Editorial

Endoscopic Ultrasound Guided Fine Needle Aspiration: Results are Reproducible

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Whether symptomatic or not, pancreatic masses are a source of concern for both patients and their managing physicians alike, and obtaining a tissue diagnosis of pancreatic lesions is a cornerstone for proper management of these patients. Although non-invasive imaging modalities, including computerized tomography (CT) and magnetic resonance imaging (MRI) have made assessment of pancreatic lesions much more detailed and can suggest a probable diagnosis, there is no substitute for obtaining a tissue sample. Multiple approaches have been pursued, with the aim of obtaining tissue from the pancreas; CT or ultrasound-guided biopsies have been traditionally used, but more recently endoscopic ultrasound (EUS) has found its place in both the staging of pancreatic neoplasms as well as the acquisition of tissue.[1] The acquisition of tissue is done through EUS-guided fine needle aspiration (FNA), with the advantage of being in close proximity to the pancreas with a higher spatial resolution.

EUS has emerged as a sensitive as well as a safe approach in the evaluation of pancreatic neoplasms. In a meta-analysis, comprised of 33 studies (with a total number of 4984 patients) that used malignant cytology as the only positive endpoint, the pooled sensitivity of EUS-FNA for malignant cytology was 85% (95% confidence interval [CI], 84 to 86%), specificity was 98% (95% CI, 97 to 99%), positive predictive value (PPV) of 99% and negative predictive value (NPV) of 65%.[2] There were no major complications reported, and minor complications ranged from 1% to 2%, and occurring more commonly when EUS-FNA was performed on cystic lesions compared to those on solid ones. Of note, only 22 or 25 gauge needles were used for EUS-FNA.[2] In a second meta-analysis, the morbidity (0.98%) and mortality (0.02%) associated with EUS-FNA were also relatively low, consisting mainly of pancreatitis (0.44%) and post-procedural pain (0.34%).[3] In a subgroup analysis, studies conducted in North America had a higher sensitivity compared to those performed in Europe (85% vs 78%),[2] which might suggest regional variability; however, it should be noted that there was a smaller number of European compared to North American studies included in that meta-analysis (6 versus 23, respectively).[2]

A retrospective, multicenter study[4] incorporated 1075 patients and 41 endoscopists from 21 centers performing EUS. Overall, 56% had an advanced 4th year endoscopy training, and 63% had performed >1000 EUS procedures; there was a wide variation in the diagnostic rate per endoscopist, ranging from 52% in the first quartile to 85% in the third quartile.[4] Factors associated with increased odds ratio (OR) for a positive diagnostic yield of malignancy included older age (OR 1.03), female patient sex (OR1.47), and greater short-axis diameter of the sampled lesion (OR 1.04). Those associated with a decreased OR included the location of the mass in the pancreatic head (OR 0.62), and an increasing number of FNA passes into the mass (OR 0.80). In the study by Savides *et al*,[4] there was no influence of the number of cases performed per endoscopist on the yield of the EUS, but on the contrary, some of the lowest yields were found in endoscopists performing high volumes. This observation may be explained by the rationale that higher volume endoscopists might biopsy more subtle lesions while those who perform lower volumes only complete procedures on more obvious masses, thereby increasing their yield.[4]

Multiple studies have been conducted with the aim of trying to enhance the yield of tissue obtained through EUS-FNA; histological analysis resulted in a higher sensitivity over cytology[5] and the use of 22-gauge or 25-gauge FNA-needles did not result in any difference in diagnostic yield.[6] It is not clear whether trucut needle biopsies carry a greater yield compared to EUS-FNA.[7,8] In the meta-analysis by Hewitt *et al*,[2] a subgroup analysis showed that there was a non-statistical improvement in sensitivity (88% vs. 80%) for examinations where a pathologist was present.

In this issue of the Saudi Journal of Gastroenterology, Baghbanian *et al*.,[9] present a case series of EUS-FNAs of solid pancreatic neoplasms, conducted at a single center in Iran. A total of 53 patients were included in the study with a follow-up period, after the EUS-FNA, ranging from 6 to 12 months. The study included only solid lesions, excluding those with a mixed or cystic nature. In the majority of the cases (81%), the

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masses were in the head of the pancreas, with more than half of all lesions having an ultimate diagnosis of adenocarcinoma (68%). A final diagnosis was reached either through EUS-FNA or, when that was not possible, a surgical specimen; alternate methods of diagnosis included CT guided biopsy, ascitic fluid analysis, or clinical follow-up for 12 months.

On hypothesis testing, the factors associated with a lower yield for EUS-FNA cytology results were found by the authors to be: Younger age patients (52 ± 7.5 vs. 66 ± 7.5 years), and lesions less than 3 cm in size. All these variables have been previously noted in the multicenter study by Savides *et al*.[4] Furthermore, Baghbanian *et al*, found that EUS-FNA had a sensitivity, specificity, PPV, NPV and accuracy with regards to diagnosing adenocarcinoma of 88, 100, 100, 70 and 90%, respectively. These figures are also similar to those in the meta-analysis by Hewitt *et al*.[2]

Although, the study results are in keeping with literature, all the EUS-FNA procedures were performed by a single operator and the samples obtained were examined by a single experienced cytopathologist. This might influence the generalizability of the results as it is widely recognized that EUS is an operator-dependent procedure.[10] Furthermore, it is not clear from the study how many passes were performed on the lesions, and whether an on-site cytopathologist or cytotechnologist was available for assessing the adequacy of the samples. Although this was not found to be a relevant factor in the meta-analysis by Hewitt *et al*,[2] it would have added to the completeness of the report of the study. Also, the study analysis and reporting were based on hypothesis testing, which is understandable given the small number of individuals included in the study; this reporting method detects differences between groups but it does not quantify this difference as is the case with relative risks or odds ratios, and cannot detect confounding by other variables not accounted for by the investigators.

However, this study does add to literature that EUS-FNA is a well established tool for clinicians to keep in their armamentarium, when confronted with the work up of pancreatic masses, and that results of trials conducted in North America and Europe can be reproduced in other areas of the world.

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