

Answering reviewers

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Title: Is endoscopic ultrasonography essential for endoscopic resection of small rectal neuroendocrine tumors?

Reviewer#1: This article suggested that EUS may not be necessary when we decide the treatment strategy for small rectal NETs ≤ 10 mm. The comments were below 1. If the pathological diagnosis after resection was not NETs, for example, leiomyoma, lymphoma, lymphangioma, or SMT-like adenocarcinoma, treatment method might be different. Thus, the authors need to get more information by means of biopsy or something. 2. The authors use the terms "Is or Ila" with SMT, but these terms should be used for epithelial lesions. 3. As the authors said, the follow-up interval was quite short. If they had data about long term follow-up for the candidates, the reliability of their findings would raise, because rectal NETs progress very slowly.

(response)

Thank you for reviewing.

1. Actually, we did not perform biopsy before endoscopic resection because biopsy can make fibrosis and it will be hard to remove submucosal lesion. After removing, we evaluated the pathologic finding, we enrolled just in case of rectal NETs. I think rectal NET has endoscopic morphologic features, it is not hard to distinguish other subepithelial lesions. We added "We did not perform biopsy before ER because biopsy can induce fibrosis and complicate removal of the submucosal lesion. After endoscopic removal, all resected specimens were evaluated histologically using light microscopy at both low and high power magnifications." in Methods.

2. The terms "Is or Ila" are revised as suggested by the reviewer. "Is or Ila" are

revised “sessile or slightly elevated” and “IIb” is revised “flat” by Paris classification.

3. The reviewer is correct. As we stated in discussion, one of limitations of our study is short-term follow-up duration. “Of the 120 lesions evaluated, 23 had follow-up at ≥ 24 mo.” is in results. We followed up 7 patients of over 3 years, they did not recur until now and we added range (154-2148 days) in table 1.

Reviewer#2: Thank you for your work and I have some comments as below; how many patients were included in the study? 118 or 120 it is not clear. if there is patient with more than one tumor please give information about it and correct the number in table according to that. the mean values should be given with standard deviation or you should give median with range. a Patient with LV invasion required additional surgery; What kind of surgery had been done? In discussion section you mentioned that incidence of NET in Kore is 48%, it is so high since the overall incidence of colon cancers is less than that? please explain. you mentioned that Lymph node metastasis in tumors less than 10 mm is 9,7. This rate is not low so do you think that additional treatment like as adjuvant radiotherapy or lymphadenectomy is needed?

(response)

Thank you for reviewing.

1. A total of 120 small rectal NETs in 118 patients were included in this study. Among the 132 rectal NETs that were treated with endoscopic resection, 118 patients with a total of 120 small (≤ 10 mm) rectal NETs were enrolled in this study. We added the sentence that “Two of the patients had two small rectal NETs each.” in methods. I revised like this; “One hundred and eighteen patients (76 men and 42 women, with a mean age of 50.7 ± 11.4 years (range 18-77 years)) with a total of 120 rectal NETs were enrolled in this study. Two patients had two rectal NETs each.” in results

2. We added standard deviation and range in age and follow-up periods. We revised median follow-up with SD and mean follow-up with range in the table 1.

3. A patient with LN invasion took low anterior resection surgery. We revised “Lymphovascular invasion was found in 1 patient who had a 6-mm tumor that required additional surgical therapy of low anterior resection.”

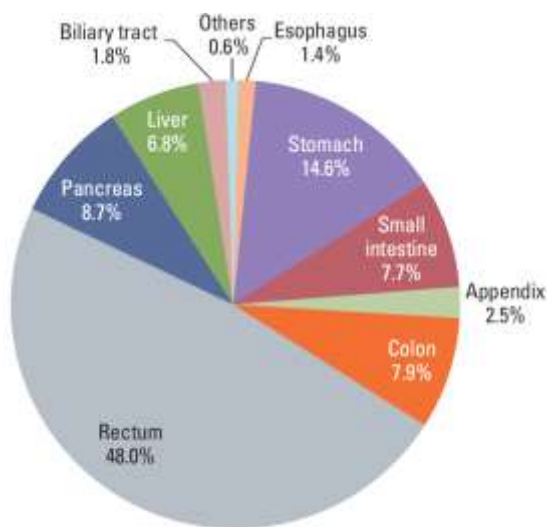


Fig. 1. Distribution of 4,951 gastroenteropancreatic neuroendocrine tumors according to the organ system.

4. We mentioned that incidence of NET in Korea is 48%, it is confusing expression. 48% means the ration of rectal NET among gastroenteropancreatic neuroendocrine tumors [Cancer Res Treat 2012;44:157-65]. We revised the sentence “The overall incidence of rectal NETs is rapidly increasing, and the incidence in Korea, in particular, has reached 48% among gastroenteropancreatic NETs”

5. Reviewer has made an important point. 9.7% is not low. As we mentioned in discussion, risk factors (size, muscularis propria invasion, histologic grade, lymphovascular invasion, neural invasion, atypical endoscopic feature) are important to predict metastasis. Our study and recent Korean study [Turk J Gastroenterol 2014;25:657-660] showed low metastasis rate in small rectal NETs. We added “In our study, lymphovascular invasion was found in 1 patient. However, more studies are needed to verify the low metastasis rate in recent studies.” in discussion. So I do not think that additional therapy is necessary in small rectal NETs removed by endoscopic procedure.