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RETROSPECTIVE STUDY

Endoscopic ultrasound-guided fine-needle aspiration for suspected malignancies adjacent to the gastrointestinal tract

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Abstract

AIM: To investigate the impact of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) in association with a multidisciplinary team evaluation for the detection of gastrointestinal malignancies.

METHODS: A cohort of 1019 patients with suspected malignant lesions adjacent to the gastrointestinal tract received EUS-FNA after a standardized multidisciplinary team evaluation (MTE) and were divided into 4 groups according to their specific malignant risk score (MRS). Patients with a MRS of 0 (without detectable risk of malignancy) received only EUS without FNA. For patients with a MRS score ranging from 1 (low risk) - through 2 (intermediate risk) - to 3 (high risk), EUS-FNA cytology of the lesion was planned for a different time and was prioritized for those patients at higher risk for cancer. The accuracy, efficiency and quality assessment for the early detection of patients with potentially curable malignant lesions were evaluated for the whole cohort and in the different classes of MRSs. The time to definitive cytological diagnosis (TDCD), accuracy, sensitivity, specificity, positive and negative predictive values, and the rate of inconclusive tests were calculated for all patients and for each MRS group.

RESULTS: A total of 1019 patients with suspected malignant lesions were evaluated by EUS-FNA. In 515 patients of 616 with true malignant lesions the tumor was diagnosed by EUS-FNA; 421 patients with resectable lesions received early surgical treatment, and 94 patients received chemo-radiotherapy. The overall diagnostic accuracy for the 1019 lesions in which a final diagnosis was obtained by EUS-FNA was 0.95. When patients were stratified by MTE into 4 classes of MRSs, a higher rate of patients in the group with higher cancer risk (MRS-3) received early treatment and EUS-FNA showed the highest level of accuracy (1.0). TDCD was also shorter in the MRS-3 group. The number of patients who received surgical treatment or chemo-radiotherapy was significantly higher in the MRS-3 patient group (36.3% in MRS-3, 10.7% in MRS-2, and 3.5% in MRS-1).

CONCLUSION: EUS-FNA can effectively detect a curable malignant lesions at an earlier time and at a higher rate in patients with a higher cancer risk that were evaluated using MTE.

Key words: Gastrointestinal neoplasm; Endoscopic ultrasonography; Clinical scoring system; Fine needle aspiration; Clinical decision support system

Core tip: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) has become paramount in establishing a diagnosis for all suspected malignant lesions of the gastrointestinal tract. Due to its increasing demand, the diagnostic yield of EUS-FNA and the length of time to determine a definitive cytological diagnosis may not be satisfactory in clinical practice. We found that EUS-FNA, when combined with the clinical evaluation of malignancy risk, was associated with a reliable level of accuracy. When prioritized for those patients with the highest clinical suspicion of cancer risk, EUS-FNA provides a shorter time to diagnosis for those patients with a higher cancer risk who can benefit from early therapy.

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INTRODUCTION

Endoscopic ultrasound (EUS) provides excellent visualization of almost all of the submucosal layers of the gastrointestinal tract as well as the organs and structures adjacent to the gastrointestinal tract, including mediastinal lymph nodes. However, the ability of EUS to differentiate between inflammatory masses and cancer is limited[1-3]. With the advent of curvilinear echoendoscopes, transesophageal, transgastric, trans-duodenal or trans-rectal endoscopic ultrasound guided fine needle aspiration (EUS-FNA) biopsies have become common practice. The role of EUS-FNA has also become paramount in establishing a correct tissue diagnosis in patients with abnormal lymph nodes during the diagnosis of unexplained mediastinal lymphadenopathy and during the staging of non-small-cell lung cancer (NSCLC) when histo-pathological findings may guide the correct therapeutic management[4-6].

Due to emerging evidence that supports its utility[7,8], the indications and requests for EUS-FNA for all suspected malignant lesions are increasing despite its limited availability. Given the increasingly widespread clinical use of EUS-FNA, it seems justified to implement strategies to prioritize the procedure for those patients with resectable disease who can benefit from early surgical treatment and for those patients with unresectable malignancies who can take advantage of specific chemotherapy or radiation therapy.

