Original Article

Can cereal-based oral contrast agents-assisted ultrasound become an alternative to non-contrast magnetic resonance imaging (MRI) in radiological follow-up for pancreatic cystic lesions?

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Background: Pancreatic cystic lesions (PCLs) are recommended to be examined by magnetic resonance imaging (MRI), yet MRI still has limitations, such as high costs, the risk of triggering claustrophobia, and relatively low availability compared with ultrasound. Oral contrast agents-assisted ultrasound has been used to examine the gallbladder and stomach, but whether oral contrast agents could improve the accuracy of transabdominal ultrasound (TAUS) for PCLs and could be a potential alternative to non-contrast MRI for PCL follow-up has not been studied. This study aimed to explore the value of cereal-based oral contrast agents in improving the accuracy of PCLs during TAUS.

Methods: This is a prospective cohort study. Patients with PCL who were admitted to our center between January 2023 and January 2024 were enrolled, and TAUS was performed before and after taking cereal-based oral contrast agents. The imaging quality of the PCL was measured by structural visualization scores. The structural visualization scores of oral contrast agent-assisted ultrasound and non-contrast MRI were also compared.

Results: A total of 27 patients with PCLs were enrolled, and 30 PCLs were detected. The sonolucency of the PCL improved after oral contrast agent administration. Before taking the agent, only 30% of patients had satisfactory sonolucency; after taking the oral contrast agent, the corresponding proportion reached 80% (P=0.002). The structural visualization score of the PCL determined by oral contrast agent-assisted TAUS was higher than that determined without the aid of an agent [1 (0–6) *vs.* 1 (0–3), P=0.001], which was mainly reflected in the increase in the number of visible septa after taking the agent. No significant difference was detected between the structural visualization score of the PCL examined by oral contrast agent-assisted TAUS and that examined by non-contrast MRI and the correlation between the 2 types of scores were satisfactory [1 (0–6) *vs.* 2 (0–7), P=0.070, Spearman correlation factor r=0.880].

Conclusions: This study used a structured scoring system to confirm that cereal-based oral contrast agents could improve the ultrasound quality of PCLs, and the correlation between the quality of oral contrast agent-assisted ultrasound and non-contrast MRI findings on PCLs was satisfactory. Further research to improve visualization of PCLs on TAUS using oral contrast agents could result in TAUS being a potential alternative to MRI in the follow-up of PCLs in resource-limited situations.

Keywords: Pancreatic cystic lesion (PCL); transabdominal ultrasound (TAUS); oral contrast agent; magnetic resonance imaging (MRI)

Submitted Feb 26, 2024. Accepted for publication Jun 25, 2024. Published online Jul 26, 2024.
doi: 10.21037/qims-24-367
View this article at: https://dx.doi.org/10.21037/qims-24-367

Introduction

Pancreatic cystic lesions (PCLs) are a heterogeneous group of diseases that mainly include serous cystic neoplasm (SCN), mucinous cystic neoplasm (MCN), intraductal papillary mucinous neoplasm (IPMN), solid pseudopapillary neoplasm (SPN), and neuroendocrine tumor (NET) (1). Patients with PCLs are often asymptomatic, and PCLs are more likely to be detected during radiological examinations (2). Thus, although the incidence of PCL can reach 24% in anatomical studies (3), the rate of PCL detection via radiological examinations is not high (4). The structural features and malignant potential of PCLs vary according to the pathological type (5). For example, the malignant potential of IPMNs can reach 40% (6). The management of different PCLs also varies according to several features of PCLs, including the pathological type, size, and growth rate (7). For certain PCLs, long-term follow-up is enough; however, for some PCLs, such as IPMNs, surgical treatment is necessary when some worrisome features are observed, such as the size of IPMN exceeding 3 cm (8). Therefore, choosing a proper method of PCL follow-up is highly important, as is providing additional information on PCLs for physicians to assist the decision-making of a suitable management approach. These patients need appropriate imaging examination methods.

