## REVIEW

243  Endoscopic ultrasound in oncology: An update of clinical applications in the gastrointestinal tract  
*Valero M, Robles-Medranda C*

## MINIREVIEWS

255  Endoscopic recommendations for colorectal cancer screening and surveillance in patients with inflammatory bowel disease: Review of general recommendations  
*Huguet JM, Suárez P, Ferrer-Barceló L, Ruiz L, Monzó A, Durá AB, Sempere J*

## ORIGINAL ARTICLE

### Retrospective cohort study

263  Endoscopic resolution and recurrence of gastric antral vascular ectasia after serial treatment with argon plasma coagulation  
*Garg S, Aslam B, Nickl N*

### Observational Study

267  Utility of the balloon-overtube-assisted modified over-the-wire stenting technique to treat post-sleeve gastrectomy complications  
*Ponte A, Pinho R, Proença L, Silva J, Rodrigues J, Sousa M, Silva JC, Carvalho J*

### Randomized Controlled Trial

273  Multicenter randomised controlled trial comparing the high definition white light endoscopy and the bright narrow band imaging for colon polyps  
*Singh R, Cheong KL, Zorrion Cheng Tao Pu L, Mangira D, Koay DSC, Kee C, Ng SC, Rerknimitr R, Aniwan S, Ang TL, Goh LK, Ho SH, Lau JYW*

## CASE REPORT

282  Bladder urothelial carcinoma extending to rectal mucosa and presenting with rectal bleeding  
*Aneese AM, Manuballa V, Amin M, Cappell MS*
World Journal of Gastrointestinal Endoscopy
Volume 9 Number 6 June 16, 2017

ABOUT COVER
Editorial Board Member of World Journal of Gastrointestinal Endoscopy, Alexander Klaus, MD, MHSc, Associate Professor, Chief Doctor, Department of Surgery, Sisters of Charity Hospital Vienna, Vienna, Vienna 1060, Austria

AIM AND SCOPE
World Journal of Gastrointestinal Endoscopy (World J Gastrointest Endosc, WJGE, online ISSN 1948-5190, DOI: 10.4253) is a peer-reviewed open access (OA) academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians. WJGE covers topics concerning gastroscopy, intestinal endoscopy, colonoscopy, capsule endoscopy, laparoscopy, interventional diagnosis and therapy, as well as advances in technology. Emphasis is placed on the clinical practice of treating gastrointestinal diseases with or under endoscopy.

We encourage authors to submit their manuscripts to WJGE. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great clinical significance.

INDEXING/ABSTRACTING
World Journal of Gastrointestinal Endoscopy is now indexed in Emerging Sources Citation Index (Web of Science), PubMed, and PubMed Central.

FLYLEAF
I-III Editorial Board

EDITORS FOR THIS ISSUE
Responsible Assistant Editor: Xiang Li
Responsible Science Editor: Jin-Xin Kong
Responsible Electronic Editor: Shun-Liang Wu
Proofing Editor-in-Chief: Lian-Sheng Ma

NAME OF JOURNAL
World Journal of Gastrointestinal Endoscopy
ISSN
ISSN 1948-5190 (online)
LAUNCH DATE
October 15, 2009
FREQUENCY
Monthly
EDITORS-IN-CHIEF
Atsushi Imagawa, PhD, Director, Department of Gastroenterology, Mitoyo General Hospital, Kani-cho, Kagawa 769-1695, Japan
Juan Manuel Herrerias Gutierrez, PhD, Academic Fellow, Chief Doctor, Professor, Unidad de Gestión Clínica de Aparato Digestivo, Hospital Universitario Virgen Macarena, Sevilla 41009, Sevilla, Spain

EDITION BOARD MEMBERS
All editorial board members resources online at http://www.wjgnet.com/1948-5190/editorialboard.htm

EDITORIAL OFFICE
Xue-Xia Song, Director
World Journal of Gastrointestinal Endoscopy
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

PUBLICATION DATE
June 16, 2017
COPYRIGHT
© 2017 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non-commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
http://www.wjgnet.com/bpg/gerinfo/204

ONLINE SUBMISSION
http://www.f6publishing.com
Endoscopic ultrasound in oncology: An update of clinical applications in the gastrointestinal tract

Manuel Valero, Carlos Robles-Medranda

Manuel Valero, Carlos Robles-Medranda, Gastroenterology and Endoscopy Division, Instituto Ecuatoriano de Enfermedades Digestivas, University Hospital OMNI, Guayaquil 090505, Ecuador

Author contributions: Both authors contributed to this paper.

Conflict-of-interest statement: The authors have no conflict of interests.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Manuscript source: Invited manuscript

Correspondence to: Carlos Robles-Medranda, MD, Head of the Endoscopy Division, Gastroenterology and Endoscopy Division, Instituto Ecuatoriano de Enfermedades Digestivas, University Hospital OMNI, Av. Abel Romeo Castillo y Av. Juan Tanca Marenco, Torre Vitalis, Mezanine 3, Guayaquil 090505, Ecuador. carlosoakm@ieced.com.ec
Telephone: +593-4-2109180
Fax: +593-4-2109180

Received: January 28, 2017
Peer-review started: February 12, 2017
First decision: March 28, 2017
Revised: April 10, 2017
Accepted: May 3, 2017
Article in press: May 5, 2017
Published online: June 16, 2017

Abstract
An accurate staging is necessary to select the best treatment and evaluate prognosis in oncology. Staging usually begins with noninvasive imaging such as computed tomography, magnetic resonance imaging or positron emission tomography. In the absence of distant metastases, endoscopic ultrasound plays an important role in the diagnosis and staging of gastrointestinal tumors, being the most accurate modality for local-regional staging. Its use for tumor and nodal involvement in pre-surgical evaluation has proven to reduce unnecessary surgeries. The aim of this article is to review the current role of endoscopic ultrasound in the diagnosis and staging of esophageal, gastric and colorectal cancer.

Key words: Endoscopic ultrasound; Staging; Esophageal cancer; Gastrointestinal cancer; Gastric cancer; Colorectal cancer

© The Author(s) 2017. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Endoscopic ultrasound (EUS) has an important role in staging, establishing prognosis and optimizing therapeutic decisions. Also, it has proved to be a useful alternative therapeutic modality in surgery. In terms of cost-benefit, it reduces the number of unnecessary diagnostic or therapeutic procedures, leading to lower morbidity and mortality rates and reduced cost in cancer treatment. This review summarizes the current role of EUS in the diagnosis and staging of esophageal, gastric and colorectal cancer.

Valero M, Robles-Medranda C. Endoscopic ultrasound in oncology: An update of clinical applications in the gastrointestinal tract. World J Gastrointest Endosc 2017; 9(6): 243-254 Available from: URL: http://www.wjgnet.com/1948-5190/full/v9/i6/243.htm DOI: http://dx.doi.org/10.4253/wjge.v9.i6.243

INTRODUCTION
Endoscopic ultrasound (EUS) was first used in 1980
as a technology prototype for pancreatic cancer evaluation\[^{[6]}\]. It was designed as a combination of two techniques, endoscopy and ultrasound, allowing the visualization of the gastrointestinal mucosa as well as the tract wall in deep and surrounding structures. In 1989 its standardized indications in clinical practice were described\[^{[2]}\]. Due to the constant evolution of this technology, it is now considered an important diagnostic and therapeutic method in the oncology field. EUS has an important role in staging, establishing prognosis and optimizing therapeutic decisions\[^{[3]}\]. Also, it has proved to be a useful alternative therapeutic modality in surgery. In terms of cost-benefit, it reduces the number of unnecessary diagnostic or therapeutic procedures, leading to lower morbidity and mortality rates and reduced cost in cancer treatment\[^{[4,5]}\]. The TNM classification (American Joint Committee on Cancer, AJCC) is the most accepted staging classification and is based on the analysis of local tumor invasion (T), lymph node involvement (N) and distant metastasis (M). Staging usually begins using noninvasive imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET), which are generally better than EUS for excluding M. In the absence of metastasis, EUS has proved to be an accurate modality for assessing T and N\[^{[2]}\]. Moreover, the development of EUS-related technology such as fine needle aspiration (FNA), high frequency catheter probe, elastography and contrast enhancement has helped to improve EUS staging accuracy. EUS indications in oncology is therefore increasing\[^{[6]}\]. The aim of this review is to summarize the current role of EUS in the staging of esophageal, gastric and colorectal cancer.

