Rectal Cancer and Anal Sphincter Disorders

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Introduction

In 2015 within the USA, it is estimated that 40,000 new cases of primary de novo rectal cancer will be diagnosed [1]. Their prognosis is most impacted by the extent of primary tumor invasion (T stage), the presence and number of lymph nodes involved (N stage), involvement of the circumferential resection margin (CRM), and the presence of distant metastasis (M stage). Staging and therapy depend on presurgical imaging modalities that include computed tomography (CT), magnetic resonance imaging (MRI), and EUS. The determined stage is the key in deciding which patients may benefit from neoadjuvant therapy as well as the most appropriate surgical approach (Fig. 27.1).

The diagnostic accuracy of EUS in rectal cancer staging has recently been questioned and criticized as clinical practice and literature do not appear to support the early very positive reports. A German multicenter, prospective, quality assurance study evaluated 7000 patients between 2000 and 2008 and compared radial EUS findings to surgical pathology T stage without the use of neoadjuvant therapy [2]. While the T stage concordance was only 65 %, increasing procedure volumes improved their results. The frequency of under- and overstaging was 18 and 17 %, respectively. Another report from a US center conducted between 1993 and 2007 revealed that EUS nodal evaluation with imaging alone without FNA did not reliably identify patients with nodal disease. Their opinion was based on the finding of a 29 % false-positive rate and because 23 % of patients were understaged when compared to surgical pathology as the gold standard [3]. The conclusions of both reports have uncertain applicability to current practice, given that they evaluated radial EUS alone using technology dating back to the early 1990s. Current practice routinely incorporates linear imaging, FNA assessment of indeterminate nodes, and improved ultrasound technology.

The objective of this chapter was to provide a comprehensive overview using historical and current data to help understand the incremental benefit of EUS versus alternative imaging modalities for assessing patients with primary de novo rectal cancer, following neoadjuvant therapy and during postoperative disease surveillance utility. We also explore potential novel interventions.

Case Study

Initial Presentation

A 62-year-old male presented with a 2-week history of intermittent hematochezia. A digital rectal examination identified the distal border of a

Electronic supplementary material The online version of this chapter (doi: 10.1007/978-1-4939-2320-5_27) contains supplementary material, which is available to authorized users. Videos can also be accessed at http://link.springer.com/chapter/10.1007/978-1-4939-2320-5_27.

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L. S. Lee (ed.), *ERCP and EUS,* DOI 10.1007/978-1-4939-2320-5_27,

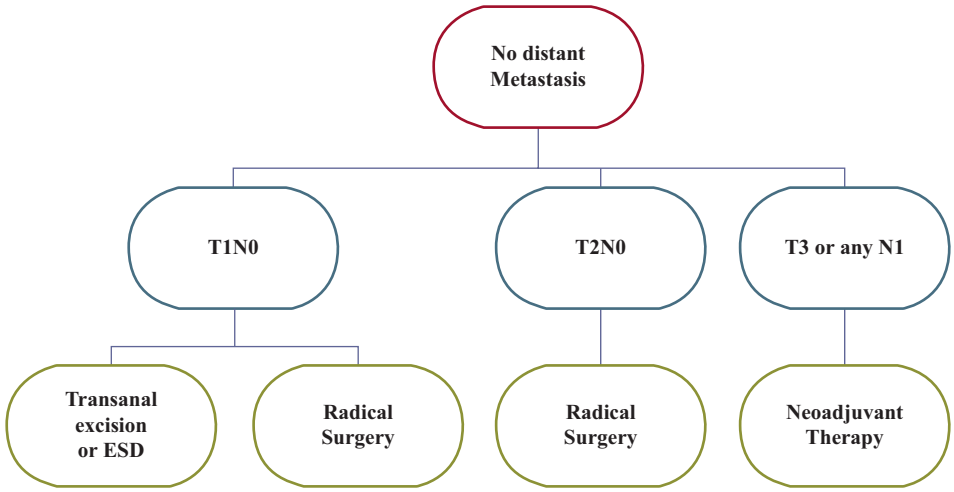

Fig. 27.1 Management algorithm for nonmetastatic primary rectal cancer (*ESD* endoscopic submucosal dissection)

posterior lateral wall ulcerated mass. Endoscopic examination revealed a traversable 4-cm friable ulcerated polypoid mass with its distal border located at the distal valve of Houston, occupying 75% of the luminal circumference. Mucosal biopsies confirmed the presence of adenocarcinoma. Abdominal CT revealed no evidence of metastatic disease. Pelvic MRI identified an enhancing 4-cm mass located approximately 7 cm from the anal verge with questionable extension through the muscularis propria and into the mesorectal fat. There was no involvement of the mesorectal fascia, with a 6 mm distance to the circumferential resection margin, and no evidence for invasion into adjacent structures. In addition, indeterminate 3- to 5-mm lymph nodes were found within the mesorectal fat. A rectal EUS examination was recommended.

What Are Useful Pearls for Initial Primary Rectal Cancer Assessment?

Anorectal Anatomy

The rectum extends from the upper end of the anal canal to the rectosigmoid junction and is approximately 12 cm in length [4]. It is subdivided into proximal, middle, and distal thirds. The surgically defined anal canal measures 2.5–4 cm in length with two-third above the dentate line and one-third below the dentate line [5]. The anatomic anal canal corresponds to the distal one-third of the surgical anal canal and spans from the dentate line to the anorectal verge. Above the dentate line, the anal canal is lined by columnar epithelium, whereas it is lined by squamous epithelium distal to the dentate line. The anal transitional zone corresponds to an approximately 10-mm-long segment between the columnar and squamous epithelial zones where the mucosa is of variable histology [6].

The rectal wall is composed of mucosa, submucosa, and muscularis propria. The mucosa comprises two wall layers: an outer hyperechoic layer (the interface between mucosa and the ultrasound probe) and an inner hypoechoic wall layer. The third wall layer is hyperechoic and represents the submucosa. The muscularis propria or fourth wall layer is composed of an outer longitudinal and inner circular smooth muscle layer. The inner circular smooth muscle becomes thickened distally and continues as the internal anal sphincter and the outer longitudinal muscle fuses with fibers from the levator ani [5]. The outermost layer of the sphincter complex is formed by striated muscles, the levator ani, and puborectalis muscles superiorly and by the inferior part of the external anal sphincter inferiorly.

