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LETTER – SARCOMA

Defining Rupture in Gastrointestinal Stromal Tumor: Semantics and Prognostic Value

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In their editorial, Asare and Feig[1] comment on our proposal for a definition of tumor rupture in gastrointestinal stromal tumor (GIST) presented in *Annals of Surgical Oncology*.[2] They discuss the weak evidence base, discount the inclusion of certain criteria, and discourage its clinical application.

The facts we have considered are as follows:

1. Tumor rupture is an established risk factor in GIST, generally accepted as having negative prognostic implications.
2. There has been no universally accepted definition of the term *tumor rupture*.
3. In the absence of a strict, universally accepted definition, its independent prognostic influence has been hard to demonstrate consistently across various studies.
4. As a non-specific term, *rupture* has an inherent vagueness and is liable to individual differences in interpretation.

Our definition is based on the Oslo criteria, which have identified patients at particularly high risk of recurrence in a population-based cohort of 410 patients, including 52 patients with tumor rupture, systematically followed long term.[3] Indeed, we agree that the numbers are few, but, to the best of our knowledge, this Norwegian study includes more patients with tumor rupture (and reports their natural history) than any other, excluding pooled analyses and trials in high-risk patients.

Given the universally accepted prerequisite that tumor rupture can be either spontaneous or iatrogenic, any break in the natural lining or containment of the tumor could literally be termed *rupture* with a possibility for peritoneal dissemination. Such a definition would potentially include needle biopsy, R1 resection, serosal tumor penetration, piecemeal resection, microscopic adjacent infiltration, etc. In our opinion, one important 'take-home' message from our definition is that it distinguishes between minor defects of tumor integrity, which have no prognostic impact based on available data (and thus would not be considered rupture), and major defects with prognostic significance (and thus termed *rupture*). This distinction is not semantic; it is a distinction based on differences in clinical outcomes. We believe there is no point in defining tumor rupture if not considered clinically relevant.

A patient with tumor rupture according to our proposed definition has a poor prognosis. The clinical application of this definition is, however, another matter. We proposed this definition so that it may be used and either validated or refined prospectively. Multidisciplinary teams will obviously have the latitude to interpret the relevance and applicability of the definition on an individual patient basis. For instance, an incisional biopsy of a small gastric GIST with an indolent mutation should probably not entail lifelong imatinib treatment, even if it is, de facto, tumor rupture. That is the nature of clinical medicine.

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Numbers in sarcoma surgery are small. Our definition is based on the limited available evidence, however scarce, and an interpretation of this evidence. As we explicitly state, this definition will now have to be validated in prospective studies. If terms are not revised and updated as data become available, they will become obsolete. Asare and Feig recommend adherence to a "long-standing, established definition". No study to date has yet specifically applied such a definition, which does not exist, and therefore cannot be commonly shared.

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