Pancreatology 19 (2019) 2–9

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

Systematic review and meta-analysis: Prevalence of incidentally detected pancreatic cystic lesions in asymptomatic individuals

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ARTICLE INFO

Article history:
Received 11 September 2018
Received in revised form
18 November 2018
Accepted 27 November 2018
Available online 28 November 2018

Keywords:
Pancreatic cyst
Prevalence
Incidental
Mucinous

ABSTRACT

Background & aims: Pancreatic cystic lesions (PCLs) are frequent incidental findings. As most PCLs require costly diagnostic evaluation and active surveillance, it is important to clarify their prevalence in asymptomatic individuals. We therefore aimed at performing a systematic review and meta-analysis to determine it.

Methods: a systematic search was conducted and studies meeting inclusion criteria were included. The prevalence of PCLs was pooled across studies. A random effect model was used with assessment of heterogeneity.

Results: 17 studies, with 48,860 patients, were included. Only 3 were prospective; 5 studies were conducted in the US, 7 in Europe, 4 in Asia and 1 in Brazil. The pooled prevalence of PCLs was 8% (95% CI 4–14) with considerable heterogeneity ($I^2 = 99.5\%$). This prevalence was higher in studies of higher quality, examining older subjects, smaller cohorts, and employing MRCP (24.8% vs 2.7% with CT-scan). The pooled rate of PCLs was four times higher in studies conducted in the US than in Asia (12.6% vs 3.1%). 7 studies reported the prevalence of mucinous lesions, with a pooled rate of 4.3% (95% CI 2–10; $I^2 = 99.2\%$), but of 0.7% only for worrisome features or high risk stigmata.

Conclusion: The rate of incidentally detected PCLs is of 8%. Mucinous lesions are the most common incidentally detected PCLs, although they rarely present with potential indication for surgery. The observed different rates in the US and other geographic Areas suggest that different protocols might be necessary to help balancing costs and effectiveness of follow-up investigations in asymptomatic subjects.

Introduction

Pancreatic cystic lesions (PCLs) are frequent incidental findings diagnosed during abdominal ultrasonography or cross-sectional imaging. The increasingly widespread use and the improved detection accuracy of imaging tests have led to an epidemic of PCLs with prevalence rates reported as high as 40%, in a clinical scenario that might be considered that of a "technology-related disease" [1].

PCLs comprise different entities, each of them with peculiar biological behavior ranging from benign to premalignant or frankly malignant neoplasms [2]. Mucinous pancreatic cystic lesions are associated with a potential risk to develop malignancy and deserve either an active treatment or surveillance [3], while serous cysts are benign lesions [4]. Intraductal Papillary Mucinous Neoplasms (IPMNs) represent the most common PCL. According with current guidelines [5–8] they should be treated surgically in the presence of major symptoms, morphological changes often defined as high risk stigmata (HRS), or when malignancy is demonstrated by cytology. In the presence of an IPMN of the branch ducts (BD-IPMN) with size exceeding 30 mm or thickened and enhanced cystic wall or non-enhancing mural nodule or moderate main duct dilatation (5–9 mm) or in presence of abrupt change in pancreatic duct caliber with distal gland atrophy (characteristics usually named worrisome features –WF–), surgery might be considered and endoscopic ultrasound (EUS) with or without aspiration/biopsy is

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https://doi.org/10.1016/j.pan.2018.11.014
1424-3903/

indicated to better analyze the morphology/cytology of the PCL, in order to stratify the risk of malignancy.

However, the vast majority of IPMNs are BD-IPMNs without any of the above mentioned signs and in patients who would be fit for surgery, these lesions require follow-up by means of Magnetic Resonance Imaging (MRI) with contrast medium and cholangiopancreatography (MRCP) or with EUS with specific time intervals.

In a recent meta-analysis [9] the risk of malignant transformation of these lesions has been calculated to be equal to 7/1000 per year, and despite the need to maintain surveillance in the long-term is debated [10], recent data suggest that it cannot be stopped after 5 years [11–13].

The surveillance of PCLs, and particularly of IPMNs, has become a challenge for health\insurance systems considering their substantial costs and resource burden. Moreover, the sustainability of a surveillance policy depends on the actual prevalence of PCLs in the general population. It is, therefore, important to clarify as accurately as possible the prevalence of PCLs, and particularly of mucinous cystic lesions, in subjects without a history of pancreatic disease. However, these data are sparse, heterogeneous, with a wide range of prevalence rates, but no systematic and comprehensive analyses examined this issue. The present systematic review and meta-analysis aimed at evaluating the prevalence of incidentally diagnosed PCLs, particularly mucinous lesions.

