Surgery of the pancreatic cystic echinococcosis: systematic review

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Abstract: The prevalence of pancreatic cystic echinococcosis (PCE) in the world is low ranging between 0.2% and 0.6%. The diagnosis of PCE is easy when it is associated to other location such as liver, it became difficult when PCE was isolated simulating other diagnosis such as pseudocyst, a choledochal cyst, serous or mucinous cystadenoma and cystadenocarcinoma. This systematic review aimed to provide evidencebased answer to the following questions: (I) what are the efficient tools to affirm the diagnosis of isolated PCE and (II) what are the best therapeutic strategy for the PCE? An electronic search was performed by two authors (W Dougaz, I Bouasker). Medline, Scopus, Embase, Web of Science, Google Scholar and Cochrane collaboration were consulted. The keywords used were "cyst", "echinococcosis", "hydatid cyst" and "pancreas". All abstracts were analyzed followed by extraction of the full text by the same two authors (W Dougaz, I Bouasker), all divergences were resolved by discussion with C Dziri. Recommendations were based on Oxford's classification: (I) what are the efficient tools to affirm the diagnosis of PCE? ---ultrasound remains the cornerstone of diagnosis. Magnetic resonance imaging (MRI) reproduces the ultrasound defined features of CE better than computed tomography (CT). MRI with heavily T2-weighted series is preferable to CT. Pancreatic duct MRI should be promising to identify a fistula between PCE and pancreatic duct (level of evidence 3-recommendation B); (II) what are the best therapeutic strategy for the PCE? --surgery is the main treatment of PCE. Open approach is validated. The decision depends of the location of PCE: head versus body and/or tail of the pancreas (level of evidence 5-recommendation D): for the head of the pancreas, the tendency is toward conservative surgery. For body and/or tail of the pancreas, the tendency is toward radical surgery. Medical treatment (albendazole) should be prescribed 1 week before surgery and 2 months during postoperative period (level II evidence and grade C recommendation).

Keywords: Pancreas; echinococcosis; cyst, hydatid cyst; surgery; systematic review

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Cystic echinococcosis (CE) is still a continuing health problem in the world (1). CE is a parasitic disease caused by the tapeworm *Echinococcus granulosus*. The tapeworm lives usually in the intestine of dog, called the "definitive host". The tapeworm eggs are passed in the feces and are ingested by sheep, called the "intermediate host". The eggs penetrate the intestinal wall of the sheep, and reach the liver using the portal vein, where they develop into a cyst. Afterward, in particular circumstances, they passed through the liver and reach all other viscera. *Echinococcus* infestation occurs in humans when they accidentally ingest tapeworm eggs (1).

After 30 years [1977–2005], the average annual surgical

incidence rate slightly dropped, from 15 to 12.6/100,000 inhabitants/year, proving that this zoonosis remains a problem of public health in Tunisia (2). CE is localized in the liver for 60% to 70% (1). CE can be disseminated to other viscera such as pancreas owing to hematogenous contamination.

In 1975, Kattan (3) reported a prevalence of 0.25%: two PCE out of 780 cases of CE affecting various organs operated on in one surgical unit in Baghdad during the period 1963–1975. In Banat (central of Europe) (4), an epidemiological study was performed on 505 adults, CE was rarely found in pancreas (0.2%). The plain radiographs, ultrasound images and computed tomography (CT) scans of 357 CE seen between 1978 and 1998 were reviewed by Dahniya *et al.* (5). One PCE was reported with a prevalence of 0.3%. In the east of Azerbaijan (6), prevalence of PCE is 0.6%. Of 265 extra pulmonary hydatid cysts collected from 1990 to 2007, Bellil *et al.* found one CE located in the pancreas corresponding to 0.4% (7). Finally, the prevalence of PCE in the world ranges between 0.2% and 0.6%.

The diagnosis of PCE is easy when it is associated to other location such as liver, it became difficult when PCE was isolated simulating other diagnosis such as pseudocyst, a choledochal cyst, serous or mucinous cystadenoma and cystadenocarcinoma. There is no consensus concerning surgical management in medical literature. This systematic review aimed to provide evidence based answer to the following questions: (I) what are the efficient tools to affirm the diagnosis of isolated PCE? and (II) what are the best therapeutic strategy for the PCE?

