Reviewer's report

Title: Quantitative Modeling of the Physiology of Ascites in Portal Hypertension

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Reviewer: Beate Appenrodt

Reviewer's report:

Levitt