As an economical, convenient, and safe imaging technique, ultrasound is an important examination method for screening and monitoring PCLs. At present, the most commonly used ultrasound method for detecting cystic pancreatic lesions is fasting transabdominal examination, but the sensitivity of identifying the structures of the PCL could be further improved via this method. Although magnetic resonance imaging (MRI) is recommended as a PCL examination approach by guidelines (7,9), it still has limitations, such as high costs, the risk of triggering claustrophobia, and relatively low availability compared with ultrasound. Endoscopic ultrasonography (EUS) can improve the accuracy of identifying PCLs compared with transabdominal ultrasonography but is less commonly used since it is an invasive examination.

Oral contrast agents have emerged to assist transabdominal ultrasonography in recent years. The major type of oral contrast agent uses cereal powder as its main ingredient and can quickly fill the stomach after gelatinization of the starch, and thus expel gases inside the stomach so that the PCL behind the stomach can be displayed more clearly (10). Consequently, oral contrast agents have been found to be valuable for improving the accuracy of transabdominal ultrasonography for detecting gastric and bile duct lesions (11,12) and for identifying the structure of a normal pancreas (13). However, no studies have evaluated whether oral contrast agents improve the visualization accuracy of the internal structure of the PCL during transabdominal ultrasound (TAUS).

In this study, PCL patients were prospectively enrolled and underwent TAUS before and after taking cereal-based oral contrast agents. The value of cereal-based oral contrast agents in improving the accuracy of PCLs during TAUS was explored, and the accuracy of oral contrast agent-assisted TAUS PCL images and non-contrast MRI PCL images were also compared. We present the following article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-24-367/rc).

Methods

Patients

This is a prospective cohort study. Patients with PCL who were admitted to Peking Union Medical College Hospital between January 2023 and January 2024 were prospectively enrolled. The inclusion criteria were as follows: (I) PCL found by previous imaging, and (II) aged 18–80 years. The exclusion criteria for patients were as follows: (I) diabetes, (II) a history of pyloric obstruction, (III) allergic to cereal-based oral contrast agents, (IV) acute pancreatitis, and (V) missing data. Patients were followed-up until a surgery for PCL was conducted, or the follow-up time had reached least 3 months. The patients who were lost to follow-up within 3 months and did not receive surgery were excluded from the study. The sex, age, symptoms, reasons for undergoing surgery/aspiration (when applicable), type of surgery (when applicable), and the pathological subtypes (if available) were recorded. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics committee of Peking Union Medical College Hospital (No. I-24PJ0102), and informed consent was provided by all individual participants.

TAUS imaging before and after taking oral contrast agents

TAUS scans were performed by a Philips IU22 or a Philips EPIQ color Doppler ultrasound instrument (Philips, Amsterdam, Netherlands) with a convex array transducer at a frequency of 2–5 MHz. The patients fasted for at least 8 hours and underwent traditional ultrasound scans. Then, they were administered oral contrast agents, and a traditional ultrasound scan was performed again. The oral ultrasound contrast agent (Huzhou East Asia Pharmaceutical Products Co., Ltd., Huzhou, China) was prepared according to the manufacturer's instructions. Then, 50 g of the oral contrast agent was mixed with 450 mL of boiled water. The sonograph was analyzed separately by 2 radiologists specializing in ultrasound with at least 5 years of experience and who were blinded to the pathological results, clinical diagnoses, and other radiological data to reduce information bias. When disagreement occurred between the 2 doctors, conclusions were reached after consulting a third doctor specializing in ultrasound for more than 20 years.

Ultrasonography and MRI

The sonolucency of the cystic lesions in the images was analyzed, the imaging quality of the PCL before and after administration of the oral contrast agent was scored according to the structure of the PCL, and the PCL structures were graded as follows: A was defined as the number of septa in the PCL, which was equal to the number of locules –1 (e.g., for uniocular cysts, A =0). B was defined as the septum/wall thickness score, which was 1 (either the septum or wall was thicker than 2 mm) or 0 (no septum/wall was thicker than 2 mm). C was defined as the papillary structure score, which was 1 (presence of at least 1 papilla in the cyst) or 0 (no papilla were present in the cyst). D was defined as the calcification score, which was the number of calcifications in the lesion. E was defined as the pancreatic duct score, which was 1 (the pancreatic duct was wider than 2 mm) or 0 (the pancreatic duct was not wider than 2 mm). The structure visualization score was defined as A+B+C+D+E, and the structural visualization scores of the PCL sonographs before and after taking the oral contrast agent were recorded. For participants who also underwent MRI, the structural visualization score of the MRI images of the PCL was also recorded.

