Accuracy of Endoscopic Ultrasound in Staging of Early Rectal Cancer

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Endoscopic ultrasound can be highly accurate for the staging of neoplasms in early rectal cancer.

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Colorectal cancer is the second most common cause of cancer death in the US, with one-third of all colorectal cancers occurring within the rectum. Each year, an estimated 40 000 Americans are diagnosed with rectal cancer (RC).[1,2] The prognosis and treatment of RC depends on both T and N stage at the time of diagnosis.[3-5] According to the most recent National Comprehensive Cancer Network guidelines from May 2019, patients with T1 to T2N0 tumors should undergo transanal or transabdominal surgery upfront, whereas patients with T3 to T4N0 or any TN1 to 2 should start with neoadjuvant therapy for better locoregional control, followed by surgery.[6] Therefore, the appropriate management of RC requires adequate staging.

Endoscopic ultrasound (EUS), magnetic resonance imaging (MRI), and computed tomography (CT) are the imaging techniques currently used to stage RC. In a meta-analysis of 90 articles published between 1985 and 2002 that compared the 3 radiologic modalities, Bipat and colleagues found that MRI and EUS had a similar sensitivity of 94%, whereas the specificity of EUS (86%) was significantly higher than that of MRI (69%) for muscularis propria invasion.[7] CT was performed only in a limited number of trials because CT was considered inadequate to assess early T stage. For perirectal tissue invasion, the sensitivity of EUS was statistically higher than that of CT and MRI imaging: 90% compared with 79% and 82%, respectively. The specificity estimates for EUS, CT, and MRI were comparable: 75%, 78%, and 76%, respectively. The respective sensitivity and specificity of the 3 imaging modalities to evaluate lymph nodes were also comparable: EUS, 67% and 78%; CT, 55% and 74%; and MRI, 66% and 76%.

The role of EUS in the diagnosis and treatment of RC has long been validated.[1,2-5] A meta-analysis of 42 studies involving 5039 patients found EUS to be highly accurate for differentiating various T stages.[8] However, EUS cannot assess iliac and mesenteric lymph nodes or posterior tumor extension beyond endopelvic fascia in advanced RC. Notable heterogeneity was found among the studies in the meta-analyses with regard to the type of equipment used for staging, as well as the criteria used to assess the depth of penetration and nodal status. The recent introduction of phased-array coils and the development of T2-weighted fast spin sequences have improved the resolution of MRI. The MERCURY trial showed that extension of tumor to within 1 mm of the circumferential margin on high-resolution MRI correctly predicted margin involvement at the time of surgery in 92% of the patients.[9] In the retrospective study by Balyasnikova and colleagues, MRI was found to correctly identify partial submucosal invasion and suitability for local excision in 89% of the cases.[10]

Therefore, both EUS and MRI are useful, more so than CT, in assessment of the depth of tumor invasion, nodal staging, and predicting the circumferential resection margin. The use of EUS, however, does not preclude the use of MRI, or vice versa. Rather, the 2 modalities can complement each other in staging and proper patient selection for treatment.[11]

Despite data supporting the value of EUS in staging RC, its use is limited by a high degree of operator dependence and a substantial learning curve,[12-17] which may explain the low EUS accuracy observed in some reports.[7,13,15] Given the presence of recognized alternatives such as MRI, we decided to reevaluate EUS accuracy for the staging of RC outside high-volume specialized centers and prospective clinical trials.

METHODS

A retrospective chart review was performed that included all consecutive patients undergoing rectal ultrasound from January 2011 to

August 2015 at the US Department of Veterans Affairs Medical Center (VAMC) in Memphis, Tennessee. Sixty-five patients with short-stocked or sessile lesions < 15 cm from anal margin staged T2N0M0 or lower by endorectal ultrasound (ERUS) were included. The patients with neoplasms staged in excess of T2 or N0 were excluded from the study because treatment protocol dictates immediate neoadjuvant treatment, the administration of which would affect subsequent histopathology.