Methods

An electronic search in several medical databases was performed by two authors (W Dougaz, I Bouasker). Medline, Scopus, Embase, Web of Science, Google Scholar and Cochrane collaboration were consulted. The keywords used were "cyst", "echinococcosis", "hydatid cyst" and "pancreas". All abstracts were analyzed followed by extraction of the full text by the same two authors (W Dougaz, I Bouasker) and all divergences were resolved by discussion with C Dziri.

All full text of original articles, case report, and small series, reporting isolated PCE, with limitations to English, French, Spanish and Italian languages, were retained by W Dougaz and I Bouasker. Assessment of methodology (W Dougaz, I Bouasker) was to check that every full text should contain demographic data, complaints, physical examination, and cyst location, hydatid serology, imaging features, operative findings, operative procedures and postoperative course. All divergences were resolved by discussion with C Dziri. As concerns operative procedures and according to the expert consensus published in 2010 (8), we considered that radical surgery aims to remove cysts completely "total cystectomy": laminated and germinal layers with or without adventitial layer called "pericyst". Therefore, "total cystectomy" for the PCE included: closed or open total pericystectomy with or without resection of the pancreas and enucleation. On the other hand, we considered conservative surgery as "partial cystectomy", in which the cyst content is sterilized and removed after opening, with the pericyst partially resected which is called "unroofing procedure" for others (8). We also considered conservative surgery all anastomosis between cysts and digestive tract and mini invasive surgery or percutaneous treatments (percutaneous drainage or PAIR technique which consisted to perform a puncture, aspiration, and injection of protoscolicid solution followed by re-aspiration) (8).

We excluded articles reporting PCE associated to cysts localized in other abdominal organs, literature reviews and editorials.

A descriptive analysis was performed. Qualitative variables were mentioned with its percentage, quantitative variables were reported with their mean value \pm standard deviation when the distribution is normal otherwise with median value and interquartile range. Recommendations were based on Oxford's classification (9).

Results

We retrieved 81 articles from 2001 to 2017, 41 articles (10-30) were retained (31-50) (*Figure 1*), published in 30 journals according to the eligibility criteria. Sixty-two patients were enrolled in this systematic review, extracted from 36 articles of cases report and five articles reporting small series. This sample included 37 women and 25 men living in Mediterranean countries, South Africa, Iran and India. The mean age was 34.76±18.03 years [median age, 32.00 years; interquartile ranges (IQR), 20.00–48.50 years; range: 4.00–72.00 years]. The main symptom was pain localized in the epigastria (69%) or in the upper left quadrant (31%). Pain was associated to vomiting in 16%, jaundice in 26% owing to a compression of the common bile duct and fever in 8%. Acute pancreatitis may reveal a PCE in 15%.

Physical examination showed an abdominal mass in 32%. Ultra-sonography (US) and CT scan were the most



Figure 1 PRISMA diagram showing selection of articles for review.

performed exam respectively in 71% in 90%. Hydatid serology is not very helpful, it has a low sensitivity 62%. Cyst was localized in the head (31%), in the body (22%) and in the tail (47%). PCE compressed the common bile duct in 16 patients who had cyst in the head (26%). Cyst size was reported in 49 patients out of 62, the median diameter was 70 mm (IQR, 41–100 mm and range, 24–180 mm).

Open approach was performed in 95% and laparoscopic approach in 5%. Radical surgery was performed in 32 patients (52%): five duodenopancreatectomies (8%), one central pancreatectomy, 20 distal pancreatectomies (32%) associated to splenectomy in 16 cases. Six patients underwent pericystectomy. A conservative surgery was performed in 30 cases (48%): 27 unroofing procedures, one cystic digestive anastomosis and two patients had percutaneous drainage associated to injection of albendazole in the cystic cavity.