Statistical analysis

The estimated sample size was calculated based on the results of the pre-experiment: the proportion of a satisfying sonolucency by TAUS was 40% before taking the oral contrast agent, and 70% after taking the oral contrast agent. Therefore, the estimated sample size was 20. This sample size would provide the trial with 80% power to reject the null hypothesis at a 2.5% significance level (with non-inferior hypothesis). Data analysis was performed using SPSS 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as the median and range or mean ± standard error of mean (SEM). The structural visualization scores of the patients before and after taking oral contrast agents were compared by the Wilcoxon test. The sonolucency of the PCL before and after oral contrast agent administration was compared via the McNemar test. The correlation between the structural visualization scores of the sonographs after taking the oral contrast agent and the structural visualization scores of the MRIs were analyzed by the Spearman correlation test. A P value <0.05 was considered to indicate statistical significance.

Results

Patient clinical characteristics

A total of 27 patients with PCL were enrolled and analyzed (*Figure 1*), including 11 males and 16 females, with a median age of 52 (22–72) years. The median follow-up time was 9 (1–27) months, with 5 patients receiving surgery within 3 months due to worrisome features having been observed through imaging. A total of 3 patients experienced abdominal pain before the detection of PCL, 1 patient had symptoms of abdominal discomfort after eating, 1 patient had jaundice, and the remaining 22 patients had no obvious symptoms before the detection of PCL. Among the 27 patients, 10 patients underwent surgery or aspiration biopsy because high-risk features were observed by imaging or serum examination, or certain symptoms persisted. A total of 7 patients underwent surgery, and the pathological results revealed that 3 had MCNs, 1 had SCN, 2 had IPMNs, and 1 had an SPN. The reasons for undergoing surgery, types of surgery, and corresponding pathology of these 7 patients are listed in *Table 1*. Among 3 patients who underwent PCL aspiration biopsy, no malignant tumor cells were found in their aspiration samples. The remaining 17 patients had regular follow-up for their PCLs.

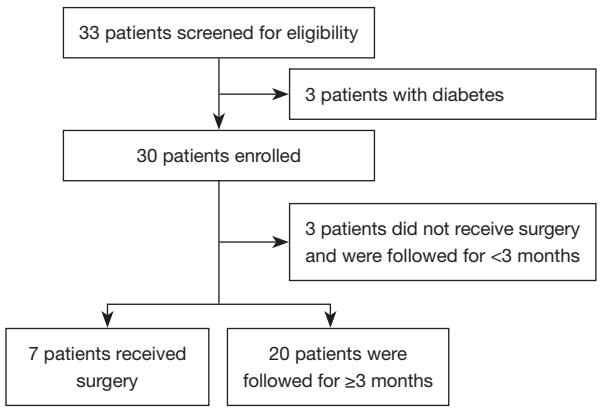

Figure 1 The diagram of patient enrollment.

Sonographic features of PCL

A total of 30 PCLs were detected in 27 patients; 3 lesions were found in 1 patient, and 2 lesions were found in 1 patient. All PCLs could be observed before the application of the oral contrast agent. Among the lesions, 9 lesions were located at the head of the pancreas, 11 were located at the body of the pancreas, and 10 were located at the tail of the pancreas. The median maximum diameter of the lesions before taking the oral contrast agent was 2.7 (range, 0.43–7.3) cm, and the median maximum diameter of lesions after taking the oral contrast agent was 2.4 (range, 0.60–8.4) cm. Moreover, there was no significant difference between the maximum diameter of the PCL before and after taking the oral contrast agent (P=0.596).

