

THE VALUE OF ENDO RECTAL ULTRASOUND

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ABSTRACT

In the last twenty years, endorectalultrasound (ERUS) has become the primary method for locoregional staging of rectal cancer. ERUS is the most accurate modality for assessing local depth of invasion of rectal carcinoma into the rectal wall layers (T stage). Lower accuracy for T2 tumors is commonly reported, which could lead to sonographic overstaging of T3 tumors following preoperative therapy. Unfortunately, ERUS is not as good for predicting nodal metastases as it is for tumor depth, which could be related to the unclear definition of nodal metastases. The use of multiple criteria might improve accuracy. Failure to evaluate nodal status could lead to inadequate surgical resection. ERUS can accurately distinguish early cancers from advanced ones, with a high detection rate of residual carcinoma in the rectal wall. ERUS is also useful for detection of local recurrence at the anastomosis site, which might require fine-needle aspiration of the tissue. Overstaging is more frequent than understaging, mostly due to inflammatory changes. Limitations of ERUS are operator and experience dependency, limited tolerance of patients, and limited range of depth of the transducer. The ERUS technique requires a learning curve for orientation and identification of images and planes. With sufficient time and effort, quality and accuracy of the ERUS procedure could be improved.

RECTAL EUS

Intraluminal rectal ultrasound examination of rectal lesions can be done with a rigid probe or a flexible echoendoscope. For the purpose of this discussion, both techniques are considered

EUS. EUS has been used to stage rectal cancer since the early 1980s. A recent publication evaluating all EUS studies from 1986 to 2003 in which more than 50 patients were enrolled showed an overall accuracy of 81.8% .2 Although most of the studies had accuracies of 85% to 95%, the composite number was influenced by two large studies, each of which contained more than 400 patients; in these studies, accuracy was lower (i.e., 63.3% and 69%; refs. 3, 4). As with MRI, most inaccuracy results from overstaging of T2 lesions, as EUS cannot reliably distinguish an irregular outer rectal wall image as being due to peritumoral inflammation or transmural tumor extension. Stenotic lesions may present difficulty, as the probe may not be able to traverse the lesion, leading to suboptimal staging. This problem is greater with rigid probes. Catheter probe EUS, which can be done with a standard endoscope, may aid in obtaining accurate tumor staging in the setting of a malignant stenosis. A well-known clinical caveat is that obstructing tumors usually represent at least T3 disease. EUS nodal staging accuracy is less than that of tumor staging and ranges from 70% to 75% .1, 5, 6 Flexible probes have the ability to evaluate the iliac region for adenopathy, which is clinically important because these nodes are retained in standard TMEresection. In one study,up to 28% of lymph node–positive distal tumors showed iliac adenopathy, with 6% of patients having only iliac adenopathy.7 Thus, failure to evaluate this region could lead to inadequate surgical margins in up to 6% of patients with low rectal lesions. Morphologic characteristics suggestive of malignant involvement include hypoechoic appearance, round shape, peritumoral location, and size >5 mm.8 An early study showed that lymph nodes >5 mm in size have a 50% to 70% chance of being malignant compared with only 20% of nodes <4 mm.9 EUS-guided fine-needle aspiration (FNA) allows confirmation of malignancy in suspicious nodes during the same examination, as long as the primary tumor does not lie in the path of the needle. Although initial studies differed on the role of EUS-guided FNA, a recent study of 457 patients showed the value of FNA, particularly in identifying distant malignant adenopathy.10 Seven percent of patients (32 of 457) had iliac adenopathy, with 47% of the nodes (15 of 32) having confirmed malignancy by FNA. Of note, only 47% of patients (7 of 15) with malignant adenopathy had adenopathy on CT. Three-dimensional EUS consists of the traditional transverse scan as well as coronal and sagittal scans that allow for a multiplanar display. This procedure has been found to be superior to CT and two-dimensional EUS in accurately determining tumor margins. The three-dimensional reconstruction is also thought to improve visualization of subtle protrusions of tumors infiltrating into adjacent tissues and organs, allowing for improved T and N staging. An initial study of 25 patients undergoing three-dimensional EUS, twodimensional EUS, and endorectal MRI showed no sig-

nificant difference in T- or N-stage accuracy, but it was thought that endorectal MRI and three-dimensional EUS improved understanding of the spatial relationship of the tumor due to their ability to obtain multiplanar imaging.12 A more recent study of 86 patients who underwent three-dimensional EUS, two-dimensional EUS (using a rigid probe), and four-channel multidetector CT showed T-stage accuracy of 78%, 69%, and 57%, respectively; N-stage accuracy was 65%, 56%, and 53%, respectively.11 However, examiner errors in interpretation were found in 47% of two-dimensional EUS studies and 65% of three-dimensional EUS studies. When these images were correctly interpreted, T-stage accuracy improved to 91% for three-dimensional EUS and 88% for two-dimensional EUS and N-stage accuracy improved to 90% and 76%, respectively. This study shows promise for three-dimensional EUS while highlighting the highly operator-dependent nature of EUS data.

