Journal of Gastrointestinal & Digestive System

Klingenberg-Noftz et al., J Gastrointest Dig Syst
2016, 6:2
http://dx.doi.org/10.4172/2161-069X.1000405

Research Article Open Access

EUS Guided Fine-needle Aspiration (EUS Guided FNA) of Pancreatic Masses: Experiences from the Beginning of the Era and Implications to the Present Day

Rolf D. Klingenberg-Noftz[1*], Leimin Sun[2], Nils Homann[3] and Diether Ludwig[4]

[1]*Department of Gastroenterology and Internal Medicine, DRK-Hospital Grevesmuehlen, Kluetzer Strasse 13-15, 23939 Grevesmuehlen, Germany*

[2]*Sir Run Run Shaw Hospital, Zhejiang University, Hangzhou Zhejiang, China*

[3]*Medical Clinic II, Sauerbruchstrasse 7, Wolfsburg Hospital, 38440 Wolfsburg, Germany*

[4]*Clinic for Internal Medicine, Segeberg Hospitals, Am Kurpark 1, 2379 Bad Segeberg, Germany*

[*]**Corresponding author:** Rolf D. Klingenberg-Noftz, MD, Department of Gastroenterology and Internal Medicine, DRK-Hospital Grevesmuehlen, Kluetzer Strasse 13-15, 23936 Grevesmuehlen, Germany, Tel: +49 3881 726 601; Fax: +49 3881 726 609; E-mail: rolf.klingenberg-noftz@drk-kh-gvm.de

Rec date: Nov 23, 2015; **Acc date:** Mar 23, 2016; **Pub date:** Mar 29, 2016

Abstract

Background: The work-up of pancreatic mass lesions requires an orchestrated employment of different diagnostic means. The "best", meaning the most sufficient and goal achieving diagnostic pathway, remains to be established and has to be adopted according to each individual patient.

The technique of endoscopic ultrasound (EUS) has been established with a high yield of diagnostic value regarding pancreatic lesions. In combination with fine needle aspirations of the suspected area guided by EUS (EUS guided FNA) the diagnostic value of pancreatic lesions is boosted with regard to the final diagnosis in a clinical setting.

Patients and Methods: During a 36-month period, 142 consecutive patients were referred to us for suspected pancreatic disease and evaluated for this study. Work-up for pancreatic lesions was performed including EUS and EUS-guided FNA. Definite diagnosis was established by explorative/curative laparoscopy/laparotomy or follow-up for up to 36 months in the aftermath of first admission. Results regarding diagnostic precision of EUS guided FNA cytology were evaluated retrospectively and correlated with other diagnostic means performed.

Results: 142 patients underwent work-up for pancreatic mass lesions of unknown genesis. EUS guided FNA was performed in all patients with a total of 13 (9.2%) minor complications (local control achieved), 2 (1.4%) major complications (1× bleeding, 1× perforation) and no fatal complication.

Cytology obtained by EUS guided FNA found malignancy in 52(37%) and absence of malignant disease in 70 (49%) cases. Cytology has not rendered a definite result in 20 (14%) cases. Final diagnosis resulted in 42% (n = 59) malignant disease, 42% (n = 60) benign disease, 10 cases (7%) remained without definite diagnosis and 13 patients (9%) left hospitalization or were lost to follow-up before completing the diagnostic work-up. Sensitivity of EUS guided FNA regarding malignant pancreatic disease was 83.7%, the specificity was 95.1% (positive predictive value 93.2%, negative predictive 87.9%).

Conclusion: According to our data, originating from the advent of the EUS era, EUS-FNA is a safe and efficient method in the diagnostic work-up of pancreatic mass lesions. Its complication rate is small, but complications occur at a relevant level, reflecting on the learning curve and the necessary expertise of the examiner with regard to the method.

However, EUS supported by FNA obtained cytology, is the diagnostic measure of choice regarding the work up of pancreatic mass lesions, even though the possibility and meaning of false negative results, varying specimen quality, adverse reactions and operator dependancy have to be taken in account with regard to the use of the method and the interpretation of its results. These problems remain unchanged up to the present day.

