

ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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Endoscopic Ultrasound in the Evaluation of Adrenal Masses

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G&H Could you describe when and how endoscopic ultrasound is utilized in the evaluation of adrenal masses?

ME Endoscopic ultrasound (EUS) is usually utilized in the evaluation of enlarged adrenal glands or adrenal masses in the context of suspected or confirmed malignancies. In particular, it is used when evaluating patients with either lung cancer or suspected metastatic disease from other cancers such as melanoma or gastrointestinal malignancies that have a predilection for spreading to the adrenal glands. The left adrenal gland is identified through the gastric approach, whereas the right adrenal gland is identified through the duodenal approach.

G&H When evaluating these patients with EUS, how can adrenal masses be differentiated from pheochromocytoma?

ME On rare occasions, primary adrenal masses may be encountered in these patients, and a word of caution should be mentioned in this scenario. When evaluating adrenal masses without known malignancy such as melanoma or lung cancer, the diagnosis of pheochromocytoma should always be kept in mind. Clues can be obtained from patients who have uncontrolled hypertension or a history of palpitations that are short-lived. Fine needle aspiration (FNA), in this particular scenario, might be contraindicated, as it might lead to adrenal hypertension crisis. Typically, a hormonal profile should be obtained first by checking 24-hour urine collection for creatinine,

total catecholamines, vanillylmandelic acid, and metanephrines to rule out pheochromocytoma prior to FNA.

G&H Could you discuss the feasibility and safety of EUS in the diagnosis and staging of adrenal gland malignancies?

ME Our experience here at the University of Alabama, which is likely the most extensive in the nation, suggests that EUS-FNA of the left and right adrenal glands are extremely safe. These conclusions are based upon the fact that the only organs traversed and punctured are the intestinal wall, specifically the stomach for the left adrenal gland and the duodenum for the right adrenal gland. In comparison to the percutaneous approach for evaluating adrenal masses, which occasionally requires traversing other organs such as the pancreas or the liver to reach either adrenal gland, the EUS-guided approach is safer. In addition, the short distance from the echoendoscope to the target, whether the left or right adrenal gland, provides an advantage in safety.

It should be noted that most gastroenterologists without training in EUS do not normally encounter these clinical scenarios and that most referrals for this indication come to us not from gastroenterologists but from thoracic surgeons, pulmonologists, oncologist surgeons, or urologists, as these patients are initially referred to these specialists for management of their problems or abnormalities. It is quite obvious, however, from lecturing across the country on this topic at lung cancer conferences, that our ability to sample the adrenal gland in a safe and minimally invasive fashion is unfortunately not well understood among pulmonologists or surgeons at other institutions. However, when these physicians do learn that we are able to sample the right or left adrenal gland, they are quite receptive and positive in regard to the use

of EUS in the targeting of these lesions in a minimally invasive fashion.

G&H What other clinical benefits does the use of EUS show over the percutaneous approach, the previous standard diagnostic option for evaluating adrenal masses?

ME As mentioned above, most of these patients are referred to us by thoracic surgeons, pulmonologists, or oncology surgeons who understand the ability of EUS to target these organs safely; however, the percutaneous approaches with either ultrasound, percutaneous ultrasound-guided FNA or computed tomography (CT)-guided FNA, are still utilized in other institutions. At our institution, however, most of these patients are now referred to EUS because of our success rate and safety profile when approaching these lesions. Complications that are associated with the percutaneous approach include bleeding and pancreatitis, which are not encountered in EUS evaluation of the adrenal glands because, as mentioned above, other organs are not traversed with EUS. The other advantage that EUS has over previous methods is the ability to target very small lesions (eg, 5 mm) that CT scans, at this point, are not able to detect or target. EUS-FNA is even more advantageous when comparing adrenalectomy for diagnostic purposes, even when performed laparoscopically.

G&H Could you describe the interface between EUS and other diagnostic techniques for evaluating adrenal masses?

ME The best example would be the interface between EUS and integrated positron emission tomography-computed tomography (PET-CT). This technology, which combines PET and CT scans, relies upon metabolic imaging and has significantly enhanced the detection of adrenal metastases from lung cancer. For example, when a patient has confirmed or suspected lung cancer, the first test they usually undergo at our institution after a CT scan of the chest and abdomen is integrated PET-CT, which usually gives us an idea of whether there is a focus of metastases in the adrenal gland and provides a target for easier sampling with EUS-guided FNA. PET-CT reports standardized uptake value (SUV) with its use, and the higher the SUV value, the more likely that the focus in the adrenal glands is malignant. However, there is overlap between inflammation, infection, and malignancy; therefore, obtaining tissue is mandatory in any PET scan showing abnormal uptake or increased SUV value, based upon the current guidelines adopted by thoracic surgeons and pulmonologists.

G&H Are there any limitations or contraindications associated with EUS evaluation of adrenal masses?

