ORIGINAL ARTICLE

Endoscopic Ultrasound Guided Fine-Needle Aspiration of Solid Pancreatic Lesions: Predictive Factors to Obtain an Adequate Diagnostic Sample

Federico Salom, Kenneth Ernest, William Piedra

Departamento de Gastroenterología, Hospital México, Universidad de Costa Rica,

San José, Costa Rica

ABSTRACT

Introduction Endoscopic ultrasound fine-needle aspiration has a crucial role in tissue acquisition of solid pancreatic lesions. Conflicting data exists regarding the impact of rapid on-site cytopathology evaluation and the type of needle used to improve the diagnostic yield. **Aims and Methods** A retrospective observational study from patients that had a pancreatic endoscopic ultrasound fine-needle aspiration, from a tertiary referral center was performed. Factors that correlated with an adequate tissue acquisition for cytological diagnosis after performing pancreatic endoscopic ultrasound fine-needle aspiration were evaluated. Patient's demographics, lesions size and location, type of needle used, rapid on-site cytopathology evaluation and final pathological diagnosis were obtained. The population was divided in two groups, according to the acquisition of a diagnostic sample. The baseline characteristics were compared with t-test and Fisher's exact test, for continuous and categorical variables, respectively. Uni and multivariate logistic regression models were elaborated in order to establish the correlation between our covariates and the odds for viable tissue acquisition. **Results** We collected data from 126 patients, 55.5% were women. The mean age was 61.59±12.18 years (range 21-85). The pancreatic lesion average size was 37.03±13.28 mm (range 8-70 mm). Most lesions were located in the head of the pancreas (73.8%). Regular fine-needle aspiration needles were used in 83.3% of the procedures. Most of them were 22-gauge needles (86.5%). Rapid on-site cytopathology evaluation was available in 32.5% of the procedures. A suitable diagnostic sample was obtained in 108 (85.7%) of the patients. After controlling other covariates, only the presence of rapid on-site cytopathology evaluation was significant (p=0.021, OR: 11.89) for diagnostic tissue acquisition. **Conclusion** Endoscopic ultrasound fine-needle aspiration is the standard of care for tissue acquisition of solid pancreatic lesions. Whenever available, rapid on-site cytopathology evaluation should be used, to increase the diagnostic yield of this procedure.

INTRODUCTION

Solid pancreatic lesions are caused mainly by malignant diseases, and its incidence has increased progressively over the past 30 years. [1] Pancreatic adenocarcinoma is the most frequent histopathological diagnosis (90%), [2, 3] but other tumors have been described including, pancreatic endocrine tumors, lymphomas and metastatic lesions to the pancreas. Differential diagnosis of solid pancreatic lesions should also include benign diseases such as focal chronic pancreatitis and autoimmune pancreatitis [4].

Endoscopic Ultrasound (EUS) in the last two decades has become crucial for pancreatic cancer staging, but it's most relevant strength is the possibility of achieving histological diagnosis through EUS-Fine-Needle Aspiration (FNA). This technique is the first line procedure for tissue acquisition and cytopathological diagnosis, with sensitivity between 64% to 85% and specificity between 75% to 100% [5]. The EUS-FNA result will impact the management in 50%-66% of the cases [6]. Many variables are involved in the chances of obtaining a suitable diagnostic sample through EUS-FNA [7]. Regarding FNA devices, different needle sizes are available, going from 25 to 19-gauge needles. There are also different needle designs to choose from (conventional needles, reverse bevel needles and the newly developed Fine-Needle Biopsy (FNB) prototype). The chosen FNA technique is also crucial to improve the results. The use of suction, stylet, number of needle-passes, and the presence of a Rapid On-Site Cytopathological Examination (ROSE); are variables that could affect the odds of obtaining an adequate diagnostic sample. The utility of ROSE and the type of needle used to improve diagnostic yield, have been a matter of debate in recent years [8, 9].