The rectum is surrounded by mesorectal fat containing lymph nodes, superior hemorrhoidal

vessels, and fibrous tissue collectively known as the mesorectum. The mesorectum is continuous with the fat of the sigmoid mesocolon superiorly and usually thicker along the posterior rectum in its intraperitoneal portion and on occasion is absent anteriorly. It is bound circumferentially by the mesorectal fascia. This fascia extends inferiorly and coalesces with Denonvilliers' fascia in men anteriorly, and anterior to this fascia are the seminal vesicles and prostate gland. Conversely in women, the anterior mesorectal fascia coalesces with rectovaginal fascia, anterior to which is the vagina. The mesorectal fascia forms an important barrier to the radial spread of upper and middle third rectal tumors and forms the plane of dissection used in total mesorectal excision (TME).

Nodal drainage of the rectum occurs initially to the perirectal lymph nodes within the mesorectum [7]. The majority of nodes follow the rectal blood supply and are located superiorly and posteriorly. The common path of nodal spread is along the superior rectal artery into the apical mesorectum and the inferior mesenteric artery into the sigmoid mesocolon. The middle rectal artery arises from the internal iliac artery directly and the inferior rectal artery arises from the internal pudendal artery, a branch of the anterior division of the internal iliac artery. The inferior and middle rectal arteries anastomose at the anorectal junction and, although uncommon, distal rectal cancers can spread to the nodes along the internal pudendal and internal iliac arteries.

Table 27.1 The 2010 American Joint Committee on Cancer (AJCC) staging system for primary rectal cancer

TNM	
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through the muscularis propria into pericolorectal tissues
T4a	Tumor penetrates to the surface of the visceral peritoneum
T4b	Tumor directly invades or is adherent to other organs or structures
Nx	Regional lymph nodes cannot be assessed
N0	No regional nodal metastasis
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 subserosa, mesentery, or non peritonealized pericolic or perirectal tissues without regional nodal metastasis
N2	Metastasis in 4 or more regional lymph nodes
N2a	Metastasis in 4–6 regional lymph nodes
N2b	Metastasis in 7 or more regional lymph nodes
Mx	Presence of distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
M1a	Metastasis confined to one organ or site (i.e., liver, lung, ovary, nonregional node)
M1b	Metastases in more than one organ/site or the peritoneum

What Is the TNM Staging System for Rectal Cancer?

The tumor node metastasis (TNM) system of the American Joint Committee on Cancer (AJCC) and the International Union against Cancer (UICC) has become the worldwide standard for staging colorectal cancer [8, 9]. The TNM system classifies the primary tumor (T) stage based on the depth of tumor invasion into and through the rectal wall. Nodal substations classified as regional lymph nodes for rectal cancer are perirectal, inferior mesenteric, sigmoid mesenteric, lateral sacral, presacral, sacral promontory, internal pudendal, internal iliac, superior rectal, middle rectal, and inferior rectal. Involvement of lymph nodes outside these groups, such as in the external or common iliac substations, is considered to be distant metastases (M stage) (Table 27.1).

EUS Technique

The examination is performed following a full colonoscopy preparation or 2 Fleets enemas and flexible sigmoidoscopy with a patient lying in the

left lateral decubitus position to facilitate optimal visualization. The necessary features to document for endoscopic evaluation are highlighted in Fig. 27.2. The middle valve of Houston is thought to be a surrogate marker for the anterior peritoneal reflection, and the location of a tumor, if proximal or distal to the anterior peritoneal reflection, has important surgical planning implications.

Following advancement of the echoendoscope to the sigmoid colon, air or CO_2 is aspirated as the echoendoscope is withdrawn in order to improve acoustic coupling. The use of either a radial or a linear echoendoscope is a personal preference. Starting with a radial echoendoscope is very reasonable to readily visualize the rectal wall layers and assess for lymph nodes. In addition to aspirating air, water will likely be needed to fill the rectum to enhance imaging. The patient can be rotated to shift the water and allow it to submerge the mass. Care must be taken to establish the relationship of the distal tumor border to the seminal vesicles in men and the cervix in females. The presence or absence of adjacent organ involvement to include the prostate, bladder, and seminal vesicles in men, and the bladder, vagina, and cervix in women should also be noted. In addition, the perirectal and perisigmoid space should be evaluated for the presence of lymph nodes or omental lesions, irrespective of whether a radial or a linear echoendoscope is used. The advantage of beginning with the linear echoendoscope is the ability to image and FNA using the same instrument.

Endosonographically, the rectal wall is seen as five alternating hyper- and hypoechoic layers. A tumor that extends no deeper than the mucosa or submucosa is classified as a T1 lesion (Video 27.1). If the lesion enters the muscularis propria (hypoechoic fourth layer) but does not breach through, it is a T2 lesion (Fig. 27.3). Deeper penetration through the muscularis propria layer, extending beyond the rectal wall and into the surrounding perirectal fat, is consistent with a T3 lesion (Fig. 27.4). Finally, a T4 lesion implies direct invasion into an adjacent organ, i.e., the prostate gland, vagina, and bladder (Fig. 27.5).

EUS evaluation of this 4-cm distal rectal cancer revealed hypoechoic wall thickening to 11 mm with pseudopodia formation and 2-mm infiltration beyond the muscularis propria.

What Are the T Staging Pitfalls?

