

## Is the Bleeding Time Prolonged in Oral Anticoagulant Treatment?

Sir,

In a recent issue of *Thrombosis and Haemostasis*, Dr. Marongiu et al. (1) made some comments on a study of ours on bleeding time techniques (2). We thank Dr. Marongiu and co-authors for their interest, and we like to answer their remarks.

To summarise our study: we compared three bleeding time techniques: Ivy, Simplate II parallel to the antecubital crease ("horizontal" i.e. perpendicular to the forearm) and Simplate II perpendicular to the antecubital crease ("vertical", i.e. parallel to the forearm). We tested the sensitivity and specificity of the three methods by comparing test performance in healthy volunteers, half of whom had received 500 mg acetylsalicylic acid. We also tested the specificity for primary hemostasis by performing bleeding times in patients on oral anticoagulant treatment. The three tests performed equally well (or poorly!) in detecting an aspirin induced defect of primary hemostasis, whereas we found no prolonged bleeding time with any of the tests in anticoagulated patients.

Marongiu et al. comment on the latter part of our study, with reference to their previous work in which they found prolonged bleeding times in anticoagulated patients during an overdose phase (3). They list several hypotheses for the seemingly discrepant results. These include that in our study the control subjects from whom the reference values were obtained were younger than the anticoagulated patients, and the rather high reference range we found for the Simplate methods. They also suggest an analysis which takes the intensity of anticoagulation into account.

We agree with these hypotheses, that were also explicitly discussed in our paper. Since prolonged bleeding times have been found in patients with severe hemophilia (4), it seems logical to expect the bleeding time to be prolonged in patients who are overanticoagulated. Our study, however, had a practical rather than a theoretical purpose. The "ideal" bleeding time technique should be sensitive and specific for primary hemostasis defects, i.e. platelet function, and insensitive for moderate defects in the clotting system. In fact, we expected the horizontal Simplate II to perform poorly in this respect, since it is so much more traumatic than the Ivy, and, to a lesser extent, than the vertical Simplate II. As it turned out, none of the three techniques was sensitive to a moderate anticoagulation effect.

Although we recognise that, due to practical reasons, the control subjects were younger than the anticoagulated patients (mean ages 26 and 55 years), we think that the weak relation between bleeding time and age would not cause any major effects (5). Moreover, it does not influence our comparison of three techniques. As can be seen from Figure 3 of our paper (2), most patients had bleeding times several minutes below the cut-off point.

We have no clear-cut explanation for the high reference range for the Simplate technique, although similarly high ranges have been reported by others (6). Again, however, since the reference ranges were obtained within the same study and all tests were performed by the same two investigators, we do not think that this could have affected the result. In our view, this just demonstrates again that the Simplate device is not standardised at all. Machereel et al. (7) have convincingly demonstrated differences between different batches of the Simplate device. We feel that the Ivy technique, when performed by a well-trained technician with a steady hand, offers more guarantee for standardisation than the Simplate device.

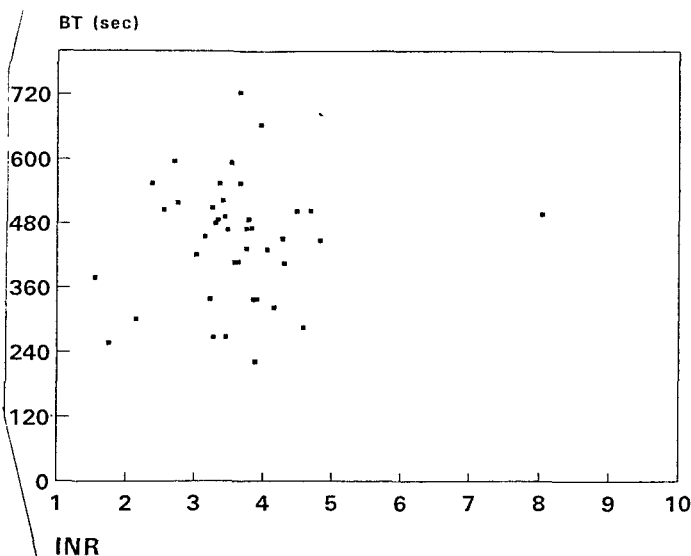


Fig. 1 Bleeding time (Simplat II in horizontal direction) and intensity of anticoagulation. The bleeding time is shown as measured with the Simplate II device in horizontal direction, in patients who received oral anticoagulant treatment. The intensity of the anticoagulation (as INR) is set out on the X-axis. Linear regression coefficient for the bleeding time for each unit of INR: 9.8 (SE 17).

Finally, we have re-analysed our data to see if the bleeding times were associated with the intensity of anticoagulation. As the figure shows for the Simplate II in horizontal direction, no association could be discerned (similarly for the Ivy and vertical Simplate – data not shown).

This does not rule out the possibility of prolonged bleeding times in excessive anticoagulation, since most of our patients were within the therapeutic range. Such a prolongation is likely. We do not think, as suggested by Marongiu et al., that this might imply an impaired platelet function in chronic anticoagulation, since prolonged bleeding times have been observed in severe clotting factor deficiencies.

In conclusion: the bleeding time may be sensitive to severe coagulation defects, but is insensitive to mild or moderate defects of secondary hemostasis.

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