—Original Article—

Diagnostic value of EUS-guided SF6 pancreatography for pancreatic cystic lesions on cyst communication with the pancreatic duct

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ABSTRACT

Background and Objectives: ERCP remains the reliable method to determine whether pancreatic cystic lesions (PCLs) and pancreatic duct communicate when other modalities (computed tomography, magnetic resonance imaging, and EUS) fail. However, complications after ERCP are still a risk that should not be ignored. In this study, we evaluated the value of EUS-guided SF6 pancreatography (ESP) for the diagnosis of PCLs focusing on pancreatic cyst communication with the pancreatic duct. **Patients and Methods:** We reviewed the database of medical records to retrieve the clinicopathological data of the patients with PCLs who had undergone ESP, and analyzed the diagnostic value of ESP to determine communication between the cyst and the pancreatic duct. The inclusion criteria were as follows: (1) PCLs were pathologically diagnosed by postsurgery specimen or through-the-needle biopsy and (2) ESP was performed to determine communication between the pancreatic cyst and the pancreatic duct. **Results:** Pathological diagnosis confirmed communication with the pancreatic duct in all eight patients with positive pancreatography, among whom seven were branch-duct–intraductal papillary mucinous neoplasm (BD-IPMN) and one was the main duct-IPMN. Pathological diagnosis confirmed noncommunication with the pancreatic duct in 20 of the 21 patients with negative pancreatography, among whom 11 were mucinous cystic neoplasm, 7 were serous cystic neoplasm, 1 was solid pseudopapillary neoplasm, 1 was pancreatic pseudocyst, and 1 was BD-IPMN. The accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of ESP to determine communication between the pancreatic cyst and the pancreatic duct were 96.6% (28/29), 88.9% (8/9), 100% (20/20), 100% (8/8), and 95.2% (20/21), respectively. **Conclusions:** ESP achieved high accuracy to determine communication between the pancreatic cyst and the pancreatic duct.

Key words: communication, EUS-guided SF6 pancreatography, pancreatic cystic lesion, pancreatic duct

INTRODUCTION

Pancreatic cystic lesions (PCLs) can be divided into neoplastic and nonneoplastic lesions. The most

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commonly encountered neoplastic PCLs are serous cystic neoplasm (SCN), mucinous cystic neoplasm (MCN), and intraductal papillary mucinous neoplasm (IPMN), whereas the most commonly encountered nonneoplastic PCLs are pancreatic pseudocyst (PPC).[1-4] Treatments vary between different types of PCLs, so precise diagnosis before treatment are often required.

For the diagnosis of PCLs, computed tomography (CT) and magnetic resonance imaging (MRI)/magnetic resonance cholangiopancreatography (MRCP) are usually the first choices.[5-8] If the diagnosis is still not clear, EUS and EUS-guided fine-needle aspiration can then be performed. Cyst fluid can be sent for chemical analysis and cytology. Through-the-needle biopsy (TTNB) has recently been reported to acquire tissue from the cystic wall or intracystic septums for histopathology.[9,10] Cyst fluid analysis and cytology are less sensitive and specific than TTNB, but TTNB is currently not routinely used clinically.

It is very important for the differential diagnosis of PCLs to accurately determine whether the cyst communicates with the pancreatic duct.[8,11] Usually, IPMN communicates with the pancreatic duct, whereas MCN, SCN, and solid pseudopapillary neoplasm (SPN) do not communicate with the pancreatic duct. PPC could be either communicated or not with the pancreatic duct. At present, endoscopic ERCP remains the reliable method to determine whether PCLs and pancreatic ducts communicate when other modalities (CT, MRI, and EUS) fail.[12] However, complications after ERCP, including postoperative pancreatitis, are still a risk that should not be ignored.

Sulfur hexafluoride (SF6) has widely been used as a contrast agent for ultrasonography and proved to be safe.[13-15] However, to our knowledge, it has not been reported in the literature to inject SF6 into the pancreatic cyst to perform pancreatography to determine communication between the cyst and the pancreatic duct. Therefore, in the present study, we analyzed clinicopathological data of patients with PCLs and evaluated the value of ESP for the diagnosis of PCLs focusing on possible pancreatic cyst communication with the pancreatic duct.

PATIENTS AND METHODS

Design and patients

We reviewed the database of medical records to retrieve the clinicopathological data of the patients with PCLs who had undergone ESP in First Medical Center of Chinese PLA General Hospital between April 2015 and February 2021 and analyzed the diagnostic value of ESP to determine communication between the cyst and the pancreatic duct. The inclusion criteria were as follows: (1) PCLs were pathologically diagnosed by postsurgery specimen or TTNB and (2) ESP was performed to determine communication between the pancreatic cyst and the pancreatic duct. The present study was in accordance with the ethical standards of Ethics Committee of Chinese PLA General Hospital and with the Helsinki Declaration.