The sonolucency of the PCL improved after the patients were administered the oral contrast agent compared with that during fasting. Before taking the oral contrast agent, a

Table 1 Information of patients who underwent surgery

Patient No.	Location of PCL	Reason for undergoing surgery	Type of surgery	Pathology
1	Pancreatic tail	A mural nodule was detected in MRI	Spleen-preserving distal pancreatomy	Mucinous cystic neoplasm
2	Pancreatic head	A dilated pancreatic duct was detected in MRI	Pancreaticoduodenectomy	Intraductal papillary mucinous neoplasm
3	Pancreatic tail	Presence of symptom (abdominal pain)	Spleen-preserving distal pancreatomy	Serous cystic neoplasm
4	Pancreatic tail	Elevation of serum CA19-9	Spleen-preserving distal pancreatomy	Mucinous cystic neoplasm
5	Pancreatic tail	Cyst fluid cytology indicated high-grade dysplasia	Distal pancreatectomy with splenectomy	Mucinous cystic neoplasm
6	Pancreatic body	A solid component was detected in MRI	Middle pancreatectomy	Solid-pseudopapillary neoplasm
7	Pancreatic head and body	A dilated pancreatic duct was detected in MRI	Pancreatectomy	Intraductal papillary mucinous neoplasm

PCL, pancreatic cystic lesion; MRI, magnetic resonance imaging; CA19-9, carbohydrate antigen 19-9.

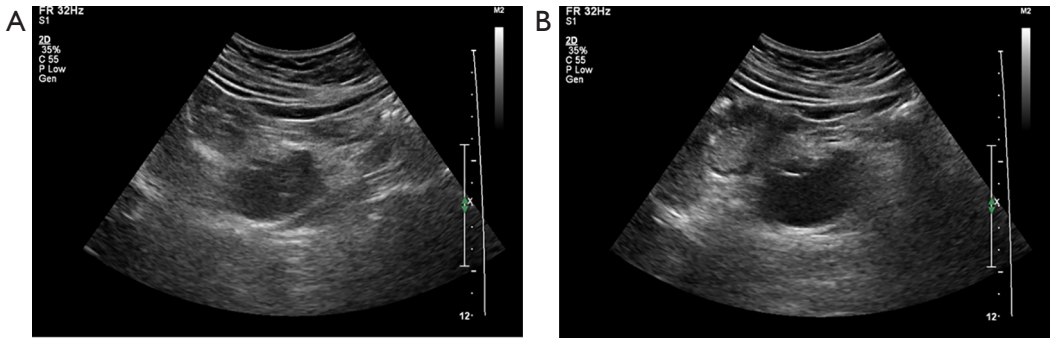

Figure 2 The ultrasound images of a 66-year-old male patient with a PCL located in the head of pancreas. Before taking cereal-based oral contrast agent (A), the sonolucency of PCL was poor, while after taking the agent (B), the sonolucency was satisfying. FR, frame rate; S1, speed 1; C, compress; P, persistence; Gen, general; PCL, pancreatic cystic lesion.

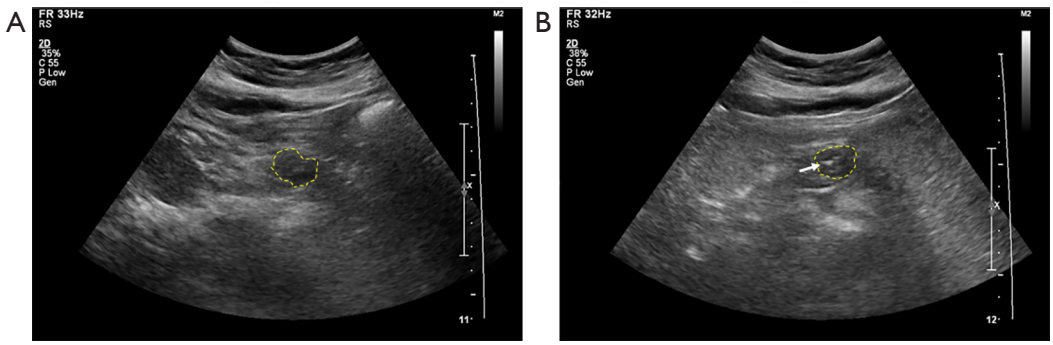

Figure 3 The ultrasound images of a 66-year-old female patient with a PCL (marked in yellow) located in the body of pancreas. Before taking cereal-based oral contrast agent (A), only 1 septum thicker than 2 mm was observed, and no papillary structure or calcification was observed, so the structural visualization score for this PCL was 2. After taking the agent (B), some anechoic areas became more obvious, and a total of 5 lobules were observed, so the septa number was consequently defined as 4. The thickness of the septum exceeded 2 mm, and 1 calcification was observed (arrow), so the structural visualization score after taking the agent was 6. FR, frame rate; RS, resolution-speed; C, compress; P, persistence; Gen, general; PCL, pancreatic cystic lesion.