For the 37 patients included in the final analysis, ERUS results were compared with surgical pathology to ascertain accuracy. The resections were performed endoscopically or surgically with a goal of obtaining clear margins. The choice of procedure depended on size, shape, location, and depth of invasion. All patients underwent clinical and endoscopic surveillance with flexible sigmoidoscopy/EUS every 3 to 6 months for the first 2 years. We used 2 different gold standards for surveillance depending on the type of procedure performed to remove the lesion. A pathology report was the gold standard used for patients who underwent surgery. In patients who underwent endoscopic resection, we used the lack of recurrent disease, determined by normal endoscopic and endoscopic ultrasound examination, to signify complete endoscopic resection and therefore adequate staging as an early neoplasm.

RESULTS

From January 2011 to August 2015, 65 rectal ultrasounds were performed. All EUS procedures were performed by 1 physician (C Ruben Tombazzi). All patients had previous endoscopic evaluation and tissue diagnoses. Twenty-eight patients were excluded: 18 had T3 or N1 disease, 2 had T2N0 but refused surgery, 2 had anal cancer, 3 patients with suspected cancer had benign nonneoplastic disease (2 radiation proctitis, 1 normal rectal wall), and 3 underwent EUS for benign tumors (1 ganglioneuroma and 2 lipomas).

Thirty-seven patients were included in the study, 3 of whom were staged as T2N0 and 34 as T1N0 or lower by EUS. All patients were men ranging in age from 43 to 73 years (mean, 59 years). All 37 patients underwent endoscopic or surgical resection of their early rectal neoplasm. The final pathologic evaluation of the specimens demonstrated 14 carcinoid tumors, 11 adenocarcinomas, 6 tubular adenomas with high-grade dysplasia, and 6 benign adenomas. The preoperative EUS staging was confirmed for all patients, with 100% sensitivity, specificity, and accuracy. None of the patients who underwent endoscopic or surgical transanal resection had recurrence, determined by normal endoscopic and endoscopic ultrasound appearance, during a mean of 32.6 months surveillance.

DISCUSSION

EUS has long been a recognized method for T and N staging of RC.[1,3-5,7,8] Our data confirm that, in experienced hands, EUS is highly accurate in the staging of early rectal cancers.

The impact of EUS on the management of RC was demonstrated in a Mayo Clinic prospective blinded study.[1] In that cohort of 80 consecutive patients who had previously had a CT for staging, EUS altered patient management in about 30% of cases. The most common change precipatated by EUS was the indication for additional neoadjuvant treatment.

However, the results have not been as encouraging when ERUS is performed outside of strict research protocol. A multicenter, prospective, country-wide quality assurance study from > 300 German hospitals was designed to assess the diagnostic accuracy of EUS in RC.[13] Of 29206 patients, 7096 underwent surgery, without neoadjuvant treatment, and were included in the final analysis. The correspondence of tumor invasion with histopathology was 64.7%, with understaging of 18% and overstaging of 17.3%.[13] These numbers were better in hospitals with greater experience performing ERUS: 73% accuracy in the centers with a case load of > 30 cases per year compared with 63.2% accuracy for the centers with < 10 cases a year. Marusch and colleagues had previously demonstrated an EUS accuracy of 63.3% in a study of 1463 patients with RC in Germany.[14] Another study based out of the UK had similar findings. Ashraf and colleagues performed a database analyses from 20 UK centers and identified 165 patients with RC who underwent ERUS and endoscopic microsurgery.[15] Compared with histopathology, EUS had 57.1% sensitivity, 73% specificity, and 42.9% accuracy for T1 cancers; EUS accuracy was 50% for T2 and 58% for T3 tumors. The authors concluded that the general accuracy of EUS in determining stage was around 50%, the statistical equivalent of flipping a coin.