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Abbreviations EUS Endoscopic ultrasound; FNA Fine-needle aspiration; ROSE Rapid onsite cytopathology examination
Correspondence Federico Salom
Departamento de Gastroenterología, Hospital México, Universidad de Costa Rica. San José, Costa Rica
Tel +506 88323284
Fax + 506 22081437
E-mail fedesalom@yahoo.com

METHODS

We performed a retrospective single center study in a high volume EUS (>700 procedures per year) tertiary care hospital. Patients 18 years or older, with a solid pancreatic lesion identified either by Computed Tomography (CT) scan or Magnetic Resonance Imaging (MRI) without a clear

diagnostic etiology, sent for EUS-FNA, between December 2008 and December 2017, were included. Patients with cystic lesions, altered anatomy, high cardiovascular risk for sedation or under anticoagulation therapy that were unable to stop treatment, as well as pregnant women were excluded. Written informed consent was obtained for the endoscopic procedure in all patients.

Patient's demographics, lesions size and location, type of needle, use of ROSE and final cytopathological diagnosis were obtained. The population was divided in two groups, according to the acquisition of an adequate sample. Those with a diagnostic specimen in one group and those with a non-diagnostic specimen in the other. The baseline characteristics were compared with t-test and Fisher's exact test, for continuous and categorical variables, respectively. Uni and multivariate logistic regression models were elaborated in order to establish the correlation between our covariates and the odds for obtaining a suitable diagnostic sample.

Endoscopic Ultrasound

EUS was done under deep sedation by an anesthesiologist. The patient was placed on a left lateral position. An endosonographic evaluation of all the pancreatic gland was done with a curvilinear array endosonographic probe (Olympus America, Center Valley, Pa). Endosonographic features of the pancreatic solid lesion were analyzed. All the FNA`s were done under direct endosonographic view, with no evidence of vessels in the puncture field, previous confirmation of adequate platelet count and coagulation tests. FNA was standardized to stylet puncture and negative suction. In our center, ROSE is performed by an experienced cytopathologist. Three FNA passes were done in patients were no ROSE was available. When the cytopathologist was present the number of passes depends on the existence of adequate material after each puncture. The tissue was expressed onto the slides with stylet and/or sterile water. The slides were stained with Diff-Quik. If ROSE was not available, the material was placed on standard cytologic solution for cell block evaluation.

RESULTS

We collected data from 126 consecutive patients. 55.6% of the patients were women and 44.4% men. The mean age was 61.59±12.18 years (range, 21-85) and pancreatic lesion average size was 37.03±13.28 mm (range 8-70 mm). Most lesions were located in the head of the pancreas (73.8%). Less frequently, the lesions were located in the body (15.9%), neck (3.9%), tail (3.2%) and uncinated process of the pancreas (3.2%).

All the patients underwent EUS-FNA tissue acquisition for cytologic evaluation of solid pancreatic lesions. Conventional FNA needles were used in 83.3% of the procedures and core needles (reverse bevel) in 16.7% of the cases. Most of them were 22-gauge needles (86.5%), 25-gauge needles were used in 12.7% and 19-gauge needles in 0.8%, respectively. ROSE was available in 41 (32.5%) of the procedures done.

A suitable diagnostic sample was obtained in 108 of the patients. The final diagnosis were mainly pancreatic adenocarcinomas, (77% of the cases), followed by pancreatic endocrine tumors in 9%. Solid pseudopapillary neoplasm (4%), chronic pancreatitis (5%), and auto-immune pancreatitis (3%) were less frequent etiological diagnoses. Interestingly two metastatic tumors were diagnosed; being a melanoma and a renal cell carcinoma the final diagnosis in each case **(Figure 1)**. No serious complications were reported due to EUS-FNA, but auto-limited bleeding was seen in 2.4% of the procedures. Patients had a clinical follow-up of at least 6 months after the procedure, or during the survival length of the patient. Target lesions were considered benign if no evidence of malignancy was identified on subsequent clinical and imaging evaluation.