Keywords: EUS guided FNA; Pancreatic mass lesions; Diagnostic work-up

Introduction

Endoscopic ultrasound (EUS) guided fine needle aspiration (FNA) has initially been reported in 1992 for the diagnostic work-up of pancreatic mass lesions [1]. The technique is at present widely accepted in the differential diagnostic of pancreatic, gastrointestinal and mediastinal diseases [2-4]. It has been shown to be of value for preoperative staging, for determining surgical resectability of pancreatic or other abdominal malignancies [5-7] and especially in obtaining material in cases prone to be managed conservatively. In a multicenter prospective study of 90 patients in whom previous

diagnostic interventional radiological procedures failed to yield a definitive diagnosis, EUS-FNA has proved to be the modality of choice to establish a diagnosis [7]. It is especially useful when computerized tomography (CT) scans do not show a focal mass lesion [6,7]. At present, data addressing sensitivity of EUS vs. CT/MRI remains undecided, but EUS, performed at expert level, appears to be the most sensitive method in diagnosing pancreatic mass lesions in sizes smaller than 20 mm, even though, data remains heterogenic in total [8-10].

Besides securing cytology for defining malignant disease, EUS-FNA is also applied to differentiate benign disease, most often from chronic pancreatitis. The diagnosis of severe chronic pancreatitis with extensive calcifications, ductal dilatation as well as intraductal concrements is fairly simple. However, diagnostic difficulties arise in patients with early, mild, minimal-change, autoimmune or focal pancreatitis that present similar to pancreatic neoplasms [11]. Another diagnostic dilemma is evident with regard to following and diagnosing malignant transformation in patients with chronic pancreatitis which is considered a precancerous lesion. In this setting, percutaneous imaging procedures such as ultrasound (US) or CT frequently fail to visualize or differentiate discrete abnormalities of the parenchyma and ducts. Even though, preoperative sample aquisition may at times not be recommended in local or primarily curative setting of an undoubtedly malignant pancreatic tumor [12,13], only tissue sampling via EUS guided FNA and cytologic work-up could prevent operative intervention in a benign situation masquerading malignant disease [14,15]. But the risk of false negative FNA has to be taken in account.

Endoscopic retrograde cholangiopancreatography (ERCP) was traditionally considered to be the standard reference procedure for morphologic diagnosis in pancreatic cancer, but it carries a substantial risk of post-ERCP pancreatitis, only visualizes the intraductal system [16] only and does therefore not add any additional preoperative staging information. In the preoperative setting of potentially curative disease, routine ERCP was therefore mainly replaced by EUS. Data addressing preoperative stenting is suggestive for a variety of pre- and postoperative complications and therefore confined to cases with cholangitis, pruritus or in a palliative or neoadjuvant setting [17].

EUS pictures not only the intraductal system and vascularisation of the pancreas in great detail, but also enables visualization of all parts of the pancreas, including the head, the uncinate process, the neck, the body and the tail, as well as most of their adjacent organs or structures [18,19].

However, disadvantages of EUS appear with regard to abnormalities of the morphologic aspect of the pancreas that can present in asymptomatic patients [20]. Aging, obesity or low body mass may alter the pancreatic parenchymatic aspect as well and may add to the necessity of an experienced and well trained EUS examiner.

Since a “gold standard” for diagnosing a chronic pancreatitis by noninvasive means does not exist, histologic tissue diagnosis must still be regarded as the best reference available.

To evaluate the diagnostic accuracy of EUS-FNA and to evaluate factors influencing diagnostic accuracy, we review our initial experience with EUS-FNA in a consecutive series of 142 patients that underwent EUS guided FNA in our institution and compare the results to present day literature.