On the other hand, in this sample of 62 patients, the authors have different surgical indication according to the location of the cyst:

(I) Head (n:19): nine radical surgery (five

duodenopancreatectomies + two total resections + two enucleations) *versus* 10 conservative surgery (nine unroofing + one cystic digestive anastomosis);

- (II) Body (n:14): five radical surgery (two total resections + one central pancreatectomy + two distal pancreatectomies) *versus* nine conservative surgery (eight unroofing+ one percutaneous drainage associated to injection of albendazole in the cystic cavity);
- (III) Tail (n:29): 18 radical surgery (18 distal pancreatectomies) *versus* 11 conservative surgery (10 unroofing + one percutaneous drainage associated to injection of albendazole in the cystic cavity).

No death occurred in this sample. Postoperative morbidity included five pancreatic fistulas (one postduodenopancreatectomy + one post-distal pancreatectomy + three post-unroofing), two deep surgical site infections post-duodenopancreatectomy, and one bleeding postduodenopancreatectomy. The follow-up was mentioned for 48 patients out of 62 (77%). Median of follow-up was 11 months (IQR, 4.25–24.00 months and range values, 0–132 months). One recurrence was reported.



Figure 2 Ultrasonography showing the same patterns independently of the location.

Discussion

PCE is a rare localization with a prevalence ranging between 0.20% and 0.60%.

Clinical presentation

This systematic review showed that the main symptom was pain localized in the epigastria (69%) or in the upper left quadrant (31%), associated to vomiting in 16%, jaundice in 26% and fever in 8%. Acute pancreatitis may reveal a PCE in 15%.

Other authors reported cases with different clinical presentation. In 1957, Lebon et al. reported a case of jaundice owing to a compressive PCE of the head (51). Morton reported also an obstructive jaundice caused by an intrapancreatic hydatid cyst (52). Mzali et al. reported a PCE of the head ruptured in the common bile duct responsible of jaundice (53). In 1955, Joske (54) reported a case of a 44-year-old man who consulted for obstructive jaundice, a hydatid cyst of the head of the pancreas pressing upon the common bile duct was found. The cyst was removed and the patient developed pancreatic insufficiency and diffuse calcification of the pancreas some years later. Katkhouda et al. (55) reported a PCE of the tail responsible for chronic recurrent pancreatitis which raised diagnostic problems. Chinya et al. (18) described a hydatid cyst of the pancreas masquerading as pancreatic pseudocyst. On the other hand, PCE may mimic a cystic tumor during intervention such as a mucinous cystic neoplasia (56).

Hydatid serology

In this systemic review, hydatid serology has a low sensitivity of 62%. In the literature review of Akbulut (57), sensitivity of hydatid serology was also low (54%).

Imaging features

This systematic review showed that US and CT scan were the most performed exam respectively in 71% and 90%. PCE was localized in the head (31%), in the body (22%) and in the tail (47%). PCE compressed the common bile duct in 16 patients who had cyst in the head (26%). Cyst size was reported in 49 patients out of 62, the median diameter was 70 mm (IQR, 41–100 mm and range, 24–180 mm). Akbulut's review (57) reported 54 patients with the following distributions: 22 in the head (41%), 6 in body and neck (11%), 26 in the tail or tail and body (48%). According to Akbulut's review (57), PCE had a mean diameter of 71.3 \pm 36.1 mm (range, 26–180 mm). Safioleas *et al.* (47) found also that body and tail of the pancreas were the most common locations (4 out of 5).

US is very useful and efficient to show calcification of the cystic wall, detachment of the membrane, and several daughter vesicles corresponding to rosette pattern (58). All these signs are pathognomonic of CE. *Figure 2* shows a PCE with daughter vesicles corresponding to type III Gharbi classification (59) or CE2 of WHO-IWGE classification (60).

CT scan is efficient to detect early calcifications of the cystic wall. It is indicated when US is doubtful such as for type IV Gharbi classification which evokes a tumor, or when cyst has a big size and it is difficult to identify its localization with US (*Figure 3*).