EVALUATION OF PREMALIGNANT LESIONS

Several studies have examined the utility of ERUS in evaluating biopsy-negative villous adenomas. Approximately 30 to 40% of rectal villous adenomas contain malignancy, and roughly 10% of biopsy-negative adenomas are misdiagnosed, even when polyps with malignant features (such as induration and ulceration) are excluded. 13 The goal of using ERUS for these biopsynegative lesions prior to excision would be to better identify foci of invasive tumor in the primary lesion or in the surrounding lymph nodes, thus minimizing the risk of inadequate resection. Although there are skeptics, it is believed that, with the use of higher-resolution transducers, ERUS is capable of distinguishing reliably between T0 and T1 masses. Current studies report favorable outcomes. In a meta-analysis of 258 biopsynegative rectal adenomas, 24% of which were ultimately found to harbor undiagnosed invasive tumor, ERUS correctly identified tumor deposits in 81% of the lesions.13 In another series of 60 patients with pT0/pT1 lesions, ERUS detected invasive elements with 89% sensitivity and 88% specificity.14 Overstaging of benign lesions was most likely (1) after snare excision, when fibrosis from the scars mimic tumor penetration into deeper tissue layers; (2) due to location of lesions near the anal sphincters, obscuring visualization of the sonographic layers. These problems can be avoided by performing ERUS prior to excision, and by using higher-frequency transducers.

EVALUATING RESPONSE TO NEOADJUVANT CHEMORADIOTHERAPY

The ability of ERUS to accurately evaluate tumor response to neoadjuvant chemoradiation prior to surgical resection is hampered primarily by the effects of the chemoradiation itself: tumor necrosis, fibrosis, and peritumoral inflammation caused by therapy can significantly compromise staging accuracy. These reactions may all appear sonographically indistinguishable from residual tumor, obscuring differentiation of the five layers of the rectal wall and resulting in overstaging. Various studies have cited accuracy rates ranging from 48 to 62%, and overstaging rates ranging from 37 to 83%, with lower rates in the setting of tumors responsive to therapy (29 to 41%) versus tumors that are nonresponsive (67 to 82%).15,16,17,18 Despite its lower accuracy in this setting, many practitioners believe that ERUS is useful as a bridge between the two treatment modalities. Residual tumor, when present, is thought to be consistently limited to the region of fibrosis, permitting investigators to determine the maximum possible depth of invasion, the closest possible distance from the anorectal ring, and the possibility of sphincter involvement.

This idea has been supported in at least two studies.19,20 In one group, certain sonographic changes in the posttherapy ERUS images were noted to correlate with response of the tumor to chemoradiotherapy. If these sonographic changes are regularly confirmed in future studies as indicating response to therapy, use of ERUS in this setting may offer some patients the possibility of avoiding resection entirely.48

NEW DEVELOPMENTS IN ENDORECTAL ULTRASOUND

Endorectal Ultrasound-Guided Needle Biopsies The potential role of ERUS-guided needle biopsy in assessing suspicious lymph nodes has already been discussed. Although it is attractive in theory, there is considerable doubt as to whether the technique will ultimately improve the accuracy of ERUS N-staging. However, this technique has been used in the evaluation of primary lesions, specifically peri-anastomotic foci suspicious for local recurrence. ERUS-guided needle biopsy is technically difficult to perform with the radial probes typically used for staging because the path of the needle cannot be visualized on transverse imaging. Linear probes, however, as shown by Akasu,19 have been utilized with some success. Some investigators employ multiplane transducers, using the transverse plane images to view the anatomy and the longitudinal plane to guide the needle.21 Studies have shown that this technique increases the specificity and accuracy of ERUS in detecting local recurrence.21 One recent report also demonstrated some success in assessing metastasis to the iliac lymph nodes, raising the possibility of being able to identify those patients who might be best treated with expanded radiation fields, or with palliative therapy.18