Materials and Methods

One hundred forty two consecutive patients underwent 155 EUS-FNA procedures between January 1999 and December 2001 in the Department of Gastroenterology of the Luebeck University Hospital. These patients were referred for EUS examination for suspicion of an upper gastrointestinal or pancreatic disease. EUS was performed after an overnight fasting period > 10 hours. All procedures were taken under conscious sedation utilizing Midazolam, Buscopan, Disoprivan and (or) Ketanest-S after informed consent was obtained. Patients were evaluated initially by transabdominal ultrasound and endoscopy of the upper gastrointestinal tract. EUS was performed by using PENTAX FG-36UX linear echoendoscope with EUS-525 Ultrasound Scanner (Hitachi Medical Systems, GmbH, Germany). Either the HITACHI (Hitachi Medical Systems, GmbH, Germany) 22G, 0.7 mm catheter or the Medi-Globe (Medi-Globe GmbH, Germany), 22G, 0.7 mm catheters were used. If tissue was to be obtained transgastrically, HITACHI (Hitachi Medical Systems GmbH, Germany) 19G, 1.1 mm catheter was employed. Color Doppler was used to exclude any vessel in the path of the needle before the lesions were punctured under constant ultrasound guidance.

During the FNA procedure, the catheter was inserted into the biopsy channel and the needle tip was then advanced incrementally under real-time EUS control until the tip was seen within the lesion.

For pancreatic head or neck lesions, the ultrasound transducer was placed in the duodenal bulb. For lesions of the pancreatic body or tail and celiac lymph nodes, the transducer was placed in the proximal stomach. The stylet was removed and suction applied through a 10 ml syringes as the needle was moved 2 to 5 within the lesion. The needle was then retracted into the catheter sheth and the entire catheter was removed. The aspirate was placed on glass slides for cytology smears and air dryed. Specimens obtained were transported to pathology for cytologic evaluation in the aftermath. An average of 2 needle passes was performed and tissue aspirated. Total time of EUS and EUS guided FNA varied from 20 to 40 min.

Up to 36 months of clinical follow-up was reviewed for this study in cases with negative or inconclusive FNA diagnosis. Final diagnosis of lesions was based on conclusive results of surgery, autopsy or clinical follow-up as adopted gold standard. EUS-FNA results and clinical data were analyzed in a retrospective setting.

Results

A total of 142 patients underwent 155 EUS-FNA procedures. There were 50 women aged of 60.6 ± 11.5 yrs (mean ± SD) ant average and 92 men with mean age of 57.4 ± 12.0 yrs (mean ± SD). 133 patients (93.7%) underwent one EUS-FNA intervention, 9 patients (6.3%) underwent EUS guided FNA twice to improve specimen quality. Complications secondary to EUS guided FNA were recorded as follows: 13 patients (9.2%) suffered from mild complications, such as abdominal pain, fever, controlled by conservative measures. Two major complication occurred (1.4%), one upper GI bleeding and one gastrointestinal perforation followed by surgical intervention.

EUS guided FNA was indicated because of search for cancer with unknown primary tumor (CUP syndrome) in 78 cases (55%), staging of a cancer already diagnosed (26 cases, 19%), differential diagnostics in inflammatory or benign pancreatic disease for 19 cases (13%), unclear or other in 13% of the cases (19 patients).

Cytology		N	%	N	%
malignant		52	37		
	adenocarcinoma			30	21.1
	undifferentiated cancer			16	11.3
	lymphoma			4	3
	Neuroendocrine tumor			2	1.4
benign		70	49		
	pancreatitis			40	28.2
	normal pancreas			18	13
	cyst			7	5
	cystadenoma			5	4
unclear		20	14		

Table 1: Cytology of FNA.

EUS imaging found tumors ranging in size from <10 mm, 2 cases (1.4%), <20 mm, 22 cases (15.5%), <30 mm, 9 cases (6%), <40 mm, 30 cases (21.1%), <50 mm, 15 cases (11%), >50 mm, 7 cases (5%). In 31 cases no data about the tumor size was recorded.

According to the cytological report of obtained FNA specimens, 52 tumors were found to be of malignant origin (37%), 70 cases (49%) identified benign tumor or focal inflammation of pancreas. In 20 cases (14%) a definite diagnosis was not established (Table 1).

After follow-up (36 months) in a consumptive view of all existing clinical data, final diagnosis established malignancy in 59 cases (42%), benign disease in 60 cases (42%), while 10 cases (7%) remained without definite diagnosis after 36 months follow-up and 13 patients (9%) were lost to follow-up and could not be settled in later work up.