Materials and methods

Search strategy

A computerized literature search of the MEDLINE database did not identify any publication related to systematic review on the prevalence of incidentally diagnosed pancreatic cystic lesions in healthy subjects or in asymptomatic population. A MEDLINE search was therefore run until January 2018. Specific search terms were: *(pancreatic cyst OR pancreatic cysts OR pancreatic cystic lesions OR intraductal papillary mucinous neoplasia OR pseudocyst OR pancreatic mucinous cyst) AND (radiological technique OR magnetic resonance OR multi-detector OR radiological imaging OR EUS OR ecoendoscopic ultrasound OR tomography OR MRI OR cholangiopancreatography OR abdominal imaging OR US OR MDCT OR CT) AND (occasional OR incidental OR incidence OR prevalence OR accidentally OR asymptomatic)*. The methodology was developed from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [14].

The titles of all identified articles were screened to ascertain their relevance. Abstracts and/or full texts of selected potentially relevant papers were evaluated. Possible further articles were identified by hand-searching reference lists in order to identify potentially relevant studies, missed at our search. In the case of duplicate publications, the most recent or the most informative one in terms of number of cases or available data, was included.

Inclusion/exclusion criteria

Studies were considered if they met the following criteria: 1) written in English; 2) inclusion of patients without history of pancreatic disorders or symptoms suggestive for them; 3) all patients underwent second or third level imaging (CT-scan, MRI ± MRCP or EUS) not to investigate primarily the pancreatic gland; 4) data about prevalence and characteristics of cystic lesions were reported.

Studies were excluded if they were available as abstract only because the abstracts did not allow full data extraction. We also excluded: 1) case reports or small case series of <20 cases; 2) papers investigating the prevalence of pancreatic cystic lesions in specific subset of patient, such as liver/pancreas transplanted patients or cluster of patients with specific type of neoplastic disease.

Two independent reviewers (G.Z. and M.S.) carried out study identification and selection and resolved their disagreements by discussion or by consulting a third reviewer (G.C.). Excluded studies and the reasons for exclusion were recorded.

Data extraction and quality assessment

Two reviewers (G.Z. and M.S.) independently extracted the data from each study and resolved their disagreements by discussion or by consulting a third reviewer (G.C.).

From the studies that met the eligibility criteria, the following data were collected: 1) study: publication year, study design, study location; 2) patients: total number of asymptomatic patients evaluated, age, sex, risk factors for pancreatic disease; 3) imaging: type of imaging procedure, imaging review, indication for imaging; 4) cases: total number of patients incidentally diagnosed with PCLs, prevalence according with age; 3) cyst features: single cyst, mean/median cyst size, maximum cyst size, connection to the main duct, location, calcification, MD dilatation, worrisome features and/or high risk stigmata; 4) Cyst diagnosis: IPMN, pseudocysts, MCN, SCN; 5) extra-pancreatic cysts.

We then developed a summary table of the relevant studies listing the population characteristics and outcomes.

The quality of the studies was evaluated independently by two reviewers (GZ and MS) using the Newcastle-Ottawa Scale with a dedicated quality appraisal tool including 7 items. Studies with a score ≥7 were considered of high quality [15].

Statistical analysis

A meta-analysis of all eligible studies identified was planned using the software package Comprehensive Meta-Analysis (Biostat, Englewood, NJ, USA) using a random-effects model [16]. In addition to within-study variance, the random-effects model considers heterogeneity among studies. The corresponding 95% confidence intervals (CI) were calculated using exact methods and assuming a Poisson distribution. We present the random-effect model because we believe that the relevant variation in the risk is most likely a consequence of inter-study differences. The quantity of heterogeneity was assessed by means of the I^2 value [17]. The I^2 quantity describes the percentage of total variation across studies that is caused by heterogeneity and not by chance. We considered an I^2 value of 25% or lower as trivial heterogeneity, and an I^2 value of 75% or higher as considerable heterogeneity. Publication bias was assessed using the Begg and Mazumdar test. A p-value <0.05 was accepted as statistically significant. Before performing the analysis, we developed the following a priori hypotheses to examine whether these had any effect on the prevalence of PCLs in asymptomatic individuals and to explore reasons for any heterogeneity observed: (a) type of imaging employed to investigate the pancreas (MRCP vs MDTC or MRI); (b) sample size (<1000 or ≥ 1000 individuals); (c) mean age (≥55 or <55 years) of the analysed population; (d) area of origin (i.e. United States, European or Asian countries); (e) quality of the studies (quality score <7 or ≥7/10).

Results

Search result and study selection

The study selection process is summarized in Fig. 1. A total of 1070 references were identified by the MEDLINE search. After a primary screening of the titles, 1009 studies were excluded because they did not fit the area of interest.

