

Reviewer 1

I had the opportunity to review a paper “¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography feature and its clinical relevance in gastric lymphomas: Comparison with gastric carcinomas”, and I found very interesting. There is no problem to publish the manuscript.

Thank you very much!

Reviewer 2

This is an interesting study that compared the PET/CT findings between the gastric lymphoma and gastric carcinoma. Although it is well written, followings need to be revised before the publication.

1. It is hard to agree that there were 52 gastric lymphomas and 73 gastric carcinomas during the study period, because the incidence of gastric carcinoma is > 10 times more higher than that of the lymphoma. Furthermore, mucinous cell-type (which is too common in this study) is a rare form of gastric carcinoma. Please clarify the whole number of the gastric malignancy patients during the study period according to the cell types, and verify the percentages of the included subjects in each cell type.

As known, the incidence of gastric carcinoma is > 10 times more higher than that of the lymphoma. However, maybe more gastric lymphoma patients chose to accept ¹⁸F-FDG PET/CT to evaluate the status of the whole body than gastric carcinoma patients in our hospital. In addition, the percentages of patients with gastric lesions in studies from Wu J and Fu L were similar to that in our study.

(1) Fu L, Li H, Wang H, Xu B, Fan Y, Tian J. SUVmax/THKmax as a biomarker for distinguishing advanced gastric carcinoma from primary gastric lymphoma. PLoS One 2012;7:e50914.

69 advanced gastric carcinoma patients and 38 primary gastric lymphoma patients were included.

(2) Wu J, Zhu H, Li K, Wang XG, Gui Y, Lu GM. (18)F-fluorodeoxyglucose positron emission tomography/computed tomography findings of gastric lymphoma: Comparisons with gastric cancer. Oncol Lett 2014;8:1757-1764.

24 patients with gastric lymphoma and 43 patients with gastric cancer were included.

Based on the comments mentioned above, the whole number of the gastric malignancy patients (gastric lymphoma and gastric carcinoma) and the percentages of the included subjects in each cell type maybe were not so unreasonable. In contrast, it was comprehensible.

2. Please describe the values of SUV uptake in Table 1 using the exact SUVmax values, because the patterns of PET/CT scan used in this study is a novel one which is not confirmed yet. (1) Type I: uptake in >1/3 of the gastric wall and diffuse thickening (2) Type II: uptake in <1/3 of the gastric wall and diffuse thickening (3) Type III: local uptake and local thickening.

To avoid redundance, it was more appropriate to describe the values of SUV uptake using the exact SUVmax values in Table 2, but not in Table 1.

3. Were there differences in SUVmax between the diffuse large B cell lymphomas (DLBCL) and low grade mucosa-associated lymphoid tissue (MALT) lymphomas? In similar, were there differences in SUVmax between the mucinous adenocarcinomas and non-mucinous adenocarcinomas? Please describe in exact values.

If we were right, we thought that we had described these issues in Table 3 and Table 4, respectively. As reported, there were significant differences in SUVmax between the diffuse large B cell lymphomas (DLBCL) and low grade mucosa-associated lymphoid tissue (MALT) lymphomas (18.41 ± 7.78 vs 4.66 ± 2.72 , $P < 0.001$), and in SUVmax between the mucinous adenocarcinomas and non-mucinous adenocarcinomas (5.28 ± 2.06 vs 9.02 ± 6.14 , $P = 0.032$).

4. Please clarify the differences in THKmax values according to the cell-types and TNM staging.

As suggested, we had clarify the differences in THKmax values according to the cell-types and TNM staging in Table 3 and Table 4, respectively.

For **gastric lymphomas**

DLBCL vs MALT: 2.33 ± 1.43 vs 1.36 ± 1.25 ($P = 0.567$)

I vs II1/II2/IV: 1.52 ± 1.19 vs 2.23 ± 1.51 ($P = 0.244$)

For **gastric carcinomas**

Mucinous vs Non-mucinous: 1.75 ± 0.93 vs 2.07 ± 1.37 ($P = 0.781$)

I/II vs III/IV: 1.57 ± 0.80 vs 2.32 ± 1.50 ($P = 0.207$)

5. A multivariate analysis including all significant values on PET/CT uptake (cell type, depth of invasion, LN invasion, metastasis, etc) should be added to support the conclusion.

This study focused on the comparison of PET/CT findings between the gastric lymphoma and gastric carcinoma. In the second part (^{18}F -FDG uptake in gastric lesions) of “Result” in this manuscript, we summarized the presence of gastric ^{18}F -FDG uptake, SUVmax and SUVmax/THKmax. As illustrated in Table 2, the SUVmax was higher in patients with gastric lymphomas compared with that in patients with gastric carcinomas (13.39 ± 9.24 vs 8.35 ± 5.80 , $P < 0.001$), and SUVmax/THKmax was significantly larger in patients with gastric lymphomas in comparison with that in patients with gastric carcinomas (7.96 ± 4.02 vs 4.88 ± 3.32 , $P < 0.001$). In addition, we performed subgroup analysis based on cell type and staging in gastric lymphoma group and gastric carcinoma group, respectively. Information about depth of invasion, LN invasion, metastasis are included in staging classification. As illustrated in Table 3 and Table 4, DLBCL (18.41 ± 7.78 vs 4.66 ± 2.72 , $P < 0.001$) and the advanced Lugano stage (stage II1/II2/IV) (15.53 ± 8.87 vs 9.97 ± 8.88 , $P = 0.026$) gastric lymphoma patients showed higher SUVmax compared to MALT lymphoma and stage I gastric lymphomas (Table 3). As to the gastric carcinoma patients, the non-mucinous adenocarcinomas subgroup (9.02 ± 6.14 vs 5.28 ± 2.06 , $P = 0.032$) and the advanced TNM stage (stage III/IV) (10.57 ± 6.27 vs 5.17 ± 2.96 , $P < 0.001$) gastric carcinomas were with higher SUVmax compared to the mucinous adenocarcinomas subgroup and the stage I/II gastric carcinoma patients (Table 4).

