The Role of EUS in Rectal Cancer and Fecal Incontinence

Uzma D. Siddiqui, MD
and Harry R. Aslanian, MD

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Abstract

Endoscopic ultrasound (EUS) has emerged as an important imaging tool used in the locoregional staging of rectal cancer and assists in selecting patients with advanced disease that may benefit from neoadjuvant therapy. Studies have shown EUS to have a T staging accuracy of 80–95% and an N staging accuracy of 70–80%. EUS with fine needle aspiration (EUS-FNA) may improve accuracy in staging following surgery or neoadjuvant therapy by providing cytologic confirmation of malignancy. Future developments may include imaging with three-dimensional ultrasound and EUS-guided delivery of chemotherapeutic agents directly into tumors. In the evaluation of fecal incontinence, EUS provides information that is complementary to anorectal manometry and electromyography by providing direct views of the anal sphincter. EUS has been shown to be highly accurate (89–100%) in identifying internal or external anal sphincter defects. Furthermore, EUS has the potential to guide therapy with the delivery of injectable materials to fill sphincter defects.

Key Words: Rectal cancer, Fecal incontinence, Endoscopic ultrasound

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EUS AND RECTAL CANCER

Background

The American Cancer Society predicts that there will be over 40,000 new cases of rectal cancer diagnosed in 2008 (1). The optimal management of rectal cancer is dependent upon accurate staging at the time of diagnosis. Patients with locally advanced disease may benefit from neoadjuvant chemoradation to reduce tumor burden and perhaps allow for sphincter preserving surgeries. Better disease control has been seen in those patients with locally advanced disease (Tx with N1 or N2; T3 or T4 with N0) who undergo neoadjuvant chemoradiation followed by surgery (2). Furthermore, the Swedish Rectal Cancer Trials showed that preoperative radiotherapy decreased local recurrence rates and improved survival in this patient population (3).

EUS Technique

Rectal endoscopic ultrasound (EUS) has emerged as an important imaging tool in the pretreatment local staging of rectal cancer. Rectal EUS is most commonly performed with a flexible radial scanning echoendoscope, but rigid ultrasound probes can also be used. In our practice, we use a standard colonoscopy preparation and routinely utilize conscious sedation, although a sigmoidoscopy preparation without sedation is also acceptable. The patient is placed in the left lateral decubitus position for the procedure. An oblique viewing echoendoscope is passed up to 35 cm under endoscopic guidance to achieve sonographic visualization of the iliac vessels. We perform the initial imaging with radial echoendoscopes which provide a 360° view and generally utilize a linear echoendoscope when fine needle aspiration (FNA) is performed to sample lymph nodes. The scope is slowly withdrawn to assess for the presence of lymph nodes (N stage). The rectum can be filled with water to enhance acoustic coupling, and the patient may be rotated to completely submerge the rectal tumor. The depth of tumor penetration into the rectal wall is assessed with identification of the mucosa, submucosa, and muscularis propria to complete the T staging.

T Staging

EUS can provide detailed images of the various rectal wall layers and can accurately determine the depth of tumor invasion into the bowel wall to establish the T stage. The new 2010 American Joint Committee on Cancer (AJCC) TNM staging of colon and rectal cancers is shown in

Table 1
2010 American Joint Committee on Cancer (AJCC) TNM staging of colon and rectal cancers

T	Primary tumor
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria
T1	Tumor invades the submucosa
T2	Tumor invades the muscularis propria
T3	Tumor invades through the muscularis propria into perirectal tissues
T4a	Tumor penetrates to the surface of the visceral peritoneum
T4b	Tumor directly invades or is adherent to other organs or structures[a]
N	Regional lymph nodes
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastasis in 1–3 regional lymph nodes
N1a	Metastasis in one regional lymph node
N1b	Metastasis in 2–3 regional lymph nodes
N1c	Tumor deposit (s) in the perirectal tissues without regional nodal metastasis
N2	Metastasis in four or more regional lymph nodes
N2a	Metastasis in 4–6 regional lymph nodes
N2b	Metastasis in seven or more regional lymph nodes
M	Distant metastasis
M0	No distant metastasis
M1	Distant metastasis
M1a	Metastasis confined to one organ or site
M1b	Metastases in more than one organ/site or the peritoneum

