The aim of this study was to evaluate if standard rotational thromboelastography (ROTEG) analysis could be used for monitoring of effects of recombinant factor VIIa (rFVIIa) on dilutional coagulopathy. Hemodilution was done in vitro as was administration of rFVIIa. The findings of the study were negative and this was attributed by the authors to methodological problems. There appear to be some methodological weaknesses in this study, which make the results difficult to interpret. In particular the authors did not attempt to distinguish among three very different causes of coagulopathy: haemodilution, hypothermia, and HES administration (and possibly also acid-base derangement). They did a very limited battery of laboratory clotting tests and did not look for markers of coagulation or fibrinolysis. These are major deficiencies.

Introduction:

The authors state that patients undergoing massive hemorrhage experience dilutional coagulopathy with crystalloid and/or colloid resuscitation. But there is a difference between dilutional coagulopathy and the coagulopathy caused by colloids, in particular hydroxyethylstarch. A previous in vitro study with TEG suggested that dilutional coagulopathy with crystalloid resuscitation is found only after 50% haemodilution is reached. Large volumes of hydroxyethylstarch transfusion are consistently associated with the development of a coagulopathy and clinical bleeding. It is unfortunate that the authors did not distinguish between these distinct causes of coagulopathy.

Materials and Methods:

The authors do not clarify whether the ROTEG and PT analyses were done with the blood warmed to body temperature. The addition of 33% colloid might have cooled the blood significantly. If the ROTEG was started immediately, it is unlikely that the blood would have had sufficient time to re-warm. This introduces a powerful confounding factor, hypothermia. Interestingly, one study found a small decrease in the PT with hypothermia and a delay in clot formation with TEG. Standard coagulation tests are automatically performed at 37 degrees and may miss the effects of hypothermia.

Hypothermia, haemodilution and HES affect platelet number, platelet function as well as other tests of coagulation besides the PT. It seems a major deficiency that the authors did not measure platelet number, platelet function and the PTT. In another study examining the effects of hemodilution with HES on coagulation, a whole battery of tests, including measurement of coagulation proteins was done. HES may also alter the pH of blood, which can in turn affect coagulation. This effect would have been lessened if the haemodilution had been done in vivo. The authors should also have measured pH.

The authors used the Wilcoxon paired test. But from their methods, it appears that there were three
specimens each time; undiluted blood, blood diluted with HES; and blood diluted with HES plus rFVII. If this is the case, perhaps Kruskal Wallis ANOVA may have been more appropriate for their analysis.

Results:
These are clearly expressed.

Discussion:
The authors do not comment on the apparent discrepancy between the PT and the CT. Both are measures of time to initial clot formation. With HES, only the PT was prolonged. The ROTEG abnormalities could be explained by platelet abnormalities (increased CFT and increased A15). One would not necessarily expect these to correct with rFVII. The authors express surprise at their results. But it seems strange to me that they should expect the same results as with Haemophilia or liver dysfunction, in which there are very low specific clotting factor concentrations. With HES haemodilution, the clotting factor concentrations may remain adequate. There are other possible mechanisms for coagulopathy, not all of which would respond to rFVII. The correction of the PT does not necessarily mean that clotting function was completely normalized. The authors speculate about large amount of thrombin generation following rFVII. They should have measured thrombin before and after rFVII and speculation would not then be necessary.

Like the authors, I do not know exactly how to interpret their results.

Additional questions:
Is the question posed by the authors new and well defined?
Yes.
Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
The methods are well described, but, as detailed above, the methods are deficient for the questions that the authors sought to answer.
Are the data sound and well controlled?
Yes.

Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes

Are the discussion and conclusions well balanced and adequately supported by the data?
No. The discussion and conclusions are confusing. There are results missing, which make it difficult to form meaningful conclusions.

Do the title and abstract accurately convey what has been found?
No. There were other things going on here besides dilutional coagulopathy (e.g. hypothermia, direct effects of HES, acid-base derangement)

Is the writing acceptable?
Yes.

References:

What next?: Reject because scientifically unsound

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests: None.