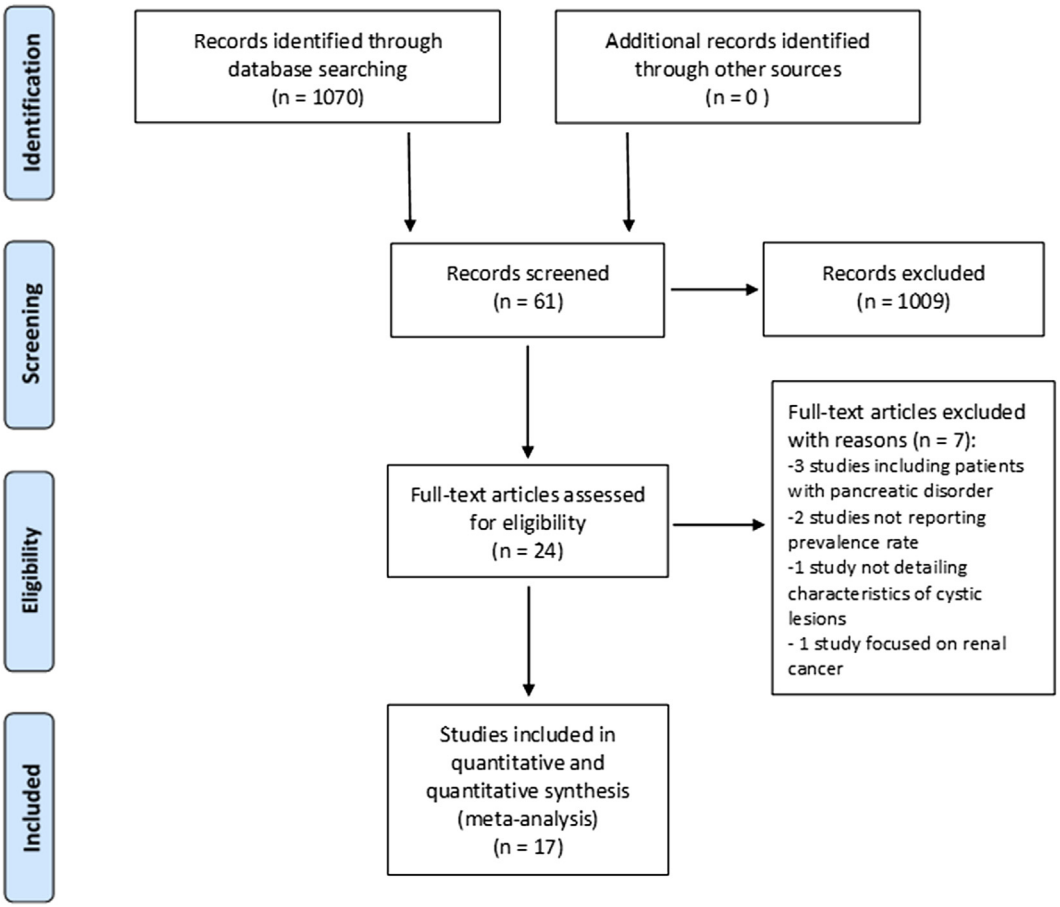

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram of assessment of studies identified in the systematic review.

The remaining 61 records were screened in more detail and 24 were considered potentially appropriate for the analysis.

Of these, 7 studies were discarded with reason: 3 studies [18–20] also enrolled patients with an history or suspect of pancreatic disorders, 2 studies [21,22] did not provide sufficient data to calculate the prevalence rate because the denominator was not expressed, 1 study [23] did not describe the characteristics of the diagnosed cystic lesions and 1 study [24] analysed a specific patients' cluster (renal tumors).

Finally, 17 studies fulfilled all inclusion criteria, and were considered both for qualitative analysis and quantitative synthesis.

Study characteristics and quality assessment

The 17 included studies were published between 2008 and 2018 [1,25–40]. Five were conducted in the USA, 7 in Europe (4 in Italy and one respectively in The Netherlands, Germany and Turkey), 4 in Asian countries (two studies both in Korea and in Japan) and one in South America (Brazil). All papers were in English language.

Three studies [30,36,39] investigated the prevalence of incidental PCLs in a specific subgroup of patients compared with controls and we included in our analysis only data concerning the latter.

Overall, 48,860 asymptomatic patients without history or clinical suspect of pancreatic disorders were included.

The descriptive characteristics of the seventeen included studies are summarized in Table 1.

All studies were mono-institutional and the study design was cross-sectional for all of them, being retrospective in 14 and prospective in 3 [25,34,35], respectively. The number of enrolled patients ranged from 110 [36] to 21,745 [37], and the percentage of males ranged from 26% [31] to 65% [28].

The mean age of the enrolled subjects ranged from 47 [31] to 68 years [39], while these data were not available in two studies [32,33]. The performed diagnostic procedures varied considerably among the studies. However, all but one study [39] in which the 192 enrolled patients underwent different investigations (either CT scan or MRI ± MRCP), employed a single diagnostic tool.

