

Fine-Needle Aspiration Biopsy of Pancreatic Masses: Failure Factors

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Abstract

Objectives: The main objective of this work is to determine the factors affecting the failure rate of pancreatic aspiration cytology, in particular the size, location, and nature of the mass as well as the size of the needle, the aspiration site, the number of passages, and realization of Fanning. **Materials and methods:** This is a retrospective study conducted in the EFD-HGE department at Ibn Sina Hospital in Rabat from March 2017 to May 2023. 138 patients with a solid or cystic pancreatic mass on imaging were included. A video-linear Pentax-type echoendoscope was used with needles of different gauges: 19G, 20G, 22G, and 25G. Statistical analysis was performed using R software and the level of significance was set at $p < 0.05$. **Results:** The sex ratio F/M was 1.35. The average age was 59 years old. The average tumor size was 40.5 mm. Fine needle aspiration (FNA) under ultrasound-endoscopy (EUS) was positive in 70% of cases: adenocarcinoma in 60% of cases, chronic pancreatitis in 9.33% of cases, neuroendocrine tumor in 8% of cases, solid and pseudo-papillary tumor of the pancreas in 4% of cases, mucinous cystadenoma with low-grade (LGD) in 1.33% of the cases, an intraductal papillary mucinous neoplasm (IPMN) in 2.66% of the cases, pancreatic tuberculosis in 1.33% of the cases. Normal pancreatic parenchyma without signs of malignancy in 13.33% of the cases. The failure rate of pancreatic fine-needle aspiration was estimated at 30% of cases (inconclusive result). By univariate analysis, we demonstrated that the risk of having an inconclusive fine needle aspiration increases on the one hand by the location of the mass at the head of the pancreas ($p = 0.02$), the presence of a cystic component ($p = 0.01$), the infiltrating character of the mass ($p = 0.01$), and on the other hand by the absence of Fanning ($p = 0.03$). However, this study did not show a significant correlation with the other factors, in particular the size of the mass, the size of the needle, the site of fine-needle aspiration, and the number of passages. No complications were noted. **Conclusion:** The failure rate of fine-needle aspiration biopsy was 30%. We demonstrated that it increases by the location of the mass at the head of the pancreas ($p = 0.02$), the presence of a cystic component ($p = 0.01$), the infiltrating character of the mass ($p = 0.01$), and the absence of fanning. An additional study with a larger sample or a multicenter study seems necessary to confirm our results.

Keywords: Ultrasound-endoscopy (EUS), pancreatic masses, EUS-guided fine-needle aspiration (FNA), EUS-guided fine-needle biopsy (FNB).

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INTRODUCTION

Endoscopic ultrasound was developed in the 1980s, to explore the pancreatic parenchyma which was generally insufficiently well visualized by ultrasound and abdominal computed tomography (CT), and then became the most widely used method for the diagnosis of solid or cystic pancreatic masses, with the possibility of fine needle aspiration cytology. The main objective of this work is to determine the factors affecting the failure rate of pancreatic aspiration cytology, in particular the size, location, and nature of the mass as well as the size of the needle, the aspiration site, the number of passage, and realization of Fanning.

MATERIALS AND METHODS

Patients

This is a retrospective study conducted in the EFD-HGE department at Ibn Sina Hospital in Rabat from March 2017 to May 2023. 138 patients with a solid or cystic pancreatic mass on imaging were included. The data were collected from the registers of EUS and the register of anatomopathological examinations of the IBN SINA hospital in Rabat. These were essentially clinical features, biological assessment, abdominal imaging, and EUS result. The latter includes the size and location of the mass, the size of the needle, the aspiration site, the number of passages performed, the complications after the operation, and the diagnosis retained.

Endoscopic ultrasound Procedure

EUS was performed under propofol sedation after a pre-anaesthetic consultation. It was performed in the left lateral decubitus position, using a PENTAX® HITACHI® sector-linear echoendoscope device. The needles used were 19 gauge (G), 20G, 22G, and 25G.

Histological examination

The samples were stored in the Cytolyt® solution and quickly sent to the anatomopathology laboratory of the IBN SINA hospital in Rabat.