The aim of this study was to assess the potential benefit of EUS-FNA when scheduled on a priority basis in patients stratified for cancer risk by a multidisciplinary team evaluation (MTE) according to a specific malignancy risk score (MRS). We evaluated a large cohort for possible benefit of EUS-FNA when patients were stratified into 4 different classes of MRS by analyzing and comparing the time to obtain a definitive cytological diagnosis (TDCD), the rate of patients who underwent surgery, and the rate of patients with unresectable lesions who could receive specific cancer treatment in different groups. Detailed analyses of accuracy and quality assessments of EUS-FNA as well as their relevance in the process of clinical decision making, were also evaluated and discussed in the whole cohort and in the different groups.

MATERIALS AND METHODS

Study design, and identification of the cohort

From November 1998 to May 2011, all patients with suspected thoracic or abdominal malignant lesions of the gastrointestinal submucosal layer as well as lesions of the organs and structures lying in close vicinity to the gastrointestinal tract including lymph nodes, were recruited in Ospedale Niguarda Ca' Granda, Milano for this study. Data were collected in a prospectively dedicated computerized database and then retrospectively analyzed 30 mo after the end of the study (November 2013, end of the study: May 2011). All relevant clinical data with cytological findings, TDCD, and final clinical diagnoses for all patients with inconclusive tests were recorded, as well as all complications associated with the procedure.

Inclusion criteria

All patients with a suspected malignant lesion who could benefit from possible treatment with surgery, chemotherapy or radiotherapy were included. All patients with a known primary tumor requiring surgical evaluation for resectability by tissue diagnosis of a suspected metastatic lesion were also included in the study provided that EUS-FNA was evaluated as technically feasible by the attending gastroenterologist (Gambitta P). The Institutional Review Board and the Ethical Committee approved the study. All patients provided written informed consent to undergo the procedure.

Criteria for MRS assessment

The clinical records of each patient were reviewed by one gastroenterologist and collegially discussed during the MTE; the team was composed of surgeons, oncologists and radiologists. Three specialists (one radiologist, one oncologist and one surgeon) expressed their clinical judgements by subjective evaluation and by objective clinical criteria following the National Comprehensive Cancer Network (NCCN) guidelines for diagnosis[9]. They assigned a score of 0 if the lesion was judged as most likely benign, or a score of 1 if the lesion was judged as most likely malignant. The final clinical score was the sum of the scores of each specialist. The clinical judgment of each single specialist was blind to the other two judgements. All patients were then divided into 4 groups with scores ranging from MRS-0 to MRS-3. Patients with MRS-0 without detectable oncological risk were submit-

ted to EUS without FNA. These patients were followed-up for at least 30 mo or until death. Further investigations were planned whenever clinically required. In all patients with MRS ranging from 1 to 3 (1 = low risk, 2 = intermediate risk, 3 = high risk of malignancy), EUS was first planned, followed by FNA.

Prioritization of the EUS-FNA and TDCD

The procedure was performed within 3 d of the MTE for patients with a MRS of 3, within 10 d for those with a MRS of 2 and within 15 d for those with a MRS of 1. TDCD was evaluated as the number of days required from the last clinical evaluation to obtain the final report of cytological evaluation. The time for the cytological processing technique did not receive any different prioritization for the whole cohort of patients and it was always performed in the shortest time possible.

EUS-FNA procedure and technique

Patients were placed in the left lateral decubitus position and were sedated with *iv* meperidine plus midazolam, according to the judgment of the endoscopist. Standard EUS was performed using either an FG-36UX or EG-383 OUT linear-array echoendoscope (Pentax) for the evaluation and staging of the lesions. Once a lesion was identified, EUS-FNA was then performed. Solid masses in the head and uncinate process of the pancreas were biopsied by a transduodenal approach with a 22 Gauge or 19 Gauge ultrasound needle (Wilson-Cook Medical Inc., United States). Following infiltration of the target lesion, the mandarin was pulled back and an excess of 50 passes into the lesion were performed before the needle was finally retracted.

Sample collection, processing, and diagnostic yield

The mandarin was reintroduced to push any collected tissue fragments that possessed a "wormlike" appearance into a cytorich red medium. This technique allowed for the optimal use of collected material avoiding the routine handling of this material as a smear, leading to a reduction in processing time[10]. No cytopathologist was present in the examination room, and the determination of adequacy was based on macroscopic inspection of the aspirate by the operator. A cloudy sediment suggesting cellularity or core tissue was used for determination of adequacy. The biopsy procedure was repeated until sufficient material was aspirated.

