%)∂ | 23(33.8%) | 27(39.7%)∂ | - | 1(1.5%)∂ | - |   | - | 2(2.9%) | - | 9(13.2%) | - | - |
| **Jang** | 318 | 114(35.8%) | 49(15.4%) | 62(19.5%) | 9(2.8%) | - | - |   | 32(10%) | 5(1.6%) | 5(1.6%) | 31(9.7%) | 5(1.6%) | - |
| **Lu**  | 108 | 11(10%)∂ | - | 26(24%) | - | - | - |   | - | 46(43%) ∂ | - | 25(23%) | - | - |
| **Kauhanen**  | 22 | 2(9%)∂ | 2(9%)∂ | 5(20.8%) | 5(22.7%) | 1(4.5%)∂ | 2(9%) |   | - |  | 3(13.6%) | 1(4.5%) | - | 1(4.5%) |
| **Duconseil**  | 148 | 77(52%) | 38(26%) | 13(9%) | 7(5%) | 8(5%)∂ | 1(0.5%) |   | 3(2%) | - | - | 1(0.5%) | - | - |
| **Khashab**  | 154 | - | - | - | - | 15(10%) | 21(13.6%) |   | 107(69.4%)∂ | 10(6.4%) | 1(0.6%) | - | - |
| **Saito**  | 48 | 16(33.3%) | - | - | - | - | - |   | 32(66.7%) | - | - | - | - | - |
| **Kim**  | 51 | - | - | 3(5.9%) | 10(19.6%) | - | 2(4%) |   | 32(62.7%) | 1(1.9%) | 1(1.9%) | 1(1.9%) | 1(1.9%) | - |
| **De Jong** | 32 | 18(56.3%)∂ | 8(32%)∂ | 1(3%) | 4(12.5%) | 1(3%)∂ | - |   | - | - | - | - | - | - |
| **Sahani**  | 130¥ | 38(29.2%) | 22(16.9%) | 6(4.6%) | 4(3.1%) | - | 16(12.3%) |   | 33(25.4%) | 5(3.8%) | 4(3.1%) | 2(1.5%) | - | - |
| **Lee**  | 63 | 14(22.2%) | 5(7.9%) | 8(15.9%) | 5(7.9%) | - | 5(7.9%) |   | 7(11.1%) | 2(3.2%) | 11(17.5%) | 5(7.9%) | 1(1.5%) | - |
| **Pongpornsub**  | 33 | 2(6%) | 5(15.2%) | 4(12.1%) | 16(48.5%) | - | - |   | 3(9.1%) | - | - | 3(9.1%) | - | - |
| **Hong**  | 31 | 15(48.4%) | - | - | - | - | - |   | 16(51.6%) | - | - | - | - | - |
| **Sainani**  | 38 | 22(57.9%) | 6(15.8%) | - | - | - | 6(15.8%) |   | 4(10.5%) | - | - | - | - | - |
| **Fisher**  | 48 | 9(18.8%)∂ | 8(16.7%)∂ | 7(14.6%) | 6(12.5%) | 5(10.4%)∂ | 1(2.1%) |   | - |  | 11(22.9%) | 1(2.1%) |  | - |
| **Visser**  | 70 | 7(10%) | 13(18.6%) | 11(15.7%) | 4(5.7%) | 2(2.9%) | 8(11.4%) |   | 7(10%) | 10(14.3%) | 2(2.9%) | 1(1.4%) | 3(4.3%) | 2(2.9%) |
| **Sperti**  | 64ὰ | 21(32.8%) | - | - | - | - | 17(26.6%) |   | 27(42.2%) | - | - | - | - | - |
| **Tann**  | 30 | 15(50%) | 2(6.7%) | - | 5(16.7%) | - | 1(3%) |   | 6(20%) | 1(3%) | - | - | - | - |
| **Song** | 53 | 31(58.5%) | 4(7.5%) | 11(20.7%) | 6(11.3%) | 1(1.9%) | - |   | - | - | - | - | - | - |
| **Gerke**  | 41ὰ | - | 9(22%) | 2(4.9%) | 14(34.1%) | - | 4(9.7%) |   | 3(7.3%) | - | 7(17%) | - | 1(2.4%) | 1(2.4%) |
| **Sperti**  | 50ὰ | 8(16%) | 5(10%) | 10(20%) | 5(10%) | 1(2%) | 4(8%) |   | 8(16%) | 5(10%) | 1(2%) | 2(4%) | 1(2%) | - |

**Table 2:** Overview of histological diagnosis of included studies; ∂ = Variation between benign/malignant not specified, ὰ= Based on a combination of pathology/FU, ¥ 130 cysts in 114 patients