Classification of pancreatic lesions

All findings were categorized as benign, malignant, or inconclusive. Adenocarcinoma, neuroendocrine tumor (NET), solid pseudopapillary tumor (TPSP), and IPMN with signs of dysplasia were considered malignant lesions. Pancreatic tuberculosis, chronic pancreatitis, and normal pancreatic parenchyma without signs of malignancy, were considered as negative for malignancy. The hemorrhagic sample was considered inconclusive (failure of fine needle aspiration).

Statistical analysis

Data entry was performed using R statistical software. Continuous variables were presented as mean \pm standard deviation, while qualitative variables were expressed as counts and percentages.

The association between FNA results and qualitative factors was analyzed using the chi-square test, revealing significance when $p < 0.05$, with a 95% confidence interval. A generalized linear model was used to estimate the relationship between fine needle aspiration results and continuous factors.

Finally, a multiple regression was carried out to evaluate the simultaneous contributions of the different factors to the results of the fine needle puncture.

RESULTS

The sex ratio F/M was 1.35. The average age was 59 years old. Fine needle aspiration under EUS had as the main indication a doubt about the tumoral nature of the mass in 58% of cases.

The EUS did not objectivize a pancreatic mass in 8% of the cases ($n = 11$): a normal aspect of the pancreas in 82% of the cases ($n = 9$) and an aspect of acute pancreatitis without individualisable mass in 18% of the cases ($n = 2$). The EUS was pathological in 92% of the cases ($n = 127$) and showed the characteristics cited below.

The average tumor size was 40.5 mm. Head locations were predominant in 50%, followed by body locations in 15%. Caudal locations in 9% of cases.

Localizations at the uncus were observed in 4% of cases. Locations at the level of the isthmus in 1% of cases. The pancreatic mass was solid in 74% of cases ($n = 94$) and cystic in 17% of cases ($n = 22$). It was solid with a cystic component in 9% of cases ($n = 11$). Calcifications were present in 9% of cases ($n = 11$). Necrosis was noted in 14% of cases ($n = 18$).

Fine needle aspiration under EES was performed in 84% of patients ($n = 107$) among the 127 whose EUS had objectified a pancreatic mass.

Size 19G needles were used in 37% of patients ($n = 39$). 20G needles were used in 16% ($n = 17$), 22G needles in 46% ($n = 49$), and 25G needles were used in 1% of patients ($n = 1$). Combined use of 22G needles with a 20G or 25G needle was noted in 1% of cases each. We performed a single passage in 6% of cases ($n = 6$), 2 passages in 54% of cases ($n = 58$), 3 passages in 32% of cases ($n = 34$), 4 passages in 6% of cases ($n = 6$), and 5 passages in 3% of cases ($n = 3$). The mean number of passages was 2.21. Fanning was performed in 40% of cases ($n = 43$). Fine needle aspiration was performed by transgastric route in 50% of cases ($n = 54$), by transbulbar route in 27% of cases ($n = 29$), by transduodenal route in 7% of cases ($n = 8$), and by transgastric route and transbulbar in 15% of cases ($n = 16$).

EUS-guided fine-needle aspiration came back positive in 70% of cases. It showed adenocarcinoma in 60% of cases, chronic pancreatitis in 9.33% of cases, neuroendocrine tumor in 8% of cases, solid and pseudo-papillary tumor of the pancreas in 4% of cases, mucinous cystadenoma with LGD in 1.33% of the cases, an IPMN in 2.66% of the cases, pancreatic tuberculosis in 1.33% of the cases. Undamaged pancreatic parenchyma without signs of malignancy was observed in 13.33% of the cases. 30% of patients ($n = 32$) had inconclusive histology (exclusively hemorrhagic sample). The procedure was redone in 9 cases and revealed: adenocarcinoma in 11% of cases ($n = 1$), chronic pancreatitis in 22% of cases ($n = 2$), and inconclusive results in 67% of cases ($n = 6$).

Diagnostic performance

We proceeded to evaluate the overall failure rate of fine-needle aspiration (rate of fine-needle aspiration whose anatomopathological result was inconclusive) then it was analyzed first according to the age and sex of the patients, then according to the characteristics of the mass (site, size, and nature) and finally to the technical modalities (size and type of the needle, number of passages, site of fine needle aspiration and Fanning).

