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RESEARCH ARTICLE

Diagnostic Yield of Endoscopic Ultrasonography–Guided Fine-Needle Aspiration (Eus-Fna) for Solid Pancreatic Masses

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Abstract

Background:

Endoscopic ultrasound-Fine-needle aspiration (EUS)-FNA is one of the most sensitive and accurate modalities, for detecting and staging pancreatic masses and for obtaining a histological diagnosis. Our stud-ies aim to assess the diagnostic yield of EUS-FNA in solid pancreatic masses. METHODS: Forty-five patients with solid pancreatic masses on im-agery were included out of 230 EUS performed between September 2018 and January 2020. All the patients, underwent EUS-FNA using 19G or 22G needles. All the masses were divided into 2 groups based on mass size: group A (< 30 mm) and group B (> 30mm). Sensitivity, nega-tive predictive value (NPV), and diagnostic accuracy were respectively evaluated. The specificity and positive predictive value were 100% in both groups. Statistical analysis was performed using SPSS, and the significance level was set at p <0.05. RESULTS: Overall, sensitivity and diagnostic accuracy were signif-icantly higher in group B (80,7% vs 46% (p=0,01), and 89,2% vs 58,8%(p=0,02)). Only the sensitivity was significantly higher with 19 G (p=0,02) in group A. In group B, the sensitivity and diagnostic accuracy were higher with 22G (71% vs 50% (p=0,6), 93,3% vs 69,5% (p=0,5), despite more passes were performed with 22G (2,55 ± 0,59 vs 1,96 ± 0,56 p = 0.001). The multivariate analysis showed that the risk of getting a negative EUS-FNA is 6,46 times higher in group A (p=0,009). CONCLUSION: The diagnostic yield of EUS-FNA is correlated at the pancreatic mass size and the risk to get a negative EUS-FNA is 6,46 times higher for masses <30mm.

Keywords: EUS-FNA, Solid mass, Needle size, Puncture route, Lesion size.

1 | BACKGROUND:

Pancreatic cancer is the seventh leading cause of death from cancer in the world. The diagnosis is often difficult at an early stage and subsequently delayed (1). The arrival of Endoscopic Ultrasound-Fine-Needle Aspiration (EUS)-FNA, allowed the diagnosis and staging of pancreatic mass lesions. It is one of the most sensitive and accurate modalities for detecting and evaluating pancreatic mass and for obtaining a histological diagnosis (2). However, many factors can affect the diagnostic yield of EUS-FNA. Our studies aim to evaluate the factors affecting the diagnostic yield of EUS-FNA in solid pancreatic masses.

2 | METHODS:

Study population:

We retrospectively included all the patients with a solid pancreatic mass, who underwent EUS-FNA using the 19G or the 22G needle, between September 2018 and January 2020 at Endoscopy and gastroenterology Unit of IBN SINA University Hospital. In total, 230 EUS with 112 FNAs were performed by two endosonographers during this period. Patients with cystic lesions were excluded from the present study (Figure1). Among all patients, four underwent surgery; 3 cases of neuroendocrine tumor (NET) and 2 cases of solid pseudopapillary neoplasm (SPN) and the final diagnosis was similar to the FNA histology (Figure 1).

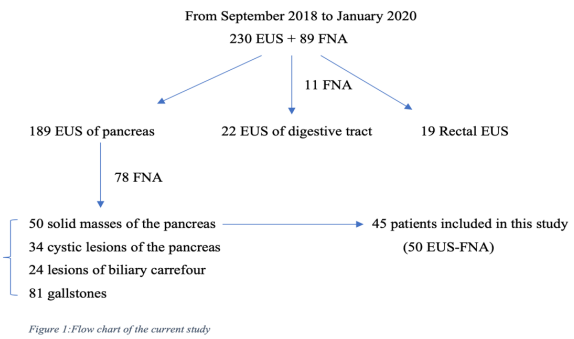

FIGURE 1: 1: Flow chart of the current study

Study design:

The study was divided into two groups based on the mean size of the pancreatic mass, obtained by endoscopic ultrasonography measurements: group A (< 30 mm) and group B (> 30 mm). Overall, fifteen patients had first negative EUS-FNA, subsequently, a second EUS-FNA was performed in 5 patients and only the final diagnosis was considered.

The main indication of the EUS-FNA was to obtain histological subtype for unresectable pancreatic cancer in 29 cases (64,5%) and suspected pancreatic cancer in 16 cases (35,5%).

EUS-FNA procedure:

The radial echoendoscope was introduced in our unit in 2015, and the linear echoendoscope became available in August 2018.