Criteria for cytological and final diagnoses

The cytological diagnoses were then categorized into three groups: (1) positive for malignancy; (2) benign; and (3) inconclusive. The cytological material obtained by EUS guided aspiration was recorded as positive (diagnostic for cancer) when malignant cells were present in the aspirate, or as benign if only benign cells from the target organ were present. However, if no cells were present or no cells from the target organ were observed, or if destroyed cytological material was found, the cytological diagnosis was recorded as inconclusive. Lymph node aspirates without lymphatic cells and without cancer cells were also recorded as cases with an inconclusive cytological diagnosis. All cytology reports that were benign, malignant or inconclusive were confirmed or invalidated by one or more of the following: (1) definitive histology by resection specimen after surgery; (2) clinical evaluation after a clinical course of at least 30 mo as a benign lesion without evidence of malignant disease, or as a malignant lesion when confirmed clinically by evaluation of the typical clinical course characteristic of malignant diseases; and (3) analysis of specimen obtained during autopsy.

Evaluation of a standard accuracy rate

True positive (TP), true negative (TN), false positive (FP) and false negative (FN) results, accuracy (AC), sensitivity (ST), specificity (SP), positive and negative predictive value (PPV, NPV), number of patients with positive and negative final diagnosis (D+, D-), likelihood ratios for a positive or negative test (+LR and -LR), and the rate of inconclusive tests (IT) were calculated. The results were calculated by standard statistical computing as follows: AC as (TP+TN)/N, ST as TP/N(D+), SP as TP/N(D-), PPV as TP/N(T+), NPV as TN/N(T-), +LR as (ST/1-SP) and -LR as SP/1-ST. To ensure that all relevant information was present we utilized the standards for reporting of diagnostic accuracy statement and checklist to improve the quality of diagnostic accuracy[11]; Inconclusive results were grouped in accordance with recent recommendations[12].

Statistical analysis

To analyze significant differences among the three groups (*i.e.*, MRS-1, MRS-2 and MRS-3) such as number of patients who underwent surgery an the mean values of TDCD a one-way ANOVA with Scheffè's *post-hoc* test was employed. A two-tailed $P < 0.05$ was considered statistically significant. SPSS 20.0 software was used for all statistical analyses and calculations.

RESULTS

Anatomical location of the lesions and surgical procedures adopted

A total of 1136 patients were evaluated. In 12 patients the procedure was abandoned, 19 patients were lost to follow up, 86 with MRS of 0 received EUS without FNA, and 1019 completed the EUS-FNA procedure.

Of the 1019 lesions evaluated by EUS-FNA, 932 were extraluminal and 87 were submucosal. In 616 patients a malignant lesion was diagnosed and the lesions in 515 patients were detected by EUS-FNA.

In 570 patients a specific treatment was adopted (455 surgical procedure and 115 chemo-radiotherapy procedures). The different anatomical locations for all the lesions, the number of patients who required surgical treatment and the different surgical procedures employed are summarized in Table 1.

Table 1 Different anatomical localizations for the 1019 lesions in which endoscopic ultrasound-guided fine-needle aspiration was employed with the 431 surgical procedures adopted

Macroscopic (> 1 cm) (*n* = 932)	Surgical procedures (*n* = 393)
512 pancreatic masses	201 pancreatic resections
135 mediastinal lymphadenopathy	44 pneumonectomy, 12 lobectomy, 14 wedge resection
107 enlarged abdominal lymph nodes	11 Debulking, 19 nephrectomy, 6 splenectomy
23 lung cancer adjacent to the esophagus	11 pneumonectomy, 2 wedge resection
21 perirectal masses	6 low anterior resection, 5 Miles' procedures
18 cancer of the extrahepatic bile duct	4 bile duct resections, 2 hepatic resections
18 perigastric masses	7 gastrectomy, 2 wedge resections
15 mediastinal masses	9 pneumonectomy
12 perirectal node	7 transanal rectal resection
13 pleural thickening and pleural effusion	7 pleurectomy, decortication
10 masses of the retroperitoneum/	3 retroperitoneal debulking
10 peritoneal thickening and ascites	4 peritonectomy
10 left lobe of the liver	3 liver resection
9 left adrenal gland	5 adrenalectomy
8 prostate nodules with rectal involvement	4 prostatectomy and rectal resection
6 ovarian cyst	5 salpingo-oophorectomy
3 thyroid	3 thyroidectomy
1 spleen	1 splenectomy
1 cyst of CBD	1 biliary duct resection
Microscopic (< 1 cm submucosal) (*n* = 87)	Surgical procedures (*n* = 23)
49 gastric	12 gastrectomy, 1 sleeve gastrectomy
14 esophageal	2 esophagectomy
13 rectal	4 low rectal ant resection
8 duodenal	2 DCP
3 colorectal anastomoses	2 redo surgery for anastomotic recurrence

CBD: Common bile duct; DCP: Duodenocephalopancreatectomy.

