

DIAGNOSTIC ACCURACY OF CONTRAST-ENHANCED PANCREATIC ULTRASOUND FOR DIAGNOSING NEOPLASTIC PANCREATIC LESIONS: A SYSTEMATIC REVIEW

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Abstract

Introduction: In recent years, there has been evidence to support the utility of contrast-enhanced ultrasound (CEUS) as a minimally invasive diagnostic technique for diagnosis of pancreatic neoplasms.

Objective: To assess the diagnostic accuracy of CEUS in distinguishing between benign and malignant pancreatic neoplasms.

Methods: A systematic review of literature published between 2012 and August 2023 was performed across several databases including PubMed, Cochrane Library, ProQuest, and Google Scholar.

Results: A total of 8 studies investigating the diagnostic utility of CEUS for benign and malignant pancreatic neoplasms were eligible for inclusion in this review. These studies included a total of 641 patients who participated in five prospective studies and three retrospective studies. Four studies included patients of Caucasian descent, while the remaining four studies included patients of Asian descent. In seven studies, 2,4 ml of Sonovue was used as the contrast agent, while in one study, 2.5 g of Levovist was used. CEUS has a sensitivity which ranges from 73.7% to 100% and specificity which ranges from 61.7% to 97.2%, and excellent accuracy for the qualitative diagnosis of benign and malignant pancreatic neoplasms.

Conclusion: CEUS has good sensitivity, specificity, and accuracy for the qualitative diagnosis of benign and malignant pancreatic neoplasms. These data demonstrate that CEUS is an important imaging tool for characterization of pancreatic tumours and is extremely successful for the diagnosis of benign and malignant pancreatic neoplasms.

Keywords: Ultrasound, Contrast enhanced, Pancreatic neoplasm, Diagnostic accuracy

INTRODUCTION

Pancreatic cancer, a common malignant tumour that frequently manifests as pancreatic adenocarcinoma, has a terrible prognosis, with an overall 5-year relative survival rate of less than 10%.¹ Based on data from the Global Cancer Observatory (GLOBOCAN) 2020, a total of 495,773 individuals received a new diagnosis of pancreatic cancer globally in the year 2020. This places pancreatic cancer as the 12th most prevalent form of malignant neoplasms. In the year 2020, pancreatic cancer accounted for an approximate total of 466,003 fatalities, so positioning it as the seventh most prevalent kind of malignant neoplasms.²

Currently, the focus is on early and curable pancreatic cancer detection³; therefore, it is necessary to develop and evaluate a new diagnostic method. Endoscopic ultrasonography (EUS) is a well-established, dependable, and safe method that provides a detailed view of pancreatic lesions with accuracy comparable to or superior to other diagnostic modalities.⁴ One limitation of EUS is its inability to differentiate between carcinoma and other causes without the use of an invasive cytological test known as EUS fine-needle aspiration (EUS FNA). This is due to the fact that most pancreatic cancers, even those with benign causes, exhibit a hypoechoic look.⁵ Furthermore, endoscopic ultrasound-guided fine-needle aspiration (EUS FNA) has both limits and substantial diagnostic advantages.⁴ The necessity arises for the development of non-invasive alternatives to endoscopic ultrasound-guided fine-needle aspiration (EUS FNA). In recent years, there has been evidence to support the utility of contrast-enhanced ultrasound (CEUS) as a minimally invasive diagnostic technique.⁶

CEUS is a non-invasive imaging technique that has diagnostic and clinical decision-making applications. CEUS can accurately depict the position, size, and characteristics of a tumour, is a sensitive imaging instrument for evaluating tumour microcirculation and perfusion, and can image dynamic vascular patterns in focal lesions. Compared to conventional ultrasound and computed tomography (CT), CEUS is more accurate at locating tumours and observing blood flow at the level of tissue perfusion⁷; therefore, it has diagnostic value in the evaluation of a variety of pathologies. CEUS imaging of tumour microvessels in real time reveals the entire blood perfusion process. Analyses of enhancement kinetics facilitate differentiation between benign and malignant tumours.

The objective of this study is to assess the diagnostic accuracy of contrast-enhanced ultrasonography in distinguishing between benign and malignant pancreatic neoplasms.

Method

This systematic review was reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines 2020.

Search Strategy

A systematic review of literature published between 2012 and August 2023 was performed across several databases including PubMed, Cochrane Library, ProQuest, and Google Scholar. The search strategy involved the following combinations of keywords: “ultrasound” or “sonography” or “ultrasonography” or “ultrasonic” or “US” AND “contrast enhanced” AND “pancreatic neoplasm” or “pancreas neoplasm” or “pancreatic cancer” or “pancreas cancer” AND “diagnostic accuracy” OR “diagnostic performance”.