In published studies, the accuracy of EUS T stage ranges from 80 to 95% compared with 65–75% for CT and 75–85% for MRI [10–12]. With respect to T stage, one particular problem for EUS is the overstaging of T2 tumors due to the difficulty in differentiating peritumoral inflammation and/or fibrosis from the cancer itself (Fig. 27.6) [13]. This tumor meets criteria for a T3 tumor because it did extend through the entire thickness of the muscularis propria into the perirectal fat and obliterated the well-defined fat–muscle interface by neoplastic pseudopodia. Accuracy of specifically T2 staging was examined in a retrospective study because this represents one major decision point in management of rectal cancers with higher T stage tumors receiving neoadjuvant therapy [14]. Both overstaging and understaging of actual T1 or T3 tumors occurred in 16% to yield a negative predictive value for identifying tumor depth of T2 or less of 84% and absence of nodal disease of 87%. Incorrect EUS staging impacted management in 23% of patients.

It is thought that all T3 rectal tumors are not clinically equivalent, with minimally invasive disease carrying a more favorable prognosis [15]. Therefore, by discriminating minimally invasive from advanced T3 disease (invasion $\leq$2 mm or >3 mm beyond the muscularis propria), preoperative EUS may provide important prognostic information. However, the challenge is that overstaging is noted more commonly in minimally invasive T3 (50%) when compared to advanced T3 disease [16]. The maximum tumor thickness of T3 cancers is also an independent prognostic factor for local and overall recurrence [17] using a cutoff value of $\geq$19 mm.

Understaging, conversely, may result from a failure to detect microscopic cancer infiltration owing to the limits of EUS resolution. Spatial resolution is improved by increasing ultrasound frequency, but at the expense of reduced depth of penetration that may compromise inspection of deeper structures. Other variables that influence the accuracy of tumor staging include operator experience and the location of the tumor within the rectum, with reduced accuracy for

DRE (digital rectal exam):

- Tumor palpated (yes/ no)
- Location (anterior, posterior)
- Fixed or mobile

Endoscopic Tumor Characteristics:

- Proximal and distal border (cm) from anal verge
- Where is the distal border in relation to the middle value of Houston?
- Circumference – 1-25%, 26-50%, 51-75%, 76-100%
- Anterior, Posterior, right or left lateral wall (circle all that apply)
- Ulceration: yes/ no
- Polypoid or sessile
- Obstruction: No, Partial (permit endoscope but not echoendoscope), Complete (no scope traverses)
- Mucosal tumor biopsies performed: yes/ no
- Tattoo placement: yes/ no

EUS (uTNM) Characteristics:

- Where is the distal border located in relation to the seminal vesicles or cervix? Above, Same level, Below
- T Stage:
  - Maximal wall thickness (mm)
  - If T3: depth of invasion beyond the muscularis propria (mm)
    minimal disease (< 3mm) or extensive disease (≥3mm)
- N Stage:
  - Peri iliac vessel, perisigmoid or perirectal node (circle all that apply)
  - Long and short axis dimensions (for all lymph nodes undergoing FNA or for most concerning appearing if FNA not performed)
  - Echogenicity, border, shape (for all lymph nodes undergoing FNA or for most concerning appearing if FNA not performed)
  - Impression of extra capsular spread: yes/ no
  - FNA: site, number of lymph nodes and number of passes per node
- **Extramural or Omental deposits**: yes/ no;
  - Size; number of deposits & number of FNA passes per deposit
  - Ascites: yes/no
  - FNA performed: yes/no, site
- **Internal Anal Sphincter involvement**: yes/ no
- **External Anal Sphincter involvement**: yes/ no
- **Other organ involvement**: yes/no, site

Fig. 27.2 Endoscopic and EUS features to be evaluated during the examination

more distal tumors [13, 18–20]. A meta-analysis of 42 studies ($n = 5039$; 1980–2008) reviewed the published data for EUS accuracy by the T stages, suggesting that EUS sensitivity is greatest for advanced disease (T3 or T4) rather than for early (T1 or T2) disease (Table 27.2) [21].

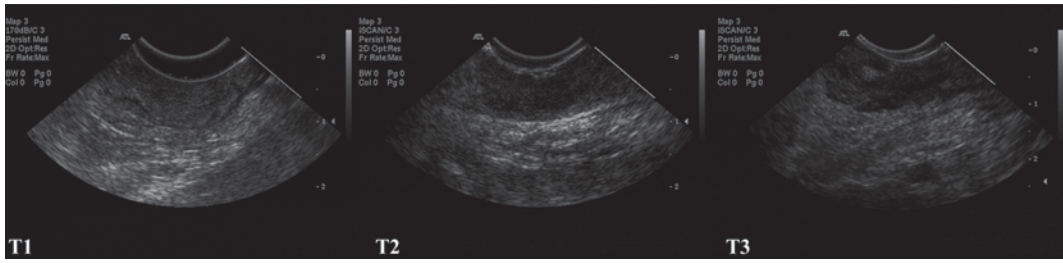

Fig. 27.3 Comparative images of the rectal wall reflecting the mural changes between T1, T2, and T3 lesions

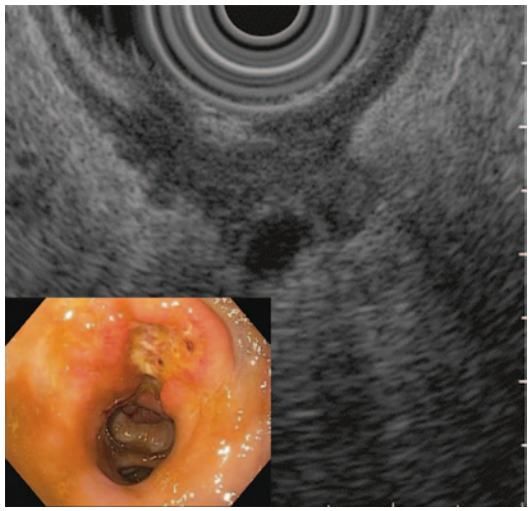

Fig. 27.4 An ulcerated friable mid-rectal T3 cancer penetrating through the muscularis propria layer, extending beyond the rectal wall and into the surrounding perirectal fat

EUS revealed a superficial T3 lesion, 3 round hypoechoic peritumoral lymph nodes as well as a 9 × 7 mm left common iliac artery lymph node. FNA of this node was performed.

What Are the Nodal (N) Staging Pitfalls?

