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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 35495

Title: Colonoscopy surveillance for advanced adenomas does not always prevent colorectal cancer

Reviewer's code: 00069988

Reviewer's country: Croatia

Science editor: Ze-Mao Gong

Date sent for review: 2017-08-05

Date reviewed: 2017-08-05

Review time: 0 Hour

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Excellent study. Only limitation is that is retrospective but due to big number of cases it has scientific impact. No additional queries.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 35495

Title: Colonoscopy surveillance for advanced adenomas does not always prevent colorectal cancer

Reviewer's code: 00503404

Reviewer's country: Canada

Science editor: Ze-Mao Gong

Date sent for review: 2017-08-05

Date reviewed: 2017-08-08

Review time: 2 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

An interesting paper, in a nice, well-described cohort, analysis is solid. One may come to a different conclusion though that current guidelines are strong enough. The interval cancer of 1.8% at the same location as the polyp is for sure less than the possible missed polyp rate even when colonoscopy is performed in a well-preped patient with good standards. So, I believe that data should be interpreted as, interval cancer rate is low but not zero. Therefore please modify discussion and conclusion. Moreover cancers at other location are for sure nothing else than missed polyp, which reflect reality. An other comment is if authors have noted any time trends and association with year of initial colonoscopy?

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 35495

Title: Colonoscopy surveillance for advanced adenomas does not always prevent colorectal cancer

Reviewer's code: 02543019

Reviewer's country: Italy

Science editor: Ze-Mao Gong

Date sent for review: 2017-08-05

Date reviewed: 2017-08-11

Review time: 6 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This paper reports the incidence of colorectal cancer in a cohort of subjects under colonoscopy surveillance after advanced/serrated adenoma resection. Data are interesting and the paper is well written. Major comments: None Minor comments: Abstract: the methods section of the abstract should be rewritten in order to better describe patients' selection. Page 6, paragraph 2. This phrase should be removed here as it describes results: "From this group 4160 patients had at least one surveillance exam following the index polypectomy for their AA/TSA/ASSA." Page 6, paragraph 3. Figure 1 should be cited in the first paragraph of the results section of the paper as it describes results and not methods. Page 8, paragraph 2. Demographic (age, sex) characteristics of the 4610 patients with surveillance colonoscopy should be reported here as well as the number and time interval of surveillance colonoscopies (e.g. using



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mean, median or quartiles...). Page 8, paragraph 3. "These 84 patients were compared to a randomly selected cohort of 252 of the AA/TSA/ASSA patients who did not develop interval CRC." Authors should better explain in the methods section why they compared these 84 patients to a randomly selected cohort and not to the entire cohort the AA/TSA/ASSA patients who did not develop interval CRC. The same comment applies to the last paragraph of page 9. Figure 1: A box with the total number of patients with AA/TSA/ASSA should be placed at the top of the flow chart.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 35495

Title: Colonoscopy surveillance for advanced adenomas does not always prevent colorectal cancer

Reviewer's code: 03476438

Reviewer's country: Belgium

Science editor: Ze-Mao Gong

Date sent for review: 2017-08-05

Date reviewed: 2017-08-20

Review time: 15 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

This study deals with an innovative, well-specified clinical question. The manuscript has been well conducted and the paper has been clearly written and is interesting. However, there are minor concerns: - The title is too risky and not supported by the conclusions of the study. - In the abstract, the introduction is long and methods are not explained at all. - There is no consensus on the definition of interval CCR. The authors should explain the concept of "interval CCR" in methods. - They use the same abbreviation (EMR) for two meanings.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 35495

Title: Colonoscopy surveillance for advanced adenomas does not always prevent colorectal cancer

Reviewer's code: 01430778

Reviewer's country: Taiwan

Science editor: Ze-Mao Gong

Date sent for review: 2017-08-05

Date reviewed: 2017-08-22

Review time: 16 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Comments on Manuscript No. 35495 The study reported the rate of CRC following index polypectomy for patients with AA/TSA/ASSA was 3 %. 1.8% of CRC developed at the index polyp site while 1.2% arose at a location distinct from the index polypectomy site. The authors tried to find the risk factors for CRC following index polypectomy. There are several issues in the study have to be addressed. 1. In the section of statistical analysis, why the authors included only cancer occurring at one year after the ultimate polypectomy? But in the section of results, the authors calculated the median time from the index polypectomy to interval cancer development was 3.5 years for patients who developed CRC after the index polypectomy was not seen on the next surveillance. The data seemed to be conflicted. 2. The authors tried to find the risk factors for the CRC following index polypectomy. The control group patients (with