Eligibility Criteria

The inclusion criteria for this study were as follows: (1) the utilisation of contrast-enhanced ultrasound (CEUS) in the diagnosis of both benign and malignant pancreatic neoplasms, either through retrospective or prospective studies; (2) studies that involved a sample size of more than 20 patients; (3) confirmation of the diagnosis of benign and malignant pancreatic neoplasms through methods such as needle biopsy, surgery and pathology, or alternative imaging techniques; (4) studies that provided reported outcomes, including values for true positive (TP), true negative (TN), false positive (FP), and false negative (FN), or data from which these values could be derived. The exclusion criteria for this study were as follows: (1) studies that did not confirm the diagnosis of benign and malignant pancreatic neoplasms using an alternate approach; (2) studies that were duplicates or did not provide adequate data; (3) case reports, reviews, letters, abstracts, or editorials. The scope of the search was restricted to research that were published in the English language.

Study Selection

The author independently reviewed titles and abstracts to determine which studies were admissible. The removal of articles with redundant or overlapping datasets. The full text of potentially pertinent studies was collected. The author independently reviewed the complete text records to determine which studies satisfied the inclusion criteria.

Data Extraction and Parameter Measured

Author independently extracted data, including author, publication date, study site, study population, and outcome measures, from eligible studies. The TP, FP, FN, and TN rates for CEUS in the diagnosis of benign and malignant pancreatic neoplasms were the primary outcome measures.

Assessment of Quality of Individual Studies

The author assessed study quality and risk of bias independently using QUADAS-2, the most recent version of QUADAS.⁸ This instrument is suggested for assessing the risk of bias and applicability of primary diagnostic accuracy studies in systematic reviews. Patient selection, index test, reference standard, and flow and timing are the four domains that make up QUADAS-2. Risk of bias and applicability were ranked as low, high, or ambiguous.

Results

The search identified 2478 results and it resulted in 2322 articles after duplicates removed. Of these, 2230 articles were excluded due to non-original articles, titles and abstract not represent the focus of interest and it resulted in 92 articles for screening. 71 articles were excluded due to not evaluating the focus of interest, full-text not available, animal studies, and inappropriate study design and it resulted in 21 articles for full-text assesment. In the end, it was determined that 8 studies investigating the diagnostic utility of CEUS for benign and malignant pancreatic neoplasms were eligible for inclusion in this review (Fig. 1). Table 1 shows the characteristics of the eight included investigations. These studies included a total of 540 patients who participated in five prospective studies and three retrospective studies. Four studies included patients of Caucasian descent, while the remaining four studies included patients of Asian descent. In seven studies, 2,4 ml of Sonovue was used as the contrast agent, while in one study, 2.5 g of Levovist was used.