Table 2 shows the high congruence of diagnosis established by EUS guided FNA with diagnoses established by consumptive view taking all clinical information and follow-up in account.

			FNA			
			benign	malignant	Chi-Square	p value
Final Diagnosis	Pancreatic	Benign	39	3	37.572	<0.0001
	Body	Malignant	7	23		
		Unsettled	6	2		
	Pancreatic	Benign	7	0	14.566	0.0007
	Head	Malignant	1	10		
		Unsettled	1	2		
	Pancreatic	Benign	6	0	16	0.0003
	Tail	Malignant	0	8		
		Unsettled	2	0		
	Pancreatic	Benign	6	0	*	*
	Cyst	Malignant	0	0		
		Unsettled	1	1		
	Total	Benign	58	3	70.96	<0.0001
	Together	Malignant	8	41		
		Unsettled	10	5		

Table 2: Comparing EUS-FNA with final diagnosis. *Chi-Square test cannot analyze when a column has no value.

Discussion

Numerous studies have shown that EUS is the single most accurate test for imaging and staging of pancreatic tumors [21-23]. In the current study, we report our experience of 142 consecutive patients that underwent EUS-FNA in a total of 155 times from January 1999 to December 2001 and compare our results and implications to present day data.

Exact preoperative staging of patients with pancreatic neoplasms is decisive with regard to patient survival [24-26]. Advanced tumor staging and declined physical status inversely correlate with patient

survival, which has basically remained unchanged during the past decade despite medical progress.

In the differential diagnosis of pancreatic mass lesions EUS guided FNA offers a high yield regarding malignancy with regard to sensitivity, specificity as well as positive and negative predictive values (Table 3).

	Detecting pancreatic cancer
Sensitivity (%)	83.7
Specificity (%)	95.1
NPV (%)	87.9
PPV (%)	93.2

Table 3: Sensitivities, specificities, NPV and PPV of EUS-FNA. NPV: Negative Predictive Value; PPV: Positive Predictive Value.

In our study, EUS-FNA was indicated for the overwhelming part, because malignant disease was suspected clinically or by prior diagnostics. Sensitivity and specificity of EUS-FNA for detecting pancreatic cancer was 87.3% and 95.1% respectively. This accuracy coincides with results of other study groups [6,27]. Most of the pancreatic mass lesions detected by EUS in our study were less than 50 mm (>75%) in diameter and were frequently undetected or postinterventionally confirmed by other image donating diagnostics such as CT scan or MRT. Current sensitivities (up to 95%) and specificities (100%) of EUS guided FNA are described in various studies and support EUS guided FNA as the method of choice for defining the histologic character of pancreatic mass lesions [28-30].

In a clinical setting pancreatic mass lesions could be evaluated evaluated by a multitude of invasive and noninvasive diagnostic measures. The optimal, meaning most successful, with regard to the definite final diagnosis, precise, considering preoperative planning, and least harmful, with regard to periinterventional complications, diagnostic pathway is yet to be established and will, however, have be adopted to each individual patient.

With regard to diagnostic accuracy some studies have shown that EUS alone is of comparable [31,32] or even greater [23,33,34] accuracy to CT scan plus ERCP with regard to the staging of pancreatic lesions. Decision making with regard to the diagnostic approach to pancreatic mass lesions, has been greatly facilitated and a straightforward diagnostic approach was recommended by recent guidelines [35]. CT scan is here described as second diagnostic step in the work-up following transabdominal ultrasonography. EUS and EUS guided FNA was recommended to be employed in succession, following picture donating radiology. However, at times, we favor EUS and obtaining material via FNA in succession of transabdominal ultrasonography, prior to CT or MRI scans, if necessary at all, when a primarily palliative setting appears. Therefore we advocate performing EUS guided FNA as early as possible in the diagnostic and staging work-up of solid pancreatic masses. This aspect is in line with growing evidence with regard to establishing protocols in neoadjuvant chemotherapy settings especially in locally advanced pancreatic cancer, for which a definite histological diagnosis must be achieved.