total of 9 PCLs (30%) had satisfactory sonolucency. After taking the oral contrast agent, a total of 24 patients (80%) with PCL had satisfactory sonolucency (P=0.002; *Figure 2*). The median structure visualization score was 1 (0–6) after the patients took the agents, and this score was significantly greater than that before the patients took the oral contrast agents [1 (0–3), P=0.001; *Figure 3*]. The number of observed septa in the 10 PCLs was changed after the agent was administered. Specifically, the number of observed septa increased in 8 PCLs, and the number decreased in 2 PCLs. For 4 PCLs, no cyst wall/septum thicker than 2 mm was observed before taking the agent, but a cyst wall/partition with a thickness >2 mm was observed after taking the agent. For 6 PCLs, no papillary structure was observed before taking the agent, but the papillary structure could be observed after taking the agent. For 1 PCL, no calcification was observed before the agent was taken, but 1 calcification was observed after the agent was taken. For 1 PCL, no dilated pancreatic duct was observed before the agent was taken, but a dilated pancreatic duct was observed after the agent was taken.

Correlation between the PCL structure visualization score on ultrasound images after taking the oral contrast agent and that on non-contrast-MRI images

Among the 27 patients, a total of 19 patients with 21 PCLs underwent non-contrast MRI. To compare the accuracy of ultrasound assisted by an oral contrast agent with that of MRI, the correlation between the PCL structure

visualization scores of these 2 examination approaches was analyzed. On MRI, the location of the PCL in 19 patients was consistent with the location detected by oral contrast agent-assisted ultrasound. The median maximum diameter of the PCL on MRI was 2.4 (0.47–5.0) cm, and no significant difference was detected between the maximal diameter of PCL on MRI and oral contrast agent-assisted ultrasound (P=0.101). No significant difference was detected between the median PCL structure visualization score determined by oral contrast agent-assisted ultrasound [1 (0–6)] and MRI [2 (0–7), P=0.070], and the PCL structure visualization scores obtained by the 2 examination approaches were significantly correlated (r=0.880, P<0.001). Among them, the septum numbers observed via oral contrast agent-assisted TAUS and non-contrast MRI were different for the 6 PCLs. A total of 5 PCLs had more septa observed via MRI, and 1 PCL had fewer septa. In 2 PCLs, no cyst wall/septum thicker than 2 mm was observed during oral contrast agent-assisted ultrasound, but a cyst wall/septum thicker than 2 mm was observed during non-contrast MRI. In 4 PCLs, the numbers of papillary structures observed during the 2 examination approaches were different, and the number of papillary structures observed on MRI was greater than that observed on oral contrast agent-assisted ultrasound.

Discussion

The management of PCLs varies. For certain types of PCL, regular follow-up is essential, and these types of PCL require proper imaging technologies (14). There is room for improvement in the accuracy of transabdominal ultrasonography for accessing the PCL since the pancreas is often hidden behind gastrointestinal gases during examination (15). Therefore, it is necessary to optimize traditional ultrasound examinations to improve the detection rate of PCLs and the clarity of PCL ultrasound images. The oral contrast agent can fill the stomach and eliminate the interference of gastrointestinal gas on TAUS examination of organs in the deep area of the abdomen (11). In addition, oral contrast agents are denser in texture than plain water and therefore can remain in the gastrointestinal tract for a longer period (16), giving ultrasonographers enough time to access the PCL. This advantage is more important in the evaluation of the PCL than in the evaluation of the normal pancreas. This study was the first to explore the value of cereal-based oral contrast agents in ultrasound examinations of PCL through a prospective cohort, and for the first time, a structured score was used to quantitatively compare the clarity and sonolucency of PCL before and after taking the oral contrast agent.

