EUS for rectal disease

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The diagnostic applications for EUS have grown tremendously over the last decade. Most of the early development involved the use of EUS for upper GI indications. Until recently the rectal applications of EUS have largely remained unexplored. Several recent publications have demonstrated the usefulness of EUS in the evaluation of rectal diseases.[1-3] At our center, there has been a steady increase in the number of patients referred for rectal indications. This review describes rectal endosonographic anatomy, highlights the technical aspects of rectal EUS, and summarizes available data on the major clinical indications for rectal EUS including imaging of perianal fistulas, the evaluation of anal sphincter injuries, and the staging of rectal cancer.

ANORECTAL ANATOMY

The anal canal is formed by 2 muscular cylinders. The inner cylinder is the internal anal sphincter (IAS) and is formed by the downward continuation of the circular smooth muscle of the rectum. The outer cylinder is the external anal sphincter and is formed by the downward extension of skeletal muscle of the puborectalis. The sphincter complex comprised by these 2 cylinders is approximately 4 cm long. When examining the anorectum with a radial scanning echoendoscope, these 2 cylinders can be appreciated as 2 discrete rings. The inner hypoechoic ring of tissue represents the internal anal sphincter; the outer hyperechoic tissue ring represents the external anal sphincter (Fig. 1). The normal IAS is between 2 to 3 mm thick[4,5] and the normal external anal sphincter (EAS) is between 7 to 9 mm thick.[4,6,7] The IAS becomes thicker and more hyperechoic with age, probably reflecting collagen replacement of the IAS.[5] Conversely, the EAS tends to become thinner with age.[6]

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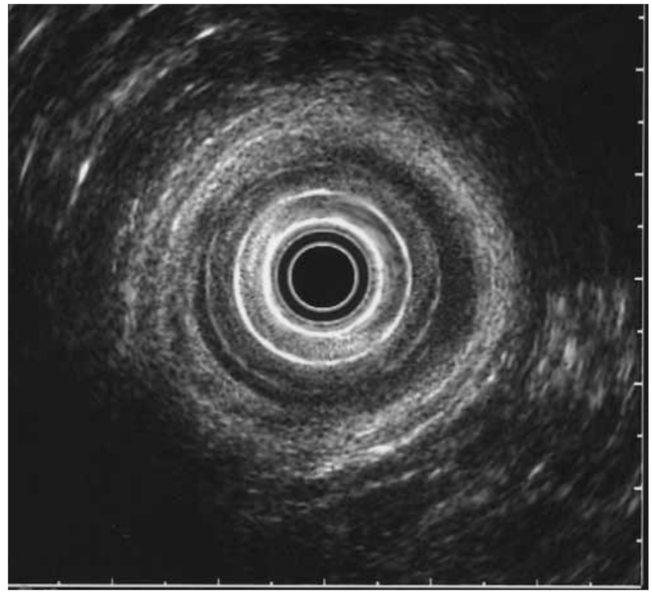

Figure 1. EUS image (radial scan) of anal sphincters. Inner hypoechoic band is the internal anal sphincter. Outer hyperechoic band represents the external anal sphincter.

The rectum itself begins at the dentate line and extends to 15 to 20 cm from the anal verge. The venous drainage from the rectum is through the superior hemorrhoidal and inferior mesenteric veins to the portal vein or through the middle and inferior hemorrhoidal veins. The lymphatic drainage follows a similar route in parallel with the vasculature. Knowledge of this anatomy is especially important when evaluating patients with rectal cancer in whom inspection of the iliac vessels and their associated lymph nodes is necessary for complete staging. These vessels and lymph nodes can typically be identified endosonographically at between 20 and 25 cm from the anal verge (Figs. 2 and 3).

TECHNIQUE

The same peroral lavage solution used for colonoscopy is also used to prepare patients for rectal EUS. This ensures that the lumen will be free of stool that can prevent adequate visualization. The examination is performed with the patient in the left lateral position. For women patients being evaluated for fecal incontinence, the examination is occasionally performed with the patient in the prone position to more clearly delineate the anterior aspect of the EAS. Frudinger et al.[8] (St. Mark's Hospital, London, UK) advocate this scanning position because they feel it provides more complete imaging of the anterior part of the EAS and improved visualization of the perineum.[8] Optimal tumor visualization may require repositioning the patient to place the region of interest in the depen-

