

October 25th 2018

Dear editor and reviewers,

Thank you very much for reviewing our manuscript. We found the comments and suggestions very helpful and constructive and we have addressed all reviewers' comments. Please see below our answers to specific comments, and the page references to the changes in the text of the manuscript (highlighted in yellow and with „Track Changes”). We are confident that you will find the new version of the manuscript much improved, and consider it for publication in your journal.

Please find enclosed the edited manuscript in Word format (file name: 42530-Edited_review.doc).

Title: Current Strategies for Malignant Pedunculated Colorectal Polyps

Authors: Adriana Ciocalteu, Dan Ionut Gheonea, Adrian Saftoiu, Liliana Streba, Nicoleta Alice Dragoescu, Tiberiu Stefanita Tenea- Cojan

Name of Journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 42530

The manuscript has been revised according to the editor's and reviewers' suggestions:

A. (1) Please check and revise the manuscript according to the CrossCheck report.

The authors' answer: The manuscript has been revised according to the CrossCheck report and missing references were inserted. We consider that data emphasised by CrossCheck such as authors' affiliation (e.g. Adrian Săftoiu, Department of Gastroenterology, Research Center of Gastroenterology and Hepatology, University of Medicine and Pharmacy of Craiova, Craiova, Romania) and statistical information taken from the cited studies should not be included in the report.

(2) The language of the manuscript is not so good. A Non-Native Speakers of English Editing Certificate is required.

The authors' answer: The manuscript has been thoroughly revised by two of the authors (DIG and AS) who have near-native English language skills and an extensive experience with scientific publications in English. A language certificate is also provided. There are stylistic and language corrections throughout the text of the revised manuscript.

(3) In order to attract readers to read your full-text article, we request that the first author make an audio file describing your final core tip. This audio file will be published online, along with your article. Please submit audio files according to the following specifications: **Acceptable file formats:** .mp3, .wav, or .aiff. **Maximum file size:** 10 MB.

The authors' answer: We added the audio file as requested.

B. Revision has been made according to the suggestions of the reviewers.

Reviewer's code: 03478635

This is an interesting review article about the current strategies for malignant pedunculated colorectal polyps. In the section for definitions, classifications and histopathological characteristics, the citation for the explanation for high-grade dysplasia may be added. In section for strategies for patients on antiplatelet therapy or anticoagulants, the definition of high risk procedures may be described more in detail. The conclusion may be revised to be concise. The careful proofreading is needed.

The authors' answer:

- In the section for „Definitions, classifications and histopathological characteristics“, two citations for the explanation for high-grade dysplasia have been added (page 5) and we corrected the reference number accordingly. [Rex DK, Hassan C, Bourke MJ. The colonoscopist's guide to the vocabulary of colorectal neoplasia: histology, morphology, and management. *Gastrointest Endosc.* 2017;86(2):253-63 [PMID:28396276 DOI: 10.1016/j.gie.2017.03.1546] and [Geramizadeh B, Marzban M, Owen DA. Malignant Colorectal Polyps;

Pathological Consideration (A review). *Iran J Pathol.* 2017;12(1):1-8 [PMCID: PMC5938718 PMID: 29760747]

- With regard to "Strategies for patients on antiplatelet therapy or anticoagulants", additional information on polypectomy as a "high risk procedure" was added and the section was reduced in order to maintain the focus on pedunculated polyps (page 15):

"The risk of bleeding as the most often adverse effect of polypectomy and particularly the higher risk of bleeding of pedunculated polyps were already described in section "Challenges in endoscopic resection techniques". Therefore, endoscopic polypectomy is considered among high risk procedures based on the risk of bleeding which is increased by the addition of antiplatelet or anticoagulant therapy. In this group of patients, the risk of haemorrhage should be balanced against the risk of thrombosis when discontinuation of therapy is performed.

These patients with MPCP and indication of polypectomy should be managed as summarised in Table 2, according to the most recent British Society of Gastroenterology (BSG) and European Society of Gastrointestinal Endoscopy (ESGE) general recommendations^[71]"

- We have improved the discussion and the conclusion in order to be more concise. Too detailed paragraphs were deleted and others were rephrased. We made a separate section for UNRESOLVED ISSUES AND AREAS FOR FURTHER RESEARCH (page 17) . Thus, "Conclusion" (page 18) was reduced to:

CONCLUSIONS

There are still unresolved issues requiring detailed recommendations according to the patient's and polyp's risk factors in order to avoid an overuse of surveillance procedures. Provided future novel imaging technologies and increased pathological recognition of high risk markers for angio- lymphatic invasion will be detected, it will be easier to decide on the optimal follow-up plan and therapy.

- Proofreading has been carefully performed and a Language certificate is provided.

Reviewer's code: 00001114

Comments to the Author: Thank you for giving me the opportunity to review the manuscript: "Current Strategies for Malignant Pedunculated Colorectal Polyps" by Dr. Ciocalteu A. This paper is well-written and comprehensive review about

this subject. This review has a lot of information including general colorectal polyp issues. Sometimes, it seems redundant and too long. Consequently, I feel topic of current strategy for malignant pedunculated colorectal polyps seems defocused. 1. I recommend the authors should write exclusively about pedunculated colorectal polyps. For example, most of sections “STRATEGIES FOR PATIENTS ON ANTIPLATELET THERAPY OR ANTICOAGULANTS”, “ADEQUATE FOLLOW- UP AFTER RESECTION” were deleted or shorten because I feel this paragraph is generality of colorectal polyps. 2. I recommend the authors use tables to explain this topics, for example, “FACTORS PREDICTING LYMPH NODE STATUS IN MALIGNANT PEDUNCULATED COLORECTAL POLYPS”.

The authors' answer:

1. - In “STRATEGIES FOR PATIENTS ON ANTIPLATELET THERAPY OR ANTICOAGULANTS”, the paragraphs from guidelines were deleted and a table was added instead in order to summarise the management for this cathegory of patients (table 2- pages 32- 33). The section was reduced to (page 15):

“The risk of bleeding as the most often adverse effect of polypectomy and particularly the higher risk of bleeding of pedunculated polyps were already described in section “Challenges in endoscopic resection techniques”. Therefore, endoscopic polypectomy is considered among high risk procedures based on the risk of bleeding which is increased by the addition of antiplatelet or anticoagulant therapy. In this group of patients, the risk of haemorrhage should be balanced against the risk of thrombosis when discontinuation of therapy is performed.

These patients with MPCP and indication of polypectomy should be managed as summarised in Table 2, according to the most recent British Society of Gastroenterology (BSG) and European Society of Gastrointestinal Endoscopy (ESGE) general recommendations^[71] “

- “ADEQUATE FOLLOW- UP AFTER RESECTION” section was shorten and we kept emphasis on pedunculated polyps (pages 15-17). The following general information was deleted:

„The recent recommendations of US Multi-Society Task Force on Colorectal Cancer endorsed by the American Society for Gastrointestinal Endoscopy^[75] address only the use of colonoscopy in the follow-up of patients with resected colorectal cancer with curative intent and insist on the fact that the colorectum

should be carefully cleared of synchronous neoplasia in the perioperative period, without any particular information on early cancer in pedunculated polyps. „

Fortunately, pedunculated polyps are unusual in the rectum. Though, rectal cancer is generally associated with a higher risk of local recurrence than in other segments of the colon, and additional considerations for surveillance^[77], such as endoscopic ultrasound for better detection of suspicious lymph nodes and recurrences^[75], are suggested.

In a long-term prospective study on 25 consecutive patients with MPCP treated with snare cautery polypectomy^[56], the author concluded that short-term outcomes after removal appeared to be similar to those with a nonmalignant polyp.

To our knowledge, to date there are no particular issues including optimal treatment and surveillance of subgroups such as synchronous colorectal cancers and malignant pedunculated polyps, multiple malignant pedunculated polyps or malignant pedunculated polyps associated to chronic inflammatory bowel disease.

2. A table was added in order to resume “FACTORS PREDICTING LYMPH NODE STATUS IN MALIGNANT PEDUNCULATED COLORECTAL POLYPS” as recommended (table 1- page 31).

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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