EUS features that accurately predict nodal metastasis have been identified in patients with esophageal cancer [22]. These conventional echo features that correlate with malignancy include an enlarged node (≥1 cm in short axis), hypoechoic appearance, round shape, and smooth border (Table 27.3). For patients with esophageal cancer, if all four abnormal morphological features are present, the accuracy for malignant invasion is 80%. However, all four features of malignant involvement are present in only 25% of malignant lymph nodes (Fig. 27.7). Unfortunately, the standard conventional EUS nodal criteria have proven inaccurate for staging many nonesophageal cancers [22–24]. No one criterion is predictive of malignancy in patients with lung, esophageal, and pancreatic cancer.

The N stage accuracy for EUS imaging in the setting of any malignancy is only 70–75% and was recently reported to be as low as 42% [25, 26]. It was previously assumed that EUS was incapable, or only seldom able, to detect benign perirectal lymph nodes. Therefore, in patients with rectal cancer, mere visualization of lymph nodes was deemed an accurate surrogate marker of nodal metastasis, thereby obviating the need for FNA. A meta-analysis [35 studies (n = 2732; 1966–2008)] of the EUS N stage accuracy in rectal cancer found that the sensitivity and specificity of EUS are moderate (approximately 75%) and concluded that further refinement in diagnostic criteria is needed to improve the diagnostic accuracy [27]. An important limitation of their analysis was the dependence on mostly studies that imaged using radial instruments alone without FNA.

Prior transrectal ultrasound studies identified a nodal size of ≥7 mm as an optimal size cutoff for predicting nodal metastases in rectal cancer, with an accuracy of 83% when compared with surgical pathology [28]. A dedicated FNA study, based on a perception that metastatic loco-regional nodes only minimally differ in morphological appearance from benign nodes, noted that the number

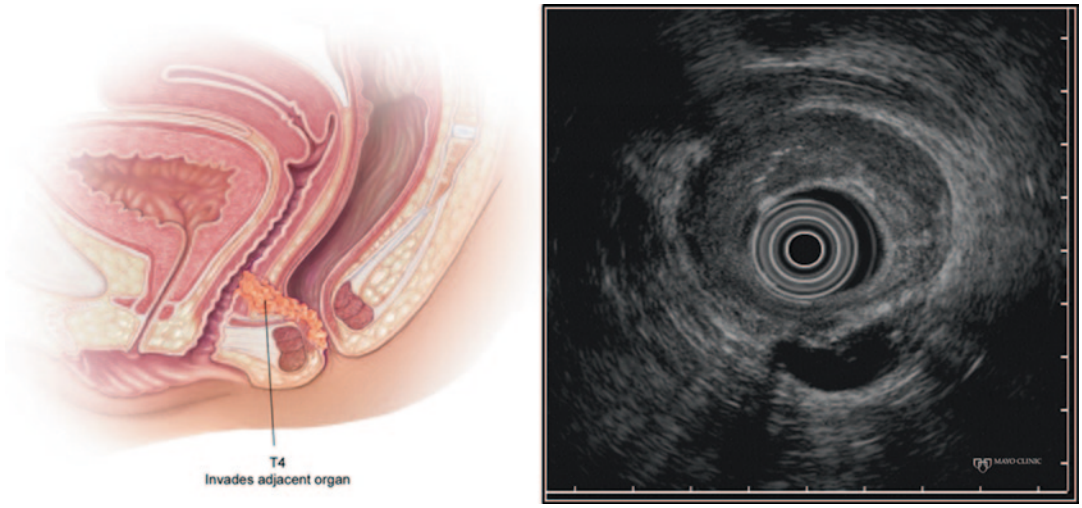

Fig. 27.5 A radial EUS examination revealing infiltration anteriorly into the vaginal wall establishing a T4 lesion

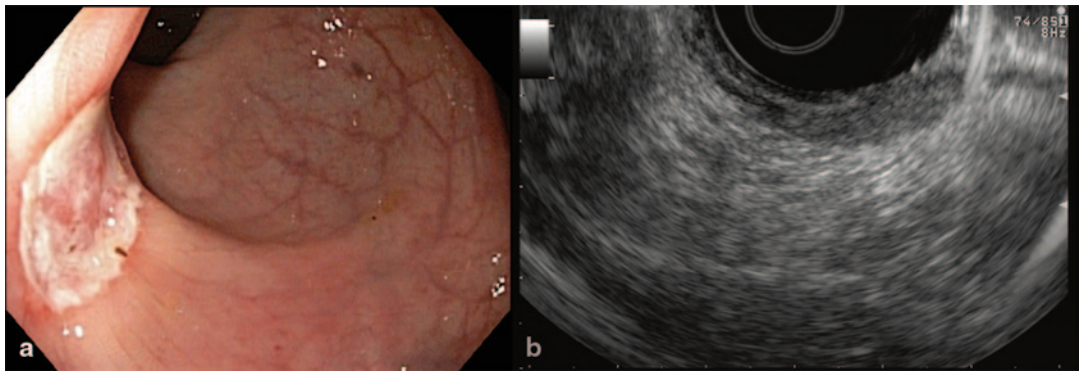

Fig. 27.6 **a** Postpolypectomy for malignancy with superficial ulceration secondary to cautery effect. **b** There is discrete mural hypoechoic change on EUS which cannot distinguish malignant from inflammatory change unless sampled by FNA

Table 27.2 EUS imaging T stage data

T stage	Sensitivity (%)	Specificity (%)
T1	88	98
T2	80	96
T3	96	91
T4	95	98

Table 27.3 EUS morphological features of benign and malignant lymph nodes

EUS features	Benign LN features	Malignant LN features
Echogenicity	Hyperechoic	Hypoechoic
Shape	Irregular	Round
Border	Irregular	Smooth
Size (short axis)	<10 mm	≥ 10 mm

of conventional malignant echo features present per lymph node did not accurately differentiate benign from malignant nodes, unless all four features were present (Table 27.4) [29]. The accuracy for each of the four conventional criteria (short axis ≥ 10 mm, hypoechoic appearance, round shape, and smooth border) for detecting malignancy is as follows: 61, 65, 51, and 51%, respectively. A lymph node short-axis length ≥ 5 mm or a hypoechoic appearance was the only