**ESOPHAGEAL CANCER**

**Characteristics of esophageal cancer and clinical implications**

The prognosis of esophageal cancer (EC) is poor because these tumors are usually detected in an advanced stage. Surgery is not possible in most cases and has a high rate of morbidity and mortality. The level of tumor invasion and lymph node metastasis will determine treatment and prognosis. Therefore, EUS plays a vital role by providing an accurate T and N staging, which allows deciding on the best treatment\[^{[7]}\]. The use of EUS evaluation in preoperative staging has led to a mortality reduction of 42.1% and a better recurrence-free survival rate, compared to patients with no EUS evaluation\[^{[8]}\]. According to the TNM classification (Table 1), superficial EC includes mucosal and submucosal involvement (Tis, T1a or T1b)\[^{[9]}\]. Patients with any nodal involvement (N\(^{+}\)) or advance tumors (T2-T4a) (Figure 1) need preoperative neoadjuvant chemoradiotherapy, whereas T1 patients with no nodal metastasis can benefit from endoscopic (Tis, T1a N0) or surgical resection (T1bN0)\[^{[10-12]}\]. When different staging methods were compared, CT, MRI and PET-scan showed themselves to be better than EUS in evaluating distant metastasis (M), however EUS proved superiority in the detection of tumor stage (T) and lymph nodes (N)\[^{[13-16]}\]. One method does not have to exclude the other. The incorporation of CT, PET and EUS in preoperative staging reduces the number of unnecessary surgical procedures from 44% to 21%\[^{[17]}\].

**The role of EUS in T staging**

EC limited to the mucosa (Tis, T1a) can be treated effectively with minimally invasive endoscopic therapy, whereas submucosal (T1b) EC carries relatively high risk of lymph node metastasis and requires surgical resection. According to a meta-analysis by Puli et al\[^{[18]}\] (49 articles), EUS sensitivity and specificity for T stage was 81.6% and 99.4%, for T1, 81.4% and 96.3%, for T2, 91.4% and 94.4%, for T3, and 92.4% and 97.4% for T4 staging, respectively. The accuracy was higher for T3-T4 lesions (> 90%) than T1-T2 (65%). However, a study by Thosani et al\[^{[19]}\] reported, on the analysis of 1019 patients with only superficial EC, that EUS sensitivity and specificity was 85% and 87% for T1a and 86% and 86% for T1b respectively, with an overall EUS accuracy for superficial EC staging of > 93%.

**The role of EUS in N staging**

The lymph node (LN) metastasis in EC is considered the main fact that influences prognosis and it depends on the number of nodes involved. This pathology has a high rate of LN involvement at an early stage. T1sm (T1b) disease has a 15% to 30% rate of LN dissemination. The 7th edition of the AJCC (Table 1) classifies the N stage according to the number of metastasized lymph nodes in N1 (1 to 2), N2 (3 to 6), and N3 (≥ 7). The use of EUS evaluation in preoperative staging has led to a mortality reduction of 42.1% and a better recurrence-free survival rate, compared to patients with no EUS evaluation\[^{[8]}\]. According to the TNM classification (Table 1)\[^{[8]}\], the presence of node metastasis indicates the need of neoadjuvant therapy. Therefore, identification of the N stage is mandatory. PET and CT have a low accuracy (51%) compared to EUS\[^{[20]}\]. The evaluation of the LN features using EUS have shown that malignant nodes tend to be larger than 1 cm, round, sharply demarcated, and hypoechoic. When all these features are present there is an 85% chance of malignancy. However, only 25% of malignant LN have all four features\[^{[21]}\]. A systematic review found that EUS has a sensitivity range of 59.5% to 100% and a specificity range of 40% to 100% for N staging\[^{[22]}\]. Puli et al\[^{[18]}\] described a EUS sensitivity for N stage of 85% and showed that the use of FNA substantially improves the sensitivity and specificity of EUS nodal staging from 85% to 97% and 85% to 96% respectively, with a low rate of complications, ranging from 0% to 2.3%. Chen et al\[^{[23]}\] found an accuracy rate of 99.4% using EUS-FNA. In patients with EC, the identification of a celiac lymph node is synonymous to LN metastasis in 90% of the cases regardless of echo features and size and...
Table 1  TNM in esophageal cancer

| Primary tumor (T) | Regional lymph nodes (N) | Distant metastasis (M) |
|-------------------|--------------------------|-----------------------|
| TXX               | NX                       | M1                    |
| T0                | NO                       | M0                    |
| Tis               | N0                       | Distant metastasis    |
| T1                | N1                       | N1                    |
| T1a               | N2                       | N2                    |
| T1b               | N3                       | N3                    |
| T2                |                             |                       |
| T3                |                             |                       |
| T4                |                             |                       |
| T4a               |                             |                       |
| T4b               |                             |                       |

Therefore indicates a poor prognosis\(^{24}\). EUS-FNA for celiac lymph node diagnosis has shown a sensitivity of 72% to 83%, a specificity of 85% to 98%, and an accuracy of 94%\(^{25}\).

Limitations
The role of EUS has some limitations. It may be less accurate for assessing the T1-T2 stage compared with T3-T4. According to some authors there is a trend to overstage the depth of the submucosal invasion, with a lower accuracy rate in early T staging (64%)\(^{26}\). The use of high frequency catheter probes may improve the diagnostic accuracy in early lesions from 83% to 92%, but the results are heterogeneous\(^{27,28}\). EUS criteria are not accurate after neoadjuvant radio-chemotherapy because EUS poorly differentiates tumor from necrosis or inflammatory reaction\(^{29}\). The presence of esophageal malignant stenosis that cannot be overcome can make TNM evaluation more difficult. A recent multi-center study suggested that routine EUS examinations may not be required in all patients with EC as the inability to advance a diagnostic gastroscope through a malignant stricture correlates 100% with locally advanced disease, so that performing a EUS does not change the treatment decision\(^{30}\).

Role of EUS in Barrett’s esophagus
EUS has long been used to evaluate Barrett’s esophagus (BE)\(^{31}\). In the case of BE associated with high-grade dysplasia (HGD) or early (T1m) esophageal adenocarcinoma (EAC), the patient may benefit from endoscopy resection, but if EUS shows an advanced disease with tumor invading the submucosal, or beyond, or lymph node involvement, endoscopic therapy may not be warranted. Qumseya et al\(^{31}\) showed in a recent meta-analysis that 14% of patients referred to EUS for BE associated with HGD or EAC will have advanced cancer (> T1sm or > N1) detected by EUS that is not amenable to endoscopic treatment and which therefore changes the therapeutic approach. With EUS it was found that 4% of these patients have advanced disease in the absence of nodules. The sensitivity and specificity for T stage was 56% and 89% and for N stage was 71% and 94 % respectively\(^{31}\). However, even the data mentioned, the American College of Gastroenterology has stated that EUS routine staging of patients with BE before EMR is unwarranted as clinical decision making will rest with the EMR findings and given the possibility of over- and under-staging in patients with superficial EAC\(^{32-35}\). In case of T1a lesions the rate of lymph node (LN) involvement is low, making these lesions optimally treated by EMR\(^{36,37}\). In patients with known T1b sm1 disease, there is conflicting data with respect to the likelihood of LN invasion\(^{38,39}\). The evidence of LN involvement, especially if substantiated by FNA, means that any attempt at endoscopic therapy would be palliative and therefore EUS may have a role in assessing and sampling regional LN, given the increased prevalence of lymph node involvement in these patients compared with less advanced disease\(^{39}\).