Patients with of MRS 0

A total of 86 patients were evaluated as MRS-0; these patients were submitted to EUS without FNA. All of these patients who exhibited no clinical evidence of malignancy as evaluated by MTE, were followed up for a period of at least 30 mo or until death. In 83 patients, the clinical evaluation of the presumed benign lesion was confirmed by further clinical investigations during the follow up period. In three patients (3.48%), a malignancy was detected at 6, 7 and 10 mo after the first clinical evaluation. In two patients, non-functioning neuroendocrine tumors of the pancreatic head and tail, considered small benign pancreatic cysts by EUS, were subsequently detected after surgical resection; in one other patient, with a pancreatic lesion evaluated as pancreatitis by EUS, an adenocarcinoma of the pancreatic head was subsequently diagnosed based on the surgical specimen.

Patients with MRS of 1-3

In 1019 patients the EUS-FNA was completed. Among 616 patients with a proven final diagnosis of cancer, EUS-FNA resulted in the detection of 511 (83%) patients with a TP diagnosis. In 431 patients the lesion was considered resectable and surgery was performed (Table 1). Ninety-four patients with unresectable lesions were submitted to different specific chemotherapies and radiation therapies as suggested by ongoing protocols. In the group of MRS of 3 we identified the highest number of patients (34.6%) who could benefit from different surgical procedures and chemo-radiotherapy.

Complications related to the procedure

Major complications occurred in two patients (0.2%). One esophageal perforation unrelated to FNA occurred during pharyngo-esophageal intubation in a patient who recovered uneventfully after 14 d in the intensive care unit (Clavien Ⅳa stage). In the other patient one sigmoid perforation that required surgery occurred (Clavien Ⅲa stage). Minor complications (Clavien Ⅱ) related to FNA were observed in five other patients.

Accuracy and efficiency and quality assessment

Table 2 shows all of the data including the number of patients with a positive and negative final diagnosis, the number of TP, TN, FP, FN diagnoses, and the number of inconclusive diagnoses. In 515 of the 616 patients with true malignant lesions (83%) the EUS-FNA was able to demonstrate the presence of malignant cells, in 359 of the 399 patients (89%) with true benign lesions, benign cells were observed. In 129 patients (12.6%), the specimen diagnosis was considered inconclusive. There were no false positive diagnoses in relation to a malignant cell diagnosis and 16 false negative diagnoses (7 of them in the pancreatic mass group). The overall diagnostic accuracy for the 1019 lesions in which a final diagnosis was obtained was 0.95 with an average of 2.2 passes per lesion (range 1 to 5). In Table 3 all values for AC, ST, SP, PPV, NPV, +LR, -LR, IT are reported, as well as the rate of patients who could receive treatment and the TDCD for each MRS group and for the whole group. TDCD and the number of patients who could receive surgical

Table 2 Cytological findings and final diagnoses of cancer *n* (%)

Cytology	Positive	Negative	Inconclusive (treated/untreated)	Patients (*n*)
Final diagnosis				
D+	515	16 (FN)	85 (55/30)	616 (TP)
D-	0 (FP)	359	44 (0/44)	403 (TN)
	515 (50.5)	375 (36.8)	129 (55/74) (12.7)	1019

D+ patients with positive final cytological diagnosis, D- patients with negative final cytological diagnosis, true positive (TP), true negative (TN), false positive (FP) and false negative (FN). Inconclusive tests are splitted into 2 groups: those that were treated (with surgery, or with chemo-radiotherapy) or those left untreated.