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index polypectomy and not later develop CRC) were “randomly” selected. The method how to random selection of control group and the ration of the method use should be explained. 3. In the section of results, the causes associated with CRC development in patients who developed interval CRC at the section site included non-adherence to the recommended surveillance interval (27.4%), incomplete resection of high risk polyp (25%) and unknown causes (30%). The causes associated with interval cancer development at another site were non-adherence to recommended surveillance interval (31.5%), unknown cause (27.8%) and incomplete colonoscopy (36.0). As we know, interval cancer is defined as “colorectal cancer diagnosed after a screening or surveillance exam in which no cancer is detected, and before the date of the next recommended exam” (Sanduleanu S, et al. Gut 2015;64:1257-1267). Therefore, the CRC developed due to non-adherence to the recommended surveillance cannot be called as interval cancer.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 35495

Title: Colonoscopy surveillance for advanced adenomas does not always prevent colorectal cancer

Reviewer's code: 03473233

Reviewer's country: Italy

Science editor: Ze-Mao Gong

Date sent for review: 2017-08-05

Date reviewed: 2017-08-23

Review time: 17 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

I read with interest the manuscript 'Colonoscopy surveillance for advanced adenomas does not always prevent colorectal cancer?' by Mouchli et al. The Authors retrospectively analysed a cohort of 4610 patients who underwent a received a diagnosis of advanced adenoma or traditional serrated adenoma or advanced sessile serrated adenoma at colonoscopy and were followed up at least with one colonoscopy, in order to determine the frequency of interval colorectal cancer (iCRC). They also nested a case-control analysis in order to evaluate some risk factors associated with the development of iCRC. Here are my comments. 1. Abstract/Results/Figure 1: I find quite misleading referring to a cohort of 14663 subjects. In fact, the paper refers to patients who had a diagnosis of AA/TSA/ASSA not associated with CRC, and with at least one surveillance colonoscopy. Only 4610 patients satisfied these criteria and this is the

number of cases that was actually studied. All the others do not add any information to the study. 2. Abstract. Please add the mean duration of follow up. 3. Abstract: please specify in the methods the inclusion criteria for patients 4. Abstract: please specify in the methods that the risk factors for iCRC were calculated on a sample of cases and controls, and report the corresponding numbers. 5. Core tip: You state that "However, screening colonoscopy has a 3.5% false negative rate for detection of CRC, resulting in 17% of patients who had undergone colon screening within 3 years being diagnosed with CRC". These figures do not appear in the main text of the paper; please report them e.g. in the introduction, with the corresponding references. 6. Introduction: please add a reference to the very first sentence. 7. Introduction/discussion: You state that "Surveillance is recommended 3 years after removal of AA, TSA, or advanced SSA". In fact, this applies to the US (please specify), but in other parts of the world different recommendations have been produced. For instance see the European guidelines for quality assurance in colorectal cancer screening and diagnosis (<http://www.kolorektum.cz/res/file/guidelines/CRC-screening-guidelines-EC-2011-02-03.pdf>), that introduced the category of intermediate risk adenomas and recommended a 1-year interval after removal of high-risk adenomas and a 3-year interval for intermediate-risk adenomas. Discussing the possible impact of the EU guidelines on your findings would be valuable for European readers. 8. Introduction. The last paragraph could be improved by clearly declaring the aims of the study. Moreover, I did not fully understand the usefulness of the last sentence. Did I miss something? 9. Methods: definition of ASSA: please define the "higher number" of synchronous polyps. 10. Results, first paragraph. You found that CRC was diagnosed in 1.67% TSA/ASSA patients and in 3.14% AA patients. Please state if this difference is statistically significant. Throughout the whole paper, AA, TSA and ASSA are considered together. However, it would be highly informative to report whether you observed any differences among the two/three categories of patients. 11. Results, second paragraph. In the text you report a series of percentages that are difficult to understand. For instance, the reader has to look at table 1 in order to understand that 47.6% vs 33.7% refer to the proportion of subjects older than 70 years. Instead, the text should be self-explicative. 12. Results, Figure 2b. The x-axis (years of follow up time) stops at 10 years, while in the text you refer to a median survival up to 15.2 years. I suggest to increase the x-axis of the Figure up to at least 16 years. 13. You included in the study patients with the index colonoscopy performed between 1990 and 2010. During this long period substantial changes in technology, procedures, knowledge about the different types of lesions took place, as well as - reasonably - in the knowhow and technical ability of endoscopists. Therefore it would be not surprising to find a significant temporal trend in the development of CRC during surveillance. I suggest to introduce the time-axis in your

analysis. 14. Discussion, last paragraph. I agree with you that “this is the first study to determine risk factors for incident CRC at the same site or at another site in the colon following polypectomy of advanced lesions.”. However there are studies about similar populations, that could be cited. See for instance, Atkin W et al. Lancet Oncol. 2017 Jun;18(6):823-834. 15. Table 1. Time interval... = 4.24, which is different from the 2.31 in text. The same difference applies to Table 3. Did I miss something? 16. Table 1 and table 3. Asterisks for statistically significant p-values are not necessary. 17. Table 1 and table 3. Please specify that p-values are referred to univariate analysis Minor 1. Core tip, last but one line: “in order to for individualize”