GASTRIC CANCER

Characteristics of gastric cancer and clinical implications
Gastric cancer (GC) is the fourth most common cancer and the second cause of cancer-related deaths (10%)\(^{40}\). An accurate staging (Table 2) can be extremely useful in providing patients with the best therapeutic option. Patients with early gastric cancer, in the presence of favorable prognosis features (well-differentiated carcinoma, limited to the mucosa, diameter < 2 cm, absence of ulceration) and no lymph node involvement
Table 2  TNM in gastric cancer

| Primary tumor (T) | TX | T0 | Tis | T1 | T1a | T1b | T2 | T3 | T4 |
|-------------------|----|----|-----|----|-----|-----|----|----|----|
| Primary tumor cannot be assessed | No evidence of primary tumor | Carcinoma in situ: Intraepithelial tumor without invasion of the lamina propria | Tumor invades lamina propria, muscularis mucosae, or submucosa | Tumor invades lamina propria or muscularis mucosae | Tumor invades submucosa | Tumor invades submucosa | Tumor invades muscularis propria | Tumor penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures | Tumor invades serosa (visceral peritoneum) or adjacent structures | Tumor invades serosa (visceral peritoneum) or adjacent structures |

Regional lymph nodes (N)

| N0 | No regional lymph node metastasis |
| N1 | Metastasis in 1-2 regional lymph nodes |
| N2 | Metastasis in 3-6 regional lymph nodes |
| N3 | Metastasis in seven or more regional lymph nodes |
| N3a | Metastasis in 7-15 regional lymph nodes |
| N3b | Metastasis in 16 or more regional lymph nodes |

Distant metastasis (M)

| M0 | No distant metastasis |
| M1 | Distant metastasis |

(N0) can benefit from endoscopic resection rather than surgical resection [41,42]. On the other hand, patients with advanced gastric cancer (T3-T4 tumors or N+) need to be treated with neoadjuvant therapy (chemotherapy, radiotherapy or both) [43,44].

CT is a frequent imaging method for the preoperative staging of GC [45]. It has a high accuracy for distant metastasis (M), however its overall accuracy for loco-regional staging (T and N stages) is low, ranging from 65% to 85% [46,47]. The CT sensitivity and specificity for N stage is 77% and 78%, respectively [48]. No better results appear to be achievable with MRI or PET [49,50].

Thus, these imaging devices are mostly used to diagnose locally advanced lesions (T3-T4 or N+) or distant metastasis than early stages of GC. On the contrary, EUS is an accurate device for the loco-regional staging [51,52] (Figure 2). The employment of EUS in the preoperative stage of GC has shown to change the therapeutic management in 30% of cases, resulting in more limited surgical resections, especially in stages T1 and T3 [53].

The role of EUS in T staging

A recent meta-analysis by Maccellini et al [54] and the Cochrane Collaboration Group (2015) evaluated 66 articles (n = 7747) about GC staged with EUS. The aim was to evaluate EUS ability to separate patients with GC who would benefit from surgery without preoperative radio-chemotherapy (T1-T2) from those with advanced tumors (T3-T4) who are likely to benefit from neoadjuvant therapy. They found EUS sensitivity and specificity to discriminate T1-T2 from T3-T4 lesions to be 86% and 90% respectively. A second analysis was made to evaluate EUS ability to discriminate between patients with superficial cancers (T1 from T2 and T1a from T1b), with the intention of identifying patients who would benefit from endoscopic resection rather than surgery. The sensitivity and specificity of EUS to distinguish T1 (early GC) from T2 (muscle-infiltrating) was 85% and 90% respectively. As for the capacity of EUS to distinguish between T1a (mucosal) vs T1b (submucosal), they showed that the sensitivity and specificity was 87% and 75% respectively. They concluded that EUS can distinguish between superficial (T1-T2) and advanced (T3-T4) primary tumors with a sensitivity and specificity greater than 85%. This performance is maintained for the discrimination between T1 and T2 superficial tumors. However, EUS diagnostic accuracy is lower when it comes to distinguishing between the different types of early tumors (T1a vs T1b) [55]. This conclusion correlates with Maccellini et al [55] previous results (2011) when they described that EUS can differentiate T1-2 from T3-4 GC with high accuracy (sensitivity of 86% and specificity of 91%). Cardoso et al [56] (2012) also showed that EUS seems to identify advanced T stage (T3 and T4) better than it identifies less advanced T stage or N stage, with a combined accuracy for T staging of 75%. Puli et al [57] (2008) evaluated 22 studies (n = 1896) and described the usefulness of EUS in GC. The sensitivity and specificity by stage were, 88.1% and 100% for T1, 82.3% and 95.6% for T2, 89.7% and 94.7% for T3, and 99.2% and 96.7% for T4. Incidentally, EUS for T stage detection was more accurate in advanced cancer than in early cancer. Kwee et al [58] (2008) showed in a systematic review (18 studies), the accuracy of EUS in differentiating mucosal (T1m) from deeper GC (> T1sm) and found that sensitivity and specificity of EUS in detecting cancerous extension beyond the mucosa ranged from 18.2% to 100% (median 87.8%) and from 34.7% to 100% (median 80.2%) respectively. They concluded that the studies showed too much heterogeneity and it is still unclear whether EUS can
Table 3  TNM in rectal cancer

| Primary tumor (T) | Regional lymph nodes (N) | Distant metastasis (M) |
|-------------------|--------------------------|------------------------|
| TX Primary tumor cannot be assessed | NX Regional lymph nodes cannot be assessed | M0 No distant metastasis |
| T0 No evidence of primary tumor | N0 No regional lymph node metastasis | M1 Distant metastasis |
| Tis Carcinoma in situ: Intraepithelial or invasion of lamina propria | N1 Metastasis in 1-3 regional lymph nodes | M1a Metastasis confined to one organ or site (for example, liver, lung, ovary, nonregional node) |
| T1 Tumor invades submucosa | N1a Metastasis in 1 regional lymph node | M1b Metastases in more than one organ/site or the peritoneum |
| T2 Tumor invades muscularis propria | N1b Metastasis in 2-3 regional lymph nodes | |
| T3 Tumor invades through the muscularis propria into pericolorectal tissues | N1c Tumor deposit(s) in the subserosa, mesentry, or non-peritonealized pericolic or perirectal tissues without regional nodal metastasis | |
| T4a Tumor penetrates to the surface of the visceral peritoneum | N2 Metastasis in 4 or more regional lymph nodes | |
| T4b Tumor directly invades or is adherent to other organs or structures | N2a Metastasis in 4-6 regional lymph nodes | |
| | N2b Metastasis in 7 or more regional lymph nodes | |
| | Distant metastasis (M) | |
| | | |

accurately differentiate between mucosal and deeper GC[58].

The role of EUS in N staging

The accuracy of EUS for N staging has shown remarkable heterogeneity of results. Mocellin et al[59] described after the evaluation of 44 studies (n = 3573) an overall sensitivity and specificity of 83% and 67% respectively[60]. Cardoso et al[61] reported accuracy for N stage of 64%, sensitivity of 74%, and specificity of 80%. These results were due to the low possibility of detecting metastasized lymph nodes that are distant from the lesion[62]. Kwee et al[63] found that sensitivity and specificity of EUS varied from 16.7% to 95.3% (median 70.8%) and 48.4% to 100% (median, 84.6%). Puli et al[64] after the analysis of 22 studies (n = 1896) reported a sensitivity for N1 of 58.2% and N2 of 64.9%. The pooled sensitivity to diagnose distant metastasis was 73.2%.

Limitations

There is a remarkable heterogeneity of the evidence currently available about the ability of EUS to differentiate T1a vs T1b tumors and to diagnose lymph node metastasis (N0 vs N+). Therefore, physicians should be cautious at the time of interpreting these results. Tumor features like size and location may affect diagnostic performance of EUS. A tumor size greater than 3 cm is associated with overstaging by EUS and decreases the diagnostic accuracy to 50%[65]. The cardia, the greater curve of upper body, the lesser curve at the incisura and the pyloric channel are the most challenging areas to examine[66].

Gastric lymphoma

Even though CT has proved useful for evaluating an abnormal gastric wall thickening, EUS, on the other hand, has shown itself to be superior for examining nodal involvement, extension and depth of tumor invasion[67]. The EUS diagnostic accuracy in gastric lymphoma is 91%-95% for T stage and 77%-83% for N stage[68,69]. The use of EUS-FNA combined with flow cytometry and immunohistochemistry can improve N staging accuracy substantially[70].