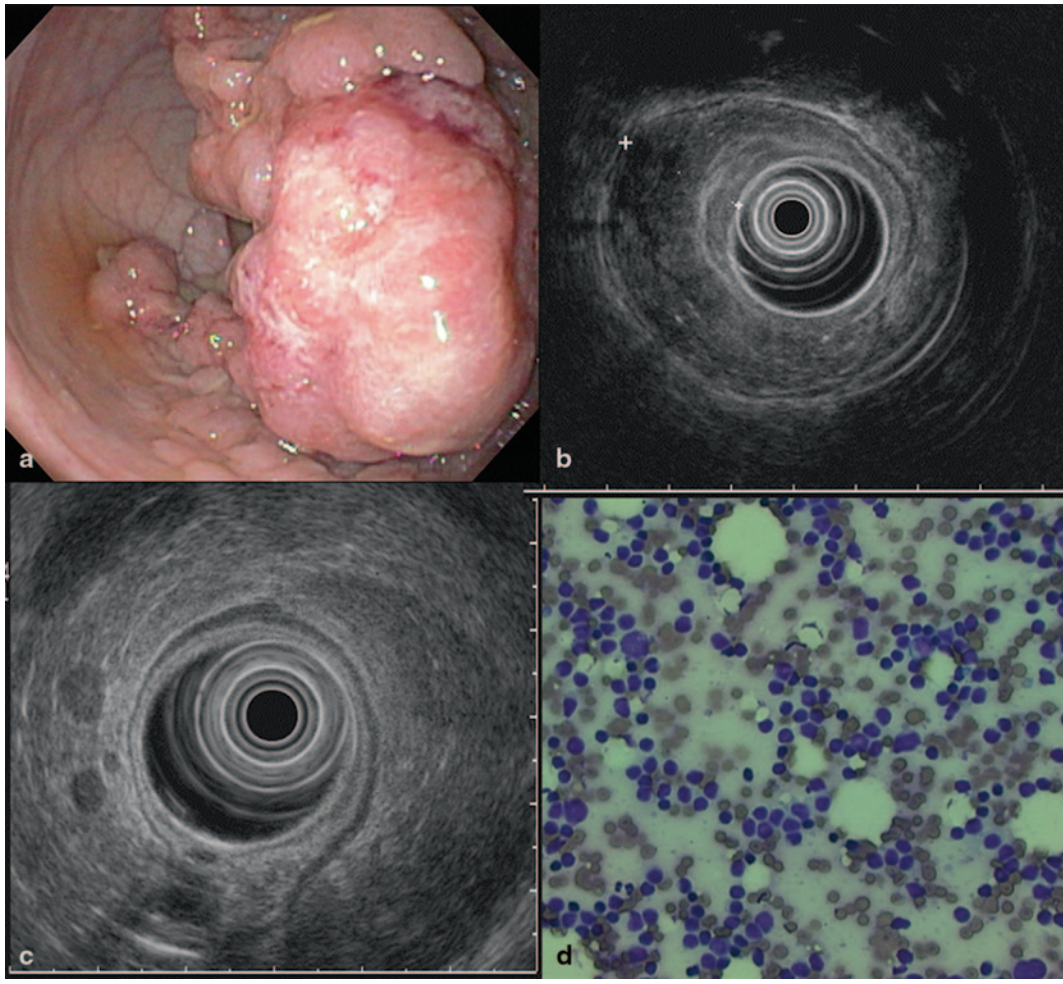

Fig. 27.7 **a**, **b** A bulky T2N1 tumor with **c** nonperitumoral lymph nodes confirmed **d** malignant by FNA

Table 27.4 Performance characteristics relative to the number of malignant EUS nodal features

	≥2 features	≥3 features	4 features
Sensitivity %	77	68	23
Specificity %	29	52	100
PPV %	53	60	100
NPV %	55	61	55
Accuracy %	54	61	61

PPV positive predictive value, *NPV* negative predictive value

EUS feature predictive of malignant infiltration. Optimum short- and long-axis lengths of 6 and 9 mm, respectively, yielded the best power distinction for malignancy (Fig. 27.8).

Using surgical histopathology specimens, Knight and colleagues assessed the performance characteristics of EUS-FNA in the setting of primary or metastatic colorectal carcinoma of perirectal masses, lymph nodes, and distant metasta-

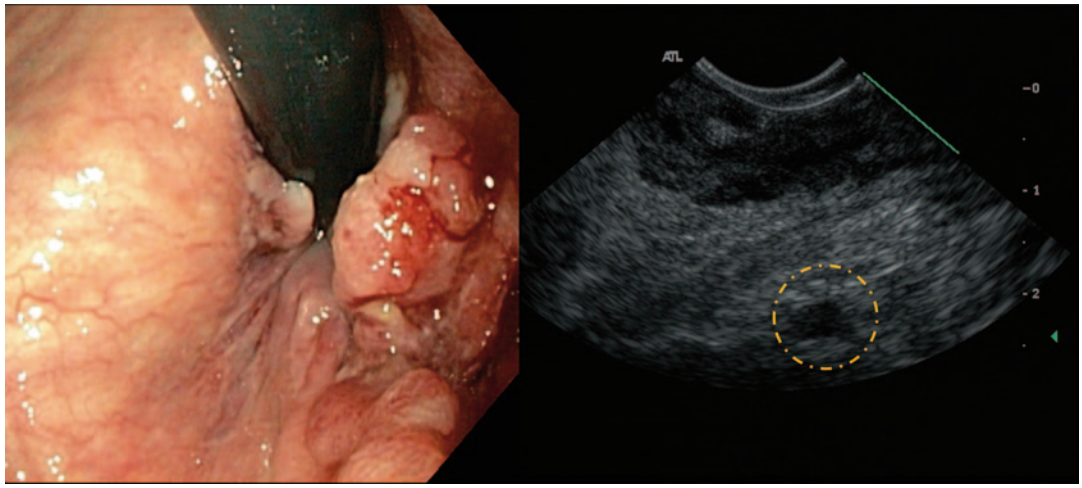

Fig. 27.8 A distal T3N1 lesion in a 54-year-old male who proceeded to neoadjuvant therapy followed by surgery. The highlighted node is perilesional and therefore not amenable to FNA. It has a hypoechoic appearance and short axis > 5mm but oval in shape with an irregular border

ses. The overall sensitivity, specificity, and positive and negative predictive values were reported as 89, 79, 89 and 79%, respectively [30].

