In Response to Reviewer #1:

1. Describe what change in stool habit? – melena/constipation/ obstipation/hematochezia

Response: Thanks for the reviewer's comment. Change in stool habit is defined as: yellow, thin, pasty stools 3-5 times a day, without mucus and blood.

2. What is a hypofractionated adenocarcinoma? – define clearly in manuscript

Response: Thanks for the reviewer's comment. According to the WHO Classification of Digestive System Tumor, hypofractionated adenocarcinoma is defined as: the cancer cells are short columnar or indefinite, arranged in small nests or strands, and basically without glandular tube structure.

3. What prompted to have the specimen re-read at the Department of Pathology of the Second Affiliated Hospital of Zhejiang University School of Medicine? Explain in manuscript

Response: Thanks for the reviewer's comment. In order to quickly improve the pathological understanding of early GI tumors in our hospital and better carry out our ESD surgery, the pathology department of our hospital has established a working exchange platform with the pathology

department of the Second Affiliated Hospital of Zhejiang University School of Medicine, and the pathology of ESD postoperative specimens is routinely exchanged and discussed with them.

4. OUTCOME – is it "One year after ESD?"

Response: Thanks for the reviewer's comment. We correct in the manuscript.

5. When should surgeons suspect it no to be prepiaroneal?

Response: Thanks for the reviewer's comment. Before treatment we can infer the pathological type from the morphology, vascular structure, and surface structure of the lesion by plain endoscopy, electronic stained endoscopy (narrow band imaging endoscopy NBI), and magnified endoscopy. And clinical staging is performed by preoperative completion of ultrasound endoscopy, CT, and MRI to clarify the depth of lesion infiltration, whether it reaches or exceeds the muscular layer, and whether there are regional lymph node metastases or distant metastases. When the depth of submucosal infiltration is ≤1000μm, it is a superficial submucosal infiltration and is an indication for endoscopic treatment; when the depth of submucosal infiltration is >1000μm, it is a deep submucosal infiltration and additional surgical treatment needs to be considered. Therefore, the surgeon can get a general conclusion by

comprehensive analysis before surgery to determine whether it is a precancerous lesion, and the gold standard is pathological results.

In Response to Reviewer #2:

1. The authors spoke in 1st person frequently. It would have been better to use passive voice.

Response: Thanks for the reviewer's comment and we improve the quality of English.

2. In case summary paragraph, the authors said "Ultrasound colonoscopy was also performed and a homogeneous hypoechoic mass about 0.52 x 0.72 cm in size was seen at the lesion, protruding into the lumen with clear borders and invading the submucosa". I think U/S cannot detect the submucosal invasion of colorectal adenoma. It is a histopathological finding.

Response: Thanks for the reviewer's comment.The normal intestinal wall has 5 echogenic rings of high-low-high-low-high in the ultrasound image. The third layer is the submucosa, which appears as a high echogenic band on ultrasound images and is the clearest and easiest to identify on ultrasound images, so it is useful as an aid in determining the depth of colon mass invasion of the colon.

3. Also in case summary paragraph, “a tubular adenoma with high-grade intraepithelial neoplasia (intramucosal carcinoma)”. colorectal adenoma with high grade dysplasia is totally different from intramucosal carcinoma.

Response: Thanks for the reviewer’s comment.High-grade intraepithelial neoplasia includes severe heterogeneous hyperplasia, carcinoma in situ and intramucosal carcinoma. To provide a more precise description of this pathology, we have made an addition stating that the pathology is an intramucosal carcinoma.

4. There are no references in the introduction section.

Response: Thanks for the reviewer’s comment and references are added in the manuscript.

5. The definition and description of colorectal adenoma with pseudoinvasion are not mentioned in the introduction.

Response: Thanks for the reviewer’s comment.Both neoplastic and non-neoplastic epithelium of the mucosa may enter the submucosa for some reason, a phenomenon known as pseudoinvasion or misplaced epithelium of the submucosa. When part of the gland of a colorectal adenoma mistakenly enters the submucosa, it is called pseudoinvasion of the adenoma.

6. There is no pathological diagnosis called “Tubular adenoma with high-grade intraepithelial neoplasia (intramucosal carcinoma)”. Either tubular adenoma with high grade dysplasia or intramucosal carcinoma.

Response: Thanks for the reviewer’s comment. High-grade intraepithelial neoplasia includes heavy heterogeneous hyperplasia of the epithelium and carcinomas that do not penetrate the mucosal muscle layer, but also includes intramucosal carcinomas.

7. For more details regarding colorectal adenoma and adenocarcinoma the authors would have been better to revise WHO classification of tumors of digestive system book, chapter of colorectal tumors.

Response: Thanks for the reviewer’s comment. The WHO (World Health Organization) classification of gastrointestinal tumors defines colorectal cancer as "an epithelial malignancy of colorectal origin, diagnosed as cancer only when the tumor penetrates the mucosal muscle to the submucosa".

8. I think there is confusion in the final diagnosis. In the paragraph of final diagnosis, the authors wrote “tubular adenoma with high-grade

intraepithelial neoplasia (intramucosal carcinoma) involving the adenolymphatic complex", while in discussion they wrote "The lesion was found to be a rare high-grade tubular adenoma of the rectum with pseudoinvasion of the submucosa only after late review of the pathology". Which one of them was the case?

Response: Thanks for the reviewer's comment. In the final diagnosis, we describe the diagnosis given by the Department of Pathology of the Second Affiliated Hospital of Zhejiang University School of Medicine. Here it may be more helpful to understand this diagnosis if we describe the concept of lymph gland complex. The intestinal mucosal collecting lymph nodules are called lymphatic gland complex when they contain crypt epithelium and often cross the mucosal muscle layer into the submucosa. And in a few cases colorectal adenomas can participate in constituting the lymphatic gland complex. It is a morphological pattern of colorectal adenoma with pseudoinfiltration of the submucosa.

In the discussion, we would like to express that the pathological findings of the rectal lesion in this patient were concluded after the pathology department of our hospital in communication with the pathology department of the Second Affiliated Hospital of Zhejiang University School of Medicine, which finally confirmed that it was a high-grade tubular adenoma of the rectum with submucosal pseudoinfiltration.

9. What did the authors mean by the term “adenolymphatic complex”?

Response: Thanks for the reviewer’s comment. What we mean by adeno-lymphatic complex is equivalent to the concept of lymphatic gland complex.

In Response to Reviewer #3:

Good work.

Response: Thanks for the reviewer's affirmation.