Abdominal MRI with or without intravenous contrast was the most commonly employed diagnostic procedure (11 studies). MRCP was also performed in 6 of them [1,29,30,38–40] with a huge variability: in two studies [1,39] it was employed in a minority of patients (respectively 19% and 15%) and in another one [29] all patients underwent MRCP and only a little part of them (20%) was investigated also with MRI with intravenous contrast.

Five studies considered exclusively MDCT scans ± contrast medium [25,26,32,33,37] and only one study [34] employed EUS.

Few studies reported patients' exposition to well known risk factors for developing pancreatic disorders (such as cigarettes smoking, alcohol consumption, increased BMI and diabetes mellitus) [1,34,38,40] and first degree family history for pancreatic diseases [1,28,38].

While a "pancreatic indication" for the diagnostic procedure was an exclusion criterion for study inclusion, the study employing EUS [34] included 6% of cases with a previous acute pancreatitis episode. As it was clarified that the episode occurred at least 3 months before the study enrolment, with pain resolution 8 weeks before the EUS and no evidence of acute fluid collection or

Table 1
General features of the 17 studies included in the quantitative analysis.

Author (year)	Country	Study Setting	Study design	Patients	Male (%)	Mean Age	Diagnostic procedure(s)	Imaging revision	Indication	Patients with PCLs (%)	Age of patients with PCLs	Patients with Mucinous lesions (%)
Kromery (2018) [40]	Germany	Single center	Retrospective	1077	521 (48.4)	55.8	WB-MRI (1.5T) +MRCP	Yes	Healthy population	494 (45.9)	60.5 (SD ± 11.6)	NR
Zerboni (2017) [39]	Italy	Single center	Retrospective	192	118 (61)	68	MDCT + c.e.; or MRI 1.5T ± c.e.; or MRCP	Yes	Not pancreas related	19 (10)	73 (95% CI 68.1–78.7)	14 (74)
Mizuno (2017) [38]	Japan	Single center	Retrospective	5296	3189 (60.2)	55.7	MRI + MRCP 3T, (thickness 3–5 mm)	Yes	No medical indication	724 (13.7)	62.6 (SD ± 10.7)	393 (54)
Chang (2016) [37]	South Korea	Single center	Retrospective	21,745	13,046 (60)	51.8	MDCT + c.e. (thickness 3 mm)	Yes	Not pancreas related	457 (2.1)	58 (SD ± 10)	383 (84)
Kim J.A. (2016) [36]	USA	Single center	Retrospective	110	49 (44.5)	47.5	MRI 1.5T (thickness 6–10 mm)	Yes	Not pancreas related	25 (22.7)	NR	NR
Ulus (2016) [35]	Turkey	Single center	Prospective	118	71 (60)	47.4	WB-MRI 1.5T	No	Healthy population	1 (0.8)	NR	1 (100)
Moris (2016) [1]	USA	Single center	Retrospective	500	252 (50)	60	MRI ± c.e. (1.5 or 3 T); MRCP 19%	Yes	Not pancreas related	208 (41.6)	63.8 (SD ± 11.2)	72 (35)
Sey (2015) [34]	USA	Single center	Prospective	341	154 (45)	59	EUS ± FNA	No	Not pancreas related	32 (9.4)	NR	NR
Ippolito (2015) [33]	Italy	Single center	Retrospective	6389	NR	NR	MDCT + c.e. (thickness 2–5 mm)	Yes	Not pancreas related	192 (3)	63 (SD ± 11)	NR
Zanini (2015) [32]	San Marino (Italy)	Single center	Retrospective	650	355 (55)	NR	16-MDCT ± c.e. (thickness 2.5 mm)	Yes	Not pancreas related	35 (5.4)	77 (53–93)	NR
de Oliveira (2015) [31]	Brazil	Single center	Retrospective	2583	672 (26)	47	MRI (3T) + c.e.	No	Not pancreas related	239 (9.3)	61 (SD ± 12.4)	NR
Matsubara (2012) [30]	Japan	Single center	Retrospective	1226	686 (56)	62	MRI (1.5 T, thickness 5 mm) and MRCP	Yes	Not pancreas related	123 (10)	69 (38–88)	NR
Girometti (2011) [29]	Italy	Single center	Retrospective	152	87 (57)	57	MRCP (1.5 T); MRI + c.e. (20%)	Yes	Not pancreas related	68 (44.7)	NR	48 (71)
de Jong (2010) [28]	Holland	Single center	Retrospective	2803	1822 (65)	51	MRI + c.e. (1.5 T)	Yes	Without medical indication	66 (2.4)	60 (SD ± 10.9)	NR
Lee (2010) [27]	USA	Single center	Retrospective	616	259 (42)	54	MRI (1.5 T, thickness 4 mm)	Yes	Not pancreas related	83 (13.5)	69 (SD ± 13)	NR
Laffan (2008) [26]	USA	Single center	Retrospective	2832	1445 (51)	58.2	16-MDCT + c.e.	Yes	Not pancreas related	73 (2.6)	NR	NR
Kim Y.S. (2008) [25]	South Korea	Single center	Prospective	2230	1338 (60)	57.5	16-MDCT + c.e.	Yes	Asymptomatic patients, CRC screening with CTC	4 (0.2)	NR	4 (100)