THREE-DIMENSIONAL ENDORECTAL ULTRASOUND

Proponents of three-dimensional ERUS (3D-ERUS) maintain that it provides superior visual images of tumor volume and the spatial relationships of tumor to surrounding anatomical structures. Two types of 3D-image construction have been reported. In some studies, transverse scanning is performed with a rigid ERUS probe to create a consecutive array of parallel sections stacked along an axis perpendicular to the images themselves. In other studies, rotational probing is performed, combining 360-degree transverse scanning with 100-degree longitudinal views.18 When reconstructed, the images have resolutions superior to those of MRI.22 3D-ERUS reportedly has several advantages over standard ERUS. Its ability to generate images in multiple planes may increase accuracy by improving diagnostic confidence, as has already been shown with MRI.21 Although the sample sizes have all been relatively small, several studies report that the accuracy of 3D-ERUS is superior to that of standard ERUS.23,24,25 The longitudinal scan planes, unique to 3D-ERUS, can precisely assess tumor size and position, facilitating accurate staging in the setting of bulky and stenotic tumors.26 Perhaps more important, the stereoscopic images generated by 3D-ERUS allow measurement and visualization of certain anatomic features, reducing interpreter error and offering potential predictive value. 3D-ERUS imaging facilitates the observer's ability to distinguish blood vessels from lymph nodes, and may enhance the precision of ERUS-guided needle biopsies.23,27 In one study, investigators were able to accurately measure the extent of circumferential infiltration, a feature shown to correlate with T-staging, lymphovascular invasion, histologic tumor differentiation, and nodal metastasis. The same group identified conical protrusions along the deep tumor margins whose numbers correlated with infiltration grade as well as T- and N-status.23,27 Like MRI, such images provide better definition of the mesorectal fascia, permitting evaluation of circumferential resection margins.28,24 These early studies suggest that 3D-ERUS may be capable of combining the high-resolution images of the rectal wall and cost-effectiveness of standard ERUS with the multiplanar and stereoscopic imaging capabilities of MRI. In time, this may make 3D-ERUS the premier imaging modality used in rectal cancer management.

ALTERNATIVE APPROACHES IN SONOGRAPHY OF RECTAL TUMORS

The difficulty in evaluating stenotic, bulky and proximal rectal tumors using the traditional rigid ERUS probe has prompted clinicians to experiment with alternative approaches to ultrasound. Transvaginal sonography employing longitudinal probes has been used in women, with some success, to evaluate stenotic tumors or rule out local recurrence following abdominoperineal resection.29 Miniaturized probes, or ''miniprobes,'' and probes on flexible scopes have also been developed and tested because of their ability to traverse these lesions. Flexible scopes are hampered by poor accuracy (49 to 59% Tstaging accuracy; 60 to 78% N-staging accuracy).30,15 Miniprobes may be inserted through colonoscopes to assess tumors in the colon as well, and to evaluate iliac lymph nodes for M-staging.18 Although some studies have reported T- and N-staging accuracies of 82 to 90% and 67 to 87%, respectively, the probes emit only high frequencies (e.g., 12.5 to 30 MHz), and therefore have poor depth of penetration and poor ability to differentiate between T3 and T4 lesions.30,31 Given the high resolution for the superficial wall, however, many surgeons believe that these miniprobes will ultimately play a role in determining the presence of malignancy in broadbased rectal polyps. Miniprobes may also serve similar functions in the evaluation of colonic polyps, potentially offering some patients the option of endoscopic local excision over colectomy.31

PREDICTIVE SONOGRAPHIC FEATURES

A small number of studies have attempted to identify sonographic features that might serve as predictors of tumor invasiveness, response to neoadjuvant therapy, and long-term outcomes. One group noted small numbers of 1–3 mm hypoechoic spots in perirectal fat at the tumor margins. These spots were found to correlate positively with lymphovascular invasion, the presence of nodal or distal metastasis, and frequency of local recurrence.32 In another study, investigators used Doppler ultrasound to grade the vascularity of 29 uT3-staged rectal tumors. Examining tumor response to chemoradiotherapy, they noted significantly higher rates of response in tumors that were more extensively vascularized and had less vascular resistance.33

CONCLUSION

Endorectal ultrasound remains the most effective diagnostic tool for evaluating rectal cancer. It is easy to perform, well-tolerated, inexpensive, and readily usable in the clinic environment. Although it is operatordependent, with a steep learning curve, the dedicated practitioner can master ERUS readily. Recent studies have reported lower levels of accuracy associated with ERUS than were reported previously; however, this is probably due to its more widespread use by lessexperienced physicians, and we expect that the reported accuracy will improve over time. In addition to its value in tumor staging, studies have shown ERUS to be useful in evaluating adenomas for foci of malignancy, assessing tumor response to neoadjuvant therapy, and in posttreatment surveillance. The ongoing development of ERUS-guided biopsies, miniprobes, and 3D-ERUS offers the potential for further improvement in staging of lymph nodes and poorly accessible tumors, as well as prediction of

response to therapy. It is clear that ERUS will remain a key element in the treatment of rectal cancer for some time.

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