Diagnostic and Interventional Endoscopy

Research Article

Evaluation of Rectal Neuroendocrine Tumors Treated with Endoscopic Resection

Levent Aktaş[1], Hakan Çamyar[2], Sezgin Vatansever[2]

[1]Divison of Internal Medicine, Department of Gastroentrology, Atatürk Training and Research Hospital, İzmir Katip Çelebi University, İzmir, Türkiye
[2]Department of Gastroenterology, Atatürk Training and Research Hospital, İzmir Katip Çelebi University, İzmir, Türkiye

Cite this article as: Aktaş L, Vatansever S. Evaluation of rectal neuroendocrine tumors treated with endoscopic resection. *Diagn Interv Endosc,* 2025, 4(1), 0133, DOI:10.5152/DiagnIntervEndosc.2025.24133.

Corresponding author: Levent Aktaş, e-mail: aktas-03@hotmail.com

Received: January 9, 2025 **Accepted:** March 24, 2025 **Publication Date:** October 14, 2025 **DOI:** 10.5152/DiagnIntervEndosc.2025.24133

Abstract

Objective: Rectal neuroendocrine tumors (rNETs) are a rare type of tumor that belong to a larger group called neuroendocrine neoplasms. These tumors are divided into two main categories: well-differentiated neuroendocrine tumors (NET G1 and G2) and poorly differentiated neuroendocrine carcinomas (NEC G3). rNETs are often not noticed because they do not show symptoms, but they can sometimes cause bowel problems or hormone-related symptoms. Small rNETs are usually treated with endoscopic resection, while larger tumors may need surgery or other treatments.

Materials and Methods: The aim of this study is to look at the clinical and histopathological features of rNETs treated with endoscopic submucosal dissection (ESD). The focus was on factors like tumor size, location, and the Ki-67 index, and how they affect patient outcomes.

Results: In this study, the average age of patients was 52.6 years, and half of them were women. Most of the tumors were located between 5 and 10 cm from the rectum (56.3%). The majority of tumors were smaller than 10 mm (81.3%), and 56.3% of them were Grade 1. There was no significant correlation between tumor size and the Ki-67 index ($r = 0.215$, $P = .424$).

Conclusion: Endoscopic submucosal dissection is a good treatment for rNETs that are smaller than 10 mm, with a high success rate in removing the tumor completely. For larger tumors or those with higher Ki-67 indices, careful monitoring is needed because they may have a higher risk of spreading.

Keywords: Endoscopic submucosal dissection, ESD, Ki-67 proliferation index, rectal neuroendocrine tumors, rNETs, tumor size

INTRODUCTION

Rectal neuroendocrine tumors (rNETs) are a rare subgroup of neuroendocrine neoplasms (NENs). According to the World Health Organization classification, these tumors are divided into two main groups: well-differentiated neuroendocrine tumors (NET G1 and G2) and poorly differentiated high-grade neuroendocrine carcinomas (NEC G3). The classification primarily relies on Ki-67 proliferation index and mitotic activity, which are critical in determining tumor grade and prognosis, as well as guiding treatment strategies.[1-3]

Rectal neuroendocrine tumors are typically asymptomatic and are often discovered incidentally during endoscopic procedures performed for unrelated conditions. Symptomatic cases may present with altered bowel habits, abdominal pain, or hormone-related symptoms such as flushing and diarrhea. The indolent nature of these tumors frequently leads to delayed diagnosis and limits treatment options at advanced stages.[1,4]

The diagnostic process includes detailed clinical evaluation, endoscopic imaging, and histopathological biopsy. Minimally invasive techniques, such as endoscopic submucosal dissection (ESD) or endoscopic mucosal resection, are recommended for small tumors (<1 cm). However, larger tumors may require surgical resection, and cases with metastatic disease often involve chemotherapy or targeted therapies.[5,6]

This study aims to retrospectively evaluate the histopathological and clinical characteristics of rNETs treated with endoscopic resection. Additionally, the study explores the impact of tumor size, localization, and Ki-67 proliferation index on clinical outcomes and disease management.

METHODS

This retrospective study included 16 patients diagnosed with rNETs who underwent ESD at the institution between 2018 and 2024. Patients were identified from the hospital's endoscopy database, and their clinical, demographic, and histopathological data were analyzed.

Endoscopic Submucosal Dissection Procedure

All patients underwent ESD without anesthesia. The procedure was performed using a high-definition colonoscope equipped with a water-jet and a dual knife. After marking the tumor margins with cautery, submucosal injection of hidroxyetilstarch and indigo carmine was applied to elevate the lesion. The tumor and its surrounding submucosal tissue were meticulously dissected en bloc. Procedural success was defined as complete resection of the lesion with clear lateral and deep margins.

Data Collection

Demographic data, including age and sex, were recorded. Tumor characteristics, such as size, localization, grade, and Ki-67 proliferation index, were retrieved from pathology reports. Patients with high-risk features (e.g., high Ki-67 index, larger tumor size) underwent 68Ga positron emission tomography (PET) imaging to evaluate potential metastatic disease.

Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM SPSS Corp.; Armonk, NY, USA). Descriptive statistics were used to summarize patient demographics and tumor characteristics. Continuous variables were expressed as mean ± SD or median (range), and categorical variables were presented as frequencies and percentages.

To assess the relationship between tumor size and Ki-67 proliferation index, Spearman's rank correlation test was employed due to the small sample size and non-parametric nature of the data. A *P*-value of <.05 was considered statistically significant.