All EUS procedures were performed under deep sedation with propofol. A linear echoendoscope (PENTAX HITACHI) was used by two endosonographers according to ESGE recommendations (3). Once the pancreatic mass has been identified, the operators measure the size in section, assess the local extension, then choose the puncture route according to the mass location, the distance between the mass and the probe and their preferences. The mass was punctured via the transgastric or the transduodenal route using 19G or 22G (Medi-globe ®). In the beginning, only 19G was available in our endoscopy unit until March 2019, 22G became available. Several needle passes were performed with fanning and the samples were directly placed in Cytolyt® according to the standard ESGE protocol (3), then sent to an advanced pathologist for analysis. All specimens were classified as malignant, benign or negative (nondiagnostic). All patients were kept under observation after the procedure (Figure 2).

Supplementary information The online version of this article (https://doi.org/xx.xxx/xxx.xx) contains supplementary material, which is available to authorized users.

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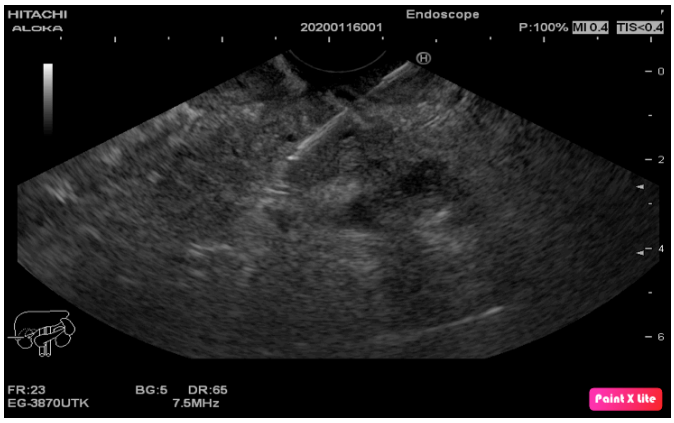

FIGURE 2: Insertion of the needleinto the pancreatic mass

The final diagnosis (4, 5):

In this study, the final diagnosis of malignancy and benignity was established based on clinical signs, biology, image features, and histopathology of the surgical specimen and the EUS-FNA.

(1) Absence of clinical, biological, imagery and EUS-FNA criteria of malignancy (with 6 months minimum of follow-up).

(2) Presence of criteria of malignancy and positive surgical specimens.

(3) Presence of clinical, biological, imaging and EUS-FNA criteria of malignancy.

(4) Presence of clinical signs, biology and imaging criteria of malignancy with negative EUS-FNA.

Outcomes measurements:

The primary outcome was the measures of the overall diagnostic yield of EUS-FNA in the pancreatic solid masses, then in each group and with each needle.

The sensitivity was defined by the percentage of malignancies diagnosed by EUS-FNA.

The diagnostic accuracy was defined by the percentage of positive histology obtained by EUS-FNA. The absence of clinical, biological, imaging and EUS-FNA criteria of malignancy was considered a true negative. The presence of clinical, biological and imaging criteria of malignancy with negative EUS-FNA, was considered to be a false negative. There were no false positives. The histology of the surgical specimens was similar to the first histology obtained by EUS-FNA.

The secondary outcomes were the measures of the difference between; the size of the mass and needle used; mass location; puncture site; the number of needle passes; fanning, and positive FNA (Table 1).

TABLE 1: Diagnostic yield in each group

	GROUP A (N=17)	GROUP B (N=28)
TRUE POSITIVE	6	22
FALSE POSITIVE	0	0
TRUE NEGATIVE	4	3
FALSE NEGATIVE	7	3

Data and statistical analysis:

Statistical analysis was done using SPSS® software (IBM, Armonk, New York, USA). The means +/- standard deviation (SD) and frequency, percentage were used respectively for quantitative variables with normal distribution and qualitative variables. The difference between the size of the mass, the number of needles passes in positive EUS-FNA was done using Student's t-test. Significance was set at $p < 0.05$.

The univariate analysis was done with Fisher's exact test. Sensitivity, specificity, positive and negative predictive value and diagnostic accuracy were calculated based on the final diagnosis and compared using Fisher's exact test. Significance was set at $p < 0.05$. The results of the multivariate analysis were studied using binary regression analysis, and only factors with

$p < 0,2$ in the univariate analysis were introduced. The significance level was set for $p < 0.05$. Data are presented with odds ratios (OR) and their respective 95% confidence intervals (CI).

3 | RESULTS:

Fifty EUS-FNA (21,7%) were performed on 45 patients over this period out of 230 EUS. The mean age was 56,42 ± 14,1 years, and the mean size of the mass was 39,46 ± 16, 82mm. There were 17 masses (37,8%) in group A and 28 masses (62,2%) in group B. The 19G needle was used in 23 cases (51,1%)

and the 22G in 22 cases (48,9%) with 2,24 ± 0,64 passes per lesion, without any major complication. The histology showed malignancy disease in 62,1% (Table 2).