In the analysis of associated clinicopathological features with SUVmax, We dichotomized patients into low (SUVmax < mean value) and high SUVmax subgroups (SUVmax ≥ mean value), and the association of SUVmax with clinicopathological features was evaluated by the chi-square test among patients with gastric lymphomas and patients with gastric carcinomas, respectively (Table 3 and Table 4).

6. In current form, this study adds little to the previous studies, so please emphasize more on the novel findings. (1) Fu L, Li H, Wang H, Xu B, Fan Y, Tian J. SUVmax/THKmax as a biomarker for distinguishing advanced gastric carcinoma from primary gastric lymphoma. PLoS One 2012;7:e50914. (2) Wu J, Zhu H, Li K, Wang XG, Gui Y, Lu GM. (18)F-fluorodeoxyglucose positron emission tomography/computed tomography findings of gastric lymphoma: Comparisons with gastric cancer. Oncol Lett 2014;8:1757-1764.

On the basis of study (1) and study (2), our study furtherly characterized the differences on the ¹⁸F-FDG PET/CT findings between gastric lymphomas and gastric carcinomas and adds several significant information to the previous studies.

First, a larger sample size in our study was an unique advantage (52 gastric lymphomas and 73 gastric carcinomas). In contrast, only 24 patients with gastric lymphoma and 43 patients with gastric cancer were included in study (2), and 38 primary gastric lymphomas and 69 advanced gastric carcinoma were included in study (1), respectively.

Second, different from study (1), which simply focused on the on FDG intensity (SUVmax) of primary lesions and its CT-detected abnormalities, including THKmax and mucosal ulcerations, our study was relatively comprehensive and complicated. In details, We reviewed and analysed the PET/CT features of gastric wall lesions including CT-detected abnormalities (THKmax and ulcerations), FDG avidity and involved region, pattern (focal/diffuse), and intensity (SUVmax). In addition, the correlation of SUVmax with gastric clinicopathologic variables was investigated by chi-square test in our study. Last but not less importantly, a ROC curve analysis was

performed to determine the differential diagnostic value of SUVmax/THKmax in gastric lymphomas with gastric carcinomas. However, Cross-validation analysis was used to distinguish advanced NHL from advanced gastric carcinoma in study (1).

Third, different from study (2), which showed that THKmax was larger in patients with gastric lymphomas compared to that in patients with gastric cancer, THKmax did not differ among gastric lymphomas and gastric carcinomas, even according to the cell-types and Lugano/TNM staging in our study. In contrast, our result was similar to that from study (1) on this issue.

Last, study (2) simply analysed the difference in the maximal thickness and SUVmax of the gastric wall lesions between the patients without and with extragastric involvement, for gastric lymphoma and gastric cancer. In the analysis of associated clinicopathological features with SUVmax, our study performed subgroup analysis based on sex, age, cell type and staging in gastric lymphoma group and gastric carcinoma group, respectively (Table 3 and Table 4). In addition, We dichotomized patients into low (SUVmax < mean value) and high SUVmax subgroups (SUVmax ≥ mean value), and the association of SUVmax with clinicopathological features was evaluated by the chi-square test among patients with gastric lymphomas and patients with gastric carcinomas, respectively (Table 3 and Table 4).

In conclusion, compared to study (1) and study (2) alone, the value of our study got improved through more comprehensive and profound investigation.

Editor

1. When you send back, please provide the format of doc, not the format of PDF.

Thank you!

We had provided the format of doc when we resubmit the revised manuscript as you suggested.

2. Please provide language a certificate letter from a professional English language editing company (Classification of the manuscript language quality evaluation is B).

For manuscripts submitted by non-native speakers of English, please provide a language certificate from one of the professional English language editing

companies mentioned in ‘The Revision Policies of BPG for Article.’

We had provided a language certificate letter from a professional English language editing company as you suggested, and the classification of the manuscript language quality evaluation from the reviewers is A.

3. The title must be informative, specific, and brief (Title should be no more than 10~12 words/60 bytes. Please revise it). Words should be chosen carefully for retrieval purposes. All nonfunctional words should be deleted, such as ‘the’, ‘studies on’, ‘observations of’, and ‘roles of’, etc.

We had done our best to present the title to be brief, informative, specific as possible, and we had changed this title as “Comparison of gastric lymphomas with gastric carcinomas on ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography” this time. As we have to use the full name of “¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography” for ¹⁸F-FDG PET/CT, the title seemed a little long.

4. A copy of the full approved grant application form(s), consisting of the information section and body section, should be provided to the BPG in PDF format.

We had provided a copy of the full approved grant application forms in PDF format when we resubmit the revised manuscript as you suggested. However, it was a little difficult for us to provide the copy of the full approved grant application forms for National Science and Technology Major Project (No.2013ZX09303001) and National Natural Science Foundation of China (No.81302003) at present, because the two applicants are being studying in America. In the end, we have to decide to delete the two projects in our manuscript.

5. Please read the core tip then provide the audio core tip: Acceptable file formats: .mp3, .wav, or .aiff. Maximum file size: 10 MB. To achieve the best quality, don’ t allow to have the noise.

We had read the core tip and had provided the audio core tip in mp3 format when we resubmit the revised manuscript as you suggested.

6. For the figures, the fonts and lines can be edited or moved. It can be made by

ppt.

We had moved the lines and edited the fonts in figure 1, figure 2 and figure 3 as suggested in the “format for manuscript revision-retrospective study” by photoshop software.