[a]Invasion of the prostate, seminal vesicles, cervix, or vagina
TNM Classification of Rectal Cancer. Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC, http://www.springerlink.com

Table 1 (4). Figure 1 demonstrates the normal rectal wall layers by EUS. If a tumor involves the mucosal layers or the submucosa, this is a T1 lesion. T2 lesions extend beyond the submucosa and into (but not beyond) the muscularis propria. T3 tumors extend beyond the muscularis propria and into the perirectal tissues but not into adjacent organs (Fig. 2). T4 lesions penetrate beyond the perirectal tissues (Table 1). In males, the prostate and seminal vesicles can be well visualized and their

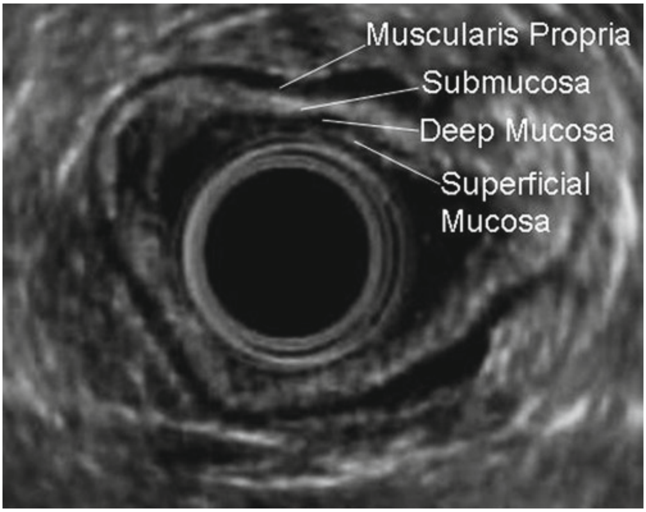

Fig. 1. Radial EUS images of the normal layers of the rectal wall.

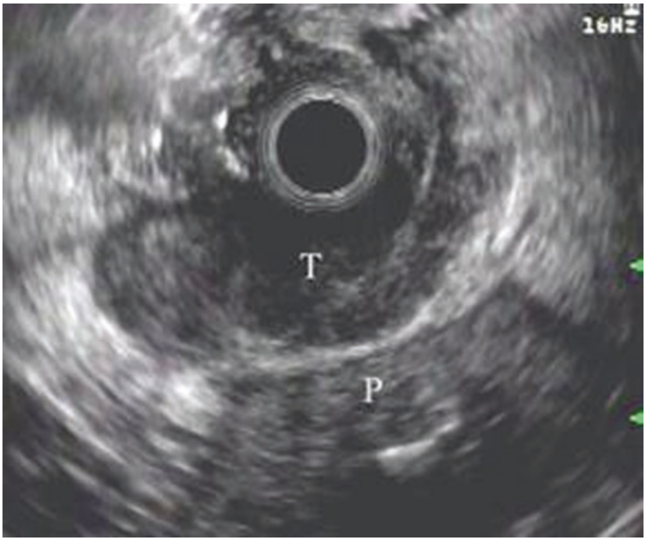

Fig. 2. Radial EUS image of a T3 rectal cancer with the hypoechoic tumor (T) extending beyond the rectal wall into surrounding fat and adjacent to, but separate from, the prostate (P).

