LETTER TO THE EDITOR

Thromboelastometry changes in myeloproliferative neoplasms—surrogate for a procoagulant haemostatic imbalance or a consequence of technical reasons?

Comment on *A. Tripodi et al. Ann Hematol (2013) 92:1633–1639*

Michael Nagler · Hugo ten Cate

Dear Editor,

With great interest, we read the article by Tripodi et al. [1] investigating the changes of global hemostatic parameters in patients with myeloproliferative neoplasms (MPN). The authors aimed to study whether global tests would be able to detect a "procoagulant imbalance" that correlates with an increased risk for thromboembolism in patients with MPN and to propose a measure for risk assessment and follow-up in clinical trials. This issue is in line with efforts to establish global measures of bleeding and thrombotic risks in a variety of clinical situations [2, 3]. However, the most important questions to give an answer on this issue are as follows: (1) Do the changes represent the thrombotic risk or are they a consequence of confounding variables? (2) Is the degree of changes relevant? We feel that these issues require critical appraisal.

The authors compared thromboelastometry measurements in patients with essential thrombocythemia (ET), primary myelofibrosis (IMF), and polycythemia vera (PV) with healthy controls. The median platelet count (PLT) in ET and IMF patients was much higher than that in PV patients and healthy controls ([1], Table 1). The influence of PLT on thromboelastometry parameters is well-established [4], and our group was able to show that PLT is a major factor of influence, independent from other factors that may affect coagulation (Fig. 1) [5]. Thus, it seems likely that observed changes are the result of a varying PLT and not an "intrinsic procoagulant imbalance". This is promoted by the fact that no differences have been found in PV patients ([1], Figure 3).

Another issue is that the investigation is based on the assumption that patients with MPN have a "procoagulant imbalance" *in general*. Most patients were on antiplatelet therapy, phlebotomy, and cytoreductive therapy, which are effective measures to reduce the thromboembolic risk in MPN patients [6]. We are convinced that a study aiming to propose a measure for risk assessment and follow-up must be done using clinical outcomes such as thromboembolic events or at least established risk factors of thromboembolic events in MPN patients [7].

The authors report on two out of nine parameters of INTEM test. A median maximum clot firmness (MCF) of 68 mm in ET and IMF (range 56–76 and 57–78, respectively) was reported versus 61 mm in healthy controls (range 51–68 mm). CFT was 47 s (30–91) in ET, 53 s (34–104) in IMF, and 71 s in controls (range 47–121). The differences were stated to be statistically significant ($p < 0.05$), but it was not reported if the analysis was corrected for multiple testing (nine parameters of INTEM test). Furthermore, given the large variability and recognized problems in reproducibility [8–10], it has to be discussed which degree of changes is considered as relevant to promote its use in clinical practice and scientific inquiry.

Development of global measures of bleeding and thrombotic risks is an important issue in thrombosis and hemostasis research. However, all validity aspects have to be mentioned to be of value in scientific inquiry and clinical practice.

M. Nagler (✉)
Department of Haematology and Central Haematology Laboratory,
Inselspital University Hospital, 3010 Berne, Switzerland
e-mail: mic.n@gmx.ch

H. ten Cate
Department of Internal Medicine, Laboratory of Clinical Thrombosis and Haemostasis, and Cardiovascular Research Institute, Maastricht University Medical Center, Maastricht, The Netherlands

Fig. 1 Changes of thromboelastometry parameters with increasing platelet count. Results of an in vitro investigation studying the impact of hematocrit level (Ht) and platelet count on thromboelastometry parameters [5] are shown (maximum clot firmness (MCF) of the INTEM test with varying platelet counts at different Ht; unpublished figure). *Box plots* display median, inter-quartile range, and range
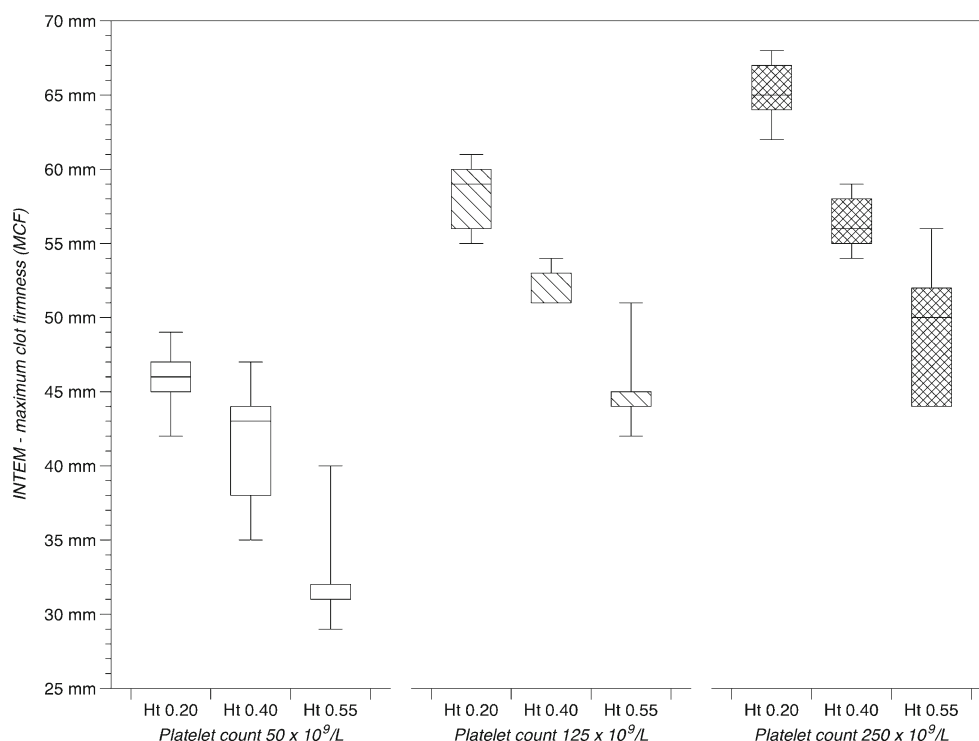
Conflicts of interest   The authors declare that they have no conflict of interest.

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