EUS has also shown a significant impact on treatment decisions. Gastric lymphoma confined to the mucosal and submucosal (T1) can simply be treated with H. pylori eradication therapy. However, if EUS shows deeper invasion, chemotherapy, radiation or surgical treatment may be necessary[71]. Moreover, EUS has proven to be useful for surveillance of recurrences at an early stage[72].

RECTAL, COLON AND ANAL CANCER

Characteristics of rectal cancer and clinical implications

Accurate staging in rectal cancer (RC) is crucial for choosing the best multimodal therapy. Treatment decisions and prognosis depends on both T and N stage of the disease at the time of diagnosis[73]. In the absence of distant metastasis (M), EUS is the most accurate imaging modality for loco-regional staging (T and N stages) of rectal tumors[74]. Stage I disease includes early rectal lesions (T1-T2 N0 M0) (Table 3). While T1 lesions can benefit from endoscopic mucosal resection or transanal endoscopic microsurgery, T2 lesions need surgery[75,76]. Stage II disease with locally advanced cancer (T3-T4 N0 M0), or stage III with lymph node metastasis (T1-4 N1-2 M0) will benefit maximally and improve recurrence-free survival when neoadjuvant radio-chemotherapy is given[77,78]. Preoperative biopsies of rectal tumors may fail to diagnose an invasive carcinoma, with up to 24% false negative results. The preoperative use of EUS reduces the rate of missed carcinomas from 21% to 3%[79]. EUS compared to other imaging modalities (CT, PET/CT, MRI) is superior and more accurate in determining T stage (EUS: 87%, CT: 76% and MRI: 77%)[70,76-77]. In N stage situations, it is also superior, but the difference is less obvious and accuracy varies between studies (EUS 63%-85%, CT 56%-79% and MRI 57%-85%)[78-82]. Usually CT and PET/CT are used for distant metastasis diagnosis[81]. It is also reported that when CT was the original mode of investigation but a further EUS was done, in 31% of the cases the mode of treatment was changed because of the result[70]. The combination of CT and EUS seems to be the most cost-effective diagnostic strategy[83]. MRI has less accuracy in the T stage than EUS does,
but provides a good definition of the circumferential resection margin (CRM). While EUS is more useful for staging early RC, MRI is indicated for staging advanced disease and defines CRM. Also, it can be used in the case of stenotic tumors, when EUS is less accurate. Thus, EUS and MRI are complementary and should be both used for preoperative staging.\(^{[81,84]}\)

RC recurrence rates range from 20% to 50%, depending on how advanced the cancer is and if neoadjuvant therapy has been administered before surgery.\(^{[85,86]}\) It has been proven that there is a significant reduction in tumor recurrence when patients undergo EUS staging compared to those who do not.\(^{[87]}\) In addition to this, EUS can be used to evaluate the colorectal anastomosis during follow-up of patients operated for RC and confirm or rule out recurrence with 97% sensitivity, 100% specificity, 100% positive predictive value (PPV), 94% negative predictive value (NPV), and an overall accuracy of 98%.\(^{[88,89]}\) One limitation that has been attributed to EUS is its difficulty in differentiating between post-operative benign lesions and recurring cancer in post-operative lesions. However, the use of EUS-guided FNA increases the specificity from 57% to 97%.\(^{[85,86]}\) Thus, EUS has a key role in both preoperative staging and follow-up after surgery.

The role of EUS in T staging

Over- or under-staging leads to changes in a patient’s treatment. Surgery instead of endoscopic resection and the use of chemoradiotherapy could be wrongly indicated when there is over-staging. On the other hand, under-staging with the lack of neoadjuvant indication could lead to an insufficient treatment. According to a recent review performed by Marone et al.\(^{[90]}\) (33 articles, n = 4976), EUS assesses the tumor penetration depth into the rectal wall with an overall accuracy for T stage of about 84%, ranging from 63% to 96%, while the reported accuracy of CT and MRI are 65%-75% and 75%-85%, respectively. They showed also that EUS accuracy for T stage is strictly related to the depth of infiltration, being lower for T2 stage than for early (T1) or advanced (T3-4) RC (T1: 88%, T2: 78.4%, T3: 85.4% and T4: 80.2%)\(^{[90]}\). Similarly, a meta-analysis (42 studies, n = 5039 patients) showed that EUS has an overall RC staging sensitivity of 81%-96% and specificity of 91%-98%, showing higher sensitivity for advanced RC (95%) than early cancer (88%). The pooled sensitivity and specificity by stage was for T1: 88% and 98%, T2: 81% and 96%, T3: 96% and 91% and T4: 95% and 98%, respectively. The authors concluded that EUS should be the imaging method of choice for the T staging of RC\(^{[91]}\) (Figure 3). Superficial RC limited to the mucosa can be resected endoscopically. EUS has a high accuracy rate in differentiating T1 from T2 lesions, ranging from 81% to 95%, with an overstaging or understaging rate of 9%\(^{[92]}\). Puli et al.\(^{[93]}\) evaluated, in a meta-analysis (11 studies, n = 1791), the efficacy of preoperative EUS in staging patients with RC confined to the mucosa (T0) and found that sensitivity was 97% and specificity 96%.

They concluded that EUS should be strongly considered for staging of early RCs\(^{[93]}\).

The role of EUS in N staging

EUS role in the determination of lymph node (LN) metastasis is less precise than T staging, with a mean accuracy of 74% (range 63%-85%)\(^{[90]}\). However, the accuracy is still better than others imaging modalities like CT (56%-79%) or MRI (57%-85%)\(^{[78-81]}\). Similarly, a meta-analysis including 35 articles showed that EUS has a sensitivity of 73% and specificity of 76% for N staging. This low EUS performance is related to the difficulty in evaluating distant metastatic LN that are out of EUS scanning, discriminating between inflammatory and metastatic LN and the tendency to overlook small metastatic LN compared to larger LN\(^{[84-86]}\). The presence of all malignant features (enlarged node ≥ 1 cm, hypoechoic appearance, round shape, and smooth border) is related to 100% of PPV for malignancy, however this situation is seen in less than 25% of cases\(^{[21]}\). It is known that there is a correlation between T stage and risk of LN involvement in patients with RC. The risk varies from 6%-11% for T1, 10%-35% for T2 and 26%-65% for T3-T4 RC\(^{[90]}\). Similarly, the EUS accuracy for N staging also depends on T staging and seems to be better for advanced disease (84% in T3 compared to 48% in T1). This is explained by the fact that in T1 lesions metastatic nodes are possibly small\(^{[90]}\). On the other hand, beside EUS limitations in N staging, EUS guided FNA can be used to balance and improve the accuracy from 75% to 87%\(^{[100]}\). EUS-FNA has a sensitivity, specificity, PPV and NPV of 89%, 79%, 89% and 79% respectively\(^{[97,101]}\). The fact that EUS-FNA has a moderate NPV (77%) for N staging means that LN metastases cannot be ruled out by a negative FNA\(^{[102]}\). Even though most perirectal nodes detected by EUS in patients with RC are metastatic, it is important to confirm this. EUS-FNA should be indicated when results change the therapeutic strategy. The presence or absence of LN metastasis in T1-T2 lesions change the stage of the patient from I to III and indicates the chemoradiotherapy strategy. EUS-FNA changes patient management in 19% of the cases\(^{[70,103]}\).