Table 3 Accuracy and efficiency and quality assessment *n* (%)

	MRS1 (*n* = 312)	MRS2 (*n* = 276)	MRS3 (*n* = 431)	Overall (*n* = 1019)
AC: (TP+TN)/N	0.97	0.87	1	0.95
ST: TP/N (D+)	0.85	0.79	0.99	0.93
SP: TP/N (D-)	1	1	1	1
PPV: TP/N (T+)	1	1	1	1
NPV: TN/N (T-)	0.97	0.76	0.95	0.90
+LR (ST/1-SP)	0	0	0	0
-LR (SP/1-ST)	6.6	4.7	100	4.2
TP	36 (3.5)	109 (10.6)	370 (36)	616 (60.4)
TN	231 (22.6)	101 (9.9)	26 (2.5)	403 (39.5)
IT	39 (12.5)	55 (19.9)	35 (8.1)	129 (12.6)
TDCD mean days (range)	25.4 (8-32)[c]	16.2 (11-24)[a]	12.4 (10-21)[a]	16.3 (8-32)
Patients TP treated with surgery or CRT	36 (3.5)[c]	109 (10.7)[a]	370 (36.3)[a]	515 (50.5)
Patients with inconclusive tests treated (surgery-CRT)	16 (9-7)	21 (12-9)	18 (13-5)	55 (34-21)

Calculation of accuracy (AC), sensitivity (ST), specificity (SP), and positive (PPV) and negative (NPV) predictive values for malignant risk score (MRS)-1, MRS-2 and MRS-3, likelihood ratios for positive and negative test (+LR, -LR) for different groups of patients. D+: Number of patients with positive final diagnosis; D-: Number of patients with negative final diagnosis; IT: Inconclusive test; TDCD: Time to definitive cytological diagnosis; CRT: Chemo-Radio-Therapy. [a]$P < 0.05$ *vs* MRS1; [c]$P < 0.05$ *vs* MRS3 according to the Scheffé *post-hoc* test.

treatment or chemo-radiotherapy were significantly different in MRS-3 patients.

DISCUSSION

In our study, the AC of the EUS-FNA was high (0.95) for the whole cohort of patients irrespectively of MTE, and ST (0.93), SP (1.0), PPV (1.0) and NPV (0.90) were all in line with results reported by other studies[13-15].

In patients with a high clinical suspicion of malignant disease, as in the MRS-3 group, the AC was higher, reaching 1 with a ST of 0.99, SP of 1, PPV 1 and NPV of 0.95. In the same group of patients with a MRS of 3, we did not find FP or FN diagnoses. The mean time to final cytological diagnosis as well as the rate of inconclusive tests were lower than that found in the other groups. Interestingly, no FP diagnoses were observed in all groups of patients. These findings represent the main advantages of EUS-FNA for the entire population of patients.

We documented 3 of 86 (3.48%) FN diagnoses in the group with a MRS of 0: These patients received EUS without FNA and two of them presented with a cystic lesion of the pancreas. It is widely accepted that the evaluation of cystic lesions of the pancreas poses a diagnostic challenge for the radiologist, the endoscopist and the pathologist[16,17]. At the moment all patients with pancreatic cystic lesions with a diameter larger than 3 cm are considered to be potentially suspect for malignant or premalignant lesions and are subjected to EUS-FNA with determination of carbohydrate antigen (CA 19-9, and CA 72-4), amylase, cyst fluid viscosity, and various stains in the fluid.

Seven of the 16 FN diagnoses were related to solid pancreatic lesions. This finding suggests the possibility that neoplastic cells can be difficult to obtain from pancreatic tumors when the perilesional pancreatic tissue has a consistent amount of inflammatory cells[18].

Although our finding of 12.6% inconclusive diagnoses is in accordance with other studies[19-21], these data can be explained by some technical aspects of the procedure itself which can present some difficulties during the puncture of the target lesion depending on several factors including the anatomical level of the lesion, the nature of the lesion itself, the small size of the lesion, and finally the absence of an onsite cytotechnologist, who verify in real time the presence of an adequate amount of tissue sampling. A consistent part of our study was performed for the evaluation of patients with focal pancreatic lesions that are often smaller than 2 cm in diameter. The accuracy of EUS-FNA in focal pancreatic lesions is usually less impressive than for mediastinal lesions[22] and the sensitivity and diagnostic accuracy of EUS-FNA for solid pancreatic lesions is reported to be strongly related to tumor size[23]. The low rate of inconclusive diagnoses by EUS-FNA in the group with a MRS of 3 (8.1% *vs* 19.9% in MRS-2 and 12.5% for MRS-1) can be explained, at least in part, by more adequate lesional and perilesional tissue in the group with the highest MRS, and above all in the group with pancreatic lesions. In these patients the cytological material obtained by the FNA can allow a more consistent and adequate sample for correct cytological evaluation[24,25].