Procedure of EUS-guided SF6 pancreatography

All EUS procedures were performed under intravenous anesthesia with a linear array echoendoscope (GF-UCT260, Olympus, Tokyo, Japan) connected to a processor featuring the color Doppler function (Prosound F75, Aloka, Tokyo, Japan). After the location of a pancreatic cyst by EUS, aspiration was performed with a 22G or 19G needle (EchoTip, Cook, Limerick, Ireland). The cyst fluid was aspirated as much as possible and then 2–5 mL diluted SF6 microbubbles (SonoVue, Bracco Diagnostics Inc, Italy) was injected into the cyst through the needle. The volume of SF6 injected was decided by the total volume of the cyst fluid aspirated by the needle. If the total volume of the cyst fluid aspirated by the needle is no more than 5 mL, then an equal volume of SF6 is injected into the cyst (ranging from 2 mL to 5 mL). If the total volume of the cyst fluid aspirated by the needle is more than 5 mL, then 5 mL of SF6 is injected into the cyst. The concentration of the diluted SF6 for intracystic injection was 1/50 of the conventional concentration used intravenously. The diluted SF6 was prepared by diluting 0.1 mL SF6 of conventional concentration to 5 mL by saline.

After injection of SF6 into the cyst, the adjacent pancreatic duct was located to observe whether microbubbles flow into the pancreatic duct from within the pancreatic cyst.

The pancreatic duct was observed for 3 min after injection of SF6. If microbubbles flow into the pancreatic duct from within the pancreatic cyst, we consider pancreatography is positive [Figure 1] and communication exists between the pancreatic cyst and the pancreatic duct. On the other hand, if microbubbles do not flow into the pancreatic duct from within the pancreatic cyst, we consider pancreatography is

negative [Figure 2] and communication does not exist between the pancreatic cyst and the pancreatic duct.

Data analysis

Continuous variables were reported as mean ± standard deviation, whereas categorical variables were reported as proportions. The accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were used to analyze the performance of ESP to determine communication between the cyst and the pancreatic duct. SPSS version 17 statistical software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

RESULTS

In total, 29 patients (8 males and 21 females) with a mean age of 48.9 (range, 31–67) years were included in our study. Patients' clinicopathological characteristics are presented in detail in Table 1.

Among the 29 patients with PCLs undergoing ESP, 6 were finally diagnosed by TTNB and 23 were diagnosed by pathology after surgery. After EUS-guided SF6 injection into the cysts, pancreatography was observed in 8 patients (positive pancreatography) and not in 21 patients (negative pancreatography).

Pathological diagnosis confirmed communication with the pancreatic duct in all eight patients with positive pancreatography, among whom seven were branch-duct-IPMN (BD-IPMN) and one was the main duct-IPMN. Pathological diagnosis confirmed noncommunication with the pancreatic duct in 20 of the 21 patients with negative pancreatography, among whom 11 were MCN,7 were SCN,1 was SPN,1 was PPC, and 1 was BD-IPMN. The accuracy, sensitivity, specificity, PPV, and NPV of ESP to determine communication between the pancreatic cyst and the pancreatic duct were 96.6% (28/29), 88.9% (8/9),

Table 1. Patients' clinicopathological characteristics

Parameter	Value, *n* (%)
Number of patients	29
Age (years), mean±SD	48.9±10.6
Sex	
Male	8 (27.6)
Female	21 (72.4)
Lesion size (cm), mean±SD	4.2±2.3
Lesion site	
Pancreatic head	11 (37.9)
Pancreatic body	5 (17.2)
Pancreatic tail	13 (44.8)
Final diagnosis	
SCN	7 (24.1)
MCN	11 (37.9)
IPMN	9 (31.0)
PPC	1 (3.4)
SPN	1 (3.4)

SCN: Serous cystic neoplasm; MCN: Mucinous cystic neoplasm; IPMN: Intraductal papillary mucinous neoplasm; PPC: Pancreatic pseudocyst; SPN: Solid pseudopapillary neoplasm; SD: Standard deviation