Limitations

EUS performance is operator-dependent and accuracy improves with experience. This fact explains the wide range of overall accuracy for T and N staging between studies (63% to 95%)\(^{[104,105]}\). A high inter-observer variability (61%-77%) has been described according to the experience of the operator, with overstaging values of 19% and understaging of 12%\(^{[104]}\). Also, EUS seems to be less accurate in restaging RC after neoadjuvant therapy (NAT), due to the limitations in differentiating inflammation, edema, necrosis and fibrosis from neoplastic infiltration, with the risk of overstaging and overtreatment\(^{[88,106,107]}\). EUS correctly predicts complete response to chemoradiation in 50%-63% of the cases. It has an overall accuracy for T stage of 48%, with 38%
of overstaging and 14% of understaging\cite{108,109}. Another limitation is that in 14% of RC there is a stricture that cannot be traversed by the echoendoscope, leading to an inaccurate T and N staging. The presence of a stricture decreases the EUS accuracy rate for T stage from 93% to 56%. When the T stages were analyzed separately, the accuracy was 76% for T1, 72% for T2, 91% for T3 and 67% for T4 stage. Moreover, there was an 11% of over-staging and 5% of under-staging errors\cite{110}. Ultrasound catheter probes can be used to compensate this limitation. A meta-analysis (10 studies, \(n = 642\)) showed a high performance using ultrasound catheter probes for T and N staging. The pooled sensitivity and specificity were for T1: 91% and 98%, T2: 78% and 94%, T3-T4: 97% and 90%, respectively. The sensitivity and specificity for N staging were 63% and 82%, respectively\cite{111}. Finally, the circumferential resection margin (CRM) is an important factor in predicting local recurrence. MRI has been described to have a better overall accuracy compared to EUS (92% vs 84%) with similar NPV (97%), especially in mid-rectum\cite{112}. However, in low RC the accuracy in both modalities is similar (87%) with a NPV of 96%\cite{113}.

**New technologies**

EUS elastography is a software application that can analyze the elastic properties of tissues (Figure 4). Harder tissue (usually malignant) appears blue which allows one to distinguish between adenocarcinomas and adenomas with high accuracy (94%)\cite{114}. It seems that EUS elastography is better in RC staging than EUS alone especially for early cancers\cite{115}. Contrast enhanced ultrasonography (CE-US) can be used to evaluate tumor...
vascularity and response to antiangiogenic treatment (Figure 5). Computed parameters can be used to quantify tumor angiogenesis and measure vascularity changes after therapy. Finally, 3D-EUS development allows spatial display of rectal and perirectal anatomy (Figure 6). It improves accuracy for both T and N staging, better than EUS alone, especially in the middle third of the rectum. Published data shows that its accuracy for N stage improves from 65% to 85% and for T stage is 97.1% for T1, 94.3% for T2, 95.7% for T3 and 98.5% for T4.

**COLON CANCER**

Despite improvements in EUS technology that allows a forward viewing, the EUS examination of the colon has proved to be less accurate for T and N staging (81% and 52.4% respectively). This decrease is due to the difficulty in evaluating the proximal colon segments and bowel movement. Mini-probe EUS can be passed through the working channel of regular colonoscopes and can be used to evaluate lesions of the entire colon compensating for some of these limitations.

**ANAL CANCER**

EUS is useful for assessing the involvement of anal sphincters in low rectal tumors and in the staging of anal squamous-cell carcinomas. Treatment decisions in anal cancer depend on sphincter invasion and EUS has an accuracy of 96%, sensitivity of 100%, specificity of 87% and NPV of 100% in evaluating it. Clinical staging of anal cancer tends to under-diagnose sphincter invasion. Most clinically classified T1-T2 patients will have T3 lesions under EUS evaluation. Giovannini et al. confirm this in a prospective multicenter study and recommend that in T1-T2 N0 tumors, a transrectal EUS should be performed. EUS can be used also to determine multimodality therapy response. A greater proportion of T1-T2 N0 lesions classified by EUS had a complete response to treatment than those classified by conventional clinical staging (94.5% vs 80%, respectively). The use of 3D-EUS in anal carcinoma seems to add some benefits in perirectal lymph node and tumor invasion detection, when compared to standard EUS, but further studies are needed.

**CONCLUSION**

Prognosis of patients with gastrointestinal cancer is strictly related to the stage of the disease at the time of diagnosis. Therefore, an accurate staging is crucial to decide the best treatment in each patient, because of the possibility of under-staging or over-staging, with subsequent mistreatments. CT scan, MRI, PET are the imaging methods that can give better information on distant disease. EUS has proven to be essential for loco-regional staging in pre-surgical evaluation. It reduces the number of unnecessary surgeries, reduces local recurrences, improves survival outcomes and guides physicians in the development of the most appropriate therapeutic strategy. It has excellent sensitivity and specificity in accurately diagnosing T and N cancer stages. FNA substantially improves EUS outcomes by enabling tissue sampling, especially for N staging. New technologies, like elastography, contrast-enhancement EUS, high-frequency probes and 3D technology are also improving EUS accuracy. On the other hand, physicians should be warned that EUS has some limitations. EUS has low accuracy in restaging RC after treatment due to the difficulty in differentiating inflammation and tissue fibrosis from residual cancer. There is also some heterogeneity in the evidence currently available about EUS results in diagnosing superficial tumors (T1a) and LN in some situations.

**REFERENCES**

1. DiMagno EP, Buxton JL, Regan PT, Hattery RR, Wilson DA, Suarez JR, Green PS. Ultrasonic endoscopy. *Lancet* 1980; 1: 629-631 [PMID: 6102631 DOI: 10.1016/S0140-6736(80)91122-8]
2. Sreenarasimhalah J. The emerging role of endoscopic ultrasonography in cancer staging. *Am J Med Sci* 2005; 329: 247-258 [PMID: 15894867 DOI: 10.1097/00004414-200505000-00006]
3. Pungpapong S, Noh KW, Wallace MB. Endoscopic ultrasonography in the diagnosis and management of cancer. *Expert Rev Mol Diagn* 2005; 5: 585-597 [PMID: 16013976 DOI: 10.1586/14737159.5.4.585]
4. Pfau PR, Chak A. Endoscopic ultrasonography. *Endoscopy* 2002; 34: 21-28 [PMID: 11778127 DOI: 10.1055/s-2002-119394]
5. Annema JT, Versteegh MI, Veselic M, Welker L, Maurad T, Sont JK, Willems LN, Rabe KF. Endoscopic ultrasound added to mediastinoscopy for preoperative staging of patients with lung cancer. *JAMA* 2005; 294: 931-936 [PMID: 11618383 DOI: 10.1001/jama.294.8.931]
6. Gan SI, Rajan E, Adler DG, Baron TH, Anderson MA, Cash BD, Davila RE, Dominitz JA, Harrison ME, Ikenberry SO, Lichtenstein D, Qureshi W, Shen B, Zuckermand M, Fanellid RD, Lee KK, Van Gulider T. Role of EUS. *Gastrointest Endosc* 2007; 66: 425-434 [PMID: 17643438 DOI: 10.1016/j.gie.2007.05.026]
7. Luo LN, He LJ, Gao XY, Huang XX, Shan HB, Luo GY, Li Y, Lin SY, Wang GB, Zhang R, Xu GL, Li J. Endoscopic Ultrasound for Preoperative Esophageal Squamous Cell Carcinoma: a Meta-Analysis. *PLoS One* 2011; 6: e158373 [PMID: 21378380 DOI: 10.1371/journal.pone.0158373]
8. Harewood GC, Kumar KS. Assessment of clinical impact of endoscopic ultrasound on esophageal cancer. *J Gastroenterol Hepatol* 2004; 19: 433-439 [PMID: 15012782 DOI: 10.1111/j.1440-1746.2003.03304.x]
9. Edge SB. Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol* 2010; 17: 1471-1474 [PMID: 20180029 DOI: 10.1245/s10434-010-0985-4]
10. Sgourakis G, Gockel I, Lang H. Endoscopic and surgical resection of T1a/T1b esophageal neoplasms: a systematic review. *World J Gastroenterol* 2013; 19: 1424-1437 [PMID: 23539431 DOI: 10.3748/wjg.v19.i9.1424]
11. Evans JA, Early DS, Chandrakshara V, Chathadi KV, Fanellid RD, Fisher DA, Foley KQ, Huang JH, Yue TL, Pasha SF, Sharaf R, Shergill AK, Dominitz JA, Cash BD. The role of endoscopy in the assessment and treatment of esophageal cancer. *Gastrointest Endosc* 2013; 77: 328-334 [PMID: 23410694 DOI: 10.1016/j.gie.2012.10.001]
12. Altorki NK, Lee PC, Liss Y, Meherally D, Korst RJ, Christos P, Valero M et al. EUS in oncology.
Determinend by endoscopic ultrasonography. Obertop H, Tytgat GN, Focken ngs P. Outcome of patients with superficial esophageal cancers: a systematic review and meta-analysis. Gastrointest Endosc 2007; 65: 377-384 [PMID: 17321235 DOI: 10.1016/j.gie.2006.12.015]