The preoperative EUS-FNA identification of extramesenteric lymph node metastases upstages 7% of primary rectal cancers. This is important because, for example, external iliac artery lymph node infiltration is outside the standard operative field for total mesorectal excision (TME). Nodal metastasis to this site typically impacts medical and surgical planning by extending the radiation fields and may indicate the need to extend the TME resection to include an extensive lymph node dissection [31]. Other markers that are associated with such metastases include serum CEA level, tumor length ≥4 cm, tumor annularity ≥50%, sessile morphology, and lymph node size. Unfortunately, these potential surrogate markers are insufficiently accurate, and EUS-FNA is necessary to identify metastasis to these nodal stations.

These findings clearly indicate the need for EUS-FNA to verify nodal status, rather than relying on nodal morphology alone, when making critical decisions regarding the use of neoadjuvant therapy. Failure to do so risks stage inappropriate therapy and in turn inappropriate patient outcomes. We now favor routine FNA because (1) improved technology allows visualization of benign lymph nodes in virtually all patients, (2) most malignant nodes in the setting of rectal cancer are less than 1 cm in size, and (3) the predictive value of imaging alone for distinguishing benign from malignant nodes remains poor.

A note of caution is that luminal fluid cytology may be positive for malignancy in 48% of luminal cancers, including rectal cancer, but is not affected by performing FNA [32]. These translocated cells may contaminate the FNA specimen and lead to false-positive FNA results. In addition, endosonographer technique and cytological misinterpretation also contribute to false-positive EUS-FNA cytology [33].

EUS-FNA of solid lesions in the lower GI tract is considered a low-risk procedure for infectious complications and does not warrant prophylactic administration of antibiotics for the prevention of bacterial endocarditis [34]. Perirectal cystic structures are considered a relative contraindication to FNA given the risk of abscess formation requiring percutaneous drainage, which has occurred despite the administration of prophylactic antibiotics [35]. If FNA is contemplated, we encourage discussion of the need and potential risks with the patients' medical and surgical staff. A recent large single-center study of 502 patients undergoing EUS-FNA of lower GI lesions, over

80 % of which were for rectal cancer, highlighted that risk factors for adverse events included pre-procedural pain, FNA of a site other than a lymph node or gut wall, and malignant cytology [36].

Case Follow-Up

The final interpretation of EUS was a superficial T3 tumor with indeterminate peritumoral nodes, but a malignant left common iliac artery lymph node, thus establishing a distal T3N1M1a rectal cancer. The patient proceeded to neoadjuvant therapy including expansion of the pelvic radiation fields. An abdominoperineal resection with an extended lymphadenectomy was subsequently performed.

Utility of EUS Compared to Other Staging Modalities

MRI Versus EUS Assessment

The role of MRI using an endorectal coil has been well established for local staging of rectal cancer [37–39]. It offers several theoretical advantages over EUS as it reveals a larger field of view and permits the study of stenotic, nontraversable tumors [18, 40, 41]. Recently, the identification of the anterior peritoneal reflection on MRI in 74 % of patients in one study is important given the impact of this landmark on surgical planning [42]. A meta-analysis of 90 articles (1995–2002) compared the utility of MRI, radial EUS without FNA, and CT for staging with histopathology correlation as the gold standard and came to the following conclusions: For T1/T2 lesions, EUS and MRI had similar sensitivity, but specificity was higher in EUS (86 vs. 69 %); for T3 tumors, the sensitivity of EUS was significantly higher than that of MRI or CT [43]. A more recent prospective study comparing radial EUS to MRI revealed that MRI was unable to visualize any T1 tumor, whereas EUS understaged all T4 tumors [44]. Furthermore, the presence of luminal stenosis and polypoid morphology was inversely associated with accuracy for either EUS or MRI.

MRI may also be used to evaluate mesorectal nodal involvement as lymph nodes may be assessed using size criteria as well as specific nodal imaging. The most reliable MRI criteria for lymph node metastasis when correlated with histological findings are an irregular contour and inhomogeneous signal [45, 46]. Many studies have evaluated the performance of MRI for assessing lymph node involvement. A meta-analysis from 2004 revealed that the sensitivity and specificity of MRI were 66 and 76 %, respectively, compared with 67 and 78 % for radial EUS without FNA and 55 and 74 % for CT [39, 43]. In another meta-analysis, there was similarly no significant difference in N staging between MRI and EUS, although EUS had a slight advantage in diagnostic specificity [47].

CT and PET-CT Versus EUS Assessment

The traditional role of CT is to identify metastatic disease as its resolution is inadequate to allow accurate distinction of the various layers, thereby limiting T stage evaluation [48, 49]. More recently, however, multislice CT has been shown useful for determining mesorectal fascia involvement, especially for tumors located in the proximal and mid-rectum with 76 % sensitivity and 96 % specificity. However, the accuracy for predicting mesorectal fascia involvement in a distal rectal cancer remains suboptimal with 66 % sensitivity and 82 % specificity [50, 51]. The CT lymph node size threshold value yielding the greatest negative predictive value for predicting nodal metastasis is 7 mm [52]. Currently, while CT combined with EUS is considered the most cost-effective staging strategy for nonmetastatic proximal rectal cancer, the emerging utility of MRI is likely to change this approach [53].