PCL = pancreatic cystic lesion; NR = not reported; MDCT = multidetector computed tomography, MRI = magnetic resonance imaging, T = tesla; MRCP = magnetic resonance cholangio-pancreatography, WB-MRI = whole body magnetic resonance imaging, EUS = endoscopic ultrasound, FNA = fine needle aspiration; CTC = computed tomography colonoscopy; CRC = colorectal cancer; c.e. = contrast-enhanced.

pseudocyst at the previous abdominal imaging, this study was not excluded.

As far as regards the quality of the included studies, the Newcastle-Ottawa score ranges from 4/10 to 9/10. Only six studies were scored as “high quality” (>7/10) [1,28,31,34,38,40].

Pooled prevalence rate of pancreatic cystic lesions

The prevalence of incidentally diagnosed pancreatic cystic lesions ranges from 0.2% to 45.9%, with a pooled prevalence of 8% (95% CI 4–14), as detailed in Fig. 2. No publication bias was found (Begg and Mazudmar Kendall's tau = −0.07, p = 0.64). There was however a considerable heterogeneity between the studies ($I^2 = 99.5\%$).

In order to explore possible reasons for this substantial heterogeneity, we repeated the analysis based on our a priori hypothesis considering different covariates (see Fig. 3). Studies with mean age of the enrolled subjects ≥55 years old [1,25,26,29,30,34,38–40] had a pooled prevalence of 11.3%, while those with mean age <55 years [27,28,31,35–37] of only 5.7%. In both cases, however, the heterogeneity was very high (I^2 >99% for both).

When we analysed the results taking into consideration the performed diagnostic procedure, the pooled prevalence of PCLs resulted 2.7% (95% CI 2–4) in the studies employing MDCT ± c.e. [25,26,32,33,37,39], without a reduction of heterogeneity ($I^2 = 93.7\%$). In the four studies using MRCP [29,30,38,40] the prevalence of PCLs was instead as high as 24.8% (95% CI 10–48), with similar heterogeneity ($I^2 = 99.5\%$). When the sample size of the studies (<1000 or ≥1000) was considered, a higher pooled prevalence was seen in studies with <1000 enrolled subjects

