Fine needle biopsy guided by contrast-enhanced harmonic versus conventional endoscopic ultrasound with macroscopic on-site evaluation for solid pancreatic lesions: abridged secondary publication

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KEY MESSAGES

1. Fine needle biopsy guided by either contrast-enhanced harmonic or conventional endoscopic ultrasound, with macroscopic on-site evaluation of specimen adequacy, achieves similarly low false-negative rates and high diagnostic accuracies when the prevalence of avascular areas in lesions is <31%.
2. Routine use of contrast-enhanced harmonic endoscopic ultrasound for fine needle biopsy may be unnecessary when dedicated needles are used for tissue acquisition and the expected prevalence of avascular areas is low in target lesions.

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Introduction

Fine needle aspiration (FNA) is the first-line diagnostic method, especially when rapid on-site evaluation by a cytopathologist is available.[1] However, FNA has limitations, including inadequate cellular acquisition and inability to provide core tissue for histological analysis.[1] Additionally, rapid on-site evaluation may be unavailable due to limited resources.

Endoscopic ultrasound (EUS)–guided fine needle biopsy (FNB) has been used to improve tissue acquisition.[1] FNB needles can collect both cells and intact core tissue for histological analysis. Macroscopic on-site evaluation (MOSE) is increasingly used to assess specimen adequacy[2] based on the presence of a macroscopic visible core (MVC), defined as whitish or yellowish tissue with an apparent bulk. EUS-guided FNB combined with MOSE provides comparable diagnostic accuracy and better tissue quality, while requiring fewer passes, relative to FNB alone.[2] Nevertheless, the reported false-negative rate is 21.3%, likely due to tumour necrosis in sizeable tumours.[2] Contrast-enhanced EUS allows better delineation of vascularity and tissue perfusion.[3] Contrast-enhanced harmonic EUS (CH-EUS) facilitates FNB of pancreatic lesions and helps avoid necrotic tissue and/or vascular structures within lesions.[3]

Puncturing avascular or necrotic areas of a tumour is a major cause of false-negative results. CH-EUS can define avascular or necrotic areas within a tumour, which may improve diagnostic accuracy. This study aimed to compare the diagnostic performance of FNB guided by either CH-EUS or conventional EUS, along with MOSE, for solid pancreatic lesions.

Methods

This prospective randomised controlled study was conducted between February 2022 and August 2023 at three tertiary referral centres in Hong Kong, Italy, and Korea. Consecutive patients aged 18 to 80 years referred for EUS-guided tissue acquisition for solid pancreatic lesions >1 cm were screened for eligibility.

Patients with coagulopathy, altered anatomy, contraindications to endoscopy, or pregnancy were excluded. Eligible patients were randomised in a 1:1 ratio to undergo FNB guided by either CH-EUS or conventional EUS.

Each pancreatic lesion was examined using a linear echoendoscope. EUS-guided tissue acquisition was performed with a 22-gauge Franseen FNB needle. The degree of suction was selected by the endoscopist. MOSE was used to assess specimen adequacy. In the CH-EUS group, CH-EUS with SonoVue was used to identify non-enhancing, avascular (necrotic) areas in the target lesion and to guide FNB to viable areas. FNB was deemed complete if the obtained MVC was ≥4 mm. If the MVC was <4 mm, FNB was repeated until a total MVC length ≥4 mm was achieved. Up to seven passes were allowed.

The primary outcome was the false-negative rate. Secondary outcomes were sensitivity, specificity, positive predictive value, negative predictive value, procedural time, and procedure-related complications.

Results

In total, 128 patients were randomised to undergo FNB guided by CH-EUS (n=64) or conventional EUS (n=64). The two groups were comparable in terms of baseline characteristics, except for the rate of pancreatic adenocarcinoma (59.4% vs 79.7%, P=0.013; Table). Avascular areas were detected in 25.0% of solid pancreatic lesions in the CH-EUS group and in 20.3% of such lesions in the conventional EUS group; detection increased to 31.3% with CH-EUS. The two groups were similar in terms of the number of passes required to achieve an MVC length ≥4 mm (1 vs 1.5) and the mean MVC length (16.8 vs 20.6 mm). Procedure time was longer in the CH-EUS group (28.9 vs 24.4 minutes, P=0.039). Procedure-related adverse event rates were low (1.6% in both groups).

For CH-EUS–guided FNB and conventional EUS–guided FNB, respectively, false-negative rates were 6.0% and 7.9%; sensitivities were 94.0% and 92.1%; specificities were 100% and 100%; and diagnostic accuracies were 95.3% and 92.2% (Table).

Discussion

Although CH-EUS increased the detection of avascular areas in solid pancreatic lesions from 25.0% to 31.3%, the false-negative rates of both CH-EUS–guided FNB and conventional EUS–guided FNB remained comparable (6.0% vs 7.9%), consistent with single-centre randomised controlled studies from Korea and Taiwan.[4,5] In the Korean study involving 240 patients, diagnostic sensitivities for malignancy were 85.8% and 88.3% for the respective FNB approaches.[4] Of note, the needle types used were heterogeneous.[4] This may have contributed to the slightly lower sensitivity. In the Taiwan study, 118 patients with solid pancreatic lesions underwent FNB guided by either CH-EUS or conventional EUS using the fanning technique.[5] There was no difference in diagnostic sensitivity (100% vs 100%) or accuracy (98.3% vs 100%).

Data regarding the false-negative rate of EUS-guided tissue acquisition using dedicated FNB needles remain scarce. Both studies from Korea and Taiwan discussed the false-negative rate of CH-EUS–guided FNB. In our prior study,[2] the false-negative rate of EUS-guided tissue acquisition using a 19-gauge conventional FNA needle was 21.3%. In contrast, the current study demonstrated false-negative rates of 6.0% and 7.9% when a dedicated 22-gauge FNB needle was used. These findings suggest that routine use of CH-EUS does not further reduce the false-negative rate when a dedicated FNB needle is used and when the prevalence of avascular areas in target lesions is <31%.

The present study has several limitations. First, the actual magnitude of effect of each modality is unknown. It is possible that the superior tissue acquisition achieved with modern dedicated FNB needles eclipsed the potential benefit of CH-EUS.[3-5] Given that dedicated FNB needles have been increasingly adopted, it may be unethical to conduct a comparative study of CH-EUS–guided FNA versus CH-EUS–guided FNB. Second, it remains uncertain how the prevalence and extent of avascular areas (necrosis) affect the false-negative rate. Although the prevalence of avascular areas within solid pancreatic lesions in our study was 31%—higher than the 16.4% reported in another study,[3] our study may have been underpowered to detect a small difference in false-negative rates between techniques. Third, a higher frequency of pancreatic adenocarcinoma was observed in the conventional EUS group. The use of a separate patient randomisation website for each study centre is likely to reduce potential bias associated with unbalanced pathological diagnoses between study groups.

Conclusion

Both CH-EUS–guided and conventional EUS–guided FNB demonstrate low false-negative rates and high diagnostic accuracies for solid pancreatic lesions. Routine use of CH-EUS may be unnecessary when the prevalence of avascular areas in target lesions is low.

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TABLE. Participant characteristics and diagnostic performance of fine needle biopsy guided by either conventional endoscopic ultrasound (EUS) or contrast-enhanced harmonic EUS (CH-EUS).

Variable	All (n=128)*	Conventional EUS (n=64)*	CH-EUS (n=64)*	P value
Age, y	66.5±10.1	67.6±9.7	65.4±10.4	0.231
Male sex	60 (46.9)	34 (53.1)	26 (40.6)	0.156
Lesion size, mm	32.3±13.5	34.0±13.4	30.7±13.5	0.168
Lesion location				
Uncinate process	12 (9.4)	5 (7.8)	7 (10.9)	0.510
Head	52 (40.6)	31 (48.4)	21 (32.8)	
Neck	13 (10.2)	6 (9.4)	7 (10.9)	
Body	28 (21.9)	12 (18.8)	16 (25.0)	
Tail	23 (18.0)	10 (15.6)	13 (20.3)	
Lesion echogenicity				
Hypoechoic	124 (96.9)	63 (98.4)	61 (95.3)	0.619
Hyperechoic	0	0	0	
Isoechoic	4 (3.1)	1 (1.6)	3 (4.7)	
Contrast enhancement pattern				
Hypoenhanced	-	-	37 (57.8)	-
Hyperenhanced	-	-	18 (28.1)	-
Isoenhanced	-	-	9 (14.1)	-
Avascular areas identified on B-mode EUS	29 (22.7)	13 (20.3)	16 (25.0)	0.526
Avascular areas identified on CH-EUS	-	-	20 (31.3)	-
Final diagnosis				
Pancreatic adenocarcinoma	89 (69.5)	51 (79.7)	38 (59.4)	0.013
Pancreatic neuroendocrine tumour	15 (11.7)	7 (10.9)	8 (12.5)	0.783
Metastatic cancer to the pancreas	5 (3.9)	3 (4.7)	2 (3.1)	>0.999
Lymphoma	1 (0.8)	0	1 (1.6)	>0.999
Solid pseudopapillary tumour	1 (0.8)	1 (1.6)	0	>0.999
Intraductal papillary mucinous neoplasm with high-grade dysplasia	2 (1.6)	1 (1.6)	1 (1.6)	>0.999
Intraductal papillary mucinous neoplasm with low-grade dysplasia	1 (0.8)	0	1 (1.6)	>0.999
Serous cystadenoma	3 (2.3)	0	3 (4.7)	0.244
Focal chronic pancreatitis	4 (3.1)	0	4 (6.3)	0.119
Autoimmune pancreatitis	3 (2.3)	1 (1.6)	2 (3.1)	>0.999
Others	4 (3.1)	0	4 (6.3)	0.119
Puncture approach				0.077
Transgastric	-	27 (42.2)	37 (57.8)	
Transduodenal	-	37 (57.8)	27 (42.2)	
No. of passes	-	1.5 (1-2)	1 (1-2)	0.480
Macroscopic visible core length, mm	-	20.6±21.0	16.8±15.9	0.259
False-negative rate, %	-	7.9	6.0	>0.999
Sensitivity, %	-	92.1	94.0	>0.999
Specificity, %	-	100.0	100.0	>0.999
Positive predictive value, %	-	100.0	100.0	>0.999
Negative predictive value, %	-	16.7	82.4	0.009
Diagnostic accuracy, %	-	92.2	95.3	0.718

* Data are presented as mean ± standard deviation, No. (%) of participants, or median (interquartile range).

Disclosure

The results of this research have been previously published in:

1. Chong CCN, Ligresti D, Kim TH, et al. Contrast enhanced EUS versus conventional EUS guided fine needle biopsy with macroscopic on-site evaluation for solid pancreatic lesions: a multicenter randomized trial. Gastrointest Endosc 2025:S0016-5107(25)02114-5.
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