Comment on "Gastrointestinal Bleeding in Small Intestinal Stromal Tumors: A Clinicopathological and Survival Analysis"

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Dear Editor,

We read with great interest the article "Gastrointestinal Bleeding in Small Intestinal Stromal Tumors: A Clinicopathological and Survival Analysis" by Fu et al[1] recently published in your journal (Vol. 37 No. 3 (2026), DOI: 10.5152/tjg.2025.25205). The authors successfully demonstrate that gastrointestinal (GI) bleeding is an independent adverse prognostic factor for small intestinal stromal tumors (SISTs), particularly in terms of relapse-free survival among patients with high-risk tumors. By linking a clinical symptom like GI bleeding with aggressive tumor characteristics such as tumor rupture and a high Ki-67 proliferation index, the authors provide valuable insights for clinical practice and risk stratification. No artificial intelligence was used during the preparation of the manuscript.

Despite the importance of this study, a careful review of the data reveals potential mathematical inconsistencies regarding the Ki-67 index that warrant clarification, particularly because Ki-67 is presented as an independent risk factor (hazard ratio [HR] = 2.585) in the multivariable analysis and is also used to support the interpretation that bleeding reflects a more proliferative and aggressive tumor biology. First, the total number of patients with Ki-67 >5% appears to have 3 different values in the same cohort of 152 patients: Table 1 reports 106 patients, Table 2 reports 65 patients, and the percentages given in the "Discussion" section (68.1% of 47 patients in the bleeding group and 51.4% of 105 patients in the nonbleeding group) correspond to approximately 86 patients. The article also states that the bleeding group had significantly higher Ki-67 expression (68.1% vs. 51.4%). However, Table 1 shows the opposite pattern: 23 of 47 patients in the bleeding group had a Ki-67 index >5% (48.9%), compared with 83 of 105 patients in the nonbleeding group (79.0%). If the data in Table 1 are correct, the proposed association between GI bleeding and higher proliferative activity is not supported by the presented data.

Additionally, this table–text discrepancy is not limited to Ki-67; the tumor rupture data show a similar mathematical inconsistency. According to Table 1, tumor rupture occurred in 17.0% (8/47) of patients in the bleeding group vs. 6.6% (7/105) of patients in the nonbleeding group. However, the "Discussion" section reports this comparison as 15.2% vs. 3.8%. These inconsistencies suggest that the underlying dataset and corresponding analysis should be rechecked.

From a pathology perspective, anatomical location significantly influences the histologic appearance and biological behavior of gastrointestinal stromal tumors (GISTs). Small intestinal and colonic GISTs are typically spindle cell tumors and may feature distinct neuropil-like anuclear areas that mimick Verocay bodies, along with regressive vascular changes such as dilated and thrombosed vessels.[2] Given that intestinal GISTs typically follow a more unpredictable clinical course than their gastric counterparts, recognition of these site-specific morphologic features is important for accurate pathologic evaluation. Notably, these regressive vascular changes may provide a potential mechanistic explanation for the GI bleeding frequently observed in these patients. However, further studies are needed to evaluate these features and determine whether they are associated with bleeding risk and overall prognosis.

As the authors highlight, the best-established prognostic parameters for GIST are mitotic activity, tumor size, and

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anatomical site.[2] However, as widely reported in the literature, tumor rupture is an important additional adverse prognostic factor. The authors appropriately note that GI bleeding is significantly associated with a higher incidence of tumor rupture. The clinical significance of this finding warrants particular attention.

As demonstrated by Hohenberger et al,[3] tumor rupture into the abdominal cavity is associated with a recurrence risk of nearly 100% and a median recurrence-free survival of only 19 months in the absence of adjuvant therapy. Because GISTs are highly vascular and fragile, mucosal infiltration or ischemic necrosis associated with GI bleeding may reflect this structural vulnerability. Therefore, patients presenting with GI bleeding may require particular surgical caution to minimize the risk of iatrogenic tumor rupture. They may be appropriate candidates for adjuvant systemic therapy following comprehensive risk assessment in accordance with current guideline recommendations.

Furthermore, pathologists can explicitly document tumor necrosis, tumor rupture, and mucosal involvement in pathology reports, in addition to standard parameters like tumor size and mitotic activity.

Molecularly, although the authors reported that 80.4% of their genetically tested cohort harbored KIT exon 11 mutations, it is also important to note that small bowel GISTs may occasionally harbor BRAF V600E mutations.[4] In addition, NF1-associated GISTs are commonly located in the small bowel.[5] Since the present study identified the small bowel as a major site associated with GI bleeding, more comprehensive molecular characterization of tumors arising at this location may provide additional biological insights into the heterogeneity of small bowel GISTs. However, molecular analysis was unavailable for 101 patients, precluding evaluation of these less common molecular subgroups. In the present study, molecular analysis could not be performed in 101 patients, and the relationship between GI bleeding and rare mutations other than KIT mutations could not be evaluated. Integrating these specific molecular profiles with morphological patterns and proliferative indices will contribute to improved patient follow-up and inform the development of future targeted therapies. Future studies incorporating broader molecular profiling may further refine the biological characterization of small bowel GISTs and their clinical implications.

In conclusion, we commend Fu et al[1] for their illuminating study connecting clinical presentations with markers of tumor aggressiveness in SISTs. Incorporating additional histological characteristics such as spindle cell morphology and specific mutational profiles such as BRAF V600E may further refine prognostic models. We respectfully suggest that the authors recheck the underlying data and analyses for Ki-67 and tumor rupture to clarify the aforementioned inconsistencies, perhaps through a corrigendum, to solidify the scientific foundation of their important findings.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

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