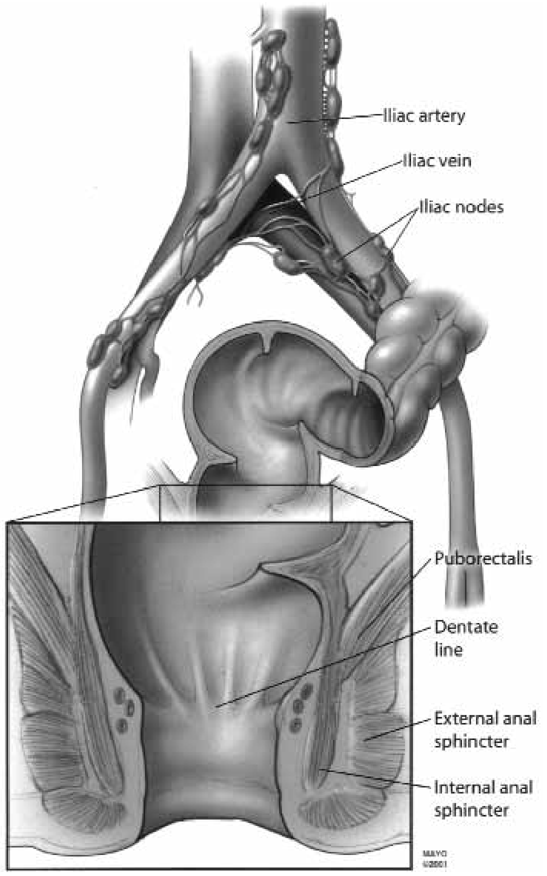

Figure 2. Diagram of rectal anatomy. Note relationship between iliac lymph nodes, rectum, and distal sigmoid colon.

dent portion of the rectum. This is particularly important for determination of the depth of invasion (T staging) of early stage, superficial lesions where the rectum is filled with water and minimal compression by the acoustic coupling balloon is desired.

Flexible sigmoidoscopy is performed prior to EUS. This serves several purposes including assessment of rectal mucosal inflammation, identification of a rectal mass if present, and evaluation of the adequacy of the preparation.

The radial scanning echoendoscope is then inserted. For patients undergoing evaluation for rectal cancer, the echoendoscope is inserted to approximately 30 cm to detect iliac lymphadenopathy. For patients being evaluated for fecal incontinence or perianal disease, it is probably sufficient to begin the examination at the rectosigmoid junction.

To examine the anal canal, the balloon is minimally inflated to reduce distortion of the canal during imaging. The echoendoscope is then gripped with one hand up against the anus to stabilize the instrument within the anal canal.

If necessary (i.e., rectal cancer with lymphadenopathy), the linear scanning echoendoscope is inserted and the lesion with endosonographic characteristics that raise a suspicion of malignancy (mass/lymphadenopathy) is targeted. Because the rectum is not a sterile environment, intravenous administration of antibiotics prophylactically before the performance of fine needle aspiration (FNA) is warranted. To further reduce the risk of infection, prophylactic treatment should be continued with oral administration of a quinolone for 48 hours after the procedure. Conscious sedation is helpful, particularly when EUS-guided FNA (EUS-FNA) is to be performed.

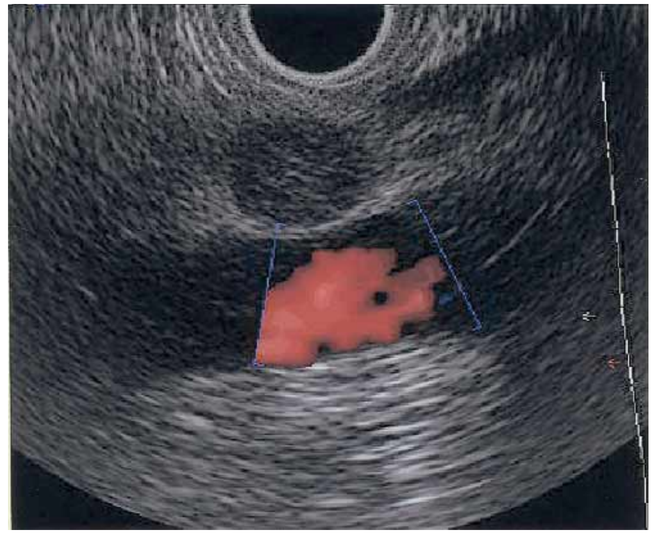

Figure 3. EUS image (linear scan) of iliac lymph node. A biopsy of this lymph node was positive for metastatic adenocarcinoma.

PERIANAL FISTULAS AND ABSCESSES

The necessity of accurately characterizing a perianal process can not be overemphasized. The risk of incomplete healing, a recurrent fistula, or even inadvertent sphincter injury is increased if fistula anatomy is incorrectly delineated or an occult abscess missed. An imaging modality should ideally provide a virtual road map that can be used to plan therapy. EUS is ideal for this purpose.

At EUS, fistulas appear as hyperechoic tracks or beads (representing air) within a larger hypoechoic tract corresponding to surrounding inflammation (Fig. 4). Patients are typically evaluated with both a radial scanning echoendoscope and an electronic biplane probe. Both instruments provide complementary information, although the biplane probe is the most useful because by applying gentle pressure with the probe, air bubbles can be visualized moving within the tract itself (Fig. 5).