The greatest portion of patients in our study was found to be diagnosed with a chronic pancreatitis (40 cases, 28.2%) by EUS and EUS-FNA. Several studies have shown that EUS is the most sensitive method in the diagnostic work-up of chronic pancreatitis [36]. Lees described endosonographic criteria to differentiate chronic pancreatitis with regard to parenchymatic (six criteria) and ductal signs (eight criteria) [37]. What however, should be considered the "gold standard" to which EUS is compared? Possible gold candidates include histology cytology, pancreatography and pancreatic function tests. Traditionally, pancreatography, via endoscopic retrograde access (ERP), was accepted as the most accurate, nonpathologic imaging method with regard to chronic pancreatitis, though yielding a substantial periinterventional risk for the patient. It was therefore replaced by MRI and MRCP which renders an even higher diagnostic accuracy compared to ERP [38]. EUS is known to produce high diagnostic values with regard to chronic pancreatitis [39,40] and is recommanded be used complementary with MRI techniques in this matter [41].

A diagnostic challenge represents the differentiation of focal chronic pancreatitis from neoplastic processes of the pancreas. With regard to this, pathologic work-up is necessary. Brand et al. prospectively evaluated focal pancreatic lesions and found that 13 of 34 patients having focal, chronic pancreatitis simulating tumor had no other associated diffuse parenchymal alteration usually present in chronic pancreatitis [42]. On the other hand, focal pancreatitis is frequently found in patients undergoing pancreatic resection for presumed cancer. However, chronic pancreatitis is considered a precancerous condition as a significantly increased risk of pancreatic cancer in all patients with chronic pancreatitis of any cause [43] is known. Malignant transformation in the condition of a chronic pancreatitis cannot be ruled out by EUS or EUS guided FNA considering false negative aspiration cytologies. This rate could be reduced by 10-15% via on-site cytopathologic examination of the specimens [44,45], but availability of a trained cytopathologist for on-site examination remains scarce. The dilemma appears unchanged and harbors a relevant and at times detrimental risk for the patient. No known diagnostic measure, including CT/MRI+MRCP, yields sufficient diagnostic safety in this matter. All necessary diagnostic means, including exploratory laparoscopy/laparotomy should, if in doubt, be employed and/or a definite follow-up, for instance (3) 6-12 months intervalls, be established [46] if reasonable.

EUS guided FNA is a safe diagnostic tool with a low complication rate conflicted to it. In our series of 142 patients, 13 (9.2%) patients experienced mild complications such as post-FNA fever or abdominal pain which ceased within two days, treated conservatively. One (0.7%) patient suffered from an upper GI bleeding after FNA, one other (0.7%) patient experienced a perforation and had to undergo surgery. Perforation is an inert risk conflicted to the employment of endoscopic techniques. Traditionally, surgical intervention, by laparoscopic or laparotomic approach, was the only choice with regard to damage control and reconstitution of gastrointestinal integrity. Recently, the development and widespread use of over the scope clipping systems, may constitute a valuable and effective alternative in a situation such as we have experienced. This technique may help to avoid a surgical approach with regard to endoscopic complication management [47].

Currently, rates of adverse events conflicted be EUS guided FNA of pancreatic masses are described to range from 0.5-2% including risk of pancreatitis and bleeding [48-50]. Discomfort, as described after FNA in our study by approximately 10% of the cases, was rarely registered in current studies. We have noted no pancreatitis in the aftermath of an EUS guided FNA. Rates for relevant complications range within currently described limits, but have to be considered to be a constant

reminder for the need for constant endoscopic training and keen awareness the regarding potential detrimental risks immanent to EUS and EUS guided FNA [51,52].

We found no evidence of needle-tract or cutaneous malignant seeding having taken place by EUS guided FNA in the histopathologic specimens. The puncture sites located in the duodenum were resected during the following surgery. Which appears to be reflected in current findings, as being restricted to single cases [48,49]. No fatal complication was recorded following interventions described in this series.

In conclusion, we have demonstrated the diagnostic value of EUS guided FNA in our single center experience originating from the beginning of the EUS era. We have found diagnostic specificities, sensitivities and rates of adverse events that are compatible to current day data and therefore support the value of EUS and EUS guided FNA in the work up of pancreatic mass lesions at present.

The method itself has proved to have stepped beyond experimental stage in the past decade and is of highest value in the hands of an experienced examiner.