relationship to the tumor is defined. Many studies have demonstrated the accuracy of EUS in T staging. Savides and Master examined results from 16 EUS studies (all included at least 70 patients) and calculated an overall EUS T staging accuracy of 83% (5). This review included earlier studies showing high EUS accuracies ranging between 76 and 90% and two more recent studies in 2002 that included over 900 patients and demonstrated lower accuracy rates of 63–69% (6, 7). Multiple comparison studies have shown that EUS has superior T staging accuracy (80–95%) when compared to CT (65–75%) (8–10). A trend toward greater accuracy versus MRI has been identified (MRI 75–85% vs. EUS 85–88%), but more studies are needed in comparison with the newer endorectal coil MRI (11–14). Differentiation between T2 and T3 tumors has presented the greatest challenge to accurate staging. Overstaging of T2 tumors has been occasionally recognized (15, 16). One study prospectively examined 80 patients with newly diagnosed rectal cancer and found that no patients were overstaged as T3 or T4, but 15% of those with T3 disease were actually understaged by EUS (17).

N Staging

Rectal EUS accuracy for regional nodal staging has been demonstrated to be between 70 and 80%, which is less accurate than EUS T staging and not significantly superior to the 65% reported accuracies of CT and MRI (9, 12, 13, 18). The presence of nodal spread is assessed in both the iliac and perirectal regions. The new 2010 AJCC staging system further delineates the N stage by the number of malignant nodes involved since this influences prognosis (Table 1) (4).

It has been previously suggested that simply visualizing lymph nodes in patients with rectal cancer indicated metastatic nodal spread and FNA was not warranted (19). We share this clinical viewpoint, and therefore do not routinely perform FNA of lymph nodes seen during rectal cancer EUS staging. However, the role of FNA in lymph node sampling remains controversial (this is discussed further in the FNA section below).

Fine Needle Aspiration

EUS-guided FNA (EUS-FNA) of visualized nodes performed via a linear echoendoscope may enhance rectal cancer staging accuracy (Figs. 3 and 4). While the addition of FNA has led to improved staging accuracy rates in tumors of the esophagus, pancreas, and lung

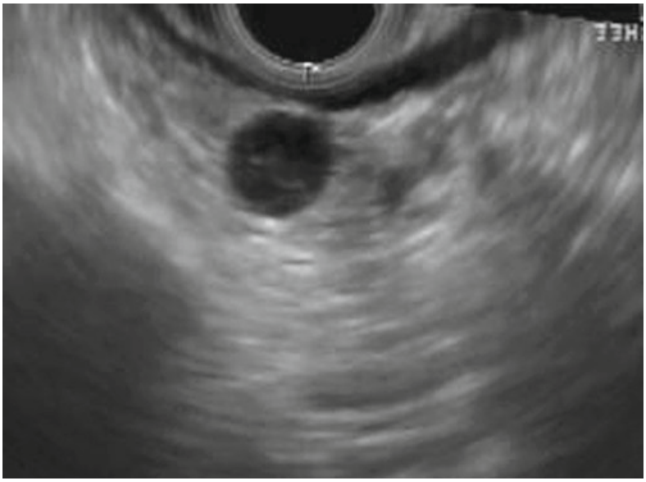

Fig. 3. Linear EUS view of a perirectal lymph node with worrisome features (hypoechoic and round with sharp borders).

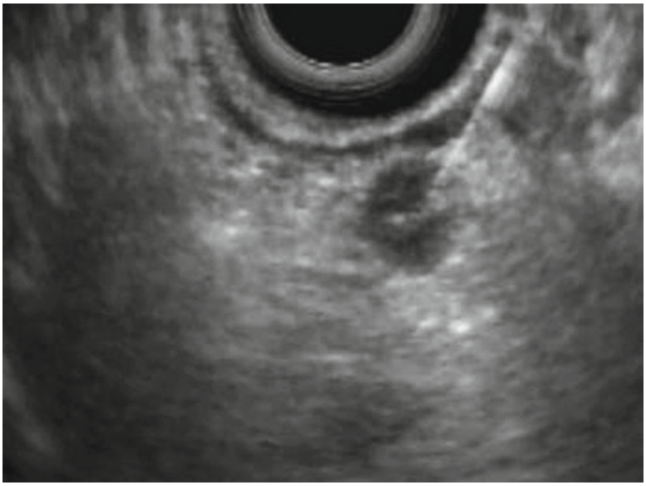

Fig. 4. Fine needle aspiration within the perirectal lymph node. Cytology confirmed the presence of malignancy.