The accuracy of US in the evaluation of perianal disease has been demonstrated in several studies.[1,9-21] In most of these, a nonendoscopic, rigid transrectal probe was used. Three prospective,

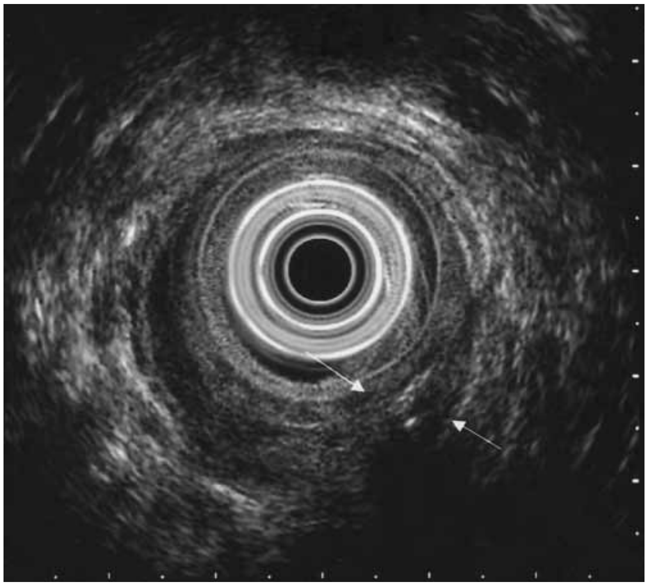

Figure 4. EUS image (radial scan) of trans-sphincteric fistula *(arrows)* in a patient with Crohn's disease. Note the hyperechoic bead of air present in hypoechoic fistula tract that disrupts the EAS and IAS at 5 o'clock. This represents air within a larger hypoechoic tract corresponding to surrounding inflammation.

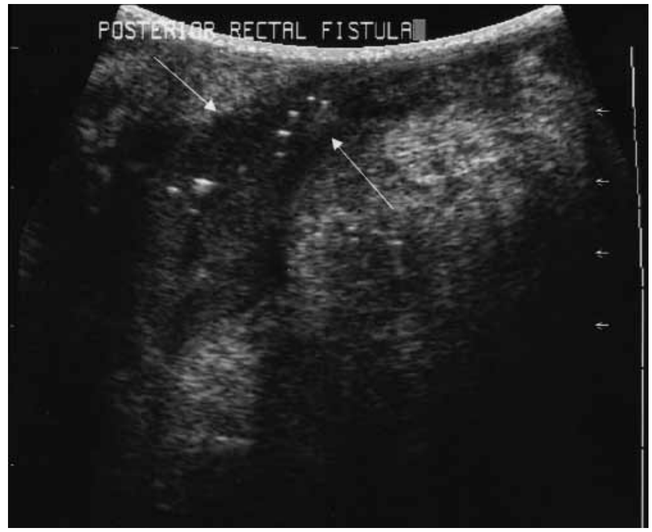

Figure 5. EUS image (linear scan) of fistula *(arrows)* in a patient with Crohn's disease. Note the hyperechoic tracks or beads (representing air) within a larger hypoechoic tract corresponding to surrounding inflammation. By applying gentle pressure with the probe these beads of air can be seen moving within the fistula tract.

blinded studies in which a flexible echoendoscope was used to evaluate perianal disease are available. One compared EUS with CT in 25 patients suspected to have perianal Crohn's disease.[13] EUS was performed at an US frequency of 5 MHz by using a radial scanning echoendoscope. Results were compared with findings at surgery, the clinical course of the patient, or both. EUS was more accurate than CT in the evaluation of perianal fistulas (respectively, 82% vs. 24%). In the other 2 studies EUS was compared with magnetic resonance imaging (MRI) in groups of patients with perianal Crohn's disease.

In the pilot study of Orsoni et al.,[21] rectal EUS, pelvic MRI, and examination under anesthesia (EUA) were compared in 22 patients with Crohn's perianal fistulas. Rectal EUS was found to be the most sensitive modality for imaging perianal fistulas caused by Crohn's disease. The agreement for fistulas with rectal EUS and pelvic MRI when compared with the surgical findings were, respectively, 82% and 50%. Rectal US in this study was performed exclusively with a 7 MHz linear scanning probe.

The results of a prospective blinded comparison study of EUS, MRI, and surgical evaluation EUA in 34 patients with suspected perianal fistulas caused by Crohn's disease was recently reported.[1] Our study demonstrated good agreement for all 3 methods with the reference-standard (EUS, 91%; MRI, 87%; EUA, 91%). In addition, the combination of any of the imaging modalities with EUA provided 100% accuracy in these patients and was the most cost-effective approach. Because an assessment of disease activity is usually necessary in these patients to formulate an appropriate treatment strategy, EUS provides an advantage over MRI by allowing colonoscopy to be performed at the same session.

