



April 15, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9921-edit.doc).

Title: Small Bowel Adenocarcinoma and Crohn's Disease Do we really know any more than we did 50 years ago?

Author: Caitlin Cahill, Philip H. Gordon, Andrea Petrucci, Marylise Boutros

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 9921

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated:

- Running title added as follows: Small bowel adenocarcinoma in Crohn's Disease
- Institution updated with postal code and city as requested: ¹ McGill University Department of Surgery / Sir Mortimer B. Davis Jewish General Hospital Colorectal Surgery G-304, Montreal, Canada H3T 1E2
- The format of the author contributions was revised according to the revision policy format as follows: Cahill C, Gordon PH, Boutros M contributed equally to this work; Cahill C, Gordon PH, Boutros M designed the research; Cahill C, Petrucci A and Gordon PH performed the research, Petrucci A performed the data collection for our institutional series; Cahill C, Gordon PH, Boutros M analyzed the data; Gordon PH, Boutros M, Petrucci A, Cahill C wrote the manuscript; Gordon PH and Boutros M revised the manuscript
- The title of the author in the Correspondence section was added as requested: Marylise Boutros MD, FRCS(C)
- The following 5 key words were added as requested: cancer risk, cancer, malignancy, incidental carcinoma, late complications of Crohn's disease, inflammatory bowel disease
- A core tip (102 words) has been added: The risk of developing small bowel adenocarcinoma is greater in patients with Crohn's disease than in the general population. Numerous risk factors for developing small bowel carcinoma in Crohn's disease have been postulated. Protective factors have been less frequently studied however several factors have been suggested. The clinical presentation of small bowel carcinoma in Crohn's disease usually mimics the presentation of a Crohn's exacerbation thus resulting in late diagnosis. The prognosis of Crohn's associated small bowel carcinoma has been noted to be poorer than the *de novo* small bowel carcinomas. There is a need to elucidate screening modalities to facilitate earlier

diagnosis and treatment.

- In the references section: We added PubMed citation numbers and DOI citations to the reference list when available. We provided the first page of the paper for those without PMID and DOI. We also added a list of all authors for each paper.

2 Revision has been made according to the suggestions of the reviewer

- Thank you for the review and the comments.
- We changed the last statement in the second paragraph of the 'Clinical Presentation' section according to the reviewer's suggestion in order to tone down the recommendation for surgery as follows: Therefore, it is prudent to consider a surgical assessment of patients with longstanding symptomatic Crohn's disease who fail to respond to conservative management.
- The prognosis section was rearranged according to suggestions of the reviewer to eliminate the mention of Widmar et al twice in the same section for the same work. The following statement was removed from the second paragraph: Widmar et al^[23] noted an average 36 month survival rate of 69.3%, with sub-group analysis as follows: node positive 49%, node negative 79.3%, localized 92.3%, and metastatic 33.3%.
- With regards to the following suggestion "In all 3 tables- I would add the odds ratio and P values if know for each of the studies cited and just add the reference # near each values. This would be much more beneficial for the readers.":
 - We had considered to do as was suggested by the reviewer in the initial submission for Tables 1 and 2 however due to use of different statistical tests, methods of reporting, completeness of reporting, heterogeneity of studies and sample sizes within studies, and generally weak study designs in the available literature, we felt that there was not sufficient clear raw data or statistical analyses to consistently report an effect measure and a significance level for each factor and citation. Thus, we felt that reporting several *p* values or ORs, whenever available, would be inconsistent and misleading; hence we opted for a narrative review. The goals of Tables 1 and 2 are to review some of the suggested risk and protective factors for small bowel adenocarcinoma in Crohn's disease that are mentioned in the literature, rather than to quantify the risks as we feel that this cannot yet be done with the available literature and data.
 - This suggestion is not applicable to Table 3 as Table 3 is simply a compilation of the histopathologies that have been noted.

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

Sincerely yours,



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