The low accuracy of EUS observed by German and British multicenter studies[13-15] was attributed to the difference that may exist in clinical trials at specialized centers compared with wider use of EUS in a community setting. As seen by our data, the Memphis VAMC is not a high-volume center for the treatment of RC. However, all our EUS procedures were performed and interpreted by a single operator (C. Ruben Tombazzi) with 18 years of EUS experience. We cannot conclude that no patient was overstaged, as patients receiving a stage of T3N0 or T > N0 received neoadjuvant treatment and were not included. However, we can conclude that no patient was understaged. All patients deemed to be T1 to T2N0 included in our study received accurate staging. Our results are consistent with the high accuracy of EUS reported from other centers with experience in diagnosis and treatment of RC.[1,3-5,17,18]

Although EUS is accurate in differentiating T1 from T2 tumors, it cannot reliably differentiate T1 from T0 lesions. In one study, 57.6% of adenomas and 30.7% of carcinomas in situ were staged as T1 on EUS, while almost half of T1 cancers were interpreted as T0.[17] This drawback is a well-known limitation of EUS; although, the misinterpretation does not affect treatment, as both T0 and T1 lesions can be treated successfully by local excision alone, which was the algorithm used for our patients. The choice of the specific procedure for local excision was left to the clinicians and included transanal endoscopic or surgical resections. At a mean follow-up of 32.6 months, none of the 37 patients who underwent endoscopic or surgical transanal resection had evidence of recurrent disease.

A limitation of EUS, or any other imaging modality, is differentiating tumor invasion from peritumoral inflammation. The inflammation can render images of tumor borders ill-defined and irregular, which hinders precise staging. However, the accurate identification of tumors with deep involvement of the submucosa (T1sm3) is of importance, because these tumors are more advanced than the superficial and intermediate T1 lesions (T1sm1 and T1sm2, respectively).

Patients with RC whose lesions are considered T1sm3 are at higher risk of harboring lymph node metastases.[18] Nascimbeni and colleagues had shown that the invasion into the lower third of the submucosa (sm3) was an independent risk factor for lower cancer-free survival among patients with T1 RC.[19] We did not measure the distance of the tumor to muscular layer in our study, but we relied on EUS to predict the circumferential tumor margins and guide the surgical resection. Of the 11 patients with T1 rectal adenocarcinomas and the 6 patients with tubular adenoma with high-grade dysplasia, all treated by local excision, none developed a local or distant recurrence during follow-up.

Unlike rectal adenocarcinomas, the prognosis for carcinoid tumors correlates not only with the depth of invasion but also with the size of the tumor. The other adverse prognostic features include poor differentiation, high mitosis index, and lymphovascular invasion.[20]

EUS had been shown to be highly accurate in determining the precise carcinoid tumor size, depth of invasion, and lymph node metastases.[20,21] In a study of 66 resected rectal carcinoid tumors by Ishii and colleagues, 57 lesions had a diameter of ≤ 10 mm and 9 lesions had a diameter of > 10 mm.[21] All of the 57 carcinoid tumors with a diameter of ≤ 10 mm were confined to the submucosa. In contrast, 5 of the 9 lesions > 10 mm invaded the muscularis propria, 6 had a lymphovascular invasion, 4 were lymph node metastases, and 1 was a liver metastasis.

In our series, 4 of the 14 carcinoid tumors were > 10 mm but none were > 20 mm. None of the carcinoids with a diameter ≤ 10 mm invaded the muscularis propria. Of the 4 carcinoids > 10 mm, 1 was T2N0 and 3 were T1N0. All carcinoid tumors in our series were low grade and with low proliferation indexes, and all were treated successfully by local excision.

CONCLUSION

We believe our study shows that EUS can be highly accurate in staging rectal lesions, specifically lesions that are T1-T2N0, be they adenocarcinoma or carcinoid. Although we could not assess overstaging for lesions that were staged > T2 or > N0, we were able to determine no understaging for all of our patients. In experienced hands, EUS remains a highly accurate staging tool for early rectal carcinoma.

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