ANAL SPHINCTER INJURY

Fecal incontinence is one of the most devastating of all physical disabilities. The associated social stigmata associated can lead to isolation. The prevalence of fecal incontinence is underestimated because of this stigma. In one series, anal sphincter tears were detected by anal endosonography in 35% of primiparous and 40% of multiparous women among whom symptoms of anal incontinence or fecal urgency were present in, respectively, 13% and 23%.[22] Until recently there was no way of obtaining direct structural evidence of sphincter injury. Heretofore, electromyography (EMG) was the primary method for assessing the integrity of the EAS. However, EMG studies were poorly tolerated because they required insertion of needles directly into the muscle. The introduction of EUS provided an accurate and relatively painless means for evaluating sphincter integrity. Several of the early transrectal US studies demonstrated that EUS was as sensitive as EMG for identification of sphincter injuries.[23-25]

At EUS, defects in the IAS appear as hyperechoic breaks in the normally hypoechoic ring; this is in contrast to EAS defects, which appear as relatively hypoechoic areas in the normally hyperechoic ring.

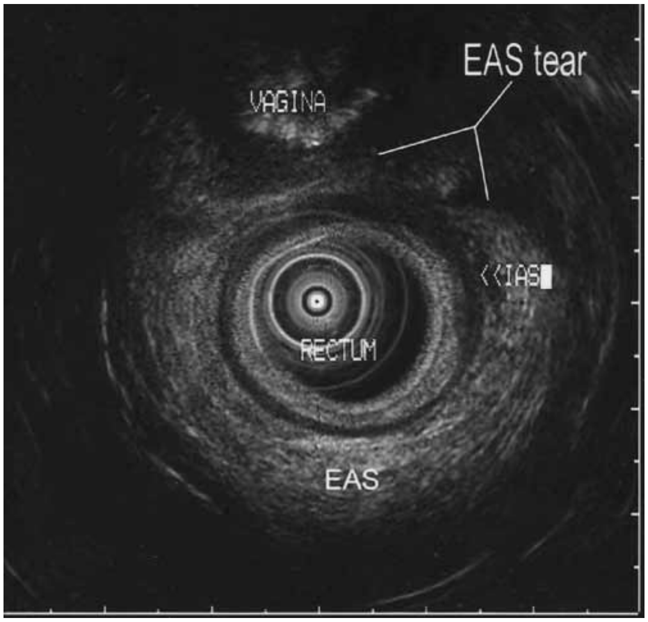

Figure 6. EUS image (sector scan) showing disruption in external anal sphincter (EAS) because of prior vaginal delivery. IAS = internal anal sphincter.

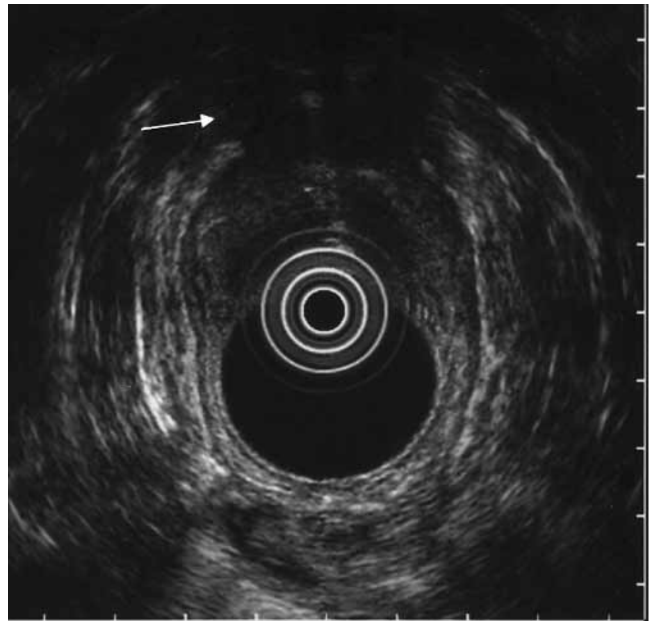

Figure 7. EUS image (sector scan) of T4 rectal cancer with involvement of prostate *(arrow)*.

This corresponds to replacement of the normal striated muscle with granulation tissue and fibrosis (Fig. 6). As mentioned previously, the examination is performed with one hand up against the anus to stabilize the echoendoscope within the anal canal. The balloon is inflated with the minimum volume of water necessary to provide acoustic contact. This limits the amount of distortion of the anal canal caused by the instrument. It is important to recognize that there is a different configuration of the anterior part of the EAS in men and women.[26] The anterior part of this sphincter seems to be shorter and slopes downward in women. This can make it difficult to demonstrate the complete 360 degree ring of the EAS in a single imaging plane.[7] This can lead to a false-positive diagnosis of an EAS defect if an endosonographer is not cognizant of this variation.

