Endoscopic ultrasonography-related diagnostic accuracy and clinical significance on small rectal neuroendocrine neoplasms

EUS on rectal NENs

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Abstract
This research aimed to examine the diagnostic accuracy and clinical significance of endoscopic ultrasonography (EUS) in the context of small rectal neuroendocrine neoplasms (NENs). A total of 108 patients with rectal subepithelial lesions (SELS) with a diameter of < 20mm were included in the analysis. The diagnosis and depth assessment of EUS was compared to the histology findings. The prevalence of NENs in rectal SELs was 78.7% (85/108). The sensitivity of EUS in detecting rectal NENs was 98.9% (84/85), while the specificity was 52.2% (12/23). Overall, the diagnostic accuracy of EUS in identifying rectal NENs was 88.9% (96/108). The overall accuracy rate for EUS in assessing the depth of invasion in rectal NENs was 92.9% (78/84). Therefore, EUS demonstrates reasonable diagnostic accuracy in detecting small rectal NENs, with good sensitivity but inferior specificity. EUS may also assist physicians in assessing the depth of invasion in small rectal NENs before endoscopic excision.

Key Words: Rectal neuroendocrine neoplasms; Endoscopic ultrasonography; Diagnosis; Depth of invasion

**Core Tip:** The diagnostic efficacy and clinical significance of endoscopic ultrasonography (EUS) on rectal neuroendocrine neoplasms (NENs) have not been well demonstrated owing to the infrequency of these particular disorders. In this manuscript, we compared the results of EUS with histology findings among a total of 108 patients with rectal subepithelial lesions with a diameter of < 20mm. We found that EUS demonstrates reasonable diagnostic accuracy in detecting small rectal NENs, with good sensitivity but inferior specificity. EUS may also assist physicians in assessing the depth of invasion in small rectal NENs before endoscopic excision.

**TO THE EDITOR**
Rectal neuroendocrine neoplasms (NENs) are diminutive but potentially malignant neoplasms. The management of NENs is contingent upon the dimensions of the tumor and the depth of its invasion. According to current consensus recommendations pertaining to the therapy of rectal NENs, it is recommended that endoscopic excision be considered as a viable approach for the treatment of small tumors (<2 cm) that are limited to the mucosa or submucosa, since these tumors have a low propensity for metastatic dissemination. While the predominant kind of rectal subepithelial lesions (SEls) consists of NENs, there exists a diverse range of other types, including small gastrointestinal tumors (GISTs), lymphangiomas, and neurilemnomas. Additionally, non-tumor diseases such as endometriosis, duplication cysts, and inflammatory lesions may also be seen in this context. Differentiating NENs from SEls is of paramount significance for the proper implementation of treatment interventions. Preoperative endoscopic ultrasonography (EUS) has been demonstrated in identifying and assessing invasion depth in rectal NENs, a critical factor in choosing the most suitable treatment approach. Nevertheless, the diagnostic efficacy and clinical significance of EUS have not
been well demonstrated owing to the infrequency of these particular disorders5-8. In this study, we investigated the diagnostic precision and clinical significance of EUS in relation to rectal NENs with a diameter of less than 20mm.

A retrospective assessment was conducted on 108 cases of rectal SELs with a diameter of less than 20mm, which were treated at Sun Yat-sen University Cancer Center from January 2010 to June 2021, after getting approval from the Ethics Committee of the Institutional Review Board. All of the lesions were removed using an endoscopic procedure and then subjected to histological examination. The criteria for inclusion were: (1) the lesion was in the rectum, at a distance of less than 15 cm from the anus, (2) the lesion had a diameter of less than 20 mm, and (3) prior to the endoscopic excision, EUS and radiography did not reveal any evidence of local lymph node involvement or distant metastases. The exclusion criteria were: (1) epithelial lesions, such as malignancy and adenoma, were eliminated from consideration in this study, and (2) no histological diagnosis. Prior to performing endoscopic excision, all patients underwent assessment via EUS to establish an EUS diagnosis and measure the depth of invasion. A blinded expert in EUS, who was blinded of the histology data, conducted a review of the ultrasonic pictures. The EUS expert then made a single diagnosis and evaluated the depth of invasion, which was then documented. The diagnosis and depth assessment of EUS was compared to the histology findings. Then diagnostic tests were used to determine the diagnostic accuracy of EUS. Prior to undergoing EUS and endoscopic excision procedures, all patients were duly informed about the possible risks and advantages associated with the interventions. Furthermore, they were required to submit written informed consent as a prerequisite for their participation. The techniques conducted in this study adhere to the guidelines outlined in the 1964 Helsinki Declaration and subsequent ethics that are pertinent to the research.