(20–25), this has not been consistently shown with rectal cancer in the past (17, 26). A contributing factor may be that perirectal lymph nodes are usually too small to visualize and may only become significantly enlarged with the involvement of metastatic disease.

Harewood et al. demonstrated that visualization alone on EUS of enlarged perirectal nodes has a higher predictive value for metastases than for nodes elsewhere in the gastrointestinal tract. There were similarly high positive predictive values for both EUS (85%) and EUS-FNA (92%) (17). In esophageal cancer patients, there have been EUS nodal features identified that predict metastatic disease: hypoechoic echotexture, well-rounded shape, smooth/sharp border, and large size (typically >1 cm) (27). However, when these EUS nodal criteria were compared to FNA results in a recently published study by Gleeson et al., only 68% of malignant lymph nodes had >or = 3 nodal features (28). The need for FNA of visualized lymph nodes will require further study.

EUS-FNA has been shown to be a feasible and safe technique for sampling both intramural and extraintestinal tumors, lymph nodes, and cystic lesions via the upper GI tract with a low risk of bacteremia, and does not routinely require administering prophylactic antibiotics (29–33). In contrast, the rectum is not a sterile field and prophylactic antibiotics are typically given with rectal EUS-FNA, despite the lack of data specifically supporting this practice. Levy et al. identified asymptomatic bacteremia in 2 of 100 patients undergoing EUS-FNA of the lower GI tract and concluded that the procedure should be considered low risk for infectious complications, and does not warrant prophylactic antibiotics for the prevention of bacterial endocarditis (33). Furthermore, if antibiotics are given, there is variation regarding the timing (before, during or after the procedure) and duration (one time dose or continue for 48–72 h following the procedure). Sasaki et al. showed that EUS-FNA of submucosal lesions and masses extrinsic to the rectum and colon could be safely performed without complications when a single dose of antibiotics was given following EUS-FNA (34). In contrast, a recent case report by Mezzi et al. described the formation of a pelvic abscess complicating EUS-FNA of a rectal lesion despite one dose of antibiotics being given during the procedure (35). The patient presented 5 days later complaining of rectal pain and fever, leading the authors to suggest continuing antibiotics for several days following the procedure. The most recent American Society of Gastrointestinal Endoscopy guideline regarding antibiotics prophylaxis for GI endoscopy states that there is "insufficient data to make firm recommendations" for antibiotic prophylaxis during EUS-FNA of solid lesions along the lower GI tract (36). Therefore, endoscopists should assess on a case by case basis. It is currently our practice to give a single dose of antibiotics prior to the performance of rectal EUS-FNA; however, more studies are needed to determine what role, if any, prophylactic antibiotics play in this setting.

Clinical Significance of EUS in Rectal Cancer Staging

Several studies have shown the clinical utility of EUS in the evaluation of rectal cancer. Harewood and Wiersema demonstrated that performing CT along with rectal EUS was the most cost-effective method for staging rectal cancer (37). Although this study showed EUS use to be associated with reduced tumor recurrence, there was no difference in mortality. Shami et al. evaluated 48 patients undergoing preoperative staging with CT and found that the addition of EUS changed management in 38% of the patients (38).

Factors Affecting EUS Accuracy

There are a number of factors that may influence rectal EUS staging accuracy. These include operator experience, stenotic tumors, and radiation therapy. Carmody and Otchy demonstrated a learning curve with rectal EUS, where accuracy rates improve with time (39). The accuracy of transrectal ultrasound staging improved from 58% during the first 12 studies to 87.5% in the remaining 24 exams. Stenotic tumors may prevent the echoendoscope from passing beyond the tumor, restricting the views obtained (40). EUS T staging accuracy has been shown to decrease following chemoradiation due to edema, necrosis, and fibrosis, which may distort the rectal wall architecture with changes that may be indistinguishable from malignancy (40, 41). It has been suggested that an influence of publication bias toward positive studies has led to the overestimation of EUS performance in rectal cancer staging (42); however, this has not been found to be a factor with EUS staging of upper gastrointestinal cancers (43).