The accuracy of EUS for detecting anal sphincter defects has been demonstrated in several prospective studies that have compared US findings to the results of surgery (sphincteroplasty).[27-37] In the largest study reported to date, US findings were prospectively compared with operative findings in 44 patients who underwent pelvic floor repair.[38] Endorectal US was 100% sensitive in detecting either IAS or EAS defects in this study population.

EUS has also been shown to be helpful in predicting outcomes of sphincteroplasty.[39,40] Endorectal US was performed in 31 patients who underwent sphincteroplasty for fecal incontinence in one study.[41] In the 21 patients in whom US documented closure of the EAS defect, 18 (86%) noted improvement in fecal incontinence. In contrast, 8 of the 10 patients who had a persistent defect in the EAS still had significant fecal incontinence.

RECTAL CANCER

According to the 1990 National Institutes of Health Consensus Conference recommendations, patients with rectal cancer that warrants adjuvant therapy are those with advanced locoregional rectal cancer (those with tumor extension into the perirectal fat and/or involvement of the mesorectal or pelvic lymph nodes (T3 or T4 with N0, Tx with N1 or N2, or stage II-III) (Fig. 7).[42] In these patients, neoadjuvant therapy followed by surgery results in better local control[43-45] and comparable or reduced toxicity when compared with standard postoperative adjuvant regimens.[46,47] The Swedish Rectal Cancer Trials, the most definitive studies confirming the benefit of preoperative radiotherapy compared with postoperative radiotherapy, demonstrate that this benefit is conferred only in patients with advanced locoregional disease (T3 or T4, N0 and Tx, N1 or N2).[48,49] Accurate staging of rectal cancer facilitates optimal selection of patients who may benefit from preoperative multimodality treatment.

Transrectal EUS has emerged as an important imaging modality for pretreatment staging of rectal cancer with superior tumor (T) staging accuracy compared to CT.[50-77] The introduction of transrectal EUS has improved the ability to delineate the histologic layers of the rectal wall, thereby improving

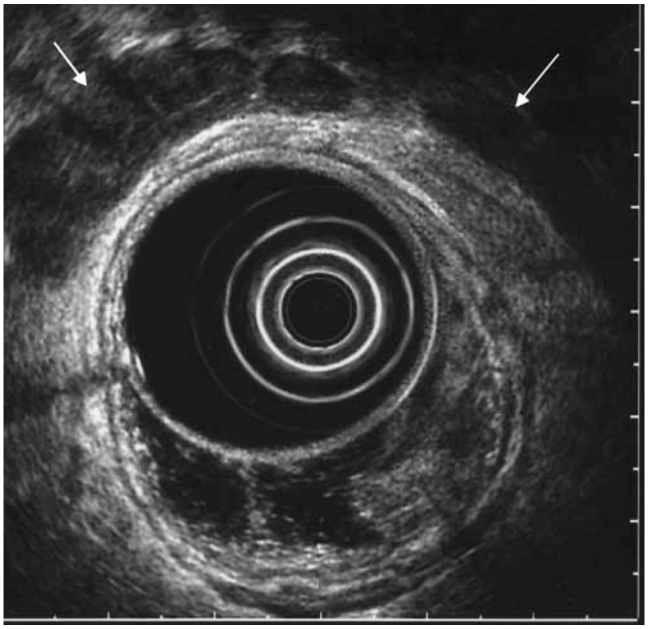

Figure 8. EUS image (sector scan) of T1 rectal cancer confined to mucosa and superficial submucosa. The seminal vesicles are noted anterior *(arrows)*.

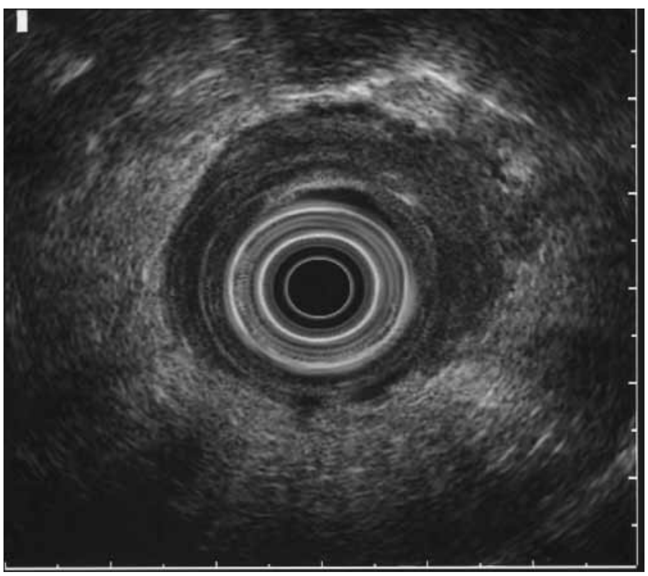

Figure 9. EUS image (sector scan) of T3 rectal cancer with frond like extension of tumor into perirectal space.