Overall, the sensitivity of the EUS-FNA procedures perform at our center was 85.7%. Patients were divided in two groups, those with a diagnostic specimen and those with a non-diagnostic specimen. Statistical evaluation of both groups was done. In the univariate analysis, there were no significant differences within groups regarding age (p=0.756), sex (p=0.619), largest (p=0.586) and smallest lesion diameter (p=0.449) **(Table 1)**. There was

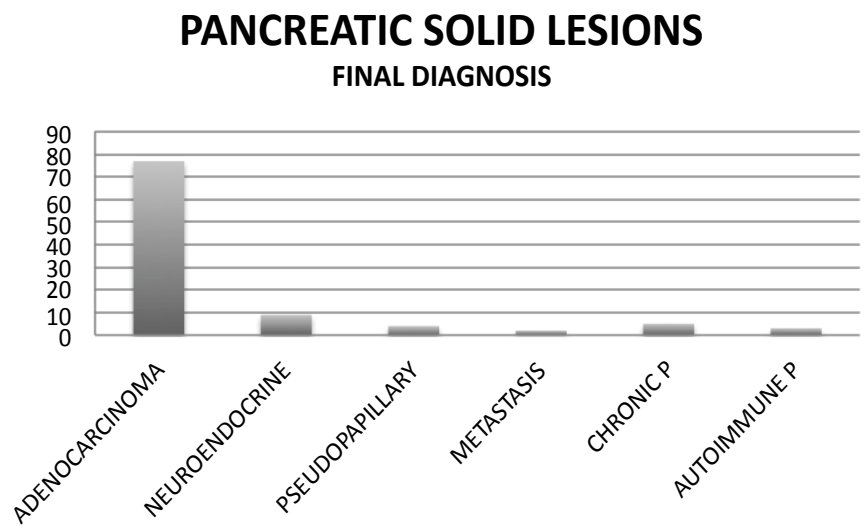

Figure 1. Final diagnosis of solid pancreatic lesions. Metastasis: A melanoma and a renal cell carcinoma the final diagnosis in each case.

Table 1. Characteristics of viable and non-viable materials.

Characteristic	Viable Material	Non-viable Material	p-value
	N=108	N=18	
Age (yr)	61.57	61.67	0.756
Mass largest diameter (mm)	36.72	38.89	0.586
Mass smallest diameter (mm)	31.2	33.22	0.449
Sex n (%)			
Male	47 (43.52)	9 (50)	0.619
Female	61 (56.48)	9 (50)	
Pancreatic site of mass n (%)			
Head	84 (77.78)	9 (50.00)	0.022
Body	14 (12.96)	6 (33.33)	
Neck	5 (4.63)	0 (0)	
Tail	3 (2.78)	1 (5.56)	
uncinate	2 (1.85)	2 (11.11)	
Needle size used n (%)			
19 G	1 (0.93)	0 (0)	0.895
22 G	93 (86.11)	16 (88.89)	
25 G	14 (12.96)	2 (11.11)	
Core-Needle Use n (%)			
Yes	18 (16.67)	3 (16.67)	1.000
No	90 (83.33)	15 (83.33)	
Number of punctures n (%)			
one	16 (14.81)	6 (33.33)	0.254
two	38 (35.19)	9 (50)	
three	50 (46.30)	1 (5.56)	
four	3 (2.77)	2 (11.11)	
five	0 (0)	0 (0)	
six	1 (0.93)	0 (0)	
ROSE n (%)			
Yes	40 (37.04)	1 (5.56)	0.007
No	68 (62.96)	17 (94.44)	

no statistical different between these two groups according to the needle size (p=0.895), regular or reverse bevel needle (p=1.000) and number of pancreatic punctures when performing EUS-FNA (p=0.254). A statistically significant difference was found regarding the presence of an adequate diagnostic specimen, for lesions located in the head the pancreas (p=0.022) and when ROSE was available (p=0.007).

We performed multivariate analysis with logistic regression for ROSE and anatomical location of the lesion. The presence of ROSE had statistical significance (OR: 11.89, 95% CI 1.45-97.79, p=0.021) for diagnostic tissue acquisition. However, we did not find significance for pancreatic lesions location (OR: 0.41, 95% CI 0.10-1.96, p=0.282).

With ROSE, an adequate diagnosis was obtained in 97.5% of the pancreatic lesions that were sampled, compared with 80% when ROSE was unavailable. Interestingly, in 60% of these patients were ROSE was used, only one FNA pass was needed to obtain an adequate diagnostic sample.

