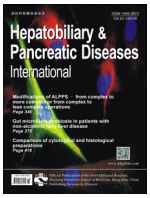
Hepatobiliary & Pancreatic Diseases International 17 (2018) 70–74

Contents lists available at ScienceDirect

Hepatobiliary & Pancreatic Diseases International

journal homepage: www.elsevier.com/locate/hbpd



Original Article/Pancreas

Diagnostic yield of EUS-FNA of small (≤15 mm) solid pancreatic lesions using a 25-gauge needle

Stefano Francesco Crinò[a,*], Maria Cristina Conti Bellocchi[a], Laura Bernardoni[a], Erminia Manfrin[b], Alice Parisi[b], Antonio Amodio[a], Nicolò De Pretis[a], Luca Frulloni[a], Armando Gabbrielli[a]

[a] *Gastroenterology and Digestive Endoscopy Unit, The Pancreas Institute, University of Verona, G.B. Rossi University Hospital, 11 P.le L.A. Scuro 10, Verona 37134, Italy*

[b] *Department of Pathology, University of Verona, G.B. Rossi University Hospital, 11 P.le L.A. Scuro 10, Verona 37134, Italy*

ARTICLE INFO

Article history:
Received 13 March 2017
Accepted 22 June 2017
Available online 31 January 2018

Keywords:
Endoscopic ultrasound
Endoscopic ultrasound-guided fine needle aspiration
Pancreatic cancer
Benign pancreatic tumors
Pancreatic neoplasms

ABSTRACT

Background: Early detection of small solid pancreatic lesions is increasingly common. To date, few and contradictory data have been published about the relationship between lesion size and endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) diagnostic yield. The aim of this study was to assess the relation between the size of solid pancreatic lesions and the diagnostic yield of EUS-FNA using a 25-gauge needle in a center without available rapid on-site evaluation.

Methods: In the retrospective cohort study, we selected patients who underwent EUS-FNA for solid pancreatic lesions with a 25-gauge needle from October 2014 to October 2015. Patients were divided into three groups (≤15 mm, 16–25 mm and >25 mm), and the outcomes were compared.

Results: We analyzed 163 patients. Overall adequacy, sensitivity, specificity and accuracy were 85.2%, 81.8%, 93.7%, and 80.4%, respectively. When stratified by size, the sensitivity and accuracy correlated with size ($P=0.016$ and $P=0.042$, respectively). Multivariate analysis showed that lesion size was the only independent factor ($P=0.019$, OR = 4.76) affecting accuracy. The role of size as an independent factor affecting accuracy was confirmed in a separate multivariate analysis, where size was included in the model as a covariate ($P=0.018$, OR = 1.08).

Conclusion: Our study demonstrates that, in the absence of rapid on-site evaluation, mass size affects the accuracy of EUS-FNA of solid pancreatic lesions.

Introduction

Early detection of solid pancreatic lesions (SPL) is increasingly common because of the widespread use of panoramic accurate abdominal imaging procedures. Small SPL are commonly discovered incidentally in asymptomatic patients during imaging studies performed for other reasons. The interest in this clinical setting is growing because of the need for an accurate diagnosis in planning patient management. Indeed, in cases of suspected pancreatic ductal adenocarcinoma (PDAC), the diagnosis of a small and often resectable tumor correlates to longer survival time [1]. Otherwise, excluding malignancy may avoid high-risk and unnecessary surgery. Similarly, for small pancreatic neuroendocrine neoplasms (pNET), the Ki-67 cytological index on preoperative biopsy specimens can be a useful metric in the management of small (<2 cm) lesions [2]. In a large multicenter retrospective study analyzing patients with small (<15 mm) SPLs [3], about 40% resulted in PDAC, 40% in pNET and 7% in metastasis from other primary tumors. This highlights the importance of correct preoperative differential diagnosis.

Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is the gold standard diagnostic tool for pancreatic masses—particularly for small lesions [4]. Several factors, including the needle type or caliber [5], number of passes, use of suction, lesion location or size, treatment method of the specimens [6], and available of rapid on-site evaluation (ROSE) can affect the diagnostic yield of EUS-FNA [7,8]. ROSE is one of the most relevant factors [9], but it is not widespread because of the low availability of cytologists.

A small (<15 mm) pancreatic lesion could be more difficult both in identification and targeting/sampling. Moreover, targeting

* Corresponding author.
E-mail address: stefanofrancesco.crino@ospedaleuniverona.it (S.F. Crinò).

https://doi.org/10.1016/j.hbpd.2018.01.010

a small lesion often requires passing the needle through some normal pancreatic tissue, which increases the risk of adverse events. Here, the choice of needle size is crucial for the technical success and safety of the procedure. A 25-gauge needle is the smallest needle available and the most easily maneuverable, especially in the duodenum where the endoscope is in an angled position.

To date, few and contradictory data have been published about the relationship between lesion size and EUS-FNA diagnostic yield [10–16].

The aim of this study was to assess the relationship between the size of SPL and the diagnostic yield of EUS-FNA using a 25-gauge needle in a center without ROSE.

Methods

Study approval and patient population

We retrospectively analyzed our prospectively collected database of EUS procedures performed from October 2014 to October 2015 at the pancreatic care center of Verona, Italy. The Institutional Ethics Committee at the University of Verona approved the study (protocol 50066).