treatment allocation by achieving more accurate determination of depth of tumor invasion (Fig. 8).[59-66] Rectal carcinoma usually appears as a hypoechoic lesion that disrupts the normal 5-layer sonographic structure of the rectal wall (Fig. 9). In published studies, the accuracy of EUS in the determination of the depth of invasion of rectal carcinoma (T stage) ranges from 80% to 95%[53,54] compared with 65% to 75% for CT and 75% to 85% for MRI.[50,55-58] With respect to T stage, the major problem with EUS is overstaging of T2 tumors (Fig. 10).[68] This is thought to be due to inflammatory infiltrate around the tumor that is sonographically indistinguishable from malignant tissue.[64,77] Understaging, conversely, may be caused by a failure to detect microscopic cancer infiltration owing to the limits of resolution of currently available EUS systems. Resolution is improved by increasing US frequency, but at the expense of a reduction in the depth of penetration, such that it may be impossible to visualize the leading edge of a tumor, which may limit the detection of invasion of adjacent organs. Other variables that influence the accuracy of tumor staging include operator experience[71,74,78] and the level of the tumor within the rectum, with reduced accuracy for more distal tumors.[71,79] Stenotic tumors are also problematic; up to 17% of lesions may be impossible to stage because of the inability to traverse the stenosis.[68] However, this is less of a problem with newer, flexible echoendoscopes. Preoperative radiotherapy also diminishes the accuracy of T-stage assessment because of increased echogenicity of the rectal wall after radiotherapy.[80]

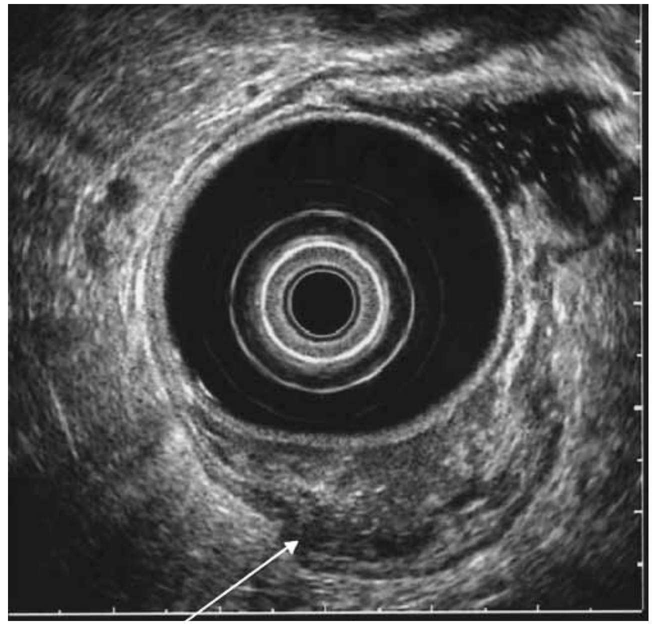

Figure 10. EUS image (sector scan) of T2 rectal cancer with focal area of tumor extension into muscularis propria *(arrow)*.

When assessing perirectal lymph nodes, no single imaging modality has been shown to be sufficiently accurate to allow confident determination of metastatic involvement. In available studies, the accuracy of EUS has been disappointing; approximately 70% to 75%[53-55,58,67-69,71-77,81] compared with 55% to 65% for CT[57,58] and 60% to 65% for MRI.[55-57] Lymph node staging by EUS is less precise than tumor staging because it is more difficult to distinguish tumor within a lymph node than to identify the depth of wall invasion. Changes detected by US that are considered to be associated with malignant involvement include hypoechoic appearance, round shape, and a reduced sonar attenuation coefficient (Fig. 11).[53,82,83] However, if only a small deposit or a micrometastasis is present in a lymph node, the characteristics of the node are unlikely to be sufficiently altered to allow detection. With reference to size alone, there is a 50% to 70% chance that a lymph node greater than 0.5 cm in diameter detected sonographically in the mesorectum will be involved by cancer; for lymph nodes smaller than 4 mm, the chance of involvement is less than 20%.[73] The incorporation of FNA with EUS is an advance in the staging of lymph nodes (N staging) associated with tumors elsewhere in the GI tract,[84-92] although heretofore its role in the evaluation of perirectal lymph nodes has not been assessed. In a recent study preliminarily reported, the role of EUS-FNA of perirectal lymph nodes in the preoperative assessment of a cohort of patients with newly diagnosed, nonmetastatic rectal cancer was defined.[93] Overall accuracy for N staging was similar (approximately 80%) for CT, EUS, and EUS-FNA. The hypothesis was that the minimal incremental increase in N staging accuracy achieved by FNA resided in the endosonographic appearance of perirectal lymph nodes. When lymph nodes with sonographic characteristics that raise a suspicion of malignant involvement are noted elsewhere in the GI tract (e.g., periesophageal, perigastric), the conventional criteria for metastatic involvement carry such uncertainty that the confirmatory cytologic assessment provided by FNA is extremely valuable.[87,91,94-98] In contrast, because of their small size and sonographic characteristics, nonmetastatic perirectal lymph nodes are typically not visualized by EUS. Therefore, EUS visualization alone has a much higher predictive value for perirectal lymph nodal metastases than for lymph nodes elsewhere in the GI tract, rendering the cytologic confirmation by EUS-FNA less valuable.

