Reviewer's report

Title: Thromboelastography on plasma reveals delayed clot formation and accelerated clot lyses in HIV-1 infected persons compared with healthy controls

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Reviewer: Marcus D. Lancé

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Major comments:
This manuscript is highly speculative and not very well supported by the presented data.
I would suggest to report a thorough analysis of coagulation factor concentrations, D-dimer and FSP. Furthermore an analysis of thrombingeneration would be worthwhile.
As there seems no values of the lipid-analysis I would suggest to leave this completely out.
Please comment on the impact of EDTA on the TEG-analysis. Although it is been applied in all analysis (and might be a structural problem) this might have an impact.
What is the purpose of stratification for smoking history? Please introduce this in the background section and mention the data-sampling in the methods section.

Detailed comments:
Abstract section:
Please avoid the last sentence (given the thromboembolic events...) as it is not shown in the current paper.
Page 3, line 4, please describe the life style factors which are specific for HIV, or are this general factors?
Page 3 lines 10-11 please re-word this sentence as it is very vague. What about the hypofibrinolytic state? ...Similarly, the flowing blood comprised of plasma and blood cells may change from its normal state to hypercoagulant, hypocoagulant and hyperfibrinolytic depending on the disease/condition of the patient.
Page 3 lines 12-14 ... Importantly, there appears to be a balance between the endothelium and the flowing blood indicating that a pro-coagulant state of one part will be counterbalanced. Please add „ under stable conditions“, because you describe a steady state.
Page 3 lines 21-22. Please re-word this sentence as HIV-infection itself does NOT cause this alterations (it is at least not proven that this is a direct action of the virus).
Page 4 lines 43-45. ..When evaluated in plasma, TEG/ROTEM provides a unique
opportunity to examine functional coagulation and especially fibrinolysis and/or fibrinolytic resistance of the fibrin clot in stored samples. Please avoid the word „unique“ and mention the disadvantage of plasma analysis in contrast to whole blood analysis which might be of importance during inflammation.

Page 5 line 63-64 ... Several articles... Please leave this sentence out.

Page 6 line 95. Please give this sentence a place more in the beginning of this section as it seems a little late here.

Page 7 line 111. Please describe more precise the platelet analysis. I guess you mean here platelet count? Please display the count in the result section.

Page 9 line 153. ....indicative of a slower thrombin generation and/or higher levels of anticoagulant factors.. This is interpretation, please leave this out here.

Page 9 line 164 pp. ...The findings were not reproduced when the analyses were performed on HIV+ and controls separately suggesting that these differences were driven by the differences in lymphocyte subsets between the two groups. Again the latter is an interpretation, which might be discussed later in the manuscript.

Page 10 line 188: ..suggesting enhanced in vivo activation of platelets. See above.

Page 11 lines 194-198 please leave the whole lipid analysis out as it does not contribute to the rest of the paper.

Page 12 lines 222-223. ... anticoagulant factors (antithrombin, protein c, protein s, FII, FVII, FIX, FX) in untreated HIV+ suggesting that impaired hepatocyte function plays a role for the IMBALANCE OF coagulation.

Page 12 lines 231-233. ... Thus, some studies have found elevated levels of d-dimer in treated HIV infected persons [18,42], in accordance with our finding of a pro fibrinolytic state of plasma. Please be more precise: ...which might be a result of a pro fibrinolytic state as we could demonstrate...

Page 12 lines 238-end of page

.. In addition to factors circulating in plasma, whole blood contains red blood cells, leukocytes, platelets and microparticles that all contribute to hemostasis [7,44-46]. Platelets are key players in coagulation and as the results of this study are based on plasma samples, soluble factors derived from platelets may influence the results....

This is a very complicated description of the fact that the analyses were done in plasma which lacks the cellular contribution to coagulation. Please re-word.

Page 13 line 243. Please comment on the fact that the level of sCD40L is inversely correlated with the R-time but only the relation sCD40L/platelet count are different between the groups. What about the induced thrombopenia due to cART therapy? Maybe the impact of this finding is not due to platelet activation? Please comment on this.

Page 14 line 270. Please add some comments on the fact that TEG was done in plasma and not in whole blood. What about EDTA? Please add comment on this
Page 14, lines 280-281. by TEG and also we found evidence for enhanced plasma activation in vivo. Please be more precise. What do you mean by „plasma activation“? As the study was performed in vitro this conclusion is supported by the data.

Page 14 lines 281-283. ... Together these findings suggest that hypocoagulability in HIV infected persons may reflect a universally adaptive response, comparable to that observed in acute critically ill patients, ensuring blood flow through an activated, procoagulant microvasculature.

Please avoid this in the conclusion. It was not topic of the investigation.
Please re-word the conclusion section as it is highly suggestive and not completely based on the results of the paper.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have no competing interests.