What is best for Endosonography Guided Fine Needle Aspiration (EUS-FNA) Samples in Solid and Cystic Lesions: Cytology, Histology or Both?

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Since its introduction in clinical practice about two decades ago, EUS-FNA has been one of the most efficient and safe methods to obtain samples from different gastrointestinal as well as extraintestinal lesions for cytological and histological analysis [1]. EUS-FNA is of cardinal importance in esophageal, lung, rectal and pancreatic cancer staging [2-4]. Apart from staging, EUS-FNA has also per se indications, representing the procedure of choice for the acquisition of cytological samples from pancreatic and biliary lesions [5,6]. Sensitivity and specificity for the diagnosis of such abnormalities range between 85 and 100% respectively regarding pancreas; sensitivity for biliary strictures varies between 43 and 86% [7,8]. These figures exceed the ones described for alternative approaches such as intraductal ERCP brushing or percutaneous puncture, which entail a higher complication rate [6]. EUS-FNA greatest advantage over the mentioned alternatives regards the real-time needle control provided during the whole operation, thanks to the fact that the device is introduced through the same plane as the ultrasound signal. This allows the endoscopist to puncture aiming towards the spots where the highest quality material presumably will be retrieved and avoid structures that may stand in the way, reducing the risk of secondary complications. In this respect, both EUS elastography and contrast enhanced EUS have been advocated to emphasize the spots within lesions where the chances of obtaining diagnostic specimens are higher. With the latter technique, it has been reported that the hypoechoenched areas within a pancreatic lesion are highly predictive of adenocarcinoma and should be targeted selectively during EUS-FNA [9].

However, several factors may ultimately influence the outcome of EUS-FNA, including the lesion’s characteristics, the presence of chronic pancreatitis, the type of needle utilized, the manipulation of the sample and also the endoscopist’s and cytologist’s experience. The standard EUS-FNA technique is well known [10-12], but ignoring its principles might lead to suboptimal outcomes. In fact, current data demonstrates that up to 30% of the patients whose cytology is labeled as negative may actually harbor malignancy [13]. In order to improve our EUS-FNA results, it is convenient to review the technique and try to correct those aspects that can be ameliorated. Nowadays we reckon that, at the time of puncturing lesions, particularly large ones, several thruscts into the periphery should be performed, since these usually yield better quality samples containing small amounts of necrotic tissue [14]. On the other hand, the influence of the needle caliber on the diagnostic yield has been evaluated in different studies, by comparing the specimens obtained with 25-gauge and 22-gauge needles. Although most of them have not found differences regarding the diagnostic outcome [15-20], it can be at least inferred that the use of a 25-gauge needle does not imply a yield loss compared to the larger needle, provides samples with a smaller blood cell component and allows an easier insertion through the echoendoscope due to its great flexibility. Sample handling after its retrieval may also influence the final result. Specimen fixation in a cell block liquid solution improves the diagnostic outcome over glass slide smearing and cytological examination, especially if there is no available cytologist in the endoscopy room [21]. One study analyzed retrospectively the diagnostic accuracy of cell block and cytological examination of EUS-FNA samples from 611 pancreatic tumors, describing 86.5% and 68% accuracy respectively (p < 0.001) [22]. Moreover, cell block enables immunocytochemical and molecular biology techniques to be applied, increasing the diagnostic yield in entities such as lymphoma [23]. However, these procedures are more expensive than glass slide cytology and their cost-benefit has been questioned by some authors [22]. Still, EUS-FNA with sample retrieval for cytological examination entails considerable drawbacks, such as the interpretation of the specimens rich in hematic, necrotic or inflammatory cells, or the definitive characterization of neoplasms that require immunohistochemical processing. EUS tru-cut biopsy needles were developed in order to overcome these flaws. Although they have been proven accurate in the diagnosis of pancreatic masses, gastric subepithelial tumors, lymphomas and necrotic neoplasms, their overall diagnostic yield remains suboptimal due to technical limitations of the tru-cut apparatus [24]. For example, Whittmann et al. [25] compared the outcome accuracy from EUS guided tru-cut biopsies and EUS-FNA in 159 patients failing to detect significant differences between them (73% vs 77% respectively). A multicentric study from Aithal et al. [26] including 95 patients, described a diagnostic accuracy of 89% in EUS guided tru-cut biopsies while EUS-FNA accuracy was 82% (p=0.21). However, studies proved that the combination of data acquired through EUS guided tru-cut biopsy and EUS-FNA ameliorates significantly the results obtained by EUS-FNA alone. In Whittmann et al.’s [25] study, the combined diagnostic accuracy reached 91%, Aithal et al. [26] placed it at 93% and a more recent study by Kipp et al. [27] showed a combined diagnostic sensitivity of 78% compared to 55% when using EUS-FNA alone (p < 0.001). Other factors, such as high costs, uncertain security profile and possible greater morbidity [28], have contributed to the criticisms against EUS guided tru-cut biopsy. In a personal view, one should add to that list the great number of blank thruscts that must be performed to retrieve a good quality specimen, which likely increases the risk of complications.