The routine use of EUS before surgery in the evaluation of rectal cancer is supported by its excellent T-staging accuracy. This improved sensitivity results in appropriate changes in preoperative therapy that would not have been made without EUS. Although FNA provides little incremental benefit in terms of patient management, its greatest potential for impacting management is in patients with early T-stage disease, and its use should be confined to this subgroup. Whether the high degree of staging accuracy offered by EUS and EUS-FNA translates into improved outcomes in terms of reduced recurrence rates and ultimately prolonged survival remains uncertain. Further long-term outcome studies focusing on the endpoint of patient survival are needed.

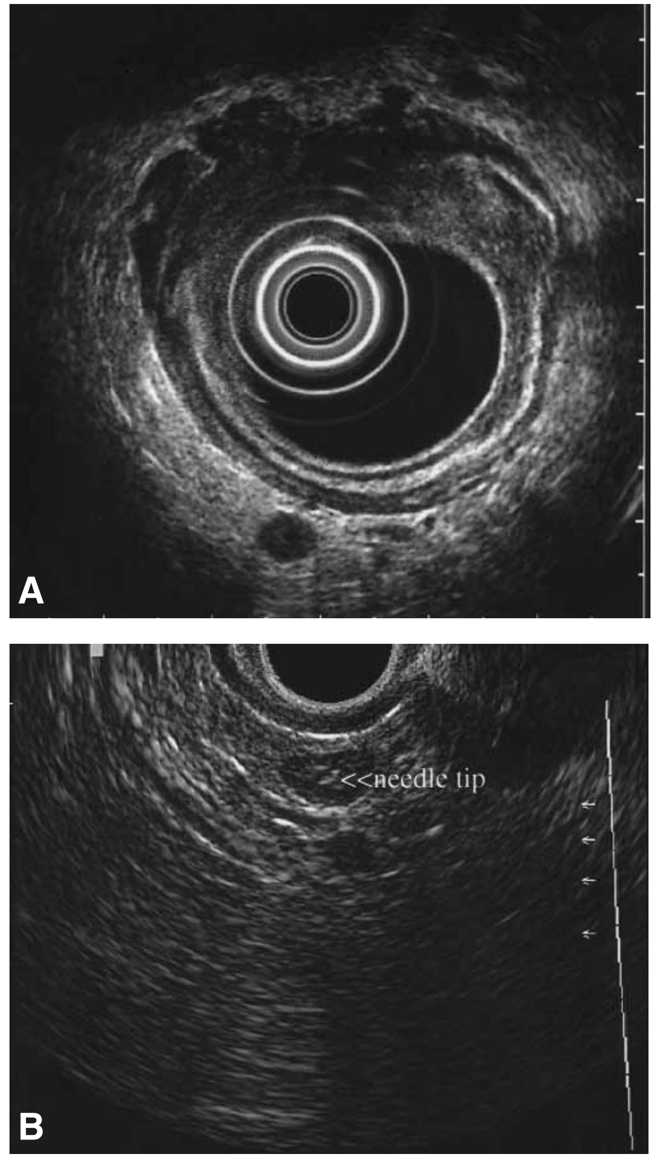

Figure 11. A, EUS image (sector scan) of T3N1 rectal cancer with 5 mm, hypoechoic, smooth bordered, round lymph node at 6 o'clock. **B,** EUS-FNA of lymph node with linear echoendoscope. The cytologic specimen aspirated was positive for metastatic adenocarcinoma.