Dyer SM, Levison DB, Chen BY, Lord SJ, Blamey S. Systematic review of the impact of lymph node staging on therapy of esophageal cancer after neoadjuvant chemoradiation. Gastrointest Endosc 1998; 48: 158-163 [PMID: 9717781 DOI: 10.1016/S0016-5107(98)70157-9]

Bang JY, Ramesh J, Hasan M, Naveeheetan U, Holt BA, Hawes R, Varadarajulu S. Endoscopic ultrasonography is not required for staging malignant esophageal strictures that preclude the passage of a diagnostic gastroscope. Dig Endosc 2016; 28: 650-656 [PMID: 27001640 DOI: 10.1111/den.12658]

Qumseya BJ, Brown J, Abraham M, White D, Wolfson H, Gupta N, Vennalaganti P, Sharma P, Wallace MB. Diagnostic performance of EUS in predicting advanced cancer among patients with Barrett’s esophagus and high-grade dysplasia/early adenocarcinoma: systematic review and meta-analysis. Gastrointest Endosc 2015; 81: 865-874.e2 [PMID: 25442088 DOI: 10.1016/j.gie.2014.08.025]

Shaheen NJ, Falk GW, Iyer PG, Gerson LB. AGC Clinical Guideline: Diagnosis and Management of Barrett’s Esophagus. Am J Gastroenterol 2016; 111: 30-50; quiz 51 [PMID: 26525079 DOI: 10.1038/ajg.2015.322]

Bergeron EJ, Lin J, Chang AC, Orringer MB, Reddy RM. Endosco-pic ultrasound is inadequate to determine which T1/T2 esophageal tumors are candidates for endoluminal therapies. J Thorac Cardiovasc Surg 2014; 147: 765-771; Discussion 771-773 [PMID: 24314788 DOI: 10.1016/j.jtcvs.2013.10.003]

Bulsiewicz WJ, Dellow ES, Rogers AJ, Pasricha S, Madanick RD, Grimm IS, Shaheen NJ. The impact of endoscopic ultrasound findings on clinical decision making in Barrett’s esophagus with high-grade dysplasia or early adenocarcinoma. Dis Esophagus 2014; 7: 409-417 [PMID: 23016606 DOI: 10.111/j.1442-2050.2012.01408.x]

Pouw RE, Heldoom N, Alvarez Herrero L, ten Kate FJ, Visser M, Busch OR, van Berge Henegouwen MI, Krishnadath KK, Weusten BL, Fockens P, Bergman JI. Do we still need EUS in the workup of patients with early esophageal neoplasia? A retrospective analysis of 131 cases. Gastrointest Endosc 2011; 73: 662-668 [PMID: 21272876 DOI: 10.1016/j.gie.2010.10.046]

Sepesi B, Watson TJ, Zhou D, Polomsky M, Little VR, Jones CE, Raymond DP, Hu R, Qiu X, Peters JH. Are endoscopic therapies appropriate for superficial submucosal esophageal adenocarcinoma? An analysis of esophagectomy specimens. J Am Coll Surg 2010; 210: 418-427 [PMID: 20347733 DOI: 10.1016/j.jacs.2010.01.003]

Pech O, Bollschweiler E, Manner H, Leers J, Ell C, Hölscher AH. Comparison between endoscopic and surgical resection of mucosal esophageal adenocarcinoma in Barrett’s esophagus at two high-volume centers. Ann Surg 2011; 254: 67-72 [PMID: 21532466 DOI: 10.1097/SLA.0b013e3181d4b168]

Leers JM, DeMeester SR, Oeezelik A, Klifpel N, Azay S, Abate E, Zehetner J, Liplham JC, Chan L, Hagen JA, DeMeester TR. The prevalence of lymph node metastases in patients with T1 esophageal adenocarcinoma a retrospective review of esophagectomy specimens. Ann Surg 2011; 255: 271-278 [PMID: 21119508 DOI: 10.1097/SLA.0b013e3181f8d42]

Nentwich MF, von Loga K, Reeh M, Uzunoglu FG, Marx A, Izbicki JR, Bogoevski D. Depth of submucosal tumor infiltration and its relevance in lymphatic metastasis formation for T1b squamous cell and adenocarcinomas of the esophagus. J Gastrointest Surg 2014; 18: 242-249; discussion 249 [PMID: 24091912 DOI: 10.1007/s11605-013-2367-2]
Valero M et al. EUS in oncology

40 Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010; 127: 2893-2917 [PMID: 21351269 DOI: 10.1002/ijc.25151]

41 Hirasawa K, Kokawa A, Oka H, Yabara S, Sasaki T, Nozawa A, Morimoto M, Numata K, Taguri M, Morita S, Maeda S, Tanaka K. Risk assessment chart for curability of early gastric cancer with endoscopic submucosal dissection. Gastrointest Endosc 2011; 74: 1268-1275 [PMID: 22015001 DOI: 10.1016/j.gie.2010.07.067]

42 Kang KJ, Kim KM, Min BH, Lee JH, Kim JJ. Endoscopic submucosal dissection of early gastric cancer. Gut Liver 2011; 5: 418-426 [PMID: 22195238 DOI: 10.5009/gnl.2011.5.4.418]

43 Paolotti X, Oba K, Burzykowski T, Michiels S, Ohashi Y, Pignon JP, Rougier P, Sakamoto J, Sargent D, Sasaki M, Van Cutsem E, Buyse M. Benefit of adjuvant chemotherapy for resectable gastric cancer: a meta-analysis. JAMA 2010; 303: 1729-1737 [PMID: 20442389 DOI: 10.1001/jama.2010.534]

44 Wagner AD, Unverzagt S, Grothé G, Grothé A, Haerting J, Fleig WE. Chemotherapy for advanced gastric cancer. Cochrane Database Syst Rev 2010; (3): CD004064 [PMID: 20238327 DOI: 10.1002/14651858.CD004064.pub3]

45 Fairweather M, Jajoie K, Sainani N, Bertagnolli MM, Wang J. Accuracy of EUS and CT imaging in preoperative gastric cancer staging. J Surg Oncol 2015; 111: 1016-1020 [PMID: 25872753 DOI: 10.1002/jso.23919]

46 Kim JW, Shin SS, Heo SH, Lim HS, Lim NY, Park YK, Jeong YY, Kang HK. The role of three-dimensional multidetector CT gastroscopy in the preoperative imaging of stomach cancer: emphasis on detection and localization of the tumor. Korean J Radiol 2015; 16: 80-89 [PMID: 2334876 DOI: 10.3348/kjr.2015.16.1.80]

47 Hur J, Park MS, Lee JH, Lim JS, Yu JS, Hong YJ, Kim KW. Diagnostic accuracy of multidetector row computed tomography in T- and N staging of gastric cancer with histopathologic correlation. J Comput Assist Tomogr 2006; 30: 372-377 [PMID: 16778609 DOI: 10.1097/01.jcatis.0000407428.20060500.00005]

48 Seeveraramn R, Cardoso R, McGregor C, Lourenco L, Mahar A, Sutrathrad R, Law C, Paszat L, Coburn N. How useful is EUS for the staging of gastric cancer? A meta-analysis. J Surg Oncol 2010; 93: 485-491 [PMID: 11725890 DOI: 10.1007/s10435-010-0581-4]

49 Yosihido K. Clinical application of ultrasound 3D imaging system in lesions of the gastrointestinal tract. Endoscopy 1998; 30 Suppl 1: A145-A148 [PMID: 9765119 DOI: 10.1055/s-2007-1001499]

50 Ahmad A, Govil Y, Frank BB. Gastric mucosa-associated lymphoid tissue lymphoma. Am J Gastroenterol 2003; 98: 975-986 [PMID: 12809817 DOI: 10.1111/j.1572-0241.2003.07424.x]