Table 2: Demographic characteristics of the patient in each group (Fisher's exact test)

Number of patients (n=45)	Group A (n=16)	Group B (n=29)	P value
The mean age in years (+/- SD)	59,8 +/- 13,2	54,5 +/- 14,5	0,2
Sex, n (%)			0,2
+Female	10 (62,5)	22 (75,86)	
+Male	6 (37,5)	7 (24,14)	
The mean size in mm (+/- SD)	26 +/- 6,01	50 +/- 12,9	0,001
Location of the mass, n (%)			0,3
+Head	12 (75)	15 (51,72)	
+Body	2 (12,5)	10 (34,48)	
+Tail	2 (12,5)	4 (13,8)	
The size of the needle, n (%)			0,5
+19G	9 (56,25)	16 (55,17)	
+22G	7 (34,75)	13 (44,83)	
Puncture route, n (%)			0,3
+Transgastric	7 (34,75)	18 (62,06)	
+Transduodenal	9 (56,25)	11 (37,94)	
The mean number of passes (+/- SD)	2,06 +/- 0,6	2,38 +/- 0,6	0,1
The final diagnosis, n (%)			0,1
+ Adenocarcinoma	5 (31,25)	17 (58,6)	
+ TNE	1 (6,25)	2 (6,9)	
+ Other maligns tumors*	0 (0)	3 (10,4)	
+ Negative	10 (62,5)	7 (24,1)	

* (2 SPN+ pancreatic Metastasis)

Primary outcomes:

Overall, sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were respectively :73,6%,100%, 100%, 41%, and 77,7%.

Sensitivity, negative predictive value (NPV), and diagnostic accuracy in groups A and B were respectively: 46,15% vs 88% (p=0,03), 36,3% vs 50% (p=0,9), 58,5% vs 89% (p=0,02). There is a significant difference in the sensitivity and diagnostic accuracy of each group, they increased significantly as the mass size increased (p=0,03 et 0,02). The negative predictive value was not significant in the groups (p=0,9).

However, the specificity and the positive predictive value (PPV) are 100% in both groups (Table 3).

TABLE 3: Diagnostic yield in each group

	Group A	Group B	p Value
Sensitivity	46,15%	88%	0,03
Specificity	100%	100%	0,001
PPV	100%	100%	0,001
NPV	36,36%	50%	0,9
Diagnostic accuracy	58,5%	89%	0,02

Fisher's exact test

The sensitivity and diagnostic accuracy with needles 19G and 22G in group A were respectively: 50% vs 33,3% (p=0,02) and 50% vs 71% (p=0,6). There is a statistically significant difference in sensitivity with needles 19G and 22G in group A.

The sensitivity and diagnostic accuracy of needles 19G and 22G in group B were: 80% vs 93,3% (p=0,6) and 69,5% vs 93,3% (p=0,5), this difference was not statistically significant (Table 4).

TABLE 4: Diagnostic yield of 19G and 22G needles in each group

	Groups	19G needle	22G needle	p Value
Sensitivity	Group A	50%	33,3%	0,02
	Group B	80%	93,3%	0,06
Diagnostic	Group A	50%	71%	0,6
accuracy	Group B	69,5%	93,3%	0,5

Fisher's exact test

Secondary outcomes:

We performed a univariate analysis of all variables that could affect the outcome of the EUS-FNA. A significant difference was found in mass sizes and the positive FNA (p=0,02) calculated using Stu-dent's t-test. No significant difference between pos-itive FNA and diameter of the needle used (p=0,5), mass location (p=0,2), puncture route (p=0,5), and number of passes (p=0,3) was found (Table 5).

Table 5 : Univariate analysis of all variables

	Histology of the FNA		
Variables	FNA + n= 28	FNA – n=17	**p value**
Mass size			0,005
+Group A	6 (13,35)	11 (24,4)	
+Group B	22 (48,9)	6 (13,35)	
Diameter of the needle			0,5
+19 G	13 (28,9)	10 (22,2)	
+22 G	15 (33,3)	7 (15,6)	
Mass location			0,2
+Head	14 (31,1)	13 (28,9)	
+Body	9 (20)	3 (6,7)	
+Tail	5 (11,1)	1 (2,2)	
Puncture route			0,5
+Transgastric	17 (37,8)	8 (17,8)	
+Transduodenal	11(24,4)	9 (20)	
Number of passes:			0,8
+1 pass	2 (4,5)	2 (4,5)	
+2 passes	16 (35,5)	11 (24,4)	
+3 passes	9 (20)	4 (8,9)	
+4 passes	1 (2,2)	0 (0)	

Fisher's exact test

Therefore, there was a significant difference in the number of passes with the 22G needle (p=0,001) (Table 6).