RECURRENT RECTAL CANCER

To achieve curative reintervention in the setting of recurrent rectal cancer, it is necessary to detect local recurrence at a resectable stage. Because local recurrences often arise extraluminally, follow-up by observation with standard video endoscopes fails to detect them at a sufficiently early stage.[99] The role of CT in this setting is limited: lesions must be at least

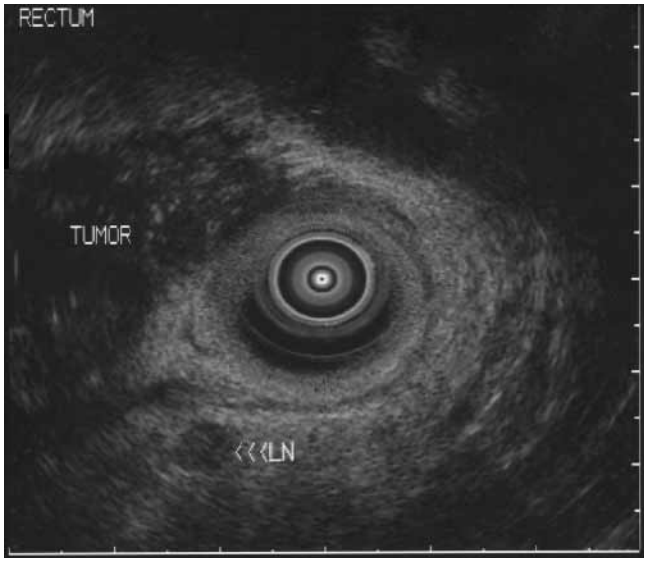

Figure 12. EUS image (sector scan) of recurrent rectal cancer arising after low anterior resection. The recurrent tumor was not apparent on endoscopy but EUS demonstrates a large perirectal mass and associated lymphadenopathy *(LN)* that was confirmed malignant by EUS-FNA.

2 cm in diameter for accurate detection,[100] and it may be difficult to distinguish local recurrence from postoperative alterations in the normal anatomy caused by fibrosis or inflammation. Furthermore, images may be obscured by artifacts produced by metal clips. Rectal EUS combines the diagnostic potential of videoendoscopy (endoluminal tumor detection) and CT (extramural tumor detection) and has proven to be a sensitive and specific method for detecting recurrence (Fig. 12). However, its performance is somewhat diminished by the postoperative or postradiation inflammatory soft tissue changes.[101] These changes obscure the mucosal layers of the rectum, making it difficult to interpret the ultrasonographic images. Nevertheless, two prospective studies have demonstrated superior performance characteristics of rectal EUS when compared with pelvic CT in detecting rectal cancer recurrence.[101,102] The sensitivity of EUS for detecting recurrence was high (100%) in both studies compared with CT (82%-85%). However, the major limitation of EUS in this setting was poor specificity because of the occasional misdiagnosis of mucosal inflammation as carcinoma. In the prospective study of Hunerbein et al.[103] EUS had a specificity of 57%. In an effort to improve specificity, these investigators evaluated the role of EUS-guided FNA in a cohort of 312 patients. EUS-FNA had an overall accuracy of 92% compared with 75% for EUS alone in the detection of recurrent rectal cancer. This superior accuracy of EUS-FNA was primarily a reflection of its superior specificity; 93% compared with 57% for CT (i.e., a false-positive FNA result is rare). Lohnert et al.[104] confirmed these findings in a study of 116 patients with tumor recurrence. Based solely on sonographic characteristics, the accuracy for detection of recurrence was 79%, but the accuracy rose to 100% when EUS-FNA was used. The greatest advantage of EUS-FNA in this study was the ability to detect extremely small pararectal recurrences, the smallest being 3 mm, thereby allowing for curative resection. In this study, 31 of 116 patients with local recurrence detected by EUS-FNA were fit candidates for curative surgery. Of these 31 patients with recurrence amenable to reoperation, 25 were detected by EUS alone, suggesting that EUS is essential if these patients are to be identified early enough to impact outcome.

Although EUS, and particularly EUS-FNA, offers benefit in detecting local recurrence, there is no consensus as to the optimal frequency or duration of follow-up in these patients. The problem of misinterpretation of postoperative changes can be reduced by performing a baseline EUS 3 months after surgery, by which time most changes are less misleading.[102] Lohnert et al.[104] performed EUS at 3-month intervals for 2 years and subsequently at 6-month intervals for 3 years after surgery. Similarly, there is no widespread agreement as to which patients should be selected for close follow-up. However, recognizing that rectal cancer recurrence rates are highest in patients with more advanced tumors at initial diagnosis and in those who undergo local excision,[105] a rational approach would be to perform the most aggressive surveillance in these patients.

CONCLUSION

The application of EUS has improved the evaluation and management of patients with a wide range of rectal diseases. EUS has been proven to be accurate and useful in the management of patients with perianal disease, fecal incontinence, and rectal cancer. Moreover, the range of potential applications for EUS in patients with rectal and anal disease continues to be delineated, and it is likely that EUS will play an even broader role in the evaluation of these patients in the future.

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