Overall Failure Rate

The overall failure rate of pancreatic fine needle aspiration is 30%. It is not influenced by age ($p = 0.09$) or patient sex ($p = 0.54$).

Fine needle aspiration failure rate according to the characteristics of the pancreatic mass

Size

To study the relationship between the failure rate of fine needle aspiration and the size of the tumor, the following parameters were considered: the major and the minor axis of the mass designated by "D" and "d", respectively, the surface (or the actual size) of the

tumor which is equal to "D x d" and finally the infiltrating character of the mass defined by "(D-d)/d".

The FNA failure rate is not influenced by the value of the major axis (p = 0.3), the minor axis (p = 0.08), or by the size of the tumor (p = 0.11). On the other hand, it has been shown that it can be influenced by the infiltrating character (p = 0.01) (Figure 1).

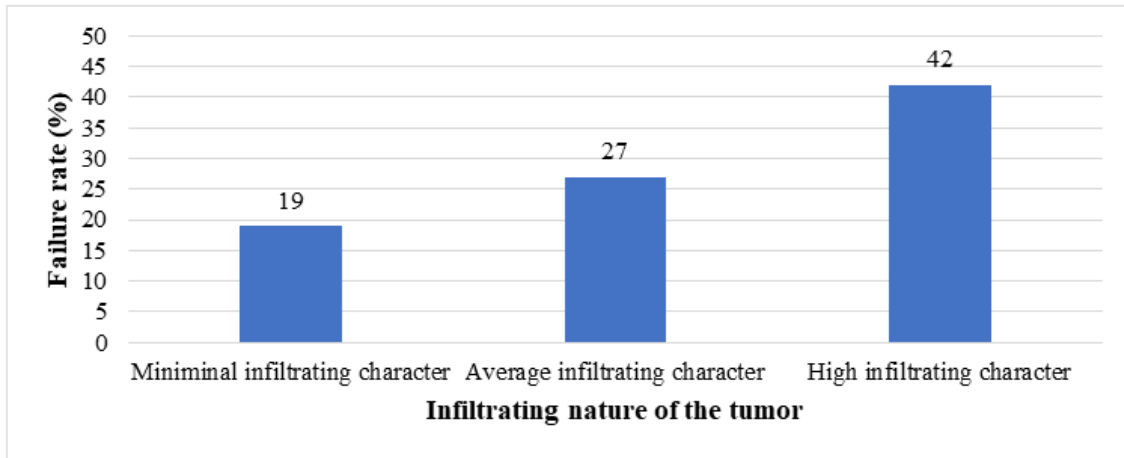


Figure 1: Fine needle aspiration failure rate according to tumor infiltration (p = 0.01)

Nature

We showed that the failure rate can be influenced by the presence or absence of a cystic component in the pancreatic mass. Indeed, this rate is 50% in the presence of a cystic component while it is estimated at 23% in its absence. This result is statistically significant (p = 0.016).

Seat

In our study, the location of the pancreatic mass in the head was found to be associated with the highest failure rate (37.28%) compared to the other locations. This result is statistically significant (p = 0.025) (Figure 2).