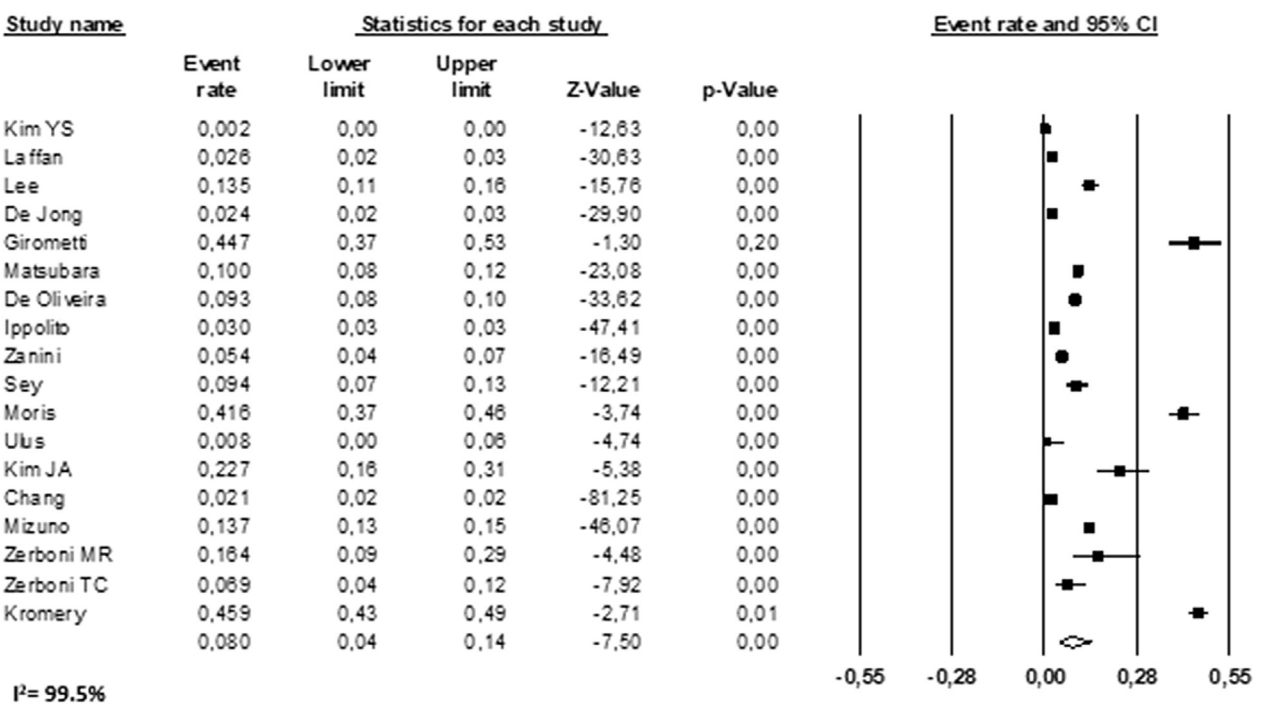

Fig. 2. Pooled prevalence of all pancreatic cystic lesions (PCLs) in the 17 examined studies. The pooled prevalence resulted of 8% (95% CI 4%–14%), with considerable heterogeneity ($I^2 = 99.5\%$).

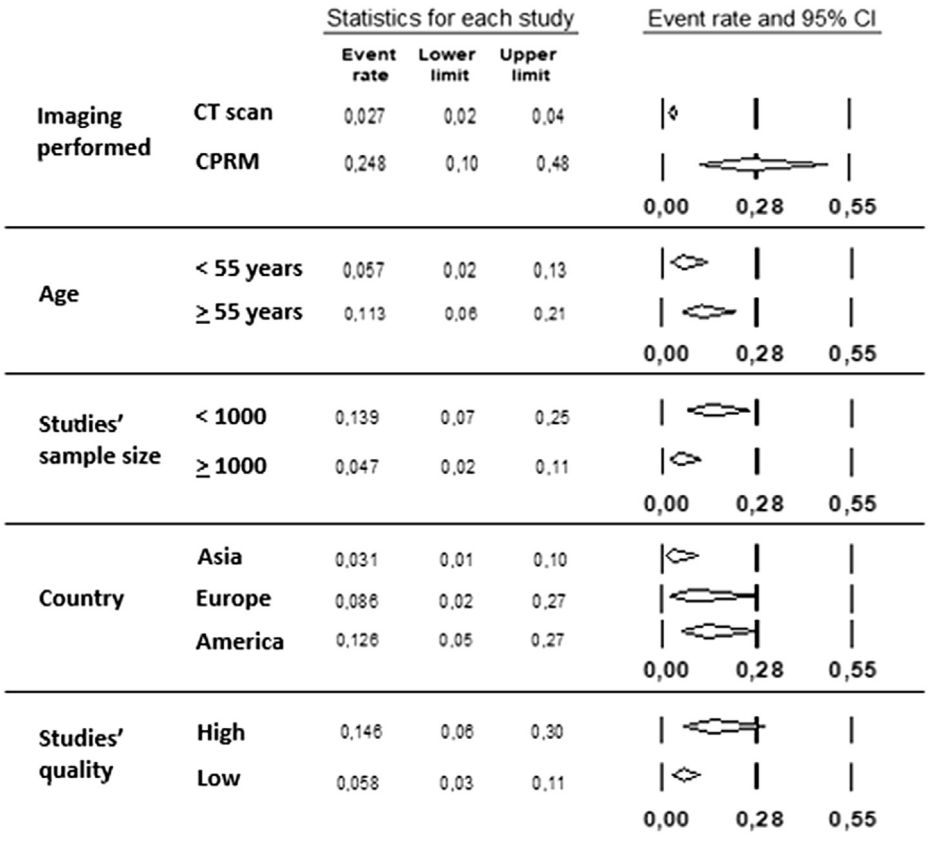

Fig. 3. Prevalence of PCLs according to variables considered a priori for sensitivity analysis: A) age (studies with mean/median population age ≥55 years compared with those with mean/median age <55 years); B) different diagnostic procedures [studies using CT scan ± medium contrast vs Magnetic Resonance Cholangio-Pancreatography (MRCP) with or without MRI]; C) sample size (<1000 vs ≥ 1000 cases); D) geographic area in which the studies were conducted (Asia, Americas and Europe); E) quality of the study (high vs low quality).

[1,27,29,32,34–36,39] (13.9%, 95% CI 7–25; $I^2 = 97.4\%$) compared to those enrolling ≥1000 people [25,26,28,30,31,33,37,38,40] (4.7%, 95% CI 2–11; $I^2 = 99.7\%$).

