

We truly appreciate the insightful and constructive comments of the reviewers. We find our manuscript greatly improved by addressing the following points.

Replies to Reviewer 1 (Reviewer's code: 00724436):

1) The high prevalence of ulcers is unusual: possible explanations should be discussed. Is it possible that the ulcers were post APC ulcers, or was it a severity feature of the radiation proctitis?

Response: We apologize for the confusion. We have added two statements in the MATERIALS AND METHODS on Line 9, Page 8 and in the DISCUSSION on Line 23, Page 13, respectively.

“The exclusion criteria for the present study included the following: (1) patients had received treatments other than medical therapy prior to APC, such as APC, formalin irrigation, fecal diversion and proctectomy.”

“According to the Vienna grading system, ulceration represents a severity feature of the radiation proctitis. Goldner et al. thought patients who had received high doses at a certain volume could develop histopathological changes such as ulcers in addition to congested mucosa or telangiectasia.”

2) The APC mode should be specified.

Response: Thank you for the excellent advice. As your suggestion, we have added a statement in the MATERIALS AND METHODS on Line 2, Page 9:

“An argon flow of 1.0~3.0 L/min at a power of 40~60 W was applied to the lesions in 1~2 -second pulses by the endoscopist, while an argon flow of 1.8 L/min at a power of 50 W was routinely adopted.”

3) The PCF is a pediatric colonoscope and not a standard colonoscope.

Response: We are sorry for the mistake. The relevant section has been revised:

“The 2.3 mm diameter front-firing APC probe was inserted through the working channel of a **therapeutic** colonoscope (PCF-Q260J; Olympus).”

4) PEG based bowel preparation is recommended before APC. The fact that some patients were prepared only with enema should be omitted.

Response: We appreciate the reviewer’s insightful comment. We admit that complete antegrade bowel preparation helps to make a clear view, which might increase the efficacy of APC. But for patients whose limited lesion range had been confirmed by previous complete colonoscopy or who could not tolerate PEG, preparation with enemas was an alternative. During the APC procedure, we used a water pump (OFP-2; Olympus) to rinse away blood or other contaminating material, which helped to make a clear view. According to the guidelines advocated by ASCRS, the use of retrograde enema, complete antegrade bowel preparation, or no bowel preparation, all appear to be safe for rectal APC procedures. (**Reference:** Paquette IM, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Treatment of Chronic Radiation Proctitis. Dis Colon Rectum 2018;61:1135-1140.)

5) A conclusion sentence is missing.

Response: Thank you for the excellent advice. As your suggestion, we have added a statement in the DISCUSSION on Line 16, Page 15:

“In conclusion, the long-term efficacy of APC for hemorrhagic CRP is uncertain in patients with telangiectasias present on more than 50% of the surface area and ulcerated area greater than 1 cm². Ulcerated area greater than 1 cm² is also a risk factor for severe complications.”

Replies to Reviewer 2 (Reviewer's code: 00503883):

1) The volume of PEG solution preparation was not described and neither how many patients were submitted of rectal enemas.

Response: Thank you for the excellent advice. As your suggestion, we have added a statement in the MATERIALS AND METHODS on Line 19, Page 8:

“Patients maintained a clear fluid diet for 24 hours before the APC procedure and underwent standard bowel preparation with 2-liter polyethylene glycol. Preparation with enemas was performed in a few patients: 8.9% (4/45) for the first APC procedure, 29.4% (5/17) for the latter procedures.”

2) The success rate of procedures was low (68.9%) when compared to medical literature (79%-100%). There was also a high rate of severe complications (13.3% of patients). We could consider patients of this study had more severe chronic radiation proctitis and were previously treated with various topics agents. But also these results were probably related to inadequate endoscopic technique: excessive argon flow or high power and contact of the probe within the rectal mucosa. The authors used a too wide range of argon flow of 1-3 L/min and probably most of them were submitted to high argon flow near to 3 L/min.

Response: We appreciate the reviewer's insightful comment. In our study, 24 patients (53.3%) were categorized as having severe radiation proctitis prior to APC therapy according to the endoscopic severity of hemorrhagic CRP based on telangiectasia distribution, the surface area involved and the presence of fresh blood. Half of the patients were treated successfully by APC. Our results were consistent with Zinicola et al. In the Zinicola et al. study, only one of the three patients with severe radiation proctitis was treated successfully by APC.

In our study, an argon flow of 1.0~3.0 L/min at a power of 40~60 W was applied to the lesions in 1~2 -second pulses by the endoscopist, while an argon flow of 1.8 L/min at a power of 50 W was routinely adopted (added in the MATERIALS AND METHODS on Line 2, Page 9). In the case of a large ulceration, the endosocopist tended to restrict the application of APC in terms of argon flow, power and time (seen in the DISCUSSION on Line 30, Page 13). Unfortunately, given that this study is retrospective, we were unable to assess the correlation between APC settings and the incidence of severe complications. In the univariate analysis, distribution of telangiectasias, surface area covered by telangiectasias and presence of fresh blood were not significantly associated with severe complications, the only risk factor was the ulceration greater than 1 cm². Further large-cohort prospective studies are warranted to assess the correlation between APC settings and the incidence of severe complications.

(**Reference:** Zinicola R et al. Haemorrhagic radiation proctitis: endoscopic severity may be useful to guide therapy. Int J Colorectal Dis 2003;18:439-444)