51 Palazzo L, Rosmayr G, Ruskone-Fournestraux A, Rougier P, Chausende R, Rambaud JC, Couturier D, Paolaggi JA. Endoscopic ultrasound staging in the local staging of primary gastric lymphoma. Endoscopy 1993; 25: 502-506 [PMID: 8287809 DOI: 10.1055/s-2007-1010358]

52 Caletti G, Fusaroli P, Togni L. EUS in MALT lymphoma. Gastrointest Endosc 2002; 56: S21-S26 [PMID: 12297744 DOI: 10.1016/S0016-5107(02)70081-3]

53 Ribeiro A, Vaquez-Sequeiros E, Wiersema MJ. EUS-guided fine-needle aspiration combined with flow cytometry and immunocytochemistry in the diagnosis of tissue lymphoma. J Gastroenterol 2003; 38: 485-491 [PMID: 12105829 DOI: 10.1007/s10120-003-0184-1]

54 Sackmann M, Morgner A, Rudolph B, Neubauer A, Thiede C, Schulz H, Kraemer W, Boersch G, Stolte M, Bayerdorffer E. Regression of gastric MALT lymphoma after eradication of Helicobacter pylori is predicted by endoscopic staging. MALT Lymphoma Study Group. Gastroenterology 1997; 113: 1087-1090 [PMID: 9322502]

55 Avalon R, Ahuja A, Deziel E, Peters B, Leone A, Tantaleo P, Perri F, Petriollo A, Scott N, Budillon A. Multidisciplinary approach to rectal cancer: are we ready for selective treatment strategies? Anticancer Agents Med Chem 2013; 13: 852-860 [PMID: 23272969 DOI: 10.2174/1871520613139900123]

56 Carriñá ET, Gheonea DJ, Sthufoi A. Advances in endoscopic ultrasound imaging of colorectal diseases. World J Gastroenterol 2016; 22: 1756-1766 [PMID: 26855535 DOI: 10.3748/wjg.v22.i5.1756]

57 Lee P, Oyama K, Homer L, Sullivan E. Effects of endorectal ultrasonography in the surgical management of rectal adenomas and carcinomas. Am J Surg 1999; 177: 388-391 [PMID: 10365876 DOI: 10.1016/S0002-9345(99)00073-2]

58 Harewood GC, Wiersema MJ, Nelson H, Macarty RL, Olson JE, Clay JE, Ahlquist DA, Jondal ML. A prospective, blinded assessment of the impact of preoperative staging on the management of rectal cancer. Gastroenterology 2002; 123: 24-32 [PMID: 12105829 DOI: 10.1053/gast.2002.34163]

59 Cederman B, Dahlberg M, Gillemius B, Pålham L, Rutqvist LE, Wilking N. Improved survival with preoperative radiotherapy in resectable rectal cancer. N Engl J Med 1997; 336: 980-987 [PMID: 9091798 DOI: 10.1056/NEJM199704303361402]

60 Randomised trial of surgery alone versus radiotherapy followed by surgery for potentially operable locally advanced rectal cancer. Medical Research Council Rectal Cancer Working Party. Lancet 1996; 348: 1605-1610 [PMID: 8961899 DOI: 10.1016/S0140-6736(96)63548-2]
diagnosis of perirectal recurrence of colorectal cancer. Dis Colon Rectum 2015; 58: 469-473 [PMID: 25850832 DOI: 10.1097/DCR.000000000000239]

90. Marone P, de Bellis M, D’Angelo V, Delrio P, Passananti V, Di Girolamo E, Rossi GB, Rega D, Tracey MC, Tempesta AM. Role of endoscopic ultrasonography in the loco-regional staging of patients with rectal cancer. World J Gastrointest Endosc 2015; 7: 688-701 [PMID: 26140096 DOI: 10.4253/wjge.v7.i7.688]

91. Pulri SR, Bechtold ML, Reddy JB, Choudhary A, Antillon MR, Brugge WR. How good is endoscopic ultrasound in differentiating various T stages of rectal cancer? Meta-analysis and systematic review. Ann Surg Oncol 2009; 16: 254-265 [PMID: 19018957 DOI: 10.1245/s10434-008-0231-5]

92. Marone P, Petruilo F, de Bellis M, Battista Rossi G, Tempesta A. Role of endoscopic ultrasonography in the staging of rectal cancer: a retrospective study of 63 patients. J Clin Gastroenterol 2000; 30: 420-424 [PMID: 10875472 DOI: 10.1097/00004836-200006000-00103]

93. Pulri SR, Bechtold ML, Reddy JB, Choudhary A, Antillon MR. Can endoscopic ultrasound predict early rectal cancers that can be resected endoscopically? A meta-analysis and systematic review. Dis Colon Rectum 2010; 53: 1221-1229 [PMID: 19517233 DOI: 10.1007/s10350-008-0862-9]

94. Bhutani MS, Hawes RH, Hoffman BJ. A comparison of the accuracy of echo features during endoscopic ultrasonography (EUS) and EUS-guided fine-needle aspiration for diagnosis of malignant lymph node invasion. Gastrointest Endosc 1997; 45: 474-479 [PMID: 9199903 DOI: 10.1016/S0016-5107(97)70167-7]

95. Gleeson FC, Clancy JE, Papachristou GI, Rajan E, Topazian MD, Wang KK, Levy MJ. Prospective assessment of EUS criteria for lymphadenopathy associated with rectal cancer. Gastrointest Endosc 2009; 69: 896-903 [PMID: 18718586 DOI: 10.1016/j.gie.2008.04.051]

96. Krajewski KM, Kane RA. Ultrasonography staging of rectal cancer. Semin Ultrasound CT MR 2008; 29: 427-432 [PMID: 19166040 DOI: 10.1053/j.sult.2008.10.005]

97. Wiersma MJ, Harewood GC. Endoscopic ultrasound for rectal cancer. Gastroenterol Clin North Am 2002; 31: 1093-1105 [PMID: 12498290 DOI: 10.1016/S0046-5107(01)00050-X]

98. Landmann RG, Wong WD, Hoefl J, Shia J, Guillem JG, Temple LK, Paty PB, Weiser MR. Limitations of early rectal cancer nodal staging may explain failure after local excision. Dis Colon Rectum 2007; 50: 1520-1525 [PMID: 17674104 DOI: 10.1007/s10350-007-9019-0]

99. Pulri SR, Reddy JB, Bechtold ML, Choudhary A, Antillon MR, Brugge WR. Accuracy of endoscopic ultrasound to diagnose nodal invasion by rectal cancers: a meta-analysis and systematic review. Ann Surg Oncol 2009; 16: 1255-1265 [PMID: 19219506 DOI: 10.1245/s10434-009-0337-4]

100. Park HH, Nguyen PT, Tran Q, Chang KJ. Endoscopic ultrasound-guided fine needle aspiration in the staging of rectal cancer [abstract]. Gastrointest Endosc 2000; 51: AB171 [DOI: 10.1016/S0016-5107(00)04420-7]

101. Knight CS, Eloubeidi MA, Crowe R, Jhala NC, Jhala DN, Chieng DC, Eltoum IA. Utility of endoscopic ultrasound-guided fine-needle aspiration in the diagnosis and staging of colorectal cancer. Diagn Cytopathol 2013; 41: 1031-1037 [PMID: 21932358 DOI: 10.1002/dc.21804]

102. Maleki Z, Eroz On, Geddes S, Li QK. EUS staging of rectal cancer: a useful diagnostic tool for perirectal and intraluminal lesions. Acta Cytol 2013; 57: 9-18 [PMID: 23221104 DOI: 10.1159/000342919]

103. Shami VM, Parmar KS, Waxman I. Clinical impact of endoscopic ultrasound and endoscopic ultrasound-guided fine-needle aspiration in the management of rectal carcinoma. Dis Colon Rectum 2004; 47: 59-65 [PMID: 14719152 DOI: 10.1016/j.dcol.2003-001-0003-0]