PET-CT often provides additional information beyond conventional staging in primary rectal cancer and is proposed for selective use in more advanced stages and when indeterminate findings exist with conventional staging [54]. Contrast-enhanced PET-CT is superior to nonenhanced PET-CT for precise definition of regional nodal status and enhances the staging/

therapy in one-third of patients [55, 56]. Some authorities suggest that the SUV_{max} value following neoadjuvant therapy predicts downstaging and a complete pathological response [57, 58]. No EUS-FNA versus PET-CT comparative study has been reported to date.

What Is the Utility of EUS Assessment Following Neoadjuvant Therapy?

Tumor response to neoadjuvant therapy is a strong predictor of disease-free survival. However, the accuracy of EUS for staging rectal cancer following such therapy is reduced markedly due to the secondary effects of postradiation edema, inflammation, necrosis, and fibrosis [59, 60]. Although few data exist, routine EUS staging following neoadjuvant therapy is discouraged [61]. The T stage accuracy following neoadjuvant therapy is 50 % [62–67]. As outcome is most accurately predicted by final pathologic stage, restaging tumors following neoadjuvant therapy is limited, and clinical correlation is most important to dictate operative and postoperative management modalities. However, FNA of nonperitumoral lymph nodes in this setting may establish the presence of residual nodal malignancy, which may offer useful information to guide further management decisions.

Is There a Role for EUS Surveillance Following Radical or Local Surgery in Rectal Cancer?

A positive CRM, serosal involvement, lymphovascular invasion, extramural venous invasion, and poor histological differentiation are important independent predictive factors for the development of local recurrence (LR) [68]. The combination of neoadjuvant therapy and total mesorectal excision has significantly reduced the incidence of LR to less than 10 %, which is greatest within the first 2 years following surgery [69, 70]. Early detection of a recurrent local tumor may result in earlier treatment and improved survival. As LR often occurs in the extraluminal region (i.e., deep to the mucosa), follow-up with forward-viewing endoscopy may fail to detect LR at a sufficiently early stage. Even EUS may be unable to visually distinguish recurrence from postoperative change related to fibrosis or inflammation, and images may be obscured by artifacts from surgically placed clips or sutures. However, FNA of the residual rectal wall or perirectal space (91 % sensitivity and 93 % specificity) may offer a diagnosis which is superior to clinical evaluation or EUS imaging alone.

There is no clear strategy for early detection of local recurrence. Two prospective studies demonstrated that EUS was superior to CT for local recurrence detection of rectal cancer [71, 72]. The sensitivity of EUS was higher (100 %) in both studies compared to CT (82–85 %). EUS was also more sensitive than digital rectal examination, CT, and CEA levels to detect LR in asymptomatic patients [73]. The optimal interval for EUS surveillance following surgical intervention is unknown. However, performing EUS every 6 months for the first 2 years following a low anterior resection may be a reasonable surveillance strategy to detect recurrent rectal cancer [74].

Local excision is an alternative management approach for superficial rectal cancers and for patients unfit for radical oncologic surgery. However, it is associated with a high local recurrence rate. Mucosal scar biopsy and EUS-FNA of either a lymph node or the deep rectal wall are methods to establish local recurrence in these patients (Fig. 27.9) [75]. In addition, EUS-FNA ± trucut biopsy (TCB) may be useful in the diagnostic evaluation of patients with extraluminal perirectal lesions to guide management [76].

Rectal implantation cysts occurring at the anastomosis following low anterior resection for rectal cancer need to be distinguished from locally recurrent rectal cancer. EUS may reveal cystic lesions at the anastomotic site with heterogeneous wall thickening, and FNA may reveal mucin containing some inflammatory cells in the absence of malignant cells [77]. EUS-FNA and TCB are sensitive for the diagnosis of malignancy in pelvic masses but carry a 7 % adverse event rate if cystic pelvic masses are sampled; there-

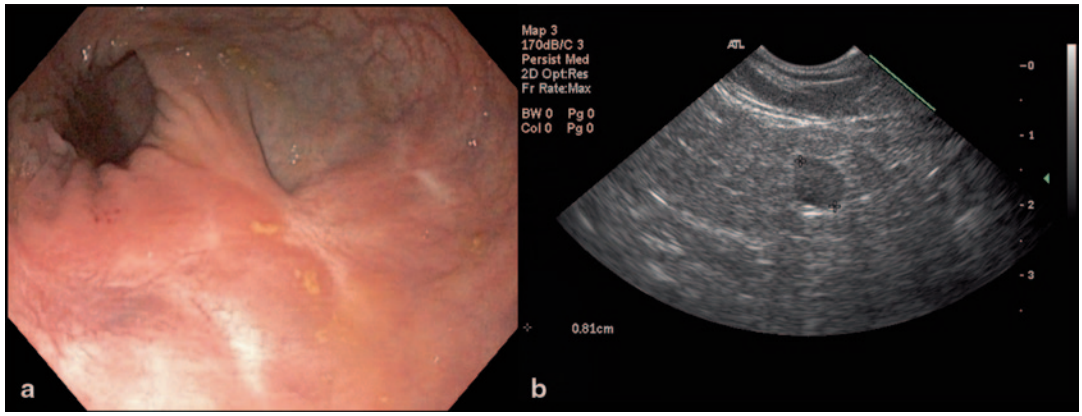

Fig. 27.9 **a** Posttransanal excision scar 18 months following local therapy. **b** EUS detected an enlarged hypoechoic non-perilesional lymph node which was positive for malignancy

fore, aspirating predominantly cystic structures is generally discouraged [78, 79].

EUS for Rectal Wall Metastases

Distant cancers rarely metastasize to the gastrointestinal wall. Such findings are estimated to account for 0.03 % of upper GI endoscopies and 0.05 % of colonoscopies [80]. The EUS appearance without FNA of secondary rectal linitis plastica is that of circumferential wall thickening affecting predominantly the submucosal and muscularis propria layers similar to primary gastric linitis plastica (Fig. 27.10) [81]. The role of FNA in the diagnosis of rectal linitis plastica secondary to prostate cancer has been reported [82]. The EUS appearance of rectal linitis plastica contrasts with processes such as rectal endometriotic implants that are either hypoechoic or heterogeneous deposits involving the fourth and fifth layer with intact mucosal layers and with local rectal cancer recurrence which usually presents in an extraluminal site [83, 84]. EUS-FNA ± TCB may confirm the diagnosis and identify the primary malignancy for metastatic lesions, which to date has included cancers originating from the bladder, breast, stomach, and cutaneous melanoma [85].