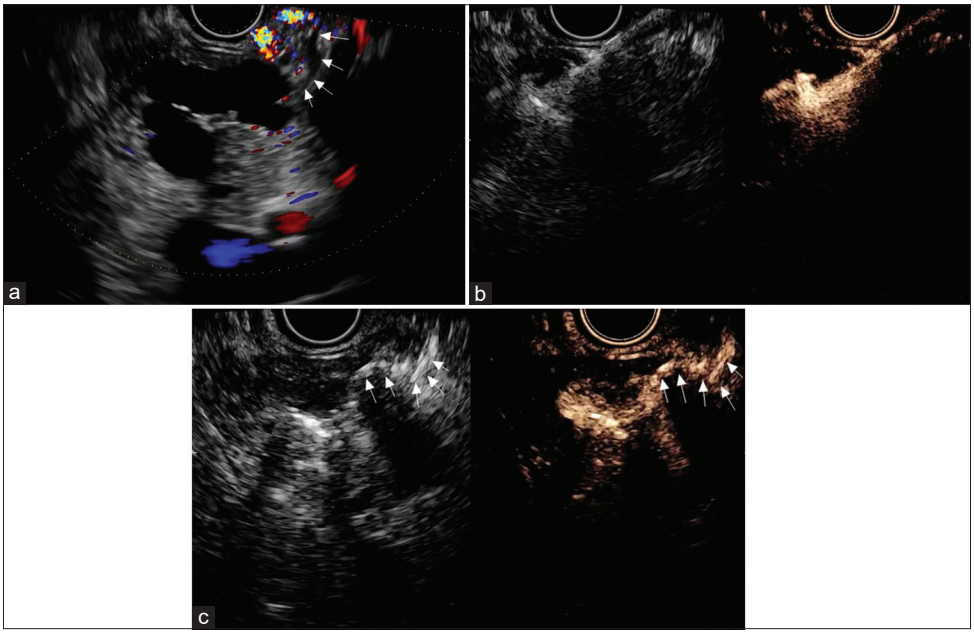

Figure 1. ESP showed communication between the pancreatic cyst and PD. (a) Before ESP, it was difficult to determine communication between the pancreatic cyst and PD by EUS (Arrows indicate PD); (b) SF6 was injected into the cyst; (c) SF6 flowed from within the cyst to PD (Arrows indicate positive pancreatography by SF6). ESP: EUS-guided SF6 pancreatography; PD: Pancreatic duct; SF6: Sulfur hexafluoride

100% (20/20), 100% (8/8), and 95.2% (20/21), respectively [Table 2].

Negative pancreatography was observed in one patient diagnosed with IPMN after operation, which was regarded as a misdiagnosis of ESP to determine communication between the pancreatic cyst and the pancreatic duct. In another patient of PPC, negative pancreatography was observed by ESP and the postsurgery pathology confirmed noncommunication between the pancreatic cyst and the pancreatic duct, in which the diagnosis of ESP was correct.

No complications were observed related to ESP.

DISCUSSION

To the best of our knowledge, the present study was the first to report injecting SF6 into the pancreatic cyst to perform pancreatography to determine communication between the cyst and pancreatic duct. We named this new method ESP. The accuracy, sensitivity, and specificity of ESP to determine communication between the pancreatic cyst and pancreatic duct were 96.6%, 88.9%, and 100%, respectively. With such primary performance, ESP might be a useful addition to the present workup for the diagnosis of PCLs.

Table 2. Comparison between EUS-guided sulfur hexafluoride pancreatography and final diagnosis on communication between pancreatic cyst and pancreatic duct

ESP	Communication by final diagnosis		Total
	Yes	No	
Positive pancreatography	8	0	8
Negative pancreatography	1	20	21
Total	9	20	29

ESP: EUS-guided SF6 pancreatography; SF6: Sulfur hexafluoride

Most PCLs are characterized by the primary imaging modalities of multidetector computed tomography (MDCT) and MRI/MRCP. Compared with MRI, MDCT is better in detecting calcifications, while MRI has advantages over MDCT by better delineating the cyst fluid content, thereby facilitating the recognition of internal septations and mural nodules.[6,16] However, because of its high spatial resolution, EUS was an excellent alternative in indeterminate patients after MRI and CT.[12,17-20] Often, it is important to evaluate the presence of communication between the cyst and pancreatic duct, especially when distinguishing IPMNs or pseudocysts from other PCLs. ERCP remains the most sensitive diagnostic modality to determine communication between PCLs and pancreatic duct but is not routinely recommended considering post-ERCP complications.[11,12]

Hence, ESP was proposed for the following reasons. First, the injection of SF6 into the cyst to perform