Ethics Comittee Approval

This study was approved by the Ethics Committee of İzmir Katip Çelebi Univeristy (Approval no: 0332 Date: December 19, 2024) and written informed consent was obtained from all patients prior to the procedure.

RESULTS

Table 1 presents the demographic characteristics of patients, tumor localization, and tumor grade.

A Spearman's rank correlation test was performed to evaluate the relationship between tumor size and Ki-67 proliferation index. No significant correlation was observed (r=0.215, *P*=.424).

Table 1. Characteristic features of patients and lesions X

Characteristics	n=16
Age	52.6 ± 10.7
Gender (female)	8 (50%)
Rectum localisation	
0-5 cm	5 (31.3%)
5-10 cm	9 (56.3%)
10-15 cm	2 (12.5%)
Size (mm)	9 (4-16)
<5 mm	2 (12.5%)
5-10 mm	10 (62.5%)
>10 mm	3 (18.8%)
Staging	
Grade 1	9 (56.3%)
Grade 2	6 (37.5%)
Grade 3	0 (0%)

DISCUSSION

Rectal neuroendocrine tumors are a rare subset of NENs, and their clinical management largely depends on tumor size, grade, and proliferative index. In this study, the majority of the tumors were ≤10 mm in size, consistent with lower metastatic potential. However, tumors >10 mm present in 18.8% of patients are known to carry a significantly higher risk of lymphovascular invasion and metastasis. This aligns with the established association between tumor size and metastatic behavior, highlighting the importance of size as a critical prognostic factor.[7,8]

Endoscopic submucosal dissection was employed in all cases and proved effective for achieving complete resection with clear margins. Endoscopic submucosal dissection's capability to provide en bloc resection minimizes recurrence risks and allows accurate histopathological evaluation. These findings reinforce ESD's role as the preferred approach for rNETs ≤20 mm without muscular invasion. However, tumors larger than this threshold or with invasive features may require surgical resection.[9]

One limitation of this study is its focus solely on tumors suitable for endoscopic resection. This introduces a selection bias, excluding more advanced or aggressive cases. Additionally, the small sample size limits statistical power, particularly in detecting correlations such as between tumor size and Ki-67 index, which showed no significant relationship (r=0.215, *P*=.424). Furthermore, the retrospective design precludes an analysis of long-term outcomes like recurrence or survival, which warrants further prospective investigation.

Patients with larger tumors or higher Ki-67 indices should be closely monitored due to their elevated metastatic risk. Incorporating advanced imaging techniques, such as 68Ga PET, and exploring biomarkers could enhance the risk stratification of rNETs. Future multicenter studies with diverse patient populations could provide stronger evidence to refine management strategies.

MAIN POINTS

- Endoscopic submucosal dissection was successfully applied for the treatment of rNETs in a single-center cohort.
- The majority of lesions were ≤10 mm and histopathologically classified as Grade 1, supporting the safety of ESD for small, well-differentiated tumors.
- En bloc resection with negative margins was achieved in all patients, enabling accurate histopathological evaluation.
- There was no statistically significant correlation between tumor size and Ki-67 proliferation index.
- Patients with lesions >10 mm or higher Ki-67 values may require closer follow-up due to their potential metastatic risk.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the Ethics Committee of İzmir Katip Çelebi University (Approval No: 0332 Date: 19.12.2024)

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – H.C., S.V.; Design – L.A.; Supervision – S.V.; Resources – H.C., S.V.; Materials – H.C., S.V.; Data Collection and/or Processing – S.V.; Analysis and/or Interpretation – L.A.; Literature Search – L.A., H.C.; Writing Manuscript – L.A., S.V.; Critical Review – S.V.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. Zheng Y, Guo K, Zeng R, et al. Prognosis of rectal neuroendocrine tumors after endoscopic resection: a single-center retrospective study. *J Gastrointest Oncol*. 2021;12(6):2763-2774. [CrossRef]
2. Shah MH, Goldner WS, Benson AB, et al. Neuroendocrine and adrenal tumors, version 2.2021, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2021 19(7):839-868.
3. Sultana Q, Kar J, Verma A, et al. A comprehensive review on neuroendocrine neoplasms: Presentation, Pathophysiology and Management. *J Clin Med*. 2023;12(15):5138. [CrossRef]
4. Hallet J, Law CH, Cukier M, Saskin R, Liu N, Singh S. Exploring the rising incidence of neuroendocrine tumors: a population-based analysis of epidemiology, metastatic presentation, and outcomes. *Cancer*. 2015;121(4):589-597. [CrossRef]
5. Levy AD, Sobin LH. Gastrointestinal carcinoids: imaging features with clinicopathologic comparison. *RadioGraphics*. 2007;27(1):237-257. [CrossRef]
6. Zhou C, Zhang F, We Y. Efficacy of endoscopic mucosal resection versus endoscopic submucosal dissection for rectal neuroendocrine tumors ≤10mm: a systematic review and meta-analysis. *Ann Saudi Med*. 2023;43(3):179-195. [CrossRef]
7. Öberg KE. Gastrointestinal neuroendocrine tumors. *Ann Oncol*. 2010;21(suppl 7):vii72-vii80. [CrossRef]
8. Sun P, Zheng T, Hu C, Gao T, Ding X. Comparison of endoscopic therapies for rectal neuroendocrine tumors: endoscopic submucosal dissection with myectomy versus endoscopic submucosal dissection. *Surg Endosc*. 2021;35(11):6374-6378. [CrossRef]
9. Hong SM, Baek DH. Endoscopic treatment for rectal neuroendocrine tumor: which method is better? *Clin Endosc*. 2022;55(4):496-506. [CrossRef]