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## Endoscopic Ultrasound-Guided Fine Needle Biopsy without Rapid On-Site Cytologic Examination: A Time to Change the Paradigm?

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See “Addition of Endoscopic Ultrasound (EUS)-Guided Fine Needle Aspiration and On-Site Cytology to EUS-Guided Fine Needle Biopsy Increases Procedure Time but Not Diagnostic Accuracy” by Rajesh N. Keswani, Kumar Krishnan, Sachin Wani, et al., on page 242-247

Over the past 2 decades, endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) has become the preferred procedure to obtain tissue for the diagnosis of gastrointestinal (GI) tract and adjacent organ lesions with acceptable accuracy and safety. EUS-FNA is reported to be a highly accurate diagnostic test for solid pancreatic neoplasms. A recent meta-analysis indicated that the pooled sensitivity and specificity for malignant cytology in solid pancreatic neoplasms was 85% and 98%, respectively.<sup>1</sup> In addition, many studies reported that the diagnostic accuracy of EUS-FNA in combination with immunohistochemistry is more than 80% for most subepithelial lesions (SET) of the GI tract.<sup>2</sup>

Although EUS-guided tissue acquisition is currently considered an accurate, safe, and relatively inexpensive method for diagnosing lesions within the GI lumen or in organs or lymph nodes adjacent to the GI tract, it has some limitations. First, to improve diagnostic accuracy, an on-site pathologist should be present. The sensitivity of EUS-guided tissue acquisition decreases by 10% to 15%, the number of needle passes increases, and the overall procedure time is prolonged in the absence of an on-site pathologist.<sup>3,4</sup> Second, for some GI tumors, including GI stromal tumors, cytology yield is limited, and core tissue is sometimes requested by cytopathologists to identify cellular arrangement and tissue architecture for ade-

quate diagnosis and subtyping.<sup>5,6</sup> These limitations lead to the need for large needles capable of obtaining core tissue. To date, the questions that many endosonographers struggle with in everyday clinical practice are “Is it necessary to obtain core tissue for improving diagnostic accuracy?” and “How could the diagnostic accuracy be improved in the absence of an on-site cytopathologist?”

With respect to pancreatic tumors, studies using EUS-guided Trucut needle biopsy to obtain core specimens failed to definitively demonstrate overall diagnostic improvement compared to EUS-FNA because of technical problems (limitation of the transduodenal approach); further, there was an increased risk of complications.<sup>7,8</sup> One randomized controlled study comparing approaches using more flexible core biopsy needles (22-gauge [G] FNA and fine needle biopsy [FNB]) for the assessment of pancreatic solid tumors found no significant difference in the diagnostic yield and accuracy, technical success, and complications.<sup>9</sup> A study by Wittmann et al.<sup>10</sup> reported that improvement of diagnostic accuracy and sensitivity was only observed in cases where a combination of FNB and FNA was performed. Thus, currently, there is no clear indication that EUS-FNB is preferable to EUS-FNA for the assessment of pancreatic lesions, unless histologic analysis is required.<sup>11</sup>

However, the situation is different for cases of GI SET and other lesions such as those involving thickening of the GI wall or lymphoma. Although the diagnostic accuracy of EUS-FNA for GI SET was reported to be approximately 50% to 70% with favorable safety, it did not always afford adequate samples for immunohistological analysis because of the small number of cells often obtained.<sup>12</sup> And while EUS-Trucut needle biopsy is more accurate than EUS-FNA for diagnosing GI mesenchymal tumors, the rigidity of the 19-G needle and

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the mechanical friction of the firing mechanism produced by the torqued echoendoscope limit its use for SETs located in the gastric antrum and duodenum, as observed in pancreatic lesions. A multicenter study using a 19-G ProCore needle to procure sufficient histologic samples revealed a diagnostic accuracy over 80% in GI SETs.<sup>12</sup> However, technical difficulty with this needle in the transduodenal passes was also a limitation.