DISCUSSION

During the evaluation of a solid pancreatic lesion, an adequate staging and histological diagnosis are essential for a proper treatment strategy. At present, EUS FNA is the most frequent procedure done for pancreatic tissue acquisition, with a high sensitivity and specificity, as described in the meta-analysis by Hewitt et al. [6]. Actually EUS-FNA appears to be the gold standard for the histological diagnosis of solid pancreatic lesions. The sensitivity of 85.7% of EUS FNA for solid pancreatic lesions obtained in our study, correlates adequately with what has been described in the literature [10]. As we expected, most of the lesions were diagnosed as pancreatic adenocarcinomas (77%) [11]. Interestingly 8% of the solid pancreatic lesions were benign diseases, either chronic pancreatitis or auto-immune pancreatitis. In all of these benign cases, no evidence of malignancy was found after 6 months of clinical and imaging follow-up. In the literature as high as 5% of pancreatectomies performed with a primary diagnosis of pancreatic cancer are later proven to be inflammatory diseases. These results strengthen even more the importance of adequate tissue acquisition, not only to provide an appropriate treatment for malignant diseases, but also to avoid unnecessary surgical procedures in benign conditions [12].

To improve the quality of the pancreatic samples obtained, technical guidelines for EUS FNA have been developed. As described above, many variables affect the odds of obtaining an adequate material for histopathological diagnosis [8]. The use of suction is recommended and neutralizing the residual negative

pressure before withdrawing the needle. No significant difference has been observed when performing EUS FNA with or without stylet [13, 14]. In our study we followed these recommendations to improve the quality of sample obtained [15, 16].

Regarding needle types, different needle sizes are equally recommended, as well as FNA versus FNB needles. We did not find any significant difference between different needle sizes or type of needle chosen [8] (standard and reverse bevel). This data correlates with a recent meta-analysis comparing FNA and FNB, which did not establish superiority of core biopsy needles in comparison to standard FNA needles in terms of diagnostic adequacy and accuracy [17, 18]. Second generation core biopsy needles have been available recently, but to our knowledge, they have not shown improvement in diagnostic accuracy, compared with standard FNA needles, [19] however they provide a better histological sample for architecture and morphological assessment. Thus, specific use of this type of needles would be a better choice when core tissue specimen is required, mainly if degree of differentiation in malignancy or molecular analysis are needed [20, 21]. The utility of ROSE has been a matter of debate. In our study, it was the only variable that influenced significantly the odds of obtaining an adequate sample when EUS FNA of solid pancreatic lesions is being performed [20]. Even though in our center the availability of this resource is not always accessible (available in 32.5% of the cases), when used, it assured a diagnostic sample in 97.5% of the cases. Diagnostic sensitivity increases when ROSE is performed, [6] with an excellent positive predictive value. Two randomized control trails have evaluated this issue with no difference in accuracy and sample adequacy. Interestingly in both studies 7 passes were done in the group of patients where ROSE was not available [22]. Different studies have proposed 2-3 passes with reverse bevel needle and 3-4 passes with regular FNA needles, with a high sensitivity (above 90%), and increasing this number have not shown to improve these results [23, 24]. In our study whenever ROSE was available, only one pass was needed in 60% of the cases, decreasing the number of passes done in this group of patients [25, 26, 27].

This study has some limitations including the retrospective evaluation of the data and the absence of a final histological confirmation in most of the cases. This issue is difficult to improve, since most of these patients either with malignant or benign diagnosis, did not undergo a surgical resection of the pancreatic lesion.

CONCLUSION

In conclusion, with our data we support the fact that EUS FNA is the standard of care for tissue acquisition from solid pancreatic lesions. It is a safe and accurate diagnostic method with very low risk of complications. Whenever available and in the absence of new generation core biopsies, ROSE should be always used. This technique will harbor a better diagnostic yield and will decrease the number of passes done, to obtain a suitable sample for an adequate cytopathological diagnosis.

Conflict of Interest

The authors disclose no financial relationships or conflict of interest relevant to this publication.

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