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ***Outcome studied*** | ***Author*** | ***Publication date*** | ***No of patients*** | ***Sensitivity*** | ***Specificity*** | ***PPV*** | ***Accuracy*** |
| **Specific diagnosis** | Du | 2017 | 68 | - | - | - | 17.30% |
|  | Jang | 2015 | 318 | - | - | - | 61.40% |
|  | Lu  | 2015 | 108 | 54.70% | 82.20% | 76.40% | 53.90% |
|  | Duconseil | 2015 | 148 | - | - | 70% | 41% |
|  | Fisher | 2008 | 48 | - | - | - | 39% |
| **Diagnosis in small <3cm cyst** | Visser | 2008 | 70 | - | - | - | 40-44% |
| **Benign *vs* Malignant cyst** | Sainani | 2009 | 30 | - | - | - | 39.5-44.7% |
|  | Jang | 2015 | 318 | 83.10% | 70% | 86.80% | - |
|  | Kauhanen  | 2015 | 31 | 83% | 76% | 45% | 77% |
|  | Lee | 2011 | 63 | 57.7-69.2% | 63.9-83.3% | 58.1-73.9% | 61.9-76.2% |
|  | Pongpornsub | 2011 | 33 | 36.30% | 100% | 100% | 76 -78.8% |
|  | Tann | 2007 | 30 | 66.7-71.4% | 87-90.5% | - | - |
|  | Gerke | 2006 | 41 | 57% | 91% | - | - |
| **Benign *vs* Malignant IPMN** | Sperti | 2005 | 50 | 94% | 65% | 73% | 80% |
| **IPMN *vs* others** | Hong | 2010 | 31 | 94% | 60% | - | 77% |
| **Prediction of aggressive lesions** | Song | 2007 | 53 | 80.60% | 86.40% | 89.30% | 0.85-0.88\* |
|  | Khashab | 2013 | 154 | 48.30% | 78.90% | 93.50% | 48% |
|  | Sahani | 2011 | 114 | - | - | 80% | - |
| **Presence of Septations** | Sainani | 2009 | 30 | 75-78% | - | 25% | 71-84.2% |
|  | Du | 2017 | 68 | 34.60% | - | - | - |
|  | Lu  | 2015 | 108 | 54.30% | - | - | - |
| **Mural Nodules** | Sainani | 2009 | 30 | 73.90% | - | - | - |
|  | Du | 2017 | 68 | 5.80% | - | - | - |
| **Ductal communication** | Lu  | 2015 | 108 | 42.90% | - | - |  |
|  | Sainani | 2009 | 30 | 85.70% | - | - | - |
|  | Song | 2007 | 53 | - | - | - | 0.77-0.79\* |

**Table 3:** Overview of Computed Tomography studies in characterising pancreatic cysts, *\*Calculation based on ROC curve analysis*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ***Outcome studied*** | ***Author*** | ***Publication date*** | ***No of patients*** | ***Sensitivity*** | ***Specificity*** | ***PPV*** | ***Accuracy*** |
| **Specific diagnosis** | Du | 2017 | 68 | - | - | - | 20.30% |
|  | Lu  | 2015 | 108 | 56.30% | 80.60% | 85.70% | 55.60% |
|  | Duconseil | 2015 | 148 | - | - | 87% | 86% |
|  | De Jong | 2012 | 62 | - | - | - | 59-63% |
|  | Visser | 2008 | 70 | - | - | - | 50% |
| **Diagnosis in small <3cm cyst** | Sainani | 2009 | 30 | - | - | - | 39.5-44.7%  |
| **Benign vs Malignant cyst** | Hwang | 2017 | 55 | 57.1%,64.3% | 78.0% ,80.5% | 50% | 75% |
|  | Kauhanen | 2015 | 31 | 83% | 82% | 63% | 87% |
|  | Lee | 2011 | 63 | 65.4-76.9% | 58.3-88.9% | 57.1-81.0% | 55.6-76.2% |
| **IPMN vs others** | Song | 2007 | 53 | 96.80% | 90.80% | 92.30% | 0.93-0.99\* |
| **Prediction of aggressive lesions** | Khashab | 2013 | 154 | 34% | 100% | 100% | 34% |
|  | Kim | 2012 | 51 | 94% | 75% | - | - |
|  | Sainani | 2009 | 30 | 78–86% | - | - | 78.9-81.6% |
| **Presence of Septations** | Du | 2017 | 68 | 46.90% | - | - | - |
|  | Lu  | 2015 | 108 | 58.80% | - | - | - |
|  | Sainani | 2009 | 30 | 91% | - | - | - |
| **Mural Nodules** | Hwang | 2017 | 55 | 57.10% | 80.50% | 50% | 74.50% |
|  | Du | 2017 | 68 | 6.30% | - | - | - |
|  | Lu  | 2015 | 108 | 55.60% | - | - | - |
|  | Duconseil | 2015 | 148 | 9% | - | - | - |
| **Ductal communication** | Sainani | 2009 | 30 | 100% | - | - | - |
|  | Song | 2007 | 53 | - | - | - | 0.92 to 0.95\* |

**Table 4:** Overview of Magnetic Resonance studies in characterising pancreatic cysts *\*Calculation based on ROC curve analysis*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ***Outcome studied*** | ***Author*** | ***Publication date*** | ***No of patients*** | ***Sensitivity*** | ***Specificity*** | ***PPV*** | ***Accuracy*** |
| **Benign *vs* Malignant cyst** | Kauhanen | 2015 | 31 | 100% | 92% | 75% | 94% |
|  | Tann | 2007 | 30 | 85.70% | 91.30% | - | - |
|  | Sperti | 2005 | 50 | 94%\* | 94%\* | 89%\* | 94%\* |
| **Benign *vs* Malignant IPMN** | Saito | 2013 | 48 | 88% | 88% | - | 88% |
|  | Hong | 2010 | 31 | 100% | 87% | - | 94% |
|  | Sperti | 2007 | 64 | 92% | 97%\* | 96% | 95% |
|  |  |  |  |  |  |  |  |

 **Table 5:** Overview of Positron Emission-Computed tomography studies in characterising pancreatic cysts *\*calculation based on PET scan*



**Table 6:** Overview of studies with direct imaging comparison *\*Calculation based on ROC curve analysis*