Tumor Recurrence

Rectal cancer recurrence often develops outside the rectal wall, which makes early detection with standard endoscopy difficult. Two studies evaluated over 200 patients and showed that EUS is superior to CT in identifying local rectal cancer recurrence (100% detection rate vs. 82–85% detection rate) (44, 45). As previously noted, mucosal inflammation and fibrosis presenting after surgery or radiation therapy can obscure or mimic sonographic changes of tumor recurrence, limiting postradiation T and N staging of EUS. However, EUS-FNA provides cytologic confirmation that can improve accuracy (42). One study of 312 patients showed that accuracy rates for detecting tumor recurrence were higher for EUS-FNA versus EUS alone (92 vs. 75%) (46).

Future EUS Applications in Rectal Cancer

Advanced sonographic imaging has been reported using different forms of three dimensional (3D)-EUS. Some studies have used single rigid 3D-EUS probes, while others utilize standard equipment with 3D reconstruction software. However, the reported data is conflicting as to whether this technology significantly improves staging accuracy versus conventional rectal EUS (47–49). More studies are needed comparing 3D-EUS with standard EUS, CT, and MRI.

EUS may also play a therapeutic role in the future management of rectal cancer based on the studies of other malignancies. As has been shown in pancreatic and esophageal cancers, it is possible that biologic agents may be injected directly into rectal tumors to achieve local control (50). Further studies are needed to evaluate other possible applications of EUS guided therapeutics.

EUS AND FECAL INCONTINENCE

Background

Fecal incontinence is an emotionally devastating ailment where the inability to control bowel movements can cause embarrassment, significantly impact quality of life, and may lead to social isolation. Because of the social stigma attached to this condition, its prevalence is likely underestimated. Reported figures suggest that more than six million people and up to 2.2% of women in the United States are affected by fecal incontinence (51, 52). Although the etiology may be multifactorial, anal sphincter injury is a common cause (especially in women during childbirth) and if clearly identified, is amenable to medical and surgical therapies. In the past, the evaluation of fecal incontinence was based upon electromyography (EMG) and anal manometry. Anal EMG has fallen out of use because of poor patient tolerability due to the insertion of needles directly into the sphincter muscle. Anal manometry is commonly used to measure the sphincter's functional ability by placing a transducer across the anal canal into the rectum and having the patient voluntarily contract their anal sphincter. In patients with fecal incontinence, anal manometry has been shown to be 60% sensitive and 78% specific for detecting sphincter defects (53). The accuracy of these tests may be limited by their inability to directly view the anal sphincter. The addition of rectal EUS and MRI in the evaluation of fecal incontinence does provide detailed images of the anal sphincter.

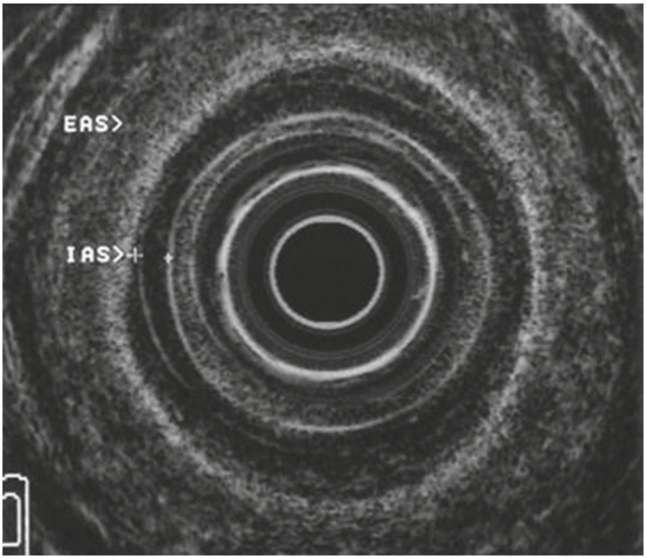

Fig. 5. Radial EUS view of normal external and internal anal sphincters (image provided by Dr. T. Savides).