Table 1 presents a comprehensive overview of the clinical data analyses conducted on a cohort of 84 patients with rectal NENs. The mean ages of the participants in the study were 44.6±13.4 years, while the average size of the lesions was 7.9±3.2 mm (range, 3-20mm). A total of 11 patients had positive vertical margins, leading to a R0 resection
rate of 86.9%, with only one case in which total resection (R0) was achieved with vascular infiltration. Based on the mitoses and Ki-67 proliferation index categorization, it was determined that 89.3% (75/84) were categorized as G1, whereas 10.7% (9/84) were categorized as G2. In 7.1% (6/84) of cases, the lesions were limited to the mucosal layer, whereas in 92.9% (78/84), the lesions extended into the submucosal layer.

Table 2 displays the diagnostic outcomes of rectal SELs in 108 patients, as determined by EUS and histology. The prevalence of NENs in rectal SELs was 78.7% (85/108). The sensitivity of EUS in detecting rectal NENs was 98.9% (84/85), while the specificity was 52.2% (12/23). The positive predictive value was 88.4% (84/95), and the negative predictive value was 92.3% (12/13). The positive and negative likelihood ratios were 2.07 and 0.02, the overall diagnostic accuracy was 88.9%, and the Youden index was 0.51.

Table 3 presents a comparison of invasion depth for rectal NENs as evaluated by EUS and histology. Out of the total of 10 rectal NENs cases infiltrating the second layer (mucosa), as determined by EUS, five cases were limited to the mucosa, while the other 5 cases demonstrated invasion into the submucosa. Out of the total of 74 rectal NENs cases infiltrating the third layer (submucosa), as determined by EUS, only one case was limited to the mucosa, while the other 73 cases demonstrated invasion into the submucosa. The overall accuracy of EUS in assessing the invasion depth of rectal NENs was 92.9% (78/84).

The current investigation revealed that EUS demonstrates a notable level of sensitivity, but accompanied by a comparatively lower level of specificity, when used for diagnosing rectal NENs. EUS accurately detected 98.9% (84/85) of rectal NENs, with just one case being misinterpreted as GIST. Out of the 23 additional rectal SELs, twelve cases (52.2%) were accurately identified and categorized as non-NENs. Moreover, eleven cases of non-NENs were inaccurately identified as NENs, including ten cases of inflammatory lesions and one case of neurilemmoma. Hence, the presence of inflammatory nodules localized into the second or third layer may potentially lead to misdiagnosis as NENs due to their comparable acoustic symptoms. Additionally, our
study revealed that EUS has reasonable accuracy in assessing the depth of invasion in rectal NENs. Nevertheless, in cases where the rectal NENs were assessed by EUS and found to be limited to the mucosa, there was a significant likelihood of inaccurate determination of the depth of invasion, indicating a shallower depth. According to the findings of our research, a significant proportion (92.9%) of rectal NENs demonstrated invasion into the submucosal layer. Therefore, in cases where rectal NENs are determined to be limited to the mucosa using EUS assessment, it is still necessary to do submucosal dissection to obtain a complete resection.

This study has limitations that should be taken into consideration. Since magnetic resonance imaging (MRI) and EUS are widely used in the diagnosis and evaluation of rectal NENs, it is meaningful to compare the results between MRI and EUS. However, it is with regret that rectal NENs included in our study were all less than 2 cm and the vast majority of them were not examined by MRI. Besides, artificial intelligence-assisted endoscopic diagnosis has been a research hotspot. Therefore, it is suggested that future research can introduce artificial intelligence to further improve the diagnostic value of EUS on rectal NENs.

In summary, EUS demonstrates acceptable diagnostic precision in identifying rectal NENs, exhibiting a commendable level of sensitivity. However, it displays a less desirable level of specificity, which poses difficulties in distinguishing NENs from other SELs, particularly inflammatory nodules. EUS may provide valuable assistance in assessing the depth of invasion for rectal NETs prior to endoscopic excision.
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