Is There a Role for EUS in Perianal Disease and Sphincter Disorders?

Perianal Fistulae and Abscess Formation

EUS is an informative imaging modality with significant impact on the treatment of Crohn's disease-associated perianal fistulae [86]. A fistula appears as a hyperechoic track within a hypoechoic region which represents air bubbles within an inflamed region. The patient's options are an endoscopic examination with either a radial or a linear echoendoscope or a nonendoscopic rigid rectal probe. A prospective blinded study compared EUS, pelvic MRI, and evaluation under anesthesia (EUA) and assessed cost-effectiveness. It revealed good agreement for the studies ($EUS = 91\,\%$; $MRI = 87\,\%$; $EUA = 91\,\%$) when compared to a surgical gold standard [87]. Examination using a 360° anorectal transducer containing a built-in three-dimensional (D) acquisition system with a gel-filled balloon with a patient in the lithotomy position is probably a superior method. In addition, MRI has emerged as an important imaging modality as it provides evaluation of the fistula within the anal canal and its relationship to the sphincter complex, other pelvic floor anatomical structures, and associated complications, i.e., abscess formation. In fact, MRI has replaced EUS in this setting

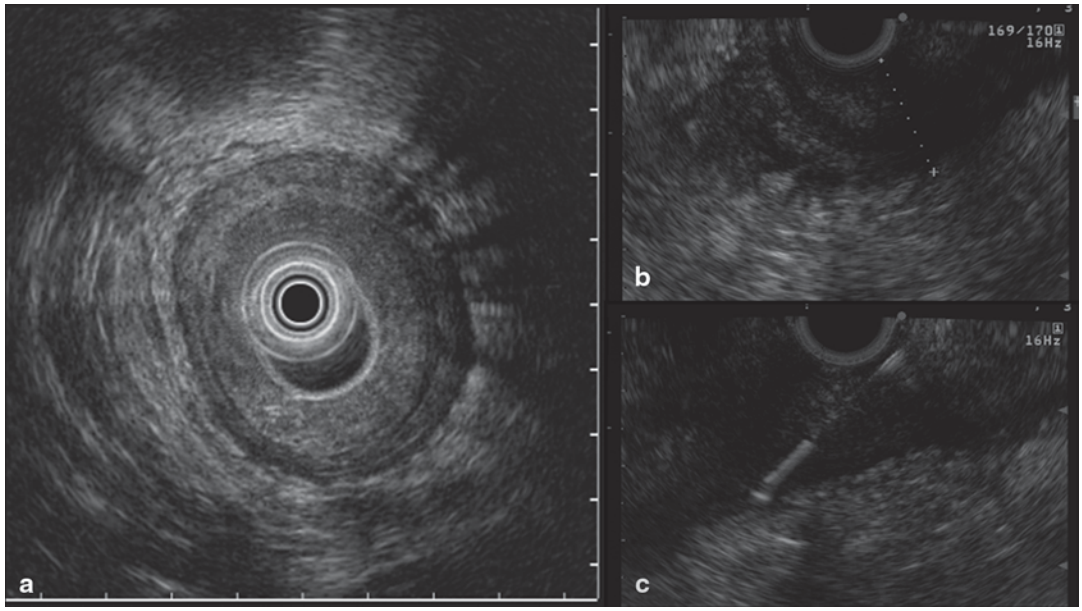

Fig. 27.10 **a**, **b** Circumferential hypoechoic mural thickening (*10 mm*) with unremarkable mucosal biopsy results. **c** However, EUS-FNA confirmed metastasis from a transitional cell cancer of the bladder, diagnosed 2 years previously

in most centers given the technical difficulty of EUS in such patients and due to surgeon preference for reviewing MRI to aid their surgical approach.

Injury to Anal Sphincter

EUS is better tolerated than electromyography, which requires needle placement directly into the sphincter complex. At 5 months postpartum, the prevalence of obstetric anal sphincter injuries in a cohort of primiparous women was 28 % [88]. The defects in the internal and external anal sphincter have different appearances on EUS. The former appears as a hyperechoic break in the normally hypoechoic ring, and the latter appears as a hypoechoic area within the normally hyperechoic ring. However, 2D and 3D transperineal sonography tools are used with increasing frequency and are becoming the gold standard to evaluate the anal sphincter complex in a proctology practice.

What Are Innovative Interventions for the Future?

EUS-guided drainage and stenting provide another option for the management of postoperative pelvic fluid collections [89]. EUS-guided drainage of abdominopelvic abscesses unrelated to diverticular disease may be another future therapeutic indication [90]. EUS fine-needle injection (FNI) with ethanol for persistent malignant pelvic lymph nodes following therapy in nonsurgical candidates has also been reported in addition to EUS-guided coil and glue placement for bleeding rectal varices [91, 92].

Key Points

- Rectal cancer T stage accuracy of EUS has room for improvement.
- FNA has emerged as an essential component of loco-regional clinical staging.

- FNA can identify M1a disease and may upstage 7% of patients presenting for evaluation.
- Staging with EUS following neoadjuvant therapy should be approached with caution.
- EUS-FNA of the rectal wall or extramural perirectal space is useful to establish local disease recurrence in the postoperative surveillance period.

Conflict of Interest The authors declare no conflict of interest.

Financial Disclosures None

Video Caption

Video 27.1 A T1 lesion with a surgical pathology gold standard revealing invasive grade 3 (of 4) adenocarcinoma ($2.7 \times 2.0 \times 0.5$ cm) invading into the submucosa but not into the muscularis propria with a negative surgical resection margin. However, a single (1 of 39) regional lymph node was positive for metastatic adenocarcinoma

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