The choice of the trans-esophageal procedure that we adopted for patients with mediastinal lymphadenopathy, in accord with other centers, most likely balanced the overall number of inconclusive tests. In our experience, this approach seems easier than a the trans-bronchial approach, facilitating detection and tissue sampling of mediastinal masses[26,27] and it most likely enables better diagnostic accuracy.

Although limitation of our study was the lack of an

accurate and reproducible method for cancer risk evaluation, our MTE was always homogeneously and uniformly carried out during the 12 years of the study, which was strictly in accord with the NCCN guidelines. This simple clinical practice allowed us to stratify patients with MRSs. In the group of MRS of 3 we found the highest number of TP tests, indicating patients who could benefit from early surgical treatment and showed the lowest number of TN tests. In the same high risk group with a MRS of 3, EUS-FNA reached the highest level of AC, ST, SP, PPV, NPV, without FP or FN diagnoses.

We conclude that a simple but standardized clinical evaluation by a multidisciplinary team can improve the diagnostic yield of EUS-FNA optimizing the clinical workup for all patients with curable malignant lesions. Our study offers some important indications on how to optimize diagnostic procedures in patients with suspected malignant lesions and can be considered a first step methodology for further evaluations of diagnostic efficiency in the setting of clinical and surgical oncology.

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COMMENTS

Background

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) has become paramount in establishing the diagnosis of all suspected malignant lesions of the gastrointestinal tract. The time to a definitive cytological diagnosis when using EUS-FNA may not be satisfactory in clinical practice due to its increasing demand during the clinical decision-making process for both benign and malignant lesions. Inadequate selection of patients may hamper the process of clinical decision making. Possible strategies to improve diagnostic efficiency in the clinical and surgical oncology settings are currently under investigation.

Research frontiers

The current study demonstrates that the practice of stratifying patients into different groups of cancer risk may improve the impact and efficiency of EUS-FNA in the early detection of those patients with malignant lesions; these patients may benefit from early surgery or chemo-radiotherapy, allowing for a very high level of accuracy in all patient groups.

Innovations and breakthroughs

Authors found that EUS-FNA was associated with a reliable level of accuracy in all patients when its use was prioritized for those patients with the highest cancer risk. EUS-FNA combined with a multidisciplinary clinical evaluation of the risk of malignancy enables a shorter time to diagnosis for those particular patients who can benefit from early therapy.

Applications

The present study offers some important indications about how to optimize diagnostic procedures in patients with suspected malignant lesions, and this report can be considered a first step methodology for further evaluations of diagnostic efficiency in the clinical and surgical oncology settings.

Peer review

This retrospective analysis was conducted in a cohort of 1019 patients with suspected malignant lesions adjacent to the gastrointestinal tract who underwent EUS-FNA during a period of 12 years. They found that EUS-FNA, when associated with a specific multidisciplinary team evaluation, enables a useful stratification of the patients on the basis of their specific cancer risk, allowing for better efficiency and a shorter time to diagnosis in those patients who can benefit from early surgery or chemo-radiotherapy treatment.

REFERENCES

1 **Rösch T**, Schusdziarra V, Born P, Bautz W, Baumgartner M, Ulm K, Lorenz R, Allescher HD, Gerhardt P, Siewert JR, Classen M. Modern imaging methods versus clinical assessment in the evaluation of hospital in-patients with suspected pancreatic disease. *Am J Gastroenterol* 2000; **95**: 2261-2270 [PMID: 11007227 DOI: 10.1111/j.1572-0241.2000.02312.x]

2 **Boujaoude J**. Role of endoscopic ultrasound in diagnosis and therapy of pancreatic adenocarcinoma. *World J Gastroenterol* 2007; **13**: 3662-3666 [PMID: 17659723]

3 **Puli SR**, Batapati Krishna Reddy J, Bechtold ML, Ibdah JA, Antillon D, Singh S, Olyaee M, Antillon MR. Endoscopic ultrasound: it's accuracy in evaluating mediastinal lymphadenopathy? A meta-analysis and systematic review. *World J Gastroenterol* 2008; **14**: 3028-3037 [PMID: 18494054 DOI: 10.3748/wjg.14.3028]

