Author's response to reviews

Title: AB0 blood group and prognosis in patients with pancreatic cancer

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Author's response to reviews: see over
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AB0 blood group and prognosis in patients with pancreatic cancer (MS: 5303993986847751)

Dear Editors,

we are pleased that you consider our manuscript entitled ‘AB0 blood group and prognosis in patients with pancreatic cancer’ for publication in BMC Cancer.

The reviewers’ comments were very helpful to improve the manuscript in form and content.

Please find our point-by-point response to the referee comments below. In the manuscript revised passages are highlighted red.

We are confident that the revised version of the manuscript will be suitable for publication in BMC Cancer.

Thank you very much for your consideration.

Sincerely, yours

Nuh N. Rahbari
Reviewer 1:

In the manuscript Rahbari et al. evaluated the ABO blood group status in pancreatic cancer progression. They verified the recent finding, that blood group 0 is associated with reduced risk of pancreatic cancer. They showed for the first time, that blood group 0 has a beneficial effect on patient survival using multivariate analysis.

The patients for this study were carefully chosen, resulting in a well-defined and characterized study group for analysis, benefiting from sample size and data recorded. This descriptive paper represents a clear and concise evaluation of data gained from a prospective clinical study of pancreatic cancer.

Discretionary Revision:
Introduction: The papers 8-11 were cited as there was an association between blood group status and pancreatic cancer found. There is one recent paper published by Gong et al (2012, 18:563-569, WJG). The authors did not find a significant association between blood group status and pancreatic cancer. Anyhow, you might want to include (cite) this article for completeness.

We agree with the reviewer’s suggestion and included cited the study by Gong et al. in our revised version of the manuscript.

Quality of written English: Acceptable for publication. There are a few typographical errors on page 9, which need correction.

We corrected the typographical errors on page 9.
Reviewer 2:

Rahbari et al. conducted a case-control study to evaluate an association between ABO blood group and prognosis in patients with pancreatic cancer in Germany. They found significant impact of blood group O on survival after surgery. Although the question of interest is interesting; however, several point must be considered in the future versions.

1) Considering the nature of the study as a cohort of pancreatic cancer patients receiving surgery evaluating survival, the analysis comparing patients cohort and other population about ABO blood group distribution looks strange. Again it is unusual to see sudden appearance of non-pancreatic cancer cohort in the first paragraph of result section. The analysis seems as if authors are trying to refer impacts of ABO blood group on pancreas carcinogenesis and it is definitely not the main focus of the study. To make the study and the paper reasonable, this reviewer recommend removing this part from the manuscript. (Major Compulsory Revisions)

We appreciate the reviewer’s comment. We agree with the reviewer that it was the primary aim of the study to evaluate the prognostic significance of ABO blood groups status in patients with pancreatic cancer. However, it was important to us to assess the distribution of the various ABO blood groups in patients with and without pancreatic cancer for the following reasons:

i. We intended to evaluate, if the prevalence of different ABO blood groups differed between patients with and without pancreatic cancer. While a potential prognostic impact of ABO blood group status may indicate a role of carbohydrates in pancreatic cancer progression differences in ABO blood group status would further underline their importance in the biology of this malignancy.

ii. Previous studies have shown an association between ABO blood groups and the incidence of pancreatic cancer.\(^1\)\(^,\)\(^2\) This studies, however, exclusively included patients with advanced pancreatic cancer who were not amenable for potentially curative resection. While these data suggest an association of ABO blood group status with a more aggressive phenotype of pancreatic cancer, there are no data on the association of ABO blood groups with early pancreatic cancer. As in our study only patients with potentially curative resection of pancreatic cancer were included, it is important to report the distribution of ABO blood groups in these patients compared to patients without pancreatic cancer.

For these reasons we are convinced that the data on the ABO blood groups in patients without pancreatic cancer should remain in the manuscript.

2) a) In the multivariate survival analysis, authors excluded 44 patients with missing value from analysis. Using complete data analysis used to induce bias in the results. Basically, authors used categorical variables for all covariate, it is interesting to see the analysis using dummy variable for missing categories. Or, authors can try multiple imputation for missing variables. (Major Compulsory Revisions)

The reviewer’s comment is appreciated. However, we kindly disagree with the reviewer’s suggestions. We indicated the number of patients with missing values in all univatiate analyses of Table 1. These patients
were excluded in all subsequent analyses including the multivariate Cox regression analysis. As of the nature of a multivariable Cox regression analysis patients with missing values for either of the included factors would not have been contributed to its results, even, if they would not have been excluded beforehand.

b) Although univariate analysis showed resection margin as a significant factor, it is not considered in the multivariate analysis. Add it in the multivariate analysis or clarify the reason in the text. (Major Compulsory Revisions)

We apologize for the lack of explanation in the initial version of the manuscript. In 2005, a revised and highly standardized protocol for the processing of pathological specimens of pancreatic resections was introduced in our institution. This change markedly increased the incidence of R1 diagnoses at our institution. As this dramatic change in the definition of R1 resections might have introduced bias, we decided not to included this factor in our multivariate analyses. To make this point clear, we added a paragraph to the methods section in the revised version of the manuscript explaining the reason, why the resection margin was not included as a factor in the multivariate analysis.

c) In the multivariate analysis, authors applied dichotomy of ABO blood groups (O vs A/B/AB). Considering results in the table 2, compared to A, other blood groups showing lower likelihood of having event. It is of interest to see the results presenting HRs for O, B, AB relative to A in the multivariate analysis. Even if authors keeps the style, it should be clarified why authors applied this dichotomy criteria in their analysis. (Major Compulsory Revisions)

We agree with the reviewer that it is interesting and important to see the HR of the blood groups 0, B, AB relative to blood group A on multivariate analysis. In the initial version of the manuscript we already provided these data in Table 3. We deliberately decided to include the results of different multivariate models (Table 3-5) to provide the reader with the most comprehensive information on the prognostic relevance of ABO blood group status in patients with pancreatic cancer while considering other known prognostic variables in this disease.

Minor point:
Authors should use ABO rather than AB0(AB zero). Same is true 'blood group 0' instead 'blood group O'. (Minor Essential Revision)

We kindly disagree with the reviewer. The correct nomenclature is ‘AB0’ as used in the initial version of the manuscript.
References:

