

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 75649

Title: Cumulative incidence and risk factors for pouch adenomas associated with familial adenomatous polyposis following restorative proctocolectomy

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02941525

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: South Korea

Manuscript submission date: 2022-03-03

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-04 13:48

Reviewer performed review: 2022-03-05 08:39

Review time: 18 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

In the present retrospective study performed on 95 patients with familial adenomatous polyposis (FAP) with proctocolectomy, Ryu et al found pouch adenomas in the 25.3% of patients and demonstrated that severe colorectal polyposis before colectomy was the main associated risk factor. Main comments: 1) A radical linguistic revision by an English native speaker is necessary. 2) In the “study population” paragraph of Methods section, Authors have reported the process of patients selection. However, this is a result and it should be moved in the appropriate section. In the above mentioned paragraph, Authors must only report inclusion and exclusion criteria. 3) Please report which was the indication to proctocolectomy: prophylaxis, cancer finding or presence of >100 polyps. This variable should be integrated in Cox multivariate analysis as well. 4) I do not understand why, in the multivariate analysis reported in Table 3, duodenal adenoma was entered in the multivariate despite a $p = 0.54$ in the univariate. Authors should enter multivariate analysis parameters significant or close to statistical significance at univariate, or variables with a relationship plausibility such as NSAID use. 5) Considering that presence of small bowel polyps at videocapsule endoscopy correlated with severity of Spiegelman classification, this agrees with the finding in table 2 about duodenal adenomas. Please comment.

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 01587889

Position: Editorial Board

Academic degree: MD, MSc, PhD

Professional title: Associate Professor, Consultant Physician-Scientist

Reviewer's Country/Territory: United States

Author's Country/Territory: South Korea

Manuscript submission date: 2022-03-03

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-10 00:51

Reviewer performed review: 2022-03-10 02:57

Review time: 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

Ryu et al. is retrospective study conducted in a single tertiary center aimed to evaluated cumulative incidence, time to development, and risk factors associated with pouch adenoma subsequent to restorative proctocolectomy with ileal pouch-anal anastomosis (RPC-IPAA) for familial adenomatous polyposis (FAP). A total of 95 FAP patients who underwent RPC-IPAA were consecutively included for a mean follow-up period of 88 months. Pouch adenomas were found in 24 (25.3%) cases with a median time of 52 months to their first formation. Tubular adenomas were detected in most patients (95.9%). There were no high-grade dysplasia or malignancies. Of the 24 patients with pouch adenoma, 13 patients removed all detected adenomas. Among the 13 patients, 4 (38.5%) patients recurred. In 11 (45.8%) patients with numerous polyps within the pouch, 7 (63.6%) patients showed pouch adenoma progression. The cumulative risk of a pouch adenoma at 5, 10, and 15 years after pouch surgery was 15.2%, 29.6%, and 44.1% respectively. Severe colorectal polyposis of more than 1000 was a significant risk factor for development of pouch adenoma (HR, 2.49; 95% CI, 1.04-5.96; p=0.041). The authors concluded that pouch adenomas occur at a fairly high rate in FAP patients who undergone RPC-IPAA. There was no spontaneous decrease or disappearance of adenoma. A high colorectal polyp count is associated with development of pouch adenoma. Thus, close endoscopic surveillance of pouch is essential and new guidelines for management of pouch adenomas are needed.

- What was the indication for RPC-IPAA for FAP? was it for adenoma prophylaxis, cancer finding or presence of >100 polyps or both. Can the authors clarify that?
- The presented data should be integrated in Cox multivariate analysis and the multivariate analysis reported in Table 3 is the



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appropriate to be used. • Why duodenal adenoma was entered in the multivariate (despite a $p = 0.54$ in the univariate). Why? • A comment is needed regarding presence of small bowel polyps at videocapsule endoscopy correlated with severity of Spiegelman classification, this agrees with the finding in Table 2 about duodenal adenomas. • Clinical characteristics of the study patients according to presence of pouch adenomas, the statistics and figures need to be carefully revisited prior to publishing this paper. • Minor language/grammatic issues.

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00562236

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor, Assistant Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: South Korea

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Reviewer chosen by: AI Technique

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Review time: 2 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
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SPECIFIC COMMENTS TO AUTHORS

Cumulative incidence and risk factors for pouch adenoma in familial adenomatous polyposis patients following a restorative proctocolectomy, by Ryu et al. is a retrospective study evaluating the risk of developing pouch adenoma after restorative proctocolectomy in patients with familial adenomatous polyposis. The study has some flaws, reported by the authors in the discussion, first of all the retrospective design that does not allow reliable conclusions, being impossible to have the same inclusion criteria for all patients. Each patients had different approaches in the management of pouch adenomas found during the follow-up. However, the number of patients analyzed, over a 30-year period is considerable, and it may add some knowledge to the topic. I have no major concern about the design of the study. No new finding with respect to the past relevant literature was found. However, the manuscript is well organized, and data presented in a simple way, but with order and they are well explained. Some flaws need to be corrected: 1. Results. Paragraph: Clinical characteristics of the study patients with and without pouch adenomas. Line 9. In patients without pouch adenoma, the use of NSAIDs was not significantly more used for the treatment of desmoid tumors, according to the statistical criteria stated by the authors in the methods section of the manuscript, though the frequency is undoubtedly higher and near the statistical significance. 2. Fig. 1. The number of patients at risk is not well aligned with time after IPAA. This should be corrected. 3. Table2. I do not understand what is the difference between: number of colorectal polyps, and colorectal polyps < or > 1000. According to the table in the group of patients without pouch adenoma the upper limit of the range is 500, whereas, below, 7 such patients had 1000 or more adenomas at the time of surgery.

The authors should explain this discrepancy, or better define the two parameters. 4.
English polishing and corrections are needed all along the manuscript.

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03668600

Position: Editorial Board

Academic degree: MD, MSc, PhD

Professional title: Professor, Staff Physician

Reviewer's Country/Territory: Brazil

Author's Country/Territory: South Korea

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-11 09:58

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Review time: 5 Days and 3 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: [Y] Anonymous [] Onymous Conflicts-of-Interest: [] Yes [Y] No
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SPECIFIC COMMENTS TO AUTHORS

The study presents valuable information in a cohort of 95 patients with FAP. Some comments: English needs revision in the whole manuscript. Please make a better sentence expressing the association of duodenal adenomas and pouch adenomas in the following sentence: "In addition, patients with duodenal adenomas developed pouch adenomas more frequently (66.7% vs 42.3%, $p=0.039$)". Assess if you tried to state that the presence of duodenal adenomas was associated with pouch adenomatosis?

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Academic degree: MD, MSc, PhD

Professional title: Associate Professor, Consultant Physician-Scientist

Reviewer's Country/Territory: United States

Author's Country/Territory: South Korea

Manuscript submission date: 2022-03-03

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2022-05-13 15:59

Reviewer performed review: 2022-05-13 16:19

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors responded to all the questions raised by the reviewer point by point fulfilling expectations and is acceptable for publication in its current version.