Magnetic resonance imaging (MRI): *Figure 4* is a T2 MRI of the same patient who had a PCE of the tail (*Figures 3,4*). Zalaquett *et al.* (61) showed that the active cysts: CE1 has a very T2 hyper-intensive rim sign and CE2 has a T2 hyper-intensive daughter cysts which is pathognomonic. The transitional cyst CE3 has a T2 hypo-intense detached membrane. As concerns inactive cysts, CE4 has a T2 iso- to hypo-intense sign and CE5 has very hypo-intense sign.

Stojkovic *et al.* (62) compared retrospectively US, MRI and CT investigations of patients with CE to determine the performance of CT and MRI in comparison to the gold standard US. He concluded that ultrasound remains the cornerstone of diagnosis, staging and follow-up of CE cysts. MRI reproduces the ultrasound defined features of



Figure 3 Computed tomography of an isolated pancreatic cystic echinococcosis.



Figure 4 Magnetic resonance imaging showing a pancreatic cystic echinococcosis of the tail.

CE better than CT. If US cannot be performed due to cyst location or patient-specific reasons MRI with heavily T2-weighted series is preferable to CT (62).

Differential diagnosis

PCE associated to CE located in the liver is the frequent situation and diagnosis of PCE is easy to confirm. However, the diagnosis of isolated PCE, in spite of all these imaging features, sometimes hesitates with choledochal cyst (23,28,33), pseudocyst (18,26,30,32,39), cystic neoplasm of pancreas (31,38), and mucinous cystic neoplasm (56).

Treatment

Surgery is the cornerstone of PCE treatment. Surgical procedures should take into account location of the cyst, presence or not of a pancreatic ductal fistula communicating with the PCE.

The literature data did not help to decide. In this systematic review, Radical surgery was performed in 32 patients (52%) and conservative surgery in 30 cases (48%). Akbulut *et al.* in their review (57) reported 29 radical surgery out of 57 patients (51%) and 28 conservative surgery (25 by open approach + three percutaneous drainage) (49%). These data testimony that there is no consensus regarding therapeutic management.

Conclusions and recommendations

All levels of evidence are low and recommendations correspond to opinions of experts

What are the efficient tools to confirm the diagnosis of PCE?

Clinical presentation is not specific. Hydatid serology has a low sensitivity of 62%. Ultrasound remains the cornerstone of diagnosis, staging and follow-up of CE cysts. MRI reproduces the ultrasound defined features of CE better than CT. MRI with heavily T2-weighted series is preferable to CT. Pancreatic duct MRI should be promising to identify a fistula between PCE and pancreatic duct (level of evidence 3—recommendation B).

What is the best therapeutic strategy for the PCE?

Surgery is the main treatment of PCE. Open approach is validated, laparoscopic approach cannot be supported by a valid data. Furthermore, laparoscopic approach for the treatment of liver CE was associated with a higher rate of extrahepatic and peritoneal recurrence than open (63).

There are two surgical options: radical *versus* conservative surgery.

The decision depends on the location of PCE: Head *versus* body and/or tail of the pancreas. On other words, on the right or on the left of the mesenteric portal vein axis (64).

- (I) Head of the pancreas: the tendency is toward conservative surgery (level of evidence 5 recommendation D);
 - No fistula with pancreatic duct: unroofing procedure with omentoplasty;
 - (ii) If there is a fistula between pancreatic duct and the PCE: anastomosis between PCE and digestive tract is indicated;
 - (iii) Duodenopancreatectomy should be reserved exceptionally for selective patients.
- (II) Body of the pancreas: the tendency is toward radical

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surgery (level of evidence 5—recommendation D);

- (i) If presence of fistula between pancreatic duct and the cyst: central pancreatectomy or anastomosis between cyst and digestive tract;
- (ii) If no fistula: unroofing procedure with omentoplasty.
- (III) Tail of the pancreas: the tendency is toward radical surgery (level of evidence 5—recommendation D).
 - (i) If presence of fistula between pancreatic duct and the cyst: distal pancreatectomy;
 - (ii) If no fistula: distal pancreatectomy or unroofing procedure with omentoplasty.

PAIR is indicated for patients who does not accept surgery or when there is an anesthesia high risk. There is no available data.

Medical treatment (albendazole) should be prescribed 1 week before surgery and 2 months during postoperative period (level II evidence and grade C recommendation) (65).

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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