Table 6: Number of passes of each needle

	19G needle (n=23)	22G needle (n=22)	p Value
Number of needle passes	1,96 +/- 0,5	2,55 +/- 0,5	0,001

Student's t-test

In multivariate analysis, independent variables included the mass size (groups A and B), the negative EUS-FNA, the location of the mass.

We found that the risk of obtaining a negative EUS-FNA is 6,46 times higher in group A (mass < 30mm) (confidence interval (CI) :1,6-26,13, p=0,009). Moreover, the mass location was not a significant factor in affecting the percentage of negative EUS-FNA (Table 7).

TABLE 4: 7: Multivariate analysis of factors could affect the percentage of negative EUS-FNA.

	Odds ratio	95% CI	p Value
Mass size:			
+Group B	1		
+Group A	6,48	1,6 -26,13	0,009
Mass location:			
+Head	1		
+Body	0,44	0,86-2,32	0,34
+Tail	0,20	0,18-2,35	0,20

4 | DISCUSSION:

Overall, sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were respectively :73,6%,100%, 100%, 41%, and 77,7%.

Crino et al. showed in their study that the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were respectively: 85.2%, 81.8%, 93.7%, and 80.4% (6).

Several studies have been interested in factors affecting the diagnostic yield of EUS-FNA

(2–7), and the first outcome is mass size. We showed through this study that the diagnostic yield is statistically correlated to the mass size, in particular for masses > 30mm in size. Sensitivity and diagnostic accuracy were respectively: 88% and 89%. By multivariate analysis, we showed that only size is considered as a potential factor to affect EUS-FNA.

Many studies have shown that the sensitivity and diagnostic accuracy increase significantly as

the size of the pancreatic mass increases. Sugiura et al. demonstrate that sensitivity and diagnostic accuracy are significantly higher for lesions >10mm in size, and increase as the lesion size increases.

In their study, they divided the patients into five groups according to the lesion size (A<1cm; B: 1-2cm; C: 2-3cm; D: 3-4cm and E>4cm), and they found that the sensitivity and the diagnostic accuracy were respectively: 89.9% vs 95% vs 97.4%; 98.5% vs 98.7% (p < 0,01) and 91.7% vs 96.4% vs 97.7% 98.6% vs 98.7% (p = 0,03) (7).

A multi-centric study including 164 patients with solid pancreatic masses, has shown that the sensitivity and diagnostic accuracy were 83% and 85% for lesions between 28,5mm and 41,3mm in size (8).

The second outcomes are the size of the needle, number of passes and fanning. Three sizes of EUS-FNA needles are commercialized: 19G, 22G, and 25G (9). The choice of the needle depends; on the mass size, the puncture route and the preference of endosonographers (10). The needle 22G is the most commonly used (11). In our study, only the sensitivity was significantly higher with the needle19G for masses with a size < 30mm (p=0,02). There was no significant difference in diagnostic accuracy (p=0,6) between needles in group A. For masses > 30mm in size, sensitivity and diagnostic accuracy were higher with the needle 22G (71% vs 50% (p=0,6), 93,3% vs 69,5% (p=0,5). This difference is not significant.

A prospective randomized trial conducted by Itoi et al. showed that the sensitivity of the needle 19G was significantly higher than 22G for the diagnosis of malignancies (12). An algorithm has been proposed by Bang et al regarding the choice of the needle (13).

By univariate analysis, we showed that there was no significant difference between the diameter of needles 19G and 22G and FNA positive: 93,3% vs 69,5% (p=0,5). A randomized trial conducted by Ramesh and al. has shown the same result regarding the performance of 19G and 22G (14).

There was no significant difference between the number of needle passes and FNA positive (p=0,8) in our studies. ESGE recommends 5 passes for solid pancreatic masses (15). LeBlanc et al. have shown that sensitivity increases as the number of passes increase with the needle 22G (16).

A randomized trial showed that there was no significant difference in diagnostic accuracy between the fanning and the standard technique (p=0,05). However, a few passes were required with fanning to establish the diagnosis of malignancy (17).

5 | CONCLUSION:

We showed in the current study, that the risk to get a negative EUS-FNA is 6,46 times higher for masses <30mm and the sensitivity of 19G needle for malignancy was higher than 22G needle for these masses.

LIST OF ABBREVIATIONS:

EUS-FNA: Endoscopic Ultrasound-Fine-needle aspiration

19G needle: 19 Gauge needle

22G needle: 22 Gauge needle

NET: Neuroendocrine tumor

SPN: Solid pseudopapillary neoplasm

SD: Standard deviation

CI: Confidence intervals

OR: Odds ratios

PPV: Positive predictive value

NPV: Negative predictive value

DECLARATIONS:

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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