Dear Editor and Editorial Staff,

Thank you for your continued support in improving this manuscript. We appreciate your thoughtful comments. We have enumerated the changes according to the editor's correspondence below.

Reviewer #1: An excellent retrospective large review of NASH patients with cirrhosis demonstrating that they are more thrombophilic than non-Nash cirrhosis and might well benefit from interventions to prevent clotting

Response:

We thank the reviewer for their positive commentary and feedback

Reviewer #2:

Comments To Authors	This manuscript investigates the link between non-alcoholic steatohepatitis and the risk of portal vein thrombosis. The topic of the paper is important and relevant. The study is well-executed and the article is well-written. My only detailed comment concerns the Discussion section. In it, the authors expound on several different therapeutic strategies to prevent or treat thromboembolic events (heparin, etc.). In the field of traumatic and surgical coagulopathy, one emerging paradigm is that of balanced intervention, according to which hypocoagulant states may be treated using a combination of procoagulant factors and anthithrombin, all supplemented in physiologically relevant amounts (J Trauma Acute Care Surg (2012) 73:S95-S102; Molecular Biosystems (2014) 10:2347-2357; Scand J Trauma Resusc Emerg Med

(2012) 20:1). Could the authors consider and discuss the possible development of this idea in application to thromboembolism? Specifically, perhaps a good strategy would be to treat thromboembolic patients (e.g., for the type of thromboembolism relevant to the subject of the manuscript) with antithrombin, with possible anticoagulation reversal using pro-coagulant factors?

Response:

We are aware of the data looking at Prothrombin complex concentrates (PCCs) in combination with antithrombin (AT) and several reports suggesting the combination of PCC-AT when used concurrently with fibrinogen may provide an alternative to restore the delicate homeostasis of coagulation and its role in both restoring normal thrombin and fibrinogen generation, however, this combination has not been well studied in liver disease. Administration of antithrombin III on conjunction with heparin has been shown to rebalance hemostasis in a solitary case report of a patient with cirrhosis and recurrent thromboembolism. Given the lack of evidence on this topic, we feel that any deep speculation is beyond the scope of our manuscript. Nonetheless, it is an intriguing avenue for future study in liver patients and we have included some commentary in our discussion.

Thank you again for your time and consideration in this manuscript. We hope we have addressed all of your concerns. Please let us know if there is anything else that needs to be addressed.

Sincerely,

Jonathan G. Stine, MD MSc, FACP
Patrick G. Northup, MD MHS