When considering the country of origin, the pooled prevalence of PCLs resulted 3.1% (95% CI 1–10; $I^2 = 99.7\%$) in studies conducted in Asia [25,30,37,38], 12.6% (95% CI 5–27; $I^2 = 99\%$) for those carried out in the Americas (either US or South America) [1,26,27,31,34,36], and 8.6% (95% CI 2–27; $I^2 = 99.6\%$) for those conducted in Europe [28,29,32,33,35,39,40].

As far as regards the quality of the studies, the six studies of "high quality" [1,28,31,34,38,40] score had a higher pooled prevalence of PCLs of 14.6% (95% CI 6–30), with $I^2 = 99.5\%$, when compared to the 11 studies with a "lower quality" score [25–27,29,30,32,33,35–37,39], which showed a pooled estimate rate was of 5.8% (95% CI 3–12), with $I^2 = 98.8\%$.

Pooled prevalence rate of mucinous cystic lesions and of lesions harbouring clinically relevant features

Seven of the 17 studies reported data on the specific type of PCLs. In these studies, the pooled prevalence of all PCLs was 7% (95% CI 2–19), with substantial heterogeneity ($I^2 = 99.6\%$) and the pooled prevalence of lesions diagnosed as of likely "mucinous nature" was 4.3% (95% CI 2–10; $I^2 = 99.2\%$) (see Fig. 4). Most of these PCLs were considered IPMNs.

Of the included 17 studies, 5 did not provide details about the morphology of the PCLs [25,36–38,40]. Of the remaining studies, 4 did not report cases with morphological aspects suggestive of "worrisome features" or "high risk stigmata" [1,26,28,29], whereas in eight studies [27,30–35,39] these characteristics were mentioned. The rate of lesions with worrisome features (WF) or high risk stigmata (HRS) such as solid nodules, thickening of the wall and main duct calibre > 5 mm ranged from 0.1% to 3.6%. The pool prevalence of either WF and/or HRS at diagnosis resulted of 0.7% (95% CI 0–1) with considerable heterogeneity ($I^2 = 85.3\%$) (see Supplementary Fig. 1).

Most of the included studies did not provide information regarding the follow-up of the incidentally diagnosed PCLs, and when available, these data were limited to a small fraction of the examined cohort.

Discussion

To our knowledge, this is the first meta-analysis investigating the prevalence of incidentally diagnosed PCLs in individuals asymptomatic for pancreatic disorders. In the present study, data from seventeen publications were analysed, resulting in a pooled prevalence rate of 8%, with a wide range (0.2%–45.9%) and considerable heterogeneity.

Only seven of the included studies provide sufficient data to define the nature of the PCLs. In these studies, the pooled prevalence of PCLs was of 7% and that of mucinous lesions was 4.3%, representing 60% of all incidentally diagnosed PCLs. However, at the time of incidental diagnosis, a minority of these lesions (0.7%) harboured features that might pose the suspicious of malignancy and an indication for surgery, such as main pancreatic duct dilation, thickened wall and mural nodules. Unfortunately, the included studies were not focused on the follow-up of these lesions, so their clinical relevance in the long-term could not be examined.

The strengths of the present study include an exhaustive literature search, rigorous statistical methods, and pooling of data to allow synthesis of all the available evidence examining the possible yield\burden of testing for pancreatic cysts in asymptomatic individuals. Nevertheless, the most relevant weaknesses of the study, as concerns many systematic review and meta-analysis, arise from the limits of the available evidence.

Most of the studies eligible for the current analysis were retrospective and for five of them the past medical history was not available; however, they include patients that were asymptomatic at the time of examination, without known health co-morbidities.

Moreover, since the included studies evaluated the radiological results collected during a long time span (up to 10 year), imaging were obtained with different machines and protocols. The authors of the studies with a longer time of recruitment considered, however, the effect of the different distribution of radiological modalities on the PCLs' rate. Moris et al. [1] tried to objectify this correlation performing an adjusted multivariate-analysis, that showed a very strong relationship between PCLs detection and both the MRI hardware and the software versions. Therefore, they confirmed the direct relationship between the number of PCLs detected and the newer MRI version used. On the other hand, Kim J.A. and colleagues [36] matched cases and controls (respectively patients affected by autosomal dominant polycystic kidney disease -ADPKD- and patients who underwent abdominal MRI imaging without history or suspect of both ADPKD and pancreatic disorders) not only for demographic characteristics but also for the timing of abdominal procedures (within 1 year of each other), in order to reduce the "technology influence" on the results.

