way to analyze our data would have been to pool all the data obtained with the two different LMWHs; major chemical, biological and clinical differences exist between these LMWHs, and there has been much debate on this issue. We believe that pooling these data would have generated many more letters to the editor!

There are few biological markers of prognosis in unstable angina. Our recent studies have focused attention on vWF as a new marker of potential interest in acute coronary syndromes. It appeared consistently as a predictive factor of outcome, and we believe it deserves attention and further evaluation in large studies. Our most recent publication demonstrated that the new anticoagulants tested in unstable angina behave better than UH with regards to vWF release. We agree it should also be confirmed. Step-by-step we are progressing in the understanding of the role of vWF in the prognosis of unstable angina, and the time has come for head-to-head comparisons between the new anticoagulant treatments. In that regard, the ARMADA study has now been completed and we will share the data very soon. I am sure that Dr. Hödl will appreciate the results.

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Enoxaparin for Acute Coronary Syndromes?

Goodman et al. (1) conclude that enoxaparin is a more effective antithrombotic treatment than unfractionated heparin (UFH) for the prevention of rebound ischemia in patients with unstable angina or non-Q-wave myocardial infarction. We suggest an alternative conclusion.

Enoxaparin’s plasma half-life is two to four times longer as compared to UFH after subcutaneous administration (2), even more when compared to UFH given intravenously, as in the Goodman et al. study. Activity against factor Xa and thrombin disappears only after more than 16 h (3), following moderate doses of enoxaparin. With high doses, as used in the ESSENCE study (1), enoxaparin’s plasma half-life is substantially longer (4).

Therefore, after stopping study drugs in the ESSENCE study, enoxaparin’s antithrombotic effect very likely lasted much longer than that of UFH. After stopping UFH, ischemic events during the 48-h monitoring period were twice as frequent as after stopping enoxaparin (45% vs. 26%), whereas there was no difference while on active treatment (25%)—compatible with an antithrombotic effect lasting about one day longer after enoxaparin. In addition, enoxaparin’s antithrombotic effect wanes much more slowly as compared to IV UFH. This may have added benefit by attenuating a heparin rebound effect.

It remains to be convincingly shown whether enoxaparin or other low-molecular-weight heparins exert superior antithrombotic effects as compared to UFH. Superior clinical benefit might be explained by pharmacokinetic differences only. For patients with acute coronary syndromes, extending the duration and slower weaning (5) of IV UFH may well be better and cheaper.

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REPLY

Pechlaner et al. suggest that our findings (1) of less rebound ischemia with enoxaparin as compared to unfractionated heparin (UFH) are simply due to the longer half-life of enoxaparin. However, the ischemic episodes (average number and duration) identified during continuous electrocardiographic monitoring were statistically significantly lower in the enoxaparin as compared to the UFH group not only during the first 12 h after drug discontinuation but also during the >12 to 24-h and even the >36 to 48-h time intervals. This suggests that the benefit seen with enoxaparin is not simply due to prolonged half-life and greater anti-Xa:IIa activity that “wanes” more slowly than UFH. Indeed, there is growing evidence supporting additional mechanisms of benefit of enoxaparin over UFH beyond the differences in pharmacokinetics; for example, the significant blunting of the rise of von Willebrand factor with enoxaparin in the first 48 h of treatment (2).

As we noted, our substudy (1) was stopped at the time of overall trial completion but prior to enrollment of an adequately powered sample size to confidently address the initial 48-h period of active