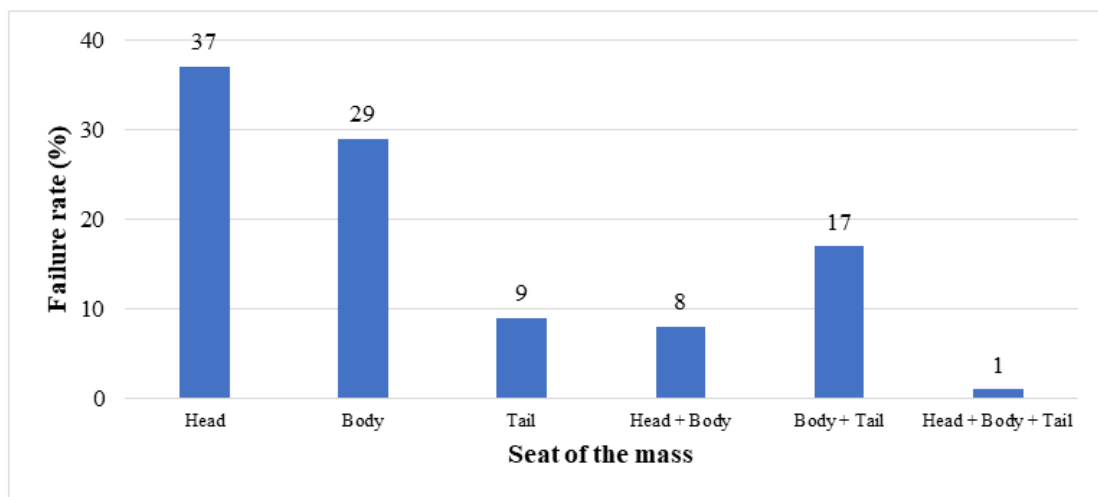


Figure 2: Fine needle aspiration failure rate according to the seat of the mass (p = 0.025)

Failure rate according to fine needle aspiration procedure

Fanning

With Fanning, the failure rate of the procedure is 17%. Without Fanning, this rate rises to 36%. These results are statistically significant (p = 0.03).

Needle size

It was found that the failure rate of fine needle aspiration was higher when using a 22G needle compared to the other sizes, but without a statistically significant difference ($p = 0.79$).

Number of passages

We found that the number of passages during fine needle aspiration did not influence its failure rate ($p = 0.9$).

Needle type

The failure rate of pancreatic fine needle aspiration was higher with FNB-type needles estimated at 33%, but this result is not statistically significant ($p = 0.38$).

Seat of procedure

We showed that the failure rate of pancreatic needle aspiration biopsy was lowest when performed transgastrically, but this result was not statistically significant ($p = 0.32$).

Multivariate analysis of factors influencing fine needle aspiration result

In this section, we studied the cyst component, seat (head), and Fanning, which were previously identified as factors influencing FNA results using multiple linear regression. We found that the cystic component and the head are always statistically significant with p values equal to 0.01 and 0.03 respectively, while the Fanning is not ($p = 0.11$).

DISCUSSION

Performance and overall failure rate of pancreatic fine needle aspiration biopsy

Endoscopic aspiration biopsy of pancreatic tumors provides a positive diagnosis in most cases [1]. Indeed, it provides a histological diagnosis in approximately 80% to 95% of cases with a sensitivity and specificity of 90% and 100%, respectively [2]. However, its failure rate with obtaining inconclusive results is estimated at 10% in some studies [3].

In our work, the failure rate of pancreatic fine needle aspiration was 30% from the first fine needle aspiration. This could be related, on the one hand, to the size of the sample and the expertise of the operator, and on the other hand, to the characteristics of the pancreatic mass, the technical modalities, and the non-availability of an immediate cytological evaluation of the sample taken [2]. Indeed, in some foreign countries, the help of a pathologist or a cytology technician (ROSE: rapid-on-site examination) is possible in the endoscopy room, allowing slides to be examined using an optical microscope [1], thus offering the possibility of having an immediate response on the quality of the samples taken and of repeating the procedure if necessary by increasing the number of passages or changing the needle size [4].

In a study conducted by Klapman *et al.*, [5], depending on the presence or not of a rapid cytological evaluation in the endoscopy room, showed an advantage of this technique ($p = 0.01$) [4].

Fine needle aspiration failure rate according to the characteristics of the pancreatic mass

Seat

A study has shown that the masses that sit at the level of the head or the uncus of the pancreas can be technically more difficult to access since the flexion of the echoendoscope hinders the exit of the needle [2]. These data are consistent with the results of our study where it was demonstrated that the failure rate of fine needle aspiration was higher if the mass was located at the level of the head ($p = 0.02$).

Size

A study by Sugiura *et al.*, [6] in 2019 demonstrated that the diagnostic yield of FNA under EUS is strongly related to the size of the mass. This efficiency increases when the size of the mass increases. They divided the patients into 5 groups according to the size of the mass (A < 1 cm; B: 1-2 cm; C: 2-3 cm; D: 3-4 cm; and E > 4 cm) and the diagnostic yield was 91.7%, 96.4%, 97.7%, 98.6%, 98.7%, respectively [7].

Other studies have shown that although large pancreatic masses offer easier access to FNA, they nevertheless have the disadvantage of being more necrotic or fibrous, thus increasing the rate of inconclusive results, given the rarity of tumor cells present in the sample [1].