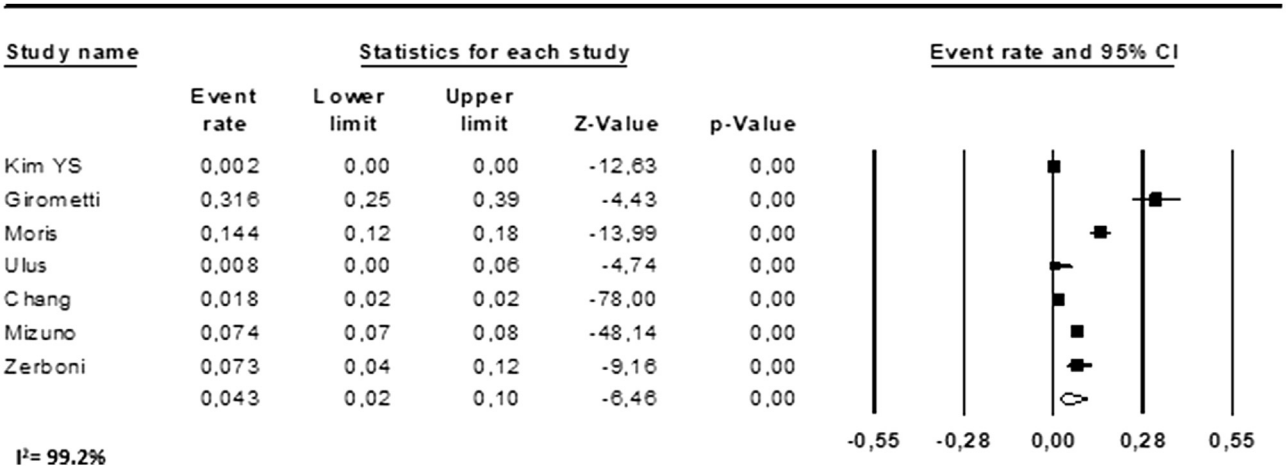

Fig. 4. Prevalence of pancreatic Mucinous Cystic Lesions in studies providing sufficient data to define the nature of the PCLs. The pooled prevalence resulted of 4.3% (95% CI 2%–10%) with considerable heterogeneity ($I^2 = 99.2\%$).

The highest [40] and one of the lowest [35] rates of PCLs were surprisingly reported by two studies using the same radiological procedure, such as whole body MRI. Paramagnetic contrast was not administrated in both, but, probably, the complementary use of MRCP in one of them [40] could explain the increasing rate of pancreatic findings, although the difference remains huge.

As mentioned before, a considerable degree of heterogeneity was present in all the conducted analyses. A number of a priori hypotheses were made to explain heterogeneity, such as age, country of origin, number of enrolled subjects, different type of abdominal cross-sectional imaging and quality of the study. However, while some of these factors influence the rate of PCLs, they could not explain heterogeneity.

The pooled estimate rate of occasional PCLs was higher in older subjects. This result is in line with previous autopsy series [41] reporting a rate of incidental PCLs of about 25%, which increases with age. The pooled rate of incidental PCLs also increased in studies enrolling a lower number of patients, in those with a higher quality score and in patients undergoing MRCP. As far as concerns the country of origin, the pooled rate of PCLs was four times higher in studies conducted in the US than in those conducted in Asia (12.6% vs 3.1%), with roughly intermediate results in Europe (see Fig. 3). This pooled data was in contrast with Laffan's et al. results [26], according to which Asians had an increased odds ratio of 3.57 (CI 95% 1.05–12.13) of having a pancreatic cyst compared with other racial groups.

A possible explanation for this difference might be that half of the studies with a better quality score were performed in the US. Also, risk factors associated with an increased risk of pancreatic cancer and of PCLs, such as diabetes and obesity [1,38,40,42] might be more common in the US. The possible role of geographical/racial differences might deserve further investigation also in view of “patients’ tailored work-up” during the management of PCLs.

Despite the limitations listed above, notably the results of the meta-analysis are similar in terms of incidence of PCLs to those of the only prospective study performed with EUS (respectively pooled rates of 8% and 9.4%), strengthening the reliability of the present data. Indeed, EUS performed after TC or MRI increases the rate of pancreatic cystic lesions undiagnosed by initial cross-sectional imaging [43]. A more recent study on this topic and employing EUS was published after our search [44]. In this study the rate of PCLs in asymptomatic subjects was as high as 24%, in line with the data from autopsy series mentioned above [41], confirming the high sensitivity of EUS in diagnosing PCLs.

In conclusion, the findings of this meta-analysis highlight the considerable high prevalence of PCLs in asymptomatic and/or apparently healthy individuals. Furthermore, taking into account both the higher prevalence of PCLs in older and asymptomatic subjects and the presence of comorbidities and the low rate of potential malignant features, radiological follow-up in this group of patients is expected not to be always cost-effective [45]. These data reinforce the need to redefine the surveillance strategy proposed by international consensus guidelines, according with a new scale of clinical risk based on individual subjects’ characteristics.

Authors’ potential competing interests

None.

Financial support

None.

Acknowledgement

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pan.2018.11.014.

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