Normal Anatomy of the Anal Sphincter

The anal sphincter consists of two distinct components, the internal and external sphincters (Fig. 5). The internal anal sphincter (IAS) consists of a 3–5 mm thick circular smooth muscle and the external anal sphincter (EAS) is a 6–10 mm thick ring of levator ani muscles (54). The IAS contributes 70–85% of the resting anal sphincter pressure and is mainly responsible for maintaining continence at rest. The IAS contributes 40% of the sphincter pressure generated after sudden distention of the rectum and the EAS reinforces anal tone during voluntary squeeze (55).

EUS Technique

With the patient in the left lateral decubitus position, the flexible radial echoendoscope (diameter of 12.7 mm) is passed into the rectum and then slowly pulled back through the anal canal with the balloon minimally inflated to minimize image distortion. As the scope is pulled out, the IAS is viewed first in the upper portion of the anal canal, and then the EAS is viewed in the lower portion. The IAS is an inner, hypoechoic ring of tissue that can become thicker and more hyperechoic with age

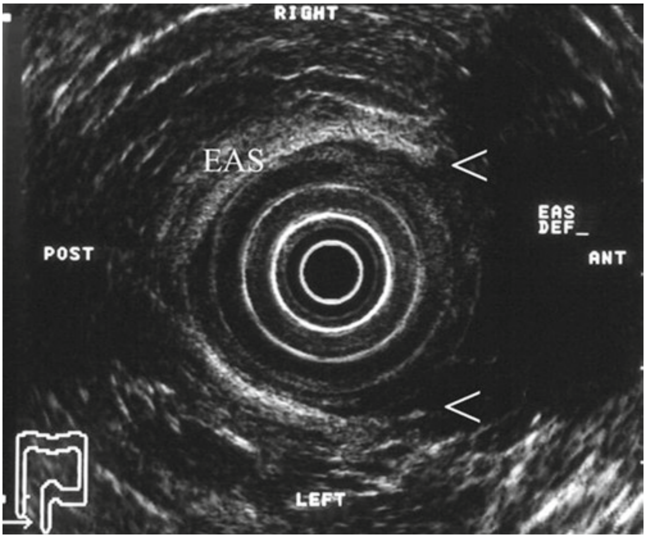

Fig. 6. Disruption of the hyperechoic external anal sphincter (EAS), with edge of tear marked with arrowheads (image provided by Dr. T. Savides).

due to collagen deposition (56–58). IAS tears appear as hyperechoic breaks in the ringed structure. The EAS is the outer, hyperechoic ring formed by the downward extension of the puborectalis muscle and tends to become thinner with age (59). Tears of the EAS appear as hypoechoic breaks (Fig. 6). A few differences between men and women should be considered when performing EUS. First, anal canal length varies from 25 mm for women to 33 mm for men (60). Second, the anterior part of the EAS is shorter, slopes more downward in women, and can make visualization of a complete ring in one plane difficult, which could lead to falsely identifying a sphincter defect (61).

EUS Accuracy in Identifying Sphincter Tears

Meyenberger et al. studied 28 patients with fecal incontinence that underwent rectal EUS prior to surgery (62). The etiology of incontinence was traumatic injury, about 50% were women, and some had both IAS and EAS defects. EUS correctly identified all 25 of IAS defects and all 10 EAS defects, but overall accuracy fell to 89% because an EAS defect was incorrectly diagnosed in three patients. Another study prospectively compared EUS to operative findings in 44 females undergoing pelvic floor repair (63). All 23 EAS defects and 21 of 22 IAS defects identified on EUS were confirmed at surgery.