We included all patients > 18 years who underwent EUS-FNA with a 25-gauge needle, standard (EchoTip Ultra, Cook Medical, Limerick, Ireland) or side-fenestrated (Echotip ProCore, Cook Medical, Limerick, Ireland), for the diagnosis of SPLs. Lesions described at EUS as cystic and repeated procedures due to inadequate first attempt were not included.

Patients were stratified into three groups based on longest lesion's diameter measured during EUS: group A (≤15 mm), group B (16–25 mm) and group C (larger > 25 mm).

Evaluation criteria

Demographic (age and gender), lesions size and location (uncinate process, head, neck, body, tail), number of needle passes, type of needles used (standard or side fenestrated), procedure related adverse events, sample adequacy, cytology results and final diagnosis were recorded for each patient.

Definitions of adverse events

Procedure-related adverse events were via clinical observations within 24 h of the procedure and were defined as follows: (1) acute pancreatitis: epigastric pain associated with at least threefold increases in serum amylase or lipase; (2) overt bleeding associated with drop in the hemoglobin level > 2 g/dL compared with pre-procedure levels; and (3) abdominal pain, i.e., pain not caused by pancreatitis or perforation requiring prolongation of hospitalization.

Cytological and final diagnosis

Cytological diagnoses were classified, according to the Bethesda classification, in "unsatisfactory", "benign", "atypical", "suspicious" and "positive for neoplasm" [17].

Those samples classified as "atypical" were included as negative for malignant lesions. Therefore, in the case of a malignant final diagnosis, the sample was considered "not accurate". Otherwise, when cytological diagnoses were reported as "suspicious", we included them as positive for malignancy.

"Diagnostic adequacy" was defined as the presence of tumor/pancreatic cells sufficient for cytopathological diagnosis in the FNA specimen.

The EUS-FNA was defined as "accurate" when the cytological diagnoses match the final diagnosis.

The final diagnosis was based on: (a) surgical pathology of the resected specimen when available; (b) biopsy specimens obtained by other modalities (i.e. percutaneous or laparoscopic biopsy when available); (c) radiological follow-up of at least 12 months. We defined lesions as malignant with any evolution such as increase in the volume, vascular infiltration or appearance of metastasis. Otherwise, benign lesions were defined as those without any radiological or clinical changes during follow-up; (d) for suspected pNET, final diagnosis was established on cytological and immunohistochemical staining (chromogranin and synaptophysin) and/or imaging features (hypervascular lesion at CT-scan positive at 68Ga-DOTATOC PET) [18].

EUS-FNA procedures and cytological method

All EUS-FNA were performed by two expert endosonographers (CSF and BL who have a current case volume of 350 FNA per year) with the patients placed in the left lateral position under deep sedation using the fanning technique [19], and the slow-pull technique [20].

The material was then posed entirely on a glass slides by reinsertion of the stylet. Alcohol-stained smears were then prepared on-site after individual passes. ROSE of the collected specimens was not available during EUS-guided sampling.

Statistical analysis

Continuous variables were assessed for normality and expressed as mean ± standard deviation (SD). The sensitivity, specificity, and accuracy (defined as the ratio of the sum of true-positive and true-negative values divided by the number of lesions) were calculated for all patients and evaluated for each group as the primary outcome. For calculation of the sensitivity, specificity and accuracy rates, EUS-FNA defined as "not adequate" were defined as false-negatives.

The Chi-square test used 2×2 or 2×3 contingency tables for categorical data; the Fisher's exact test was used for cases with small expected frequencies (<5). All tests were two-tailed. Factors affecting the accuracy of the EUS-FNA were analyzed using uni- and multivariate analyses. Multivariate analysis was carried out employing binary logistic regression. A backward stepwise technique according to Wald's test was used (probability for stepwise: entry = 0.05, removal = 0.01). Independent variables included the lesion size, the final diagnosis, the location of the lesion, the needle type used and the number of passes. Significance level was set for $P < 0.05$. Data are presented with odds ratios (OR) and their respective 95% confidence intervals (CI). SPSS software was used for statistical analysis (SPSS Inc., an IBM company, Chicago, IL, USA).

Results

We identified 167 patients, and four were lost to follow-up. Therefore, 163 patients (88 males, 75 females; mean age 60 years, range 20–85) were analyzed. The final diagnosis was defined on surgical specimens in 60 patients, on other modality biopsy specimens in 7 cases, and on radiological follow-up in 96. Final diagnosis were: 65 PDAC (39.9%), 58 pNET (35.6%), 17 focal pancreatitis (10.4%), 9 metastasis (5.5%), 5 solid-pseudopapillary neoplasm (3.1%), 3 autoimmune pancreatitis (1.8%), 2 acinar cell carcinoma (1.2%), 2 intrapancreatic lymphnodes (1.2%), 1 ganglioneuroblastoma (0.6%), and 1 schwannoma (0.6%).

The median lesion diameter was 21.3 ± 11.0 mm (range 6–70). Sixty-one lesions were ≤15 mm (37.4%), 62 had a diameter between 16–25 mm (38.0%), and 40 were larger than 25 mm (24.5%). Eighty-one were located in the pancreatic head/uncinate process (49.7%), 49 in the neck/body (30.1%), and 33 in the tail (20.2%). A