EDITORIAL

INTESTINAL RESEARCH

ISSN 1598-9100(Print) • ISSN 2288-1956(Online)
http://dx.doi.org/10.5217/ir.2014.12.3.176
Intest Res 2014;12(3):176-177

A High Risk Group in the Modified National Institutes of Health Consensus Criteria for the Gastrointestinal Stromal Tumor: A Clear Indication of the Adjuvant Imatinib

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Article: Prediction of Tumor Recurrence in Patients with Non-Gastric Gastrointestinal Stromal Tumors Following Resection according to the Modified National Institutes of Health Criteria **(Intest Res 2014;12:229-235)**

Since it is difficult to predict the prognosis of gastrointestinal stromal tumor (GIST) with the standard tumor-node-metastasis system, a system for assessment of the malignant potential according to risk stratification is commonly used in a clinical setting. Leading classification systems are the National Institutes of Health (NIH) consensus criteria,[1] the modified NIH consensus criteria,[2] the Armed Forces Institute of Pathology criteria and others. Jang et al.[3] in this issue compared the most widely used NIH criteria and the modified NIH criteria.

The NIH criteria[1] proposed before 2002 classified the prognosis of GISTs into four subgroups (very low, low, intermediate or high risk) based on mitotic count and tumor size.

The modified NIH criteria,[2] developed by Dr. Joensuu in 2008, includes the primary tumor site and tumor rupture as two additional prognostic factors to the original NIH consensus criteria. According to the modified criteria, a part of individuals belonging to the intermediate risk group based on the NIH consensus criteria are re-classified into the high risk group. Based on the NIH consensus criteria, cases with mitotic count >10/50 high power fields (HPF) and tumor size >10 cm, or those with mitotic count >5/50 HPF and tumor size >5 cm are classified as the high risk group. This classification maintains identically only when GISTs are located in the stomach according to the modified NIH criteria. In contrast, when GISTs are detected in organs other than the stomach, cases with tumor size >5 cm are included in the high risk group, regardless of the mitotic count. If the mitotic activity is >5/50 HPF in the GISTs involving non-gastric organs cases with tumor size >2 cm are also classified into the high risk group. Thus, some non-gastric GISTs formerly grouped as the intermediate risk group are re-classified as the high risk group. All cases with the presence of a tumor rupture are classified as the high risk group, as well in the modified NIH consensus criteria.

The need for re-classification has been raised to accurately determine the postoperative adjuvant Imatinib group. Although the effectiveness of postoperative adjuvant Imatinib has been clarified in the high risk group for GISTs, it still remains unclear in the intermediate risk group. The 2012 National Comprehensive Cancer Network (NCCN) guideline recommends postoperative adjuvant therapy for patients based on the following study results.[4]

Received April 21, 2014. **Revised** May 26, 2014. **Accepted** May 27, 2014.
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Financial support: None. **Conflict of interest:** None.

http://dx.doi.org/10.5217/ir.2014.12.3.176 • Intest Res 2014;12(3):176-177

A randomized trial (SSGXVIII/AIO) reported that 36 months, compared to 12 months, of adjuvant Imatinib was significantly better in extending relapse free survival and overall survival in patients with a high estimated risk of recurrence postoperatively (tumor >5 cm in size with a high mitotic rate [>5 mitoses/50 HPF] or a risk of recurrence greater than 50%).[5]

Moreover, the ACOSOG Z9001 study showed that adjuvant Imatinib significantly prolonged relapse free survival in patients with GISTs that were larger than 3 cm. In particular, the efficacy of Imatinib was noticeable in patients with a considerably higher risk of recurrence (intermediate and high-risk).[6]

When the parameters of these two studies are matched with the classification criteria, it is reasonable that the high risk group based on the modified NIH consensus criteria should be subject to adjuvant Imatinib treatment.

From the aspects of clinical effectiveness, whether a classification system can better discriminate a single high risk group requiring adjuvant chemotherapy, the modified NIH consensus criteria are considered a more effective indicator. Follow-up without specific post-operative adjuvant treatment is required for very low, low and intermediate risk groups based on the modified NIH criteria, while adjuvant Imatinib treatment is recommended for the high risk group.

In the study of Jang et al. in this issue, gastric GISTs were not included and there was no case involving a tumor rupture. For these reasons, evaluating the significance of the modified NIH criteria is difficult based on their study results. Moreover, additional chemotherapies, including postoperative use of Imatinib, were excluded to observe the natural progress of tumors. Considering the fact that the clinical effectiveness of the modified NIH criteria is critical in determining the use of postoperative adjuvant therapy, the study results would have been more useful if the differences in the prognosis had been compared between those with and without adjuvant therapy.

However, this study demonstrated that some GISTs formerly categorized as the intermediate risk group, according to the original NIH criteria, were re-classified as the high risk group, and showed a significantly high recurrence rate. The study was meaningful in that it supported the view that the high risk group classified according to the modified NIH consensus criteria is subject to adjuvant Imatinib therapy.

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