4 **Schmulewitz N**, Wildi SM, Varadarajulu S, Roberts S, Hawes RH, Hoffman BJ, Durkalski V, Silvestri GA, Block MI, Reed C, Wallace MB. Accuracy of EUS criteria and primary tumor site for identification of mediastinal lymph node metastasis from non-small-cell lung cancer. *Gastrointest Endosc* 2004; **59**: 205-212 [PMID: 14745393 DOI: 10.1016/S0016-5107(03)02692-0]

5 **Vazquez-Sequeiros E**, Norton ID, Clain JE, Wang KK, Affi A, Allen M, Deschamps C, Miller D, Salomao D, Wiersema MJ. Impact of EUS-guided fine-needle aspiration on lymph node staging in patients with esophageal carcinoma. *Gastrointest Endosc* 2001; **53**: 751-757 [PMID: 11375583 DOI: 10.1067/mge.2001.112741]

6 **Micames CG**, McCrory DC, Pavey DA, Jowell PS, Gress FG. Endoscopic ultrasound-guided fine-needle aspiration for non-small cell lung cancer staging: A systematic review and metaanalysis. *Chest* 2007; **131**: 539-548 [PMID: 17296659 DOI: 10.1378/chest.06-1437]

7 **Itoi T**, Tsuchiya T, Itokawa F, Sofuni A, Kurihara T, Tsuji S, Ikeuchi N. Histological diagnosis by EUS-guided fine-needle aspiration biopsy in pancreatic solid masses without on-site cytopathologist: a single-center experience. *Dig Endosc* 2011; **23** Suppl 1: 34-38 [PMID: 21535198 DOI: 10.1111/j.1443-1661.2011.01142.x]

8 **Pellisé Urquiza M**, Fernández-Esparrach G, Solé M, Colomo L, Castells A, Llach J, Mata A, Bordas JM, Piqué JM, Ginès A. Endoscopic ultrasound-guided fine needle aspiration: predictive factors of accurate diagnosis and cost-minimization analysis of on-site pathologist. *Gastroenterol Hepatol* 2007; **30**: 319-324 [PMID: 17662213 DOI: 10.1157/13107565]

9 National Comprehensive Cancer Network (NCCN) guidelines for detection, prevention and risk reduction. Available: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#detection

10 **Creemers K**, van der Heiden O, Los J, van Esser J, Newhall D, Djamin RS, Aerts JG. Endoscopic ultrasound fine needle aspiration in the diagnosis of lymphoma. *J Oncol* 2011; **2011**: 785425 [PMID: 21559244 DOI: 10.1155/2011/785425]

11 **Bossuyt PM**, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, Moher D, Rennie D, de Vet HC, Lijmer JG. The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. *Clin Chem* 2003; **49**: 7-18 [PMID: 12507954 DOI: 10.1373/49.1.7]

12 **Shinkins B**, Thompson M, Mallett S, Perera R. Diagnostic accuracy studies: how to report and analyse inconclusive test results. *BMJ* 2013; **346**: f2778 [PMID: 23682043 DOI: 10.1136/bmj.f2778]

13 **Rocca R**, De Angelis C, Daperno M, Carucci P, Ravarino N, Bruno M, Crocellà L, Lavagna A, Fracchia M, Pacchioni D, Masoero G, Rigazio C, Ercole E, Sostegni R, Motta M, Bussolati G, Torchio B, Rizzetto M, Pera A. Endoscopic ultrasound-fine needle aspiration (EUS-FNA) for pancreatic lesions: effectiveness in clinical practice. *Dig Liver Dis* 2007; **39**: 768-774 [PMID: 17606420 DOI: 10.1016/j.dld.2007.04.013]

14 **Eloubeidi MA**, Tamhane A. Prospective assessment of diagnostic utility and complications of endoscopic ultrasound-guided fine needle aspiration. Results from a newly developed academic endoscopic ultrasound program. *Dig Dis* 2008; **26**: 356-363 [PMID: 19188728 DOI: 10.1159/000177022]

15 **Coté GA**, Hovis CE, Kohlmeier C, Ammar T, Al-Lehibi A, Azar RR, Edmundowicz SA, Mullady DK, Krigman H, Ylagan L, Hull M, Early DS. Training in EUS-Guided Fine Needle Aspiration: Safety and Diagnostic Yield of Attending Supervised, Trainee-Directed FNA from the Onset of Training. *Diagn Ther Endosc* 2011; **2011**: 378540 [PMID: 22203780 DOI: 10.1155/2011/378540]