104. Kauer WK, Prantl L, Dittler HJ, Siewert JR. The value of endoscopic ultrasonography in colorectal cancer staging in routine diagnostics: a 10-year analysis. Surg Endosc 2004; 18: 1075-1078 [PMID: 15156388 DOI: 10.1007/s00464-003-9088-7]

105. Marusch F, Koch A, Schmidt U, Zippel R, Kuhn R, Wolff S, Prett J. Endoscopic ultrasound for rectal cancer.
Valero M et al. EUS in oncology

M, Wierth A, Gastinger I, Lippert H. Routine use of transrectal ultrasound in rectal cancer: results of a prospective multicenter study. *Endoscopy* 2002; 34: 385-390 [PMID: 11972270 DOI: 10.1055/s-2002-252992]

Maier AG, Barton PP, Neuhold NR, Herbstr B, Teley BK, Lechner GL. Peritumoral tissue reaction at transrectal US as a possible cause of overstaging in rectal cancer: histopathologic correlation. *Radiology* 1997; 203: 785-789 [PMID: 9169705 DOI: 10.1148/radiol.203.3.9169705]

Schizas AM, Williams AB, Meenaj J. Endoscopic staging of lower intestinal malignancy. *Best Pract Res Clin Gastroenterol* 2009; 23: 663-670 [PMID: 19744631 DOI: 10.1016/j.bpcg.2009.06.006]

Marone P, de Bellis M, Avallone A, Delrio P, di Nardo G, D’Angelo V, Tatangelo F, Pecori B, Di Girolamo E, Iaffaioli V, Lastoria S, Battista Rossi G. Accuracy of endoscopic ultrasound in staging and resting patients with locally advanced rectal cancer undergoing neoadjuvant chemoradiation. *Clin Res Hepatol Gastroenterol* 2011; 35: 666-670 [PMID: 21728549 DOI: 10.1016/j.clinre.2011.05.012]

Maor Y, Nadler M, Barshack I, Znora O, Koller M, Kudel Y, Fidder H, Bar-Meir S, Avidan-B. Endoscopic ultrasound staging of colorectal cancer: diagnostic value before and following chemoradiation. *J Gastroenterol Hepatol* 2006; 21: 454-458 [PMID: 16590874 DOI: 10.1111/j.1440-1746.2005.03927.x]

Vanagasus A, Lin DE, Stryker SJ. Accuracy of endoscopic ultrasound for restaging rectal cancer following neoadjuvant chemoradiation therapy. *Am J Gastroenterol* 2008; 99: 109-112 [PMID: 14687151 DOI: 10.1038/j.1463-1318.2002.252992]

Gall TM, Markar SR, Jackson D, Haji A, Faiz O. Mini-probe ultrasonography for the staging of colon cancer: a systematic review and meta-analysis. *Color Dis* 2014; 16: 01-08 [PMID: 24119196 DOI: 10.1111/coDi.12445]

Kim MJ. Transrectal ultrasonography of anorectal diseases: advantages and disadvantages. *Ultrasound* 2015; 34: 19-31 [PMID: 25492991 DOI: 10.14556/iusg.140531]

Granero-Castro P, Muñoz E, Frasso M, García-Granero A, Esclapez P, Campos S, Flor-Lorenzo B, García-Granero E. Evaluation of mesorectal fascia in mid and low anterior rectal cancer using ultrasonography and computed tomography. *Ultrasound Med Biol* 2015; 41: 516-522 [PMID: 25795355 DOI: 10.1016/j.ultrasmedbio.2014.11.019]

Wijetunge W, Kularatne D, Ippolito C, Balon Y, Grossman D. 3-D endorectal ultrasound in the staging of lower intestinal malignancy. *Ann Gastroenterol Hepatol* 2011; 15: 112-116 [PMID: 23118545 DOI: 10.1016/S1590-8658(11)60022-X]

Kim JC, Cho YK, Kim SY, Park SK, Lee MG. Comparative study of three-dimensional and conventional endorectal ultrasonography used in rectal cancer staging. *Surg Endosc* 2016; 12: 1280-1285 [PMID: 11988797 DOI: 10.1007/s00464-001-8277-5]

Kongkam P, Linlawan S, Aniwan S, Lakananurak N, Khemnak S, Sahakrutzrungruang C, Pattanauran J, Khomvilai S, Wasedopas N, Ritudit W, Bhutani MS, Kullavanijaya P. Renkmimrit R. Forward-viewing radial-array endoendoscope for staging of colon cancer beyond the rectum. *World J Gastroenterol* 2014; 20: 2681-2687 [PMID: 24627604 DOI: 10.3748/wjg.v20.i10.2681]

Bhutani MS, Nadella P. Utility of an upper endoendoscope for endoscopic ultrasonography of malignant and benign conditions of the sigmoid/left colon and the rectum. *Am J Gastroenterol* 2001; 96: 3318-3322 [PMID: 11774943 DOI: 10.1111/j.1572-0241.2001.00088.x]

Urban O, Kliment M, Fojtik P, Palti R, Orhalmai J, Vitez P, Holeczy P. High-frequency ultrasound probe sonography staging for colorectal neoplasia with superficial morphology: its utility and impact on patient management. *Surg Endosc* 2011; 25: 3393-3399 [PMID: 21590501 DOI: 10.1007/s00464-011-1737-7]

Assenat E, Thèzenas S, Samalin E, Bibeau F, Portales F, Azria D, Quenet F, Rouenet P, Simon Aubert B, Senesse P. The value of endorectal ultrasound in predicting the lateral clearance and outcome in patients with lower-third rectal adenocarcinoma. *Endoscopy* 2007; 39: 309-313 [PMID: 17354183 DOI: 10.1055/s-2007-966211]

Senesse P, Khemnissa F, Lemanski C, Masson B, Quenet F, Saint Aubert B, Simony J, Ychou M, Dubois JB, Rouanet P. Contribution of endorectal ultrasonography in preoperative evaluation for very low rectal cancer. *Gastroenterol Clin Biol* 2001; 25: 24-28 [PMID: 11275615]

Giovannini M, Seitz JF, Houvenaeghel G, Delpero JR, Rosello R, Gauthier A. Intrarectal and intravaginal echography in the evaluation of the extension and the monitoring of cancer of the anal canal. *Presse Med* 1989; 18: 1439-1440 [PMID: 2529535]

Giovannini M, Seitz JF, Rosello R, Houvenaeghel G, Delpero JR, Gauthier A. The value of endo-anorectal echography in the evaluation of the loco-regional extension and the monitoring of cancers of the anal canal. *Ann Gastroenterol Hepatol (Paris)* 1990; 26: 5-4 [PMID: 2189120]

Giovannini M, Seitz JF, Sfedj D, Houvenaeghel G, Delpero Jr. Transanorectal ultrasonography in the evaluation of extension and the monitoring of epidermoid cancers of the anus treated by radiotherapy or chemotherapy. *Gastroenterol Clin Biol* 1992; 16: 994-998 [PMID: 1493902]

Giovannini M, Bardou VJ, Barclay R, Palazzo L, Roseau G, Helbert T, Burtin P, Bouché O, Pujol B, Favre O. Anal carcinoma: prognostic value of endorectal ultrasound (ERUS). Results of a prospective multicenter study. *Endoscopy* 2001; 33: 231-236 [PMID: 11293755 DOI: 10.1055/s-2001-12860]

Tarantino D, Bernstein MA. Endoanorectal ultrasound in the staging and management of squamous-cell carcinoma of the anal canal: potential implications of a new ultrasound staging system. *Dis Colon Rectum* 2002; 45: 16-22 [PMID: 11786758 DOI: 10.1007/s10350-004-6108-1]

Christensen AF, Nielsen MB, Engellholm SA, Roed H, Svendsen LB, Christensen H. Three-dimensional anal endosonography may improve staging of anal cancer compared with two-dimensional endosonography. *Dis Colon Rectum* 2004; 47: 341-345 [PMID: 14991496 DOI: 10.1053/d CRC.2003.0056-2z]

P- Reviewer: Altonbary AY, Samiullah S, Sloomian BL
S- Editor: Ji FF  L- Editor: A  E- Editor: Wu HL