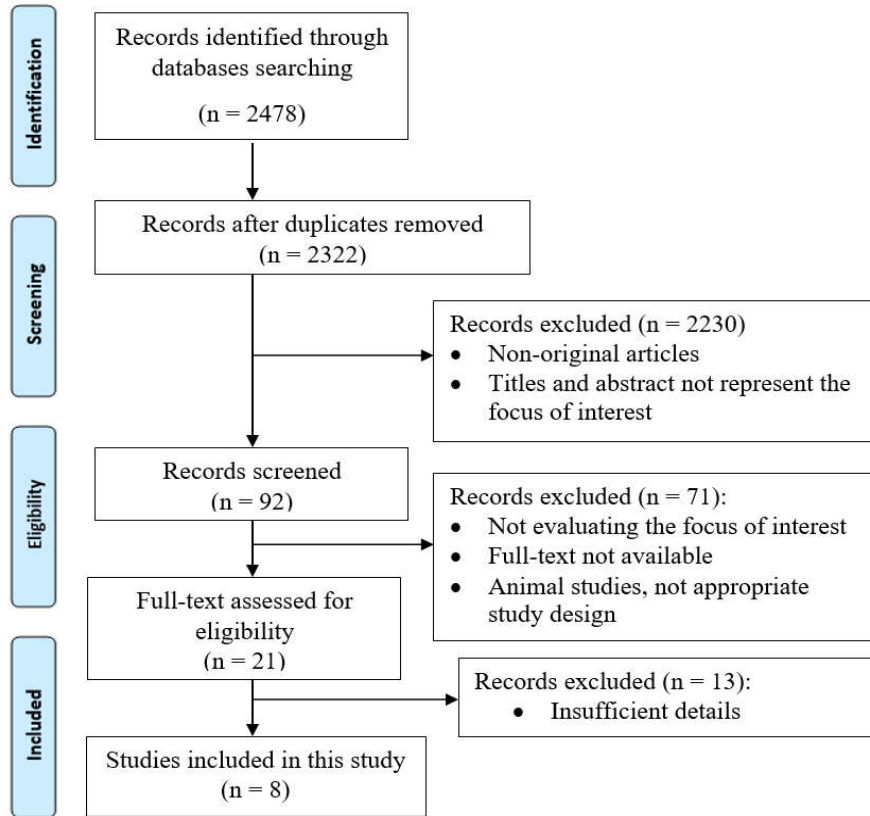


Figure 1. The search strategy based on PRISMA flow diagram

Table 1. Characteristics of the included studies

Author	Country	Race	Study design	N (male/female)	Mean or median Age (years)	Contras agent	TP	FP	FN	TN	Sensitivity	Specificity
Kurihara et al. (2012) ⁹	Japan	Asian	Prospective	22 (14/8)	67.5	Levovist 2.5 g	15	1	2	4	88.2%	NA
Xu et al. (2012) ¹⁰	China	Asian	Retrospective	52 (30/22)	51.5	Sonovue 2.4 ml	16	11	0	27	100%	78.9%
Grossjohann et al. (2012) ¹¹	Denmark	Caucasian	Retrospective	49 (26/23)	66	Sonovue 2.4 ml	38	1	6	4	86%	80%
Vasile et al. (2012) ¹²	Romania	Caucasian	Prospective	76 (38/38)	59.5	Sonovue 2.4 ml	51	4	6	15	Using time to peak of 9 second: 73.7% Using time to maximum gradient of 8.5 second: 87.7%,	Using time to peak of 9 second: 81.3% Using time to maximum gradient of 8.5 second: 65.3%
Fan et al. (2013) ¹³	China	Asian	Retrospective	90 (53/37)	55.1	Sonovue 2.4 ml	33	7	3	47	91.7%	97.2%
Ardelean et al. (2015) ¹⁴	Romania	Caucasian	Prospective	83 (34/49)	63.7	Sonovue 2.4 ml	72	1	6	4	90.7%	90%
Sun et al. (2017) ¹⁵	China	Asian	Prospective	61 (13/48)	46.9	Sonovue 2.4 ml	21	5	5	30	88.5%	65.7%
Bunganic et al. 2018 ⁶	Czech Republic	Caucasian	Prospective	107 (NA)	67.5	Sonovue 2.4 ml	69	13	4	21	94.5%	61.7%

Discussion

According to the findings of this systematic review, CEUS has a sensitivity which ranges from 73.7% to 100% and specificity which ranges from 61.7% to 97.2%, and excellent accuracy for the qualitative diagnosis of benign and malignant pancreatic neoplasms. Although the sensitivity and specificity of CEUS in differentiating benign from malignant lesion varies greatly between studies, we can say that CEUS can provide critical information that aids in the timely and correct diagnosis and management of pancreatic lesions.

Contrast-enhanced ultrasonography (CEUS) is a medical procedure that entails the utilisation of intravenous contrast agents containing microbubbles composed of perfluorocarbon or nitrogen gas. The purpose of this technique is to enhance the quality and dependability of ultrasound images. These bubbles have a significant impact on ultrasound backscatter and enhance vascular contrast. Currently, third generation contrast agents, such as SonoVue, have been extensively utilised in clinical settings. SonoVue is a formulation of SF₆ microbubbles characterised by a high molecular weight, robust microbubble stability, and excellent real-time imaging capabilities.¹⁶ Contrast-enhanced ultrasound (CEUS) plays a crucial role in the diagnosis of pancreatic neoplasms due to its high contrast and spatial resolution capabilities. Malignant pancreatic neoplasms manifest as solid focal masses inside the pancreas that exhibit a hypo-enhancing pattern compared to the surrounding normal tissue. These masses typically display an uneven distribution, an indistinct boundary, an irregular form, and peripheral enhancement. The initial onset time of the internal contrast agent is later than that of the pancreatic parenchyma, whereas the initial withdrawal time is earlier and the transition time is shorter.¹⁷ Similar to pancreatic parenchyma, benign tumours exhibit isoechoic enhancement, an even distribution, distinct boundaries, a regular shape, and time phases.¹⁶

The current study, on the other hand, had significant drawbacks. First, there was some heterogeneity among the included studies, which could be attributed to differences in ultrasound technician experience, equipment sensitivity, contrast agents, as well as case selection, size of the focal pancreatic neoplasm, clinical stage, and non-uniform gold standards. Second, the search was limited to literature published in English, which may have resulted in the omission of several studies. Finally, the methodological quality of the included studies may have influenced our findings.

Conclusion

This systematic review found that CEUS has good sensitivity, specificity, and accuracy for the qualitative diagnosis of benign and malignant pancreatic neoplasms. These data demonstrate that CEUS is an important imaging tool for characterization of pancreatic tumours and is extremely successful for the diagnosis of benign and malignant pancreatic neoplasms.

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