

Format for ANSWERING REVIEWERS

November 25, 2013

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 5196-review.doc).

Title: Synchronous and metachronous neoplasmas in gastric cancer patients: A 23-year study.

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

1 Format has been updated

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

(1) Only one patient developed metachronous neoplasm after radiotherapy alone and it was added to the manuscript. Cytostatic has been changed to cytotoxic. I have added more family history data. In 5th paragraph(discussion) are developed results of authors from 2nd paragraph(introduction). According to recent BPG's Revision Polices for brief Articles statistical P is marked as P not p. CT has been changed to computed tomography. References were corrected.

(2) I apologize but our report is retrospective study and we knew about death of 12 (6 metachronos and 6 synchronous) of all 58 patients. Three of them died of second primary cancer instead of gastric cancer. One of cases died of cardio-vascular failure. Eight of them died because of cancer spread and generalisation of disease without possibility of settlement which cancer was the reason of death. Adapted by us definition of Waren and Gates says that if the interval time between two cancers was longer than 6 mo, cancers are classified as metachronous. In metachronous cases it could be adopted that second cancer was the reason of death but if interval between them was e.g. 8 mo and the patient had generalisation of disease (ascites, distal metastases) how could we verify which cancer caused spread of disease. Late recurrence of first cancer could also be ruled out. For the sake of patients any additional (e.g. biopsy), beyond necessary, procedures were not carried out. For these reasons and the fact that not all patients were followed up or contact with them was missed, it was difficult to assess how many patients with CG really died of second primary cancer. Of course, I agree that our report is one of many similar reports in the world but our intension was to verify the previous data on Polish population and to answer if both GC groups differ in terms of selected features and it appeared that blood group and age are such characteristics.

(3) I do agree that both groups : gastric cancer and multiple gastric cancer, differ in terms of numbers and it would be more convincing to collect more multiply GC patients in prospective study. Although difference of average age between the patients with and without additional cancer was only 4 years, however statistical analysis allowed us to show difference in age.

Taking into account percentage of GC with second tumor and blood group O (which was added in manuscript) it seems that it concerned only small group(4.8%) of GC patients. However, our data in the best of our knowledge is the only one that indicated such relationship and further investigation will decide on their suitability.

(4) Our University's Committee of Ethics was informed about our research but they answered that their agreement is not necessary because it is only retrospective analysis of clinical data (we have Polish version of their decision). I did not ignore papers related to ABO blood groups and gastric cancer but publications about blood groups and other cancers cited in manuscript were the only example publication on such relationship. Of course I do agree with the reviewer's suggestion and have added more publications related to blood groups and gastric cancer. Sentence..." To the best of our knowledge, our results represent the first investigation of these associations, and they indicate that patients with gastric cancer who have blood group O should be monitored for the development of second primary tumors"....means that it is the first report that gastric cancer patients with blood group O may develop other tumors. Our data showed that gastric cancer patients with blood group O more often developed second cancer than patients with other ABO blood groups. I have corrected some minor things according to your suggestions.

(5) 1/ In our report we have assumed that the mean age was the age of gastric cancer diagnosis. Others described mean age as an age of the first diagnosed cancer or as an age of gastric cancer diagnosis like we did it. 2/Early stage was obviously based on histopathological examination after operation. Same non operated patients with distal metastatic tumor or local infiltration in CT were classified as advanced - I have added such information in manuscript. 3/ I do agree that both group: gastric cancer and multiple gastric cancer differ in terms of numbers but statistical analysis allowed comparing both groups. 4/I apologize, but in results part by mistake it was written "GC with know family history" instead of "Out of the total patients with GC patients and know stage of disease (n=727)". Obviously, it has been changed. According to your suggestion, I have added more details in results part.

Thank you very much for all helpful comments and suggestion.

3 References and typesetting were corrected

Sincerely yours,

A handwritten signature in blue ink, reading "Malgorzata Lawniczak". The signature is written in a cursive, flowing style.

Malgorzata Ławniczak, M.D.

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