Since the oral contrast agent eliminated the interference of gastric gas on the PCL to the greatest extent, the sonolucency of the PCL after oral contrast agent administration was significantly greater than that during fasting TAUS. With the improvement in sonolucency, the internal structure of the PCL became more clearly visible. In this study, the main structural characteristics of the PCL (number of septa, septum/wall thickness, papillary structure, calcification) that were of interest in the previous literature (6,17,18) were included in the quantitative evaluation, so were the high-risk features such as the dilated pancreatic duct, and it was found that the overall structural visualization score after taking the oral contrast agent was greater than that before taking the agent. After taking the oral contrast agent, the internal structure of the PCL could be more clearly observed by TAUS. The most prominent changes in the structural visualization scores before and after taking the oral contrast agent were the number of septa in the PCL, the thickening of the cyst wall/septum, and the presence of a visible papillary structure. The number of septa and the thickness of the cyst wall/septum in the PCL may be related to the pathological classification. Zhong *et al.* (18) examined the MCN and SCN by EUS and reported that the SCN tended to contain more septa and thinner cyst walls. In addition, Fan *et al.* (17) reported that the papillary structure was more likely to be present in NETs than in SCNs and MCNs. Therefore, the application of an oral contrast agent could increase the value of TAUS in the diagnosis, classification, or follow-up of PCLs.

In this study, the images of oral contrast agent-assisted ultrasound of PCLs were further compared with the non-contrast MRI images; it was found that there was no significant difference between the structured visualization scores of the oral contrast agent-assisted ultrasound images and that of the non-contrast MRI images, and the Spearman correlation factor of these two was 0.880, which indicated a good correlation. Non-contrast MRI is currently the recommended radiological examination approach for evaluating PCL (15), but this approach has limitations, such as high cost, risk of causing claustrophobia, and limited use in patients with implanted metal devices. The use of oral contrast agent-assisted TAUS not only retains the advantages of traditional ultrasound but also improves the accuracy of its image display. According to our study, the internal structures observed by oral contrast agent-assisted

TAUS and non-contrast MRI were comparable to some extent.

This study has several limitations. The number of enrolled patients was limited. Most of the patients did not undergo surgical resection, and pathological diagnoses were lacking; therefore, an in-depth analysis of the correlation between the structural visualization scores and the pathological classification was not available. Since many patients did not undergo EUS examination, the accuracy of oral contrast agent-assisted TAUS and EUS was not compared. Nevertheless, this study preliminarily explored the value of a cereal-based oral contrast agent in the examination of PCLs via TAUS and confirmed that the use of an oral contrast agent could improve the accuracy of ultrasonography via a structured scoring system. Additionally, with the assistance of an oral contrast agent, the accuracy of TAUS for accessing the PCL was comparable with that of non-contrast MRI to some extent, suggesting that oral contrast agent-assisted TAUS could be an alternative to non-contrast MRI for PCL follow-up in resource-limited area, or patients who cannot tolerate MRI, such as those with metal implants. However, a randomized and controlled comparative study on oral contrast agent-assisted TAUS and non-contrast MRI/EUS is needed to explore whether oral contrast agent-assisted TAUS could be a proper alternative to non-contrast MRI/EUS. Nonetheless, these findings provide a basis for further PCL ultrasound research on oral contrast agents.

Conclusions

Oral contrast agent has been used in TAUS for gallbladder disease, yet no study has applied it in TAUS for PCL. This prospective study used a structured scoring system to confirm that cereal-based oral contrast agent could improve the ultrasound quality of PCLs, and the correlation between the quality of oral contrast agent-assisted TAUS and non-contrast MRI findings on PCLs was satisfactory. Further research to improve visualization of PCLs on TAUS using oral contrast agents could result in TAUS being a potential alternative to MRI in the follow-up of PCLs in resource-limited situations.

Acknowledgments

Funding: The study was supported by the National High Level Hospital Clinical Research Funding of Peking Union Medical College Hospital (No. 2022-PUMCH-D-001).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-24-367/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-367/coif). All authors report that this study was supported by the National High Level Hospital Clinical Research Funding of Peking Union Medical College Hospital (No. 2022-PUMCH-D-001). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics committee of Peking Union Medical College Hospital (No. I-24PJ0102), and informed consent was provided by all individual participants.

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Cite this article as: Ji J, Shi X, Xia Y, Gao L, Luo N, Ma L, Pan A, An Y, Hu Y, Jiang Y. Can cereal-based oral contrast agents-assisted ultrasound become an alternative to non-contrast magnetic resonance imaging (MRI) in radiological follow-up for pancreatic cystic lesions? Quant Imaging Med Surg 2024;14(8):5602-5609. doi: 10.21037/qims-24-367

