

The manuscript is an invited Editorial to comment the following article published in the World Journal of Gastroenterology in 2017:

**Lee JW, Lee MS, Chung IK, Son MW, Cho YS, Lee SM. Clinical implication of FDG uptake of bone marrow on PET-CT in gastric cancer patients with surgical resection. World J Gastroenterol 2017; 23: 2385-2395 [PMID: 28428718 DOI: 10.3748/wjg.v23.i13.2385]**

The required format for the editorial article was the following:

**“Editorial article format.** Unstructured abstract: up to 200 words. Core Tip: up to 100 words.... Main text: up to 1500 words. Tables/illustrations: up to 2. References: up to 10.”.

#### **Comments to reviewer 1**

- 1) The article is an invited Editorial, so that it would be inappropriate to reformat the manuscript for a minireview.
- 2) The manuscript has been revised for the English language and a language editing certificate has been provided as required for manuscripts submitted by Non-Native Speakers of English.

#### **Comments to reviewer 2**

- 1) The article has been structured with an Introduction, two Paragraphs and the Conclusion.
- 2) To clarify the purpose of the article, a brief sentence has been inserted at the beginning of the manuscript where the aims of the manuscript are briefly resumed; the INTRODUCTION has been changed as follows:

#### **“INTRODUCTION**

Gastric cancer (GC) remains a leading cause of cancer death worldwide, with poor prognosis despite significant advances in diagnosis and treatment. Survival rates are highest in Japan, due to focused management of preventive and prognosis-related factors (*i.e.* infection and smoking, respectively)<sup>[2]</sup>, and are progressively increasing in western countries<sup>[1-3]</sup>. Prognostic factors related to GC are quite well established, such as local

extension, lymph-node involvement and presence of distant metastases, and can be adequately defined by the conventional imaging modalities, including endoscopic ultrasound (EUS), computed tomography (CT) and magnetic resonance imaging (MRI). However, some emerging prognostic factors related to the metabolism of tumour cells, such as the glucose avidity, or to the systemic inflammatory response (SIR) to the tumour can be better evaluated through the metabolic information that are provided by positron emission tomography (PET) integrated with CT, even though the role of PET/CT imaging in the evaluation of GC is still controversial.”

3) We considered that there were essentially two main topics to be discussed in the invited Editorial:

- the most relevant prognostic factors in candidates to potentially curative gastrectomy for gastric cancer (GC);
- the role of PET-TC in the evaluation of these prognostic factors.

Some prognostic factors are related to the tumour, including the anatomic site, the tumour stage according to the TNM classification, and the tumour histology. Recent studies however have also demonstrated the relevant prognostic role of the host systemic inflammatory response (SIR) to malignancy in different malignant tumours, including GC. For patients with potentially resectable locally advanced gastric cancer (AGC), the type of resection (i.e. subtotal vs total gastrectomy) and the extension of lymphadenectomy have a definite prognostic impact on tumour recurrence and survival. Various perioperative therapies have been recently proposed for resectable GC, including chemotherapy (CHT), radiotherapy and chemoradiotherapy, to be performed before and/or after surgery; even though adjuvant and neoadjuvant therapies have been demonstrated to improve prognosis after potentially curative resection of locally AGC, the optimal strategy is still debated.

Referring to the role of FDG PET/CT in GC patients, it is still questioned due to the lower sensitivity in diagnosing and staging GC than other imaging techniques, such as endoscopic ultrasound and CT scan. There is however growing evidence that FDG uptake in the primary tumour and regional lymph-nodes may be efficient in predicting prognosis of resected patients and in monitoring tumour response to perioperative treatments, and may have prognostic value that can change therapeutic strategies. Moreover, FDG uptake

of bone marrow (BM) seem to be significantly associated with SIR to GC and to represent an efficient prognostic factor after curative surgery; this is the topic discussed in the article by Lee JW published in the World Journal of Gastroenterology in 2017 and commented in our invited Editorial.

In the manuscript we had to discuss all these topics, somehow controversial in most cases, with a very limited number of references, up to 10. This is why we decided to refer to the most influential guidelines and review articles about the prognostic factors related to resectable advanced gastric cancer and about the role of FDG PET/CT in the prognostic evaluation of GC patients. Several influential studies about these topics were consulted but could not be cited. Finally, four of the articles cited in the manuscript describe the most relevant prognostic factors related to GC, two refer to the prognostic role of SIR in malignant tumours and in GC, and four describe the role of FDG PET/CT in the prognostic evaluation of GC patients, referring to FDG uptake either in the tumour or in the bone marrow.

In the light of the above, we believe that the comments of the reviewer should be reconsidered keeping into appropriate consideration the Instructions to Authors provided by the Editorial Office.

4) Ref 9) has been corrected.

5) The manuscript has been revised for the English language and a language editing certificate has been provided as required for manuscripts submitted by Non-Native Speakers of English.

### **Comments to reviewer 3**

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### **Comments to reviewer 4**

1) Abbreviations were defined in the revised manuscript.

2) To clarify the purpose of the article, the INTRODUCTION has been changed as follows:

**"INTRODUCTION**

Gastric cancer (GC) remains a leading cause of cancer death worldwide, with poor prognosis despite significant advances in diagnosis and treatment. Survival rates are highest in Japan, due to focused management of preventive and prognosis-related factors (*i.e.* infection and smoking, respectively)<sup>[2]</sup>, and are progressively increasing in western countries<sup>[1-3]</sup>. Prognostic factors related to GC are quite well established, such as local extension, lymph-node involvement and presence of distant metastases, and can be adequately defined by the conventional imaging modalities, including endoscopic ultrasound (EUS), computed tomography (CT) and magnetic resonance imaging (MRI). However, some emerging prognostic factors related to the metabolism of tumour cells, such as the glucose avidity, or to the systemic inflammatory response (SIR) to the tumour can be better evaluated through the metabolic information that are provided by positron emission tomography (PET) integrated with CT, even though the role of PET/CT imaging in the evaluation of GC is still controversial.”

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