A 22-G ProCore needle, which is more flexible than a 19-G ProCore needle, was introduced recently. A study comparing 22-G EUS-FNB with 22-G EUS-FNA demonstrated that the yield rate of the macroscopically optimal core sample and the rate of diagnostic sufficiency for EUS-FNB in GI SETs was 92% and 75%, respectively, values that are comparable to the results of a previous study using the 19-G FNB needle (91% and 82%, respectively).<sup>6</sup>

Another interesting effort to improve the diagnostic accuracy in patients with GI SETs is to combine EUS-FNA with EUS-FNB. Storch et al.<sup>13</sup> reported that the diagnostic accuracy of combining EUS-FNA and EUS-FNB was 95% in their retrospective study, even without an on-site cytopathologist. However, in general, combining EUS-FNA and EUS-FNB may increase the number of passes and result in higher costs. Currently, when one of these methods fails, the other is considered as a rescue method.

It is believed that on-site cytopathological evaluation reduces the number of inadequate FNA samples and improves the sensitivity and overall accuracy of EUS-FNA for the diagnosis of various GI tract tumors, as shown in studies on pancreatic solid tumors. However, in one study using a new EUS histology needle, the authors reported a correct diagnosis of 86% and an overall diagnostic accuracy for the detection of malignancy of 92.9% without a pathologist present for the endoscopy.<sup>14</sup> A recent study by Kim et al.<sup>6</sup> reported that the yield of histologic core sample and diagnostic sufficiency rate of EUS-FNB was higher than that of EUS-FNA for histopathological diagnosis of SET of the GI tract in the absence of an on-site pathologist. In the current issue of *Clinical Endoscopy*, Keswani et al.<sup>15</sup> reported their retrospective study comparing the diagnostic accuracy of EUS-FNB alone to a conventional sampling method of EUS-FNA with rapid on-site cytology evaluation (ROSE) followed by EUS-FNB in nonpancreatic adenocarcinoma lesions. In the group undergoing EUS-FNB alone, tissue acquisition was performed without EUS-FNA or ROSE. In the conventional group, routine EUS-FNA was attempted in the presence of an attending cytopathologist, and, if needed, EUS-FNB was attempted. The result of overall diagnostic accuracy for the EUS-FNB alone group and the EUS-FNA, EUS-FNB group was 83.7% and 84.9% ( $p=1.0$ ), respectively. Further, the procedure duration was significantly

shorter in the EUS-FNB group (58.4 minutes compared to 73.5 minutes,  $p<0.0001$ ). EUS-FNB was performed with ProCore needles. They concluded that EUS-FNB without on-site cytology provides a high diagnostic accuracy in cases of nonpancreatic adenocarcinoma lesions and that initial EUS-FNA provides no additional benefit.

The report by Keswani et al.<sup>15</sup> has some limitations. Two major limitations are the retrospective study design and the fact that the diagnostic accuracy of initial EUS-FNA in the EUS-FNA, EUS-FNB group was lower than that in other published studies. The size of the EUS-FNB needle was selected at the discretion of the endoscopist, and this factor might have led to bias. Despite these limitations, the study presents some interesting points.

There is no doubt that the presence of an on-site pathologist improves the diagnostic accuracy of EUS-guided tissue acquisition; however, many facilities cannot afford this option. Still, if the diagnostic accuracy of EUS-FNB compared to EUS-FNA (followed by EUS-FNB in certain cases) is independent of an on-site pathologist, their absence may not be a major concern. This might be encouraging to many endosonographers and induce them to prefer a core tissue using EUS-FNB rather than a cytologic sample, especially from nonpancreatic lesions. A new type of EUS-compatible core biopsy needle might accelerate such a change. Even in cases of pancreatic tumors when on-site pathologists are not available, EUS-guided core tissue sampling might replace EUS-FNA. However, it is premature to apply these conclusions to clinical practice, and further prospective randomized studies are needed to clarify the efficacy of EUS-FNB alone in the absence of on-site pathologists for the assessment of nonpancreatic tumors.

## Conflicts of Interest

The author has no financial conflicts of interest.

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