However, as controversies about the optimal diagnostic pathway regarding the work up of pancreatic mass lesions appear to have settled recently, we advocate the use of EUS and EUS guided FNA at times even sooner as recommended in the diagnostic work- up.

Securely detecting or ruling out malignant transformation in patients presenting with chronic pancreatitis and its complications remains a be to be constant challenge to the treating gastroenterologist. This dilemma has not changed since the acquisition of our data to the present day and may only be solved by careful, precise diagnostics and determined medical follow-up.

References

1. Vilmann P, Jacobsen GK, Henriksen FW, Hancke S (1992) Endoscopic ultrasonography with guided fine needle aspiration biopsy in pancreatic disease. Gastrointest Endosc 38: 172-173.
2. Chang KJ, Albers CG, Erickson RA, Butler JA, Wuerker RB, et al. (1994) Endoscopic ultrasound-guided fine needle aspiration of pancreatic carcinoma. Am J Gastroenterol 89: 263-266.
3. Wiersema MJ, Kochman ML, Chak A, Cramer HM, Kesler KA (1993) Real-time endoscopic ultrasound-guided fine-needle aspiration of a mediastinal lymph node. Gastrointest Endosc 39: 429-431.
4. Wiersema MJ, Hawes RH, Tao LC, Wiersema LM, Kopecky KK, et al. (1992) Endoscopic ultrasonography as an adjunct to fine needle aspiration cytology of the upper and lower gastrointestinal tract. Gastrointest Endosc 38: 35-39.
5. Giovannini M, Seitz JF, Monges G, Perrier H, Rabbia I (1995) Fine-needle aspiration cytology guided by endoscopic ultrasonography: results in 141 patients. Endoscopy 27: 171-177.
6. Chang KJ, Nguyen P, Erickson RA, Durbin TE, Katz KD (1997) The clinical utility of endoscopic ultrasound-guided fine-needle aspiration in the diagnosis and staging of pancreatic carcinoma. Gastrointest Endosc 45: 387-393.
7. Wiersema MJ, Vilmann P, Giovannini M, Chang KJ, Wiersema LM (1997) Endosonography-guided fine-needle aspiration biopsy: diagnostic accuracy and complication assessment. Gastroenterology 112: 1087-1095.
8. Bronstein YL, Loyer EM, Kaur H, Choi H, David C, et al. (2004) Detection of small pancreatic tumors with multiphasic helical CT. AJR Am J Roentgenol 182: 619-623.
9. Sahani DV, Bonaffini PA, Catalano OA, Guimaraes AR, Blake MA (2012) State-of-the-art PET/CT of the pancreas: current role and emerging indications. Radiographics 32: 1133-1158.
10. Dewitt J, Devereaux BM, Lehman GA, Sherman S, Imperiale TF (2006) Comparison of endoscopic ultrasound and computed tomography for the preoperative evaluation of pancreatic cancer: a systematic review. Clin Gastroenterol Hepatol 4: 717-725.
11. Hollerbach S, Klamann A, Topalidis T, Schmiegel WH (2001) Endoscopic ultrasonography (EUS) and fine-needle aspiration (FNA) cytology for diagnosis of chronic pancreatitis. Endoscopy 33: 824-831.
12. Hartwig W, Schneider L, Diener MK, Bergmann F, Büchler MW, et al. (2009) Preoperative tissue diagnosis for tumours of the pancreas. Br J Surg 96: 5-20.
13. Wolfgang CL, Herman JM, Laheru DA, Klein AP, Erdek MA, et al. (2013) Recent progress in pancreatic cancer. CA Cancer J Clin 63: 318-348.
