

Dear Editors, Dear Reviewers,

Thank you for your thoughtful review of our manuscript entitled " **INCIDENTAL ANAL ¹⁸ FDG UPTAKE: SHOULD WE FURTHER EXAMINE THE PATIENT?**" Manuscript 53494. Please find below the point-by-point replies to the comments of the reviewers.

The revised article is submitted as an attachment. Changes requested by reviewers and for formatting for World Journal of Clinical Cases are highlighted in yellow.

This study demonstrated the anal uptake of FDG and therapeutic intervention retrospectively. Although this is an important analysis on how to address the incidental anal uptake of FDG, I think there are some points that need to be explained more clearly.

Comment 1 The comparison of the patients who were offered treatment and those who were not is the main point of this article. Therefore, it is important to describe more clearly the rationale for and the definition of offering treatment. Was the decision to offer treatment decided only on the diagnosis and its severity? Are there any considerations about the patient's preference or prognosis that need to be taken into account?

We thank the reviewer for this comment. Treatments were offered in case of symptomatic disease or if there was a risk of extension and/or aggravation of the disease. The treatment was chosen according to the habits of the practitioner. The retrospective nature of the study does not make it possible to find out whether the patient's preference was taken into account. The prognosis of the primary disease was not associated with the treatment proposal or not. The text was completed as follows: "Treatments were offered in case of symptomatic disease or if there was a risk of extension and/or aggravation of the disease. The treatment was chosen according to the habits of the practitioner" (in methods) and "Among the 15 patients with progressive PET-CT (considered poor prognosis), 8 had treatment and 7 had no treatment (p=0.46) (in results).

Comment 2 The final diagnoses of the examined patients should be listed and compared between the patients who were offered treatment and those who were not. I think it is more important to detect neoplastic lesions than benign hemorrhoids.

We thank the reviewer for this comment. The diagnoses of the examined patients were listed in results section "Among the 48 patients who underwent examinations, 33 (69%) had the following anorectal diseases: haemorrhoidal disease (n=19), anal fissure (n=6), recurrence of rectal adenocarcinoma on the coloanal anastomosis (n=2), condyloma (n=3), faecal impaction (n=1), suppuration (n=1) and solitary rectal ulcer syndrome (n=1) " and reported in Figure 2. These data have been included in the table along with details of whether or not the treatment is proposed. We agree that it is more important to detect neoplastic lesion.

Comment 3 The patients who were offered treatment appear to have been symptomatic more frequently than the patients who were not offered treatment. I think it is important to detect patients who should be offered treatment among asymptomatic patients. Among the 29 asymptomatic patients, were there any differences in FDG up-take between the patients who were offered treatment and those who were not? Please consider multivariate analysis, including FDG uptake and symptoms as factors affecting the offering of treatment.

We thank the reviewer for this comment. Of the asymptomatic patients, 18/29 were diagnosed (haemorrhoidal disease (n=12), anal fissure (n=2), condyloma (n=3) and solitary rectal ulcer syndrome (n=1)) and 8/29 were offered treatment. Among the 29 asymptomatic patients, the ¹⁸FDG PET/CT metabolic parameters differed significantly between treated and untreated patients. The group of asymptomatic patients that was offered treatment had higher SUV_{max} and SUV_{mean} measurements (p= 0.03 for both) and lower MV41 and MV30 values than the group asymptomatic patients without treatment (p= 0.02 and p=0.03, respectively). The text has been modified.

In a multivariate analysis including the presence of symptoms, the diagnosis (yes) and the SUV_{mean} > 6.1 cm³, the factor significantly associated with the treatment was the SUV_{mean} > 6.1 cm³ (OR= 6.87 [1.18-29.9], p= 0.03). This data has been included in the result section.