16 **Ahmad NA**, Kochman ML, Lewis JD, Ginsberg GG. Can EUS alone differentiate between malignant and benign cystic lesions of the pancreas? *Am J Gastroenterol* 2001; **96**: 3295-3300 [PMID: 11774939 DOI: 10.1111/j.1572-0241.2001.05328.x]

17 **Scheiman JM**. Management of cystic lesions of the pancreas. *J Gastrointest Surg* 2008; **12**: 405-407 [PMID: 17957437]

18 **de la Fuente SG**, Ceppa EP, Reddy SK, Clary BM, Tyler DS, Pappas TN. Incidence of benign disease in patients that underwent resection for presumed pancreatic cancer diagnosed by endoscopic ultrasonography (EUS) and fine-needle aspiration (FNA). *J Gastrointest Surg* 2010; **14**: 1139-1142 [PMID: 20424928 DOI: 10.1007/s11605-010-1196-9]

19 **Iglesias-Garcia J**, Dominguez-Munoz JE, Abdulkader I, Larino-Noia J, Eugenyeva E, Lozano-Leon A, Forteza-Vila J. Influence of on-site cytopathology evaluation on the diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) of solid pancreatic masses. *Am J Gastroenterol* 2011; **106**: 1705-1710 [PMID: 21483464 DOI: 10.1038/ajg.2011.119]

20 **Turner BG**, Cizginer S, Agarwal D, Yang J, Pitman MB, Brugge WR. Diagnosis of pancreatic neoplasia with EUS and FNA: a report of accuracy. *Gastrointest Endosc* 2010; **71**: 91-98 [PMID: 19846087 DOI: 10.1016/j.gie.2009.06.017]

21 **Cleveland P**, Gill KR, Coe SG, Woodward TA, Raimondo M, Jamil L, Gross SA, Heckman MG, Crook JE, Wallace MB. An evaluation of risk factors for inadequate cytology in EUS-guided FNA of pancreatic tumors and lymph nodes. *Gastrointest Endosc* 2010; **71**: 1194-1199 [PMID: 20598246 DOI: 10.1016/j.gie.2010.01.029]

22 **Fritscher-Ravens A**, Topalidis T, Bobrowski C, Krause C, Thonke E, Jäckle S, Soehendra N. Endoscopic ultrasound-guided fine-needle aspiration in focal pancreatic lesions: a prospective intraindividual comparison of two needle assemblies. *Endoscopy* 2001; **33**: 484-490 [PMID: 11437040 DOI: 10.1055/s-2001-14970]

23 **Siddiqui AA**, Brown LJ, Hong SK, Draganova-Tacheva RA, Korenblit J, Loren DE, Kowalski TE, Solomides C. Relationship of pancreatic mass size and diagnostic yield of endoscopic ultrasound-guided fine needle aspiration. *Dig Dis Sci* 2011; **56**: 3370-3375 [PMID: 21688127 DOI: 10.1007/s10620-011-1782-z]

24 **Devereaux BM**, Leblanc JK, Yousif E, Kesler K, Brooks J, Mathur P, Sandler A, Chappo J, Lehman GA, Sherman S, Gress F, Ciaccia D. Clinical utility of EUS-guided fine-needle aspiration of mediastinal masses in the absence of known pulmonary malignancy. *Gastrointest Endosc* 2002; **56**: 397-401 [PMID: 12196779 DOI: 10.1067/mge.2002.126829]

25 **Harewood GC**, Wiersema MJ. Diagnosis of pancreatic cancer-EUS/FNA to the rescue? *Am J Gastroenterol* 2001; **96**: 2501-2502 [PMID: 11513201 DOI: 10.1111/j.1572-0241.2001.04090.x]

26 **Arima M**, Tada M. Endoscopic ultrasound-guided fine needle aspiration biopsy in esophageal and mediastinal diseases: clinical indications and results. *Dig Endosc* 2003; **15**: 93-99 [DOI: 10.1046/j.1443-1661.2003.00224.x]

27 **Hernandez LV**, Mishra G, George S, Bhutani MS. A descriptive analysis of EUS-FNA for mediastinal lymphadenopathy: an emphasis on clinical impact and false negative results. *Am J Gastroenterol* 2004; **99**: 249-254 [PMID: 15046212 DOI: 10.1111/j.1572-0241.2004.04052.x]

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