14. Gardner TB, Levy MJ, Takahashi N, Smyrk TC, Chari ST (2009) Misdiagnosis of autoimmune pancreatitis: a caution to clinicians. Am J Gastroenterol 104: 1620-1623.
15. Ghazale A, Chari ST, Smyrk TC, Levy MJ, Topazian MD, et al. (2007) Value of serum IgG4 in the diagnosis of autoimmune pancreatitis and in distinguishing it from pancreatic cancer. Am J Gastroenterol 102: 1646-1653.
16. Bozkurt T, Braun U, Leferink S, Gilly G, Lux G (1994) Comparison of pancreatic morphology and exocrine functional impairment in patients with chronic pancreatitis. Gut 35: 1132-1136.
17. Isenberg G, Gouma DJ, Pisters PW (2002) The on-going debate about perioperative biliary drainage in jaundiced patients undergoing pancreaticoduodenectomy. Gastrointest Endosc 56: 310-315.
18. Chak A (2000) Endoscopic ultrasonography. Endoscopy 32: 146-152.
19. Lambert R, Caletti G, Cho E, Chang KJ, Fusaroli P, et al. (2000) International Workshop on the clinical impact of endoscopic ultrasound in gastroenterology. Endoscopy 32: 549-584.
20. Catalano MF, Lahoti S, Geenen JE, Hogan WJ (1998) Prospective evaluation of endoscopic ultrasonography, endoscopic retrograde pancreatography, and secretin test in the diagnosis of chronic pancreatitis. Gastrointest Endosc 48: 11-27.
21. Mertz HR, Sechopoulos P, Delbeke D, Leach SD (2000) EUS, PET, and CT scanning for evaluation of pancreatic adenocarcinoma. Gastrointest Endosc 52: 367-371.
22. Midwinter MJ, Beveridge CJ, Wilsdon JB, Bennett MK, Baudouin CJ, et al. (1999) Correlation between spiral computed tomography, endoscopic ultrasonography and findings at operation in pancreatic and ampullary tumours. Br J Surg 86: 189-193.
23. Snady H (1994) Role of endoscopic ultrasonography in diagnosis, staging, and outcome of gastrointestinal diseases. Gastroenterologist 2: 91-110.
24. Prat F, Chapat O, Ducot B, Ponchon T, Fritsch J, et al. (1998) Predictive factors for survival of patients with inoperable malignant distal biliary strictures: a practical management guideline. Gut 42: 76-80.
25. Warshaw AL, Fernández-del Castillo C (1992) Pancreatic carcinoma. N Engl J Med 326: 455-465.
26. Murr MM, Sarr MG, Oishi AJ, van Heerden JA (1994) Pancreatic cancer. CA Cancer J Clin 44: 304-318.
27. Shin HJ, Lahoti S, Sneige N (2002) Endoscopic ultrasound-guided fine-needle aspiration in 179 cases: the M. D. Anderson Cancer Center experience. Cancer 96: 174-180.
28. Lai R, Stanley MW, Bardales R, Linzie B, Mallery S (2002) Endoscopic ultrasound-guided pancreatic duct aspiration: diagnostic yield and safety. Endoscopy 34: 715-720.
29. Varadarajulu S, Tamhane A, Eloubeidi MA (2005) Yield of EUS-guided FNA of pancreatic masses in the presence or the absence of chronic pancreatitis. Gastrointest Endosc 62: 728-736.
30. Eloubeidi MA, Jhala D, Chhieng DC, Chen VK, Eltoum I, et al. (2003) Yield of endoscopic ultrasound-guided fine-needle aspiration biopsy in patients with suspected pancreatic carcinoma. Cancer 99: 285-292.
31. Snady H, Cooperman A, Siegel J (1992) Endoscopic ultrasonography compared with computed tomography with ERCP in patients with obstructive jaundice or small peri-pancreatic mass. Gastrointest Endosc 38: 27-34.