ME The limitations or contraindications of EUS pertain to those of endoscopy and conscious sedation. First, endoscopy must be feasible; in other words, patients should not have any obstruction, strictures, or alterations in the esophagus or stomach such as gastric bypass surgery. Second, as with any other procedure, the coagulation profile and platelet counts should be normal. Beyond these two limitations, we believe that reaching the left adrenal gland is highly likely (approximately 98–100% at our institution). The right adrenal gland, particularly when enlarged, is also reasonably feasible to reach, though data remain limited to a few case studies.

G&H Could you expand on the challenges of evaluating the right adrenal gland with EUS-FNA compared to the left adrenal gland?

ME When I was in training, it was believed, and still is believed to some degree, that with EUS it is possible to find the normal left adrenal gland, but the right adrenal gland can be found only approximately 20% of the time due to its retrocaval nature, hiding behind the inferior vena cava. Until recently, it was unusual to receive a referral to sample or even consider sampling the right adrenal gland. Although a bit skeptical at the beginning, I thought that it behooved us to at least attempt to find a right adrenal gland that was enlarged, since it would be easier to find an enlarged gland, though still more challenging than finding the left gland. We conducted a small study to determine the feasibility and success of sampling enlarged right adrenal glands, to our knowledge the first such study published, and devised an approach for finding the right adrenal gland via the transduodenal approach. The left adrenal gland was much easier to identify, as we could follow the celiac axis artery; in fact, we found the left adrenal gland in nearly 100% of the cases. In contrast, for the right adrenal gland, we used the duodenal window and landmarks that were not as clarified compared to the left adrenal gland.

G&H Has there been any cost-effectiveness analysis performed on this topic?

ME I am not aware that EUS-guided FNA of the adrenal glands has been evaluated in the context of cost-effectiveness. However, I would predict that due to its high yield and low complication profile that EUS-FNA would be cost-saving compared to other alternative strategies such as surgical evaluation or CT- or percutaneous ultrasound-guided approaches.

G&H Could you describe the clinical applications of rapid onsite evaluation of EUS-FNA specimens of adrenal lesions?

ME We strongly believe that rapid onsite evaluation (ROSE) is a very helpful adjunct when performing EUS-guided FNA and, for that matter, any other form of FNA. Several studies, including one that my colleagues and I recently conducted, suggest that the yield of FNA increases when ROSE is utilized. First, ROSE ensures the assessment of adequate sampling, which is important because prior to reaching a diagnosis in any fine needle aspirate, a baseline of adequate material is needed to evaluate the specimen. Second, ROSE might suggest diagnoses that require ancillary studies such as immunohistochemical stains or fungal stains or cultures, which is advantageous. Therefore, without immediate feedback on the biopsy specimen, alternative diagnoses may not be considered. When performing EUS, the gastroenterologist can immediately sample the target in question further to provide additional samples for the pathologist to examine in the laboratory with the ancillary studies mentioned above.

In addition, from a patient management perspective, ROSE allows for the immediate communication of findings postprocedure to the patients, family members, and referring physician. Most of the patients we examine travel long distances from neighboring states and are very anxious to know the diagnosis; giving them immediate feedback regarding their diagnosis is often helpful and appreciated.

Although this has not been studied formally, we think that ROSE reduces a significant amount of physician workload in terms of follow-up communication with the patient at future dates. When we evaluate a patient, we immediately tell them if they have, for example, lung cancer, adrenal metastases, or pancreatic cancer, depending upon the lesions studied. In our view, this makes the visit comprehensive and complete in most instances. The referring physician is also called the same day and informed of the diagnosis, which is followed by a written communication by fax the next day.

G&H In addition to its diagnostic role, does EUS have a therapeutic application in managing adrenal masses?

ME A preliminary study was presented at this year's Digestive Disease Week in San Diego, California, from a

group in Brazil led by Everson Artifon. They performed alcohol injection via EUS for palliating pain in patients with enlarged adrenal glands. The same group had previously published a case report on the same topic in *Gastrointestinal Endoscopy*. In this single case report, they were able to palliate pain from the enlarged left adrenal gland in a patient. Due to the close proximity of the left adrenal gland to the celiac axis network of nerves, it is feasible that performing celiac plexus neurolysis in this group of patients could produce the same result, in terms of palliating pain. However, this has not been studied; it is a mere speculation, at this point, regarding the mechanism of pain palliation in this group of patients.

G&H What do you foresee as the next steps for future research?

ME More data are required in terms of comparative trials with EUS and the percutaneous approach. I am not aware of any study that compares, for example, CT-guided sampling of adrenal glands with the EUS-guided approach. More studies are also needed regarding improved methods to identify a normal right adrenal gland as well as pathologic ones. More experience is also needed with successfully finding and sampling the right adrenal gland in all centers in which gastroenterologists work closely together with thoracic surgeons and pulmonologists.

Suggested Reading

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