Editorial

Is EUS Here to Stay? Accuracy Is Not an Indication…

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Endoscopic ultrasound (EUS) has come a long way. Initially, despite the impressive images it provided, EUS was considered as "a procedure looking for an indication". After an explosion in EUS-related research in the last decade, EUS was validated as an accurate tool for staging luminal cancers[1,2], for diagnosing bile duct stones, for assessing structural changes of chronic pancreatitis, *etc*. With the advent of EUS-guided tissue sampling, the sensitivity and specificity of EUS images for diagnosing or excluding malignancy were taken to a whole new level of "pathologic certainty".[3] Armed with these data, endosonographers were finally able to move forward to increase the use of EUS in more and more clinical contexts.

With time, EUS has become accepted more and more widely (if not, the "standard of care") for various indications: TNM cancer staging, suspected bile duct stones, idiopathic pancreatitis, suspected chronic pancreatitis, diagnosis/staging of various cancers [gastrointestinal and non-gastrointestinal (ex: lung cancer)], management of cystic lesions, and therapeutic indications such as EUS-guided celiac plexus neurolysis (CPN) and pseudocyst drainage, *etc*. With increased availability of training opportunities, the availability of EUS has also moved out from referral centers to include increasing numbers of community hospitals. The result is that EUS has essentially completed the move from an experimental procedure to the mainstream of endoscopic management of various diseases.

With this evolution comes a new responsibility for endosonographers. Instead of focusing on what EUS can do, we need to show that EUS is what we should do. We have shown that EUS is accurate, but accuracy in itself is not an indication. Accuracy is an average value obtained by combining tests of sensitivity and specificity. Sensitivity and specificity are actually not clinically applicable parameters; since they ask the question: if we know whether a disease is present or absent; will a test be positive or negative? This assumes that the clinician knows the diagnosis before performing the test - which is obviously not a clinically useful assumption. On the contrary, predictive values are clinically useful; since they ask the question: if the test is positive or negative, what is the chance that the disease will be present or absent? The important caveat is that predictive values are strongly influenced by the pre-test probability of disease. So studies reporting predictive values must be performed in a clinically realistic context.

We have also shown that EUS results may change management. But, just because a test changes management, it doesn't mean that these changes produce better outcomes - especially if the EUS-related outcomes are not compared formally to outcomes of other modalities. It is also unclear whether results obtained with endosonographers and patients found in a university setting are comparable to those obtained in a "real world" community setting. In other words, for many indications it is time to produce more randomized trials comparing the EUS to its alternatives. For others, the existing evidence is probably sufficient to make randomized trials superfluous.

There are overwhelming data that EUS is an extremely accurate tool to diagnose extra-hepatic biliary stones in both high- and low-risk populations, compared to both endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopanereatography (MRCP); and it is clearly safer than ERCP.[4] It remains probably the most accurate modality for TNM staging of luminal cancers - with possible exception of rectal cancer, where magnetic resonance imaging (MRI) has equivalent TNM staging accuracy, but can also visualize the meso-rectal fascia (which EUS cannot).[5] EUS-guided fine needle aspiration (FNA) remains a uniquely powerful tool that provides safe, painless and accurate tissue acquisition for otherwise inaccessible lesions – with less risk of tumor seeding.[6,7] For all these indications, randomized trials are probably unnecessary, and would possibly be unethical – due to the clear empiric evidence that EUS is superior. This is particularly true for mediastinal, pancreatic, and submucosal lesions. For therapy, there are strong data, including randomized trials, that EUS-guided therapy is the best first choice for pseudocyst drainage[8] and celiac plexus neurolysis for cancer pain.[9]

However, as stated earlier, accuracy is not an indication.

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While the technical superiority of EUS for specific diagnostic indications may be clear, the influence of EUS-influenced decisions on higher outcomes such as survival, costs, and quality of life should be clarified in real-life settings. A few examples come to mind.

TNM STAGING

For esophageal cancer, our experience suggests that EUS rarely changes the indication for chemo-radiation for symptomatic patients, other than those in whom cervical (M1) nodes can be biopsied. If patients have evidence of nodal metastases by computed tomography (CT) and/or positron emission tomography (PET) scan, will EUS really change outcomes? For gastric cancer, EUS rarely, if ever, changes the indication for surgery. Although EUS may identify miniscule pockets of ascites that could signal carcinomatosis, it is often difficult to prove this by EUS-guided FNA. Could EUS simply be replaced by laparoscopy in patients with lesions unresectable by endoscopic mucosal resection? For rectal cancer, why not use MRI as the primary staging tool and reserve EUS for cases where staging is unclear or where EUS-FNA of nodes could change management?

CYSTIC LESIONS

EUS is used increasingly to evaluate indeterminate cystic lesions.[10] EUS imaging alone not unreliable enough to distinguish serous from mucinous lesions,[11] therefore EUS-guided cyst puncture is often performed for macroscopic and microscopic cyst-fluid analysis (cytology, tumor markers, mucin stains, *etc.*) and to sample solid components. While there are data showing EUS-guided cyst fluid analysis may distinguish serous from pre-malignant lesions, it is far from perfect.[12] EUS results also appear to be influencing the decision to operate or observe cystic lesions, but there are no data showing that EUS-induced changes have positively influenced survival, costs, or quality of life. Could the same (or better) outcomes be obtained by management changes determined solely by clinical variables and cross sectional imaging (CT or MRI) without EUS-cyst fluid analysis?

EUS-GUIDED THERAPY

EUS-guided cyst-gastrostomy and CPN have been successfully compared to alternatives by randomized trials. However, other drainage procedures such as hepatico-gastrostomy and pancreatico-gastrostomy still require similar trials - especially since their complication rates are not insignificant and may have been under-reported.[13]

There are certainly other examples, but those cited hopefully demonstrate that the value of EUS for standard and for newer indications may be less clear than we think. As endosonographers, we have fought hard to validate EUS and prove its technical superiority for numerous indications. In this era of economic constraints and increasing access to newer diagnostic and therapeutic modalities, it is incumbent on endosonographers to do the work to ensure that EUS is here to stay.

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