32. Rosch T, Braig C, Gain T, Feuerbach S, Siewert JR, et al. (1992) Staging of pancreatic and ampullary carcinoma by endoscopic ultrasonography. Comparison with conventional sonography, computed tomography, and angiography. Gastroenterology 102: 188-199.
33. Erickson RA, Garza AA (2001) EUS with EUS-guided fine-needle aspiration as the first endoscopic test for the evaluation of obstructive jaundice. Gastrointest Endosc 53: 475-484.
34. Tierney WM, Fendrick AM, Hirth RA, Scheiman JM (2000) The clinical and economic impact of alternative staging strategies for adenocarcinoma of the pancreas. Am J Gastroenterol 95: 1708-1713.
35. Eloubeidi MA, Decker GA, Chandrasekhara V, Chathadi KV, Early DS, et al. (2016) The role of endoscopy in the evaluation and management of patients with solid pancreatic neoplasia.
36. Snady H (2001) Endoscopic ultrasonography in benign pancreatic disease. Surg Clin North Am 81: 329-344.
37. Lees WR (1986) Endoscopic ultrasonography of chronic pancreatitis and pancreatic pseudocysts. Scand J Gastroenterol Suppl 123: 123-129.
38. Adamek HE, Albert J, Breer H, Weitz M, Schilling D, et al. (2000) Pancreatic cancer detection with magnetic resonance cholangiopancreatography and endoscopic retrograde cholangiopancreatography: a prospective controlled study. Lancet 356: 190-193.
39. Kahl S, Glasbrenner B, Zimmermann S, Malfertheiner P (2002) Endoscopic ultrasound in pancreatic diseases. Dig Dis 20: 120-126.
40. Kahl S, Glasbrenner B, Leodolter A, Pross M, Schulz HU, et al. (2002) EUS in the diagnosis of early chronic pancreatitis: a prospective follow-up study. Gastrointest Endosc 55: 507-511.
41. Pungpapong S, Wallace MB, Woodward TA, Noh KW, Raimondo M (2007) Accuracy of endoscopic ultrasonography and magnetic resonance cholangiopancreatography for the diagnosis of chronic pancreatitis: a prospective comparison study. J Clin Gastroenterol 41: 88-93.
42. Fritscher-Ravens A, Sriram PV, Krause C, Atay Z, Jaeckle S, et al. (2001) Detection of pancreatic metastases by EUS-guided fine-needle aspiration. Gastrointest Endosc 53: 65-70.
43. Lowenfels AB, Maisonneuve P, Cavallini G, Ammann RW, Lankisch PG, et al. (1993) Pancreatitis and the risk of pancreatic cancer. International Pancreatitis Study Group. N Engl J Med 328: 1433-1437.
44. Klapman JB, Logrono R, Dye CE, Waxman I (2003) Clinical impact of on-site cytopathology interpretation on endoscopic ultrasound-guided fine needle aspiration. Am J Gastroenterol 98: 1289-1294.
45. Layfield LJ, Bentz JS, Gopez EV (2001) Immediate on-site interpretation of fine-needle aspiration smears: a cost and compensation analysis. Cancer 93: 319-322.
46. Schreyer AG, Jung M, Riemann JF, Niessen C, Pregler B, et al. (2014) German Society of Digestive and Metabolic Diseases (DGVS). S3 guideline for chronic pancreatitis - diagnosis, classification and therapy for the radiologist 186: 1002-1018.
47. Changela K, Virk MA, Patel N, Duddempudi S, Krishnaiah M, et al. (2014) Role of over the scope clips in the management of iatrogenic gastrointestinal perforations. World J Gastroenterol 20: 11460-11462.
48. Paquin SC, Gariépy G, Lepanto L, Bourdages R, Raymond G, et al. (2005) A first report of tumor seeding because of EUS-guided FNA of a pancreatic adenocarcinoma. Gastrointest Endosc 61: 610-611.
49. Chong A, Venugopal K, Segarajasingam D, Lisewski D (2011) Tumor seeding after EUS-guided FNA of pancreatic tail neoplasia. Gastrointest Endosc 74: 933-935.
50. Fornari F, Civardi G, Cavanna L, Di SM, Rossi S, et al. (1989) Complications of ultrasonically guided fine-needle abdominal biopsy. Results of a multicenter Italian study and review of the literature. The Cooperative Italian Study Group. Scand J Gastroenterol 24: 949-955.
51. Carrara S, Arcidiacono PG, Mezzi G, Petrone MC, Boemo C, et al. (2010) Pancreatic endoscopic ultrasound-guided fine needle aspiration: complication rate and clinical course in a single centre. Dig Liver Dis 42: 520-523.
52. Eloubeidi MA, Tamhane A (2005) EUS-guided FNA of solid pancreatic masses: a learning curve with 300 consecutive procedures. Gastrointest Endosc 61: 700-708.