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LETTER TO THE EDITOR

Letter to the editor: new response evaluation criteria using early morphological change in imatinib treatment for patients with gastrointestinal stromal tumor

Junjie Jiang[1] · **Lisong Teng**[1]

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Dear Editor,

We read with interest the article entitled "new response evaluation criteria using early morphological change in imatinib treatment for patients with gastrointestinal stromal tumor" [1]. In this study, Ishida et al. established a new response evaluation tool based on early morphological change to predict the clinical outcome of imatinib treatment for patients with unresectable gastrointestinal stromal tumor (GIST). We would like to share some opinions.

Standardized response criteria for evaluating computed tomography (CT) imaging play a vital role in oncological management. Response evaluation criteria in solid tumors (RECIST) are the most common imaging method to assess tumor response [2]. However, on the one hand, tumor shrinkage on CT scan tend to occur at the late phase of the treatment, which cannot provide timely decision-making guidance in clinical practice; on the other hand, a morphologically detected increase in tumor size such as cystic transformation or hemorrhage is easily recognized as PD using RECIST criteria, even in case of a true pathological response, which has become known as "pseudoprogression". In addition, Choi criteria is established based on the morphological change in the extent of tumor attenuation rather than tumor size, which outperforms RECIST in the discrimination between responders and non-responders for malignant GIST treated with imatinib [3]. Furthermore, Chun et al. proposed a new tool based on early morphological change (EMC) in CT imaging, including tumor attenuation and tumor border, to predict response to molecularly targeted drugs in metastatic colorectal cancer [4].

In this study, Ishida et al. compared the predictive value of EMC, RECIST, and Choi criteria and highlighted that early evaluation with EMC could predict good outcomes in GIST patients treated with imatinib [1]. We consider that this is a pioneer work for exploring the response criteria based on multidimensional CT imaging for GIST patients. Nevertheless, we raise concerns about reproducibility and accordance of the EMC criteria. As the authors observed, the discrepancy in defining response outcome (optimal response, incomplete response, and none response) between the two radiologists occurred in 12 cases (18.2%). Similarly, Chun et al. reported that the frequency of discrepancy in scoring EMC among radiologists reached 26% [4]. We consider that the subjective definition of EMC (tumor attenuation and outline) is the leading cause of the non-negligible discrepancy. To be specific, there is no objective parameter to distinguish the difference between homogeneous and heterogeneous tumor attenuation. Meanwhile, a sharply or poorly defined tumor outline is always dependent on the judgment of clinical radiologists. More importantly, in this study, a non-negligible population (16.7%) was classified into group 2, according to the fuzzy definitions of tumor attenuation and tumor outline. Currently, a quantitative measurement for CT imaging using artificial intelligence and radiomics analysis has become a hot-spot area for tumor diagnosis and treatment evaluation [5, 6]. It is recommended to quantitatively measure the tumor attenuation and border for optimizing the evaluation of EMC and develop a predictive model based on these radiological features to predict clinical outcomes of GIST patients treated with imatinib.

In addition, the authors stated that "Active morphological response (+) (Active MR(+)) was defined as 'optimal' or 'incomplete' response, according to the previous report by Chun et al.". We noticed that, in the study by Chun et al., patients with optimal response were considered as the responders, whereas those with incomplete response or none response were the non-responders. However, in this

✉ Lisong Teng
lsteng@zju.edu.cn

[1] Department of Surgical Oncology, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China

study, patients with incomplete response were considered as the responders (Active MR(+)), whose radiological feature changes were relatively fizzy according to the EMC definition. Therefore, the potential bias might be introduced due to the grouping pattern, especially in a limited sample-size study. It would be helpful if the authors could conduct the survival analysis by grouping patients into three groups (optimal, incomplete, and none response).

Overall, this study highlights the important value of EMC in the area of response evaluation in solid tumors and overcomes the unidimensional limitation of RECIST criteria. In future, multidimensional radiological features such as tumor size, tumor attenuation, tumor outline, and intratumor vascular density could be captured and integrated using artificial intelligence and radiomics analysis to establish the precise response evaluation criteria with high reproducibility, which might bring a new revolution in the area of response evaluation in solid tumors.

Declarations

Conflict of interest All the authors declare no conflict of interest in this study.

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