In our series, we did not find a link between the size of the pancreatic mass and the failure rate of fine needle aspiration. This could be explained, by the location of the mass, which may be difficult to access, or by the presence of necrosis [2]. Furthermore, it has been shown that the failure rate of fine needle aspiration is linked to the infiltrating character of the tumor ($p = 0.01$).

Consistency

A large multicenter study, evaluating the factors associated with the optimization of the diagnostic yield of fine needle aspiration of cystic masses of the pancreas, showed that the presence of a solid component within the mass was associated with the improvement of the results ($p = 0.016$) [4]. In our series, we found that the presence of a cystic component within the mass increases the rate of inconclusive fine needle aspiration ($p = 0.01$).

Fine needle aspiration failure rate according to technical modalities

Needle size

The results of various observational studies and randomized trials conducted by Wani *et al.*, [8] in

2014 demonstrated that the use of a 25G needle was associated with better diagnostic yield compared to a 22G needle in the fine needle aspiration of pancreatic masses. Another observational study demonstrated that the diagnostic yield of fine needle aspiration was better with a 19G needle compared to a 22G needle [9].

In our series, we found that the failure rate of pancreatic fine needle aspiration was higher with 22G needles ($p = 0.79$).

Fanning

A randomized study conducted by Bang *et al.*, [10] in 2013, showed that Fanning optimizes the chances of harvesting tumor cells during the same passage within the lesion compared to standard techniques, which makes it possible to reduce the failure rate of fine needle punctures and improve diagnostic yield [10].

These data agree with the results of our work where it was shown that the failure rate of fine needle aspiration was 39.58% and 16.66%, respectively in the absence and the presence of Fanning ($p = 0.03$).

Number of passes

In two studies conducted by Volmar *et al.*, [11] and Siddiqui *et al.*, [12], the diagnostic yield of fine needle punctures of pancreatic masses was not influenced by the number of passages [11, 12]. Furthermore, other prospective and retrospective studies have suggested that many passages ranging from 5 to 7 are recommended to optimize the diagnostic yield of pancreatic fine needle puncture and reduce its failure rate. On the other hand, another study demonstrated that increasing the number of passages beyond 7 does not increase the diagnostic yield of fine needle aspiration of pancreatic masses [2].

In our series, it was found that the failure rate of fine needle aspiration was not influenced by the number of passages performed ($p = 0.9$).

Needle type

Two meta-analyses carried out in 2015 and 2017 comparing fenestrated needles (FNB) with standard needles (FNA), did not find any significant difference between these two types of needles in terms of diagnostic yield and quality of the sample obtained. However, the diagnosis was established with fewer passages (1 to 2 in general) with fenestrated needles [1, 13].

In our series, it was shown that the failure rate of pancreatic fine needle aspiration increases with FNB-type needles, but this result was not statistically significant ($p = 0.38$).

The fine needle puncture site

Pancreatic masses can be reached either transgastrically for lesions of the body and tail, or transduodenally for lesions of the head. However, the transgastric route generally remains the easiest to access since the echoendoscope remains linear allowing easy exit of the needle [2].

In our study, the transgastric route was found to be associated with the lowest failure rate of pancreatic puncture but this result was not statistically significant ($p = 0.32$).

CONCLUSION

Fine-needle puncture under EUS remains the best method for obtaining the histological diagnosis of solid or cystic pancreatic masses, in about 80% to 95% of cases according to data from the literature, with a complication rate that remains rare. In our series, EUS provided a histological diagnosis in 70% of cases with a predominance of adenocarcinoma in 60% of cases. Its failure rate is estimated at 30% according to our study with a sample qualified as hemorrhagic or inconclusive.

By univariate statistical analysis, we showed that the failure rate of fine-needle puncture under EUS depends on several factors including the seat of the mass at the head of the pancreas, the presence of a cystic component, and the infiltrating character of the mass as well as the absence of Fanning, which were associated with a statistically higher failure rate.

However, no statistically significant correlation was shown between the size of the mass, the size of the needle used, the number of passages performed, the aspiration site, and the rate of inconclusive aspiration cytology.

Nevertheless, our study had certain limitations, mainly the size of the sample, which was not large enough. Thus, an additional study with a larger sample or a multicenter study seems necessary to confirm our results.

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