In order to grant a new opportunity to histological sample retrieval through EUS-FNA a new type of needle has been recently developed (Echotip Procore, Cook Medical). The device provides EUS guided core biopsies by means of a section system and not through a tru-cut apparatus. Its diagnostic yield and security profile are still to be determined. At the moment of writing this editorial only one published study had evaluated the 19-gauge procore needle. Iglesias-Garcia et al.

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Biopsies have not displaced EUS-FNA as the EUS-based procedure to answer the question entitling this editorial, to date EUS-guided role of this ingenious technique remains to be defined. In summary, which was introduced through a 19-gauge needle [36]. The biopsy cystic wall forceps biopsy in a case series, acquired thanks to a 0.8 mm in a Spanish group has for the first time described the performance of a histological samples from the cystic wall during EUS has been studied. A volume studies.

The cyst content can be aspirated by EUS-FNA, allowing cytological and biochemical analyses with amylase and carcinoembryonic antigen (CEA) determination. The latter parameter's sensitivity to identify mucinous cysts, which is basically the goal of EUS-FNA in this area, is around 80% [30]. On the other hand, the yield of cytology in this context is very low (sensitivity below 50%) [30]. Such poor EUS-FNA outcomes regarding cystic lesions have stimulated the research for new techniques to obtain suitable specimens to improve the diagnostic yield. In the last years new devices have been proposed, like the cystic brush Echobrush (Cook Medical), which permits intracystic brushing, through a 19-gauge needle. The data reported in the literature about the diagnostic yield and security of this instrument is contradictory. A recent study compared the usefulness of intracystic Echobrush versus cytological analysis of the cyst content in 30 patients; intracystic brushing improved the cellular diagnosis of these pancreatic lesions (73% vs 36%, p=0.08), particularly in those of mucinous lineage (50% vs 18%, p=0.016) [31]. However, intracystic brushing could not be accomplished due to technical matters in 8 of 30 patients and implied 27% technical failure that was greatest in cystic lesions located in the pancreatic head. Furthermore, this study has been strongly criticized [32] because it encountered 13.6% morbidity and 4.5% mortality in patients who underwent brushing, remarkably higher than the other diagnostic and therapeutic maneuvers performed through EUS [33]. In another study, 19% morbidity rate including severe complications in 8% of the patients has also been described in relation to intracystic brushing with Echobrush in a group of 37 subjects [34]. Results in a larger patient data set have been recently published comparing the Echobrush to EUS-FNA in 127 cystic lesions out of 120 patients [35]. Adequate material was obtained in 85.1% of the lesions with Echobrush compared to 66.3% with FNA (p<0.05). Three patients had self-limited intra cystic bleeding and another one developed a perigastric abscess, all of them in the Echobrush group. Therefore, we believe that the safety profile of the Echobrush must be further assessed in high quality, large volume studies.

Just as it occurred regarding solid lesions, the possibility of obtaining histological samples from the cystic wall during EUS has been studied. A Spanish group has for the first time described the performance of a cystic wall forceps biopsy in a case series, acquired thanks to a 0.8 mm in diameter and 220 cm in length forceps (Polyscopic; Lumenis Surgical), which was introduced through a 19-gauge needle [36]. The biopsy led to the correct diagnosis of the lesions in all the cases. The future role of this ingenious technique remains to be defined. In summary, to answer the question entitling this editorial, to date EUS-guided biopsies have not displaced EUS-FNA as the EUS-based procedure of choice to retrieve tissue samples. The published studies do prove that the combination of both strategies improves each one's separate outcomes. Which lesions require implementing both approaches for their diagnosis and which may be characterized only by cytological analysis is still to be defined. Future investigations should establish how the latest technological advancements might contribute to the diagnosis of the lesions discussed above and if the histological specimens will finally prevail over cytological samples.

References


