Reviewer’s report

Title: p53 expression in patients with ulcerative colitis - associated with dysplasia and carcinoma: a systematic meta-analysis

Version: 0 Date: 12 Jun 2017

Reviewer: Julajak Limsrivilai

Reviewer's report:

The study concept is good. This is the first meta-analysis to determine the association between p53 expression and the risk of dysplasia and cancer in patients with ulcerative colitis (UC). However, the meta-analysis of the association between KRAS and TP53 mutations with IBD-associated colorectal cancer has recently been published (Du L et al., Oncotarget 2017). Please find my comments below.

1. The study by Vento et al. (ref. 16 in the manuscript) included 52 patients who underwent restorative proctocolectomy with construction of an ileal reservoir (42 patients with pouchitis, 10 patients normal ileoanal pouch), and 9 healthy subjects. The specimens in this study were ileal tissue and not colonic tissue. Should this study be included in the meta-analysis?

2. The criteria to categorize the patients/tissues into each group in this meta-analysis is confusing. The tissues without dysplasia but from the patient with UC and dysplasia were categorized as UC without dysplasia group in some studies (e.g. Friis-Ottessen et al., ref. 14 in manuscript), but were categorized as UC with dysplasia in the study by Sato et al. (ref. 25 in manuscript). Please kindly clarify this issue.

3. The authors stated that the literature search was performed up to February 13th, 2017. However, some studies may have been missed. Some examples are among the studies below.


Could the authors kindly provide the reasons for excluding these studies?

4. The authors did not include the studies which included both Crohn's disease and ulcerative colitis patients in this meta-analysis. The data would be more complete if the authors can...
obtain more information specifically for UC patients in those studies and include them in this meta-analysis. One example is the following study.


(20 of 31 IBD patients with colorectal cancer had UC)

5. In the search strategy section, Boolean operators in the search term, such as AND and OR, should be entered in uppercase letter.

6. I do not understand how the authors interpreted the results of sensitivity analysis in the section 3.5. To the best of my knowledge, sensitivity analysis is performed to investigate the validity and robustness of the meta-analysis. There are 2 main methods.

1. Applying the meta-analysis to subsets of studies based on high-quality versus low-quality studies, early studies versus late studies, and etc.

2. Applying the leave-one-out method

   In this meta-analysis, the authors stated in the Method section that they used the leave-one-out method, which is done by performing a meta-analysis on each subset of the studies obtained by leaving out exactly one study. Thus, there should be 12 meta-analyses in the sensitivity analysis in UC with dysplasia vs. without dysplasia or carcinoma (the same numbers as the numbers of studies included in the meta-analysis comparing UC with dysplasia vs. UC without dysplasia or carcinoma). If the results of each meta-analysis in these 12 meta-analyses are consistent, then there is confidence that the overall meta-analysis is robust and not dependent on any single study.

   However, in the Results section, the authors reported the results of sensitivity analysis by reporting the result of only one meta-analysis with removal of the study by Klump et al.. This looks like the way to report the results when sensitivity analysis is done by the 1st method. In this case, the authors should have stated the criteria of selection or removal of the studies for the sensitivity analysis.

7. I would like to see the grading of quality of the studies included in this meta-analysis.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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