EUS Compared to Other Modalities

EUS has been compared to other diagnostic tools used in the evaluation of fecal incontinence. Initial studies of EUS compared to EMG demonstrated that it was much better tolerated by patients and could provide similarly accurate assessments of the anal sphincter (64–66). Another study compared EUS to anal manometry and EMG in 12 patients who underwent sphincter repair (67). EUS correctly identified all the sphincter injuries and had 100% accuracy versus 75% accuracies for EMG and manometry and 50% for clinical assessment. A few studies have compared rectal EUS with MRI in detecting sphincter injuries; however, the results have varied due to different patient populations, expertise at various institutions, and study design. One study by Malouf, using consensus opinion of the gastroenterologist and surgeon as a comparison, showed that MRI and EUS were concordant in 32 patients, EUS incorrect in 6 patients, and MRI incorrect in 15 patients (68). Another report of 22 women who underwent surgery for fecal incontinence showed that MRI had a better correlation with surgical findings than EUS (69). A more recent study of 19 women undergoing surgery for fecal incontinence showed that EUS and MRI were equivalent in diagnosing anal sphincter defects (70). More prospective studies will need to be done in a greater number of patients before definitive conclusions can be made regarding the accuracies of EUS and MRI in detecting sphincter injuries.

Clinical Impact of EUS on Fecal Incontinence

Multiple studies have examined the role of EUS in predicting the therapeutic response to sphincteroplasty. Three studies showed that 76% of patients with EUS detected anal sphincter defects had improvement in symptoms following surgery (62, 71, 72). Other studies demonstrated that performing EUS before and after sphincteroplasty to demonstrate the closure of sphincter defects correlated well with the improvement in symptoms of fecal incontinence (73, 74). One study examining 31 patients found that a persistent EAS defect seen on postoperative EUS predicted the failure of symptomatic improvement (75). Hill et al., however, showed that approximately 50% of patients had symptomatic improvement regardless of the results of EUS, anal manometry, or whether surgery was performed (76). This study emphasized that while sphincter defects may have been correctly identified, conservative therapy may be effective in many cases. Additional studies are needed to determine the optimal management of patients with sphincter tears.

Future EUS Applications in Fecal Incontinence

The diagnostic accuracy in the identification of sphincter defects may potentially be improved with the application of 3D-EUS which can provide multiplanar imaging of the anal sphincter. To date, comparable results have been identified between 3D-EUS and MRI in detecting EAS defects (77). Tjandra et al. demonstrated a potential therapeutic use for EUS in fecal incontinence in a study evaluating different methods of treating patients with an injectable silicone biomaterial (PTP implants = Bioplastique™) (78). Injections into the intersphincteric space and IAS were performed and patients were randomized to delivery with EUS guidance (n = 42) or simply by palpation (n = 40). While both groups had significantly improved symptoms, this improvement was greater in the group with EUS-guided injections. Further studies are needed with long-term follow-up to see if EUS-guided therapies prove beneficial in fecal incontinence.

SUMMARY

Rectal EUS plays a significant role in the evaluation of malignant and benign diseases. EUS has emerged as an important tool used in the locoregional staging of rectal cancer and assists in selecting patients with advanced disease that may benefit from neoadjuvant therapy. Currently, EUS T staging has a high accuracy (80–95%) when performed prior to neoadjuvant therapy and in comparison to N staging (70–80%). EUS-FNA may improve accuracy but more studies are necessary to determine if this is significantly better than EUS alone. Future therapeutic roles may include EUS-guided delivery of chemotherapeutic agents directly into rectal tumors. In the evaluation of fecal incontinence, EUS provides the information that is complementary to anorectal manometry and electromyography by providing direct views of the anal sphincter. EUS has been shown to be highly accurate (89–100%) in identifying internal or EAS defects. Furthermore, EUS has the potential to guide therapy with the delivery of injectable materials to fill sphincter defects.

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