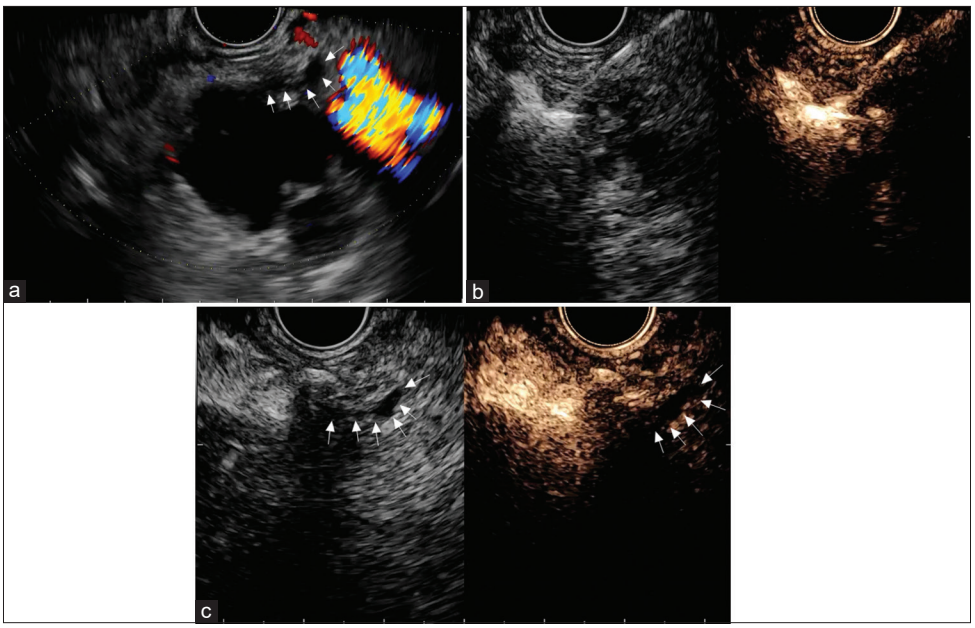

Figure 2. ESP showed no communication between the pancreatic cyst and PD. (a) Before ESP, it was difficult to determine communication between the pancreatic cyst and PD by EUS (Arrows indicate PD); (b) SF6 was injected into the cyst; (c) SF6 was not observed to flow from within the cyst to PD (Arrows indicate negative pancreatography by SF6). ESP: EUS-guided SF6 pancreatography; PD: Pancreatic duct; SF6: Sulfur hexafluoride

pancreatography is mechanically similar to the injection of contrast agent into the pancreatic duct to perform pancreatography. Second, SF6 has widely been used as a contrast agent for ultrasonography intravenously and proved its safety. Third, ESP could be performed as an addition to EUS imaging immediately after aspiration of cyst fluid for patients difficult to determine communication between PCLs and pancreatic duct. However, if a differential diagnosis of PCLs could be made by typical EUS imaging characteristics, ESP is not necessary. ESP is recommended to be used when it was helpful to make a differential diagnosis and difficult to determine communication between the pancreatic cyst and pancreatic duct by EUS as shown in Figures 1 and 2.

ESP was performed in 29 patients with PCLs in the present study and no ESP-related complications were found which otherwise might occur if undergoing ERCP. SF6 has been widely reported to be safe when used intravenously. In a retrospective study of 30,222 cases undergoing contrast-enhanced sonography of abdominal and superficial organs with SF6, no patient died as a result of any adverse reaction, and six patients (0.020%) had adverse reactions of varying degrees, including two patients (0.007%) who had signs of early anaphylactic shock that improved after active rescue.[14] SF6 also has a high safety profile when used intravesically.[21] To visualize and diagnose vesicoureteral reflux, SF6 is injected into the bladder through a urinary catheter and has an outstanding safety profile in adults and children, as well as in initial studies in pregnant women. Even not observed in our present study, the potential of adverse events might occur since SF6 is injected into the cyst which connects to the main pancreatic duct.

Our study has a few limitations. First, only one case of PPC and one case of SPN were included in the total 29 patients, so this study population did not reflect the whole spectrum of PCLs. Moreover, other PCLs not discussed in our study such as cystic pancreatic neuroendocrine neoplasm might also encounter the differentiation question of determining communication between the cyst and the pancreatic duct, which could benefit from the use of ESP. Second, our study was retrospective in a single center, which may have introduced unintended biases, and thus further multicenter prospective studies are needed.

CONCLUSIONS

We demonstrated the high accuracy of ESP to determine communication between the pancreatic cyst and the pancreatic duct.

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Conflicts of interest
Enqiang Linghu is an Associate Editor of the journal. This article was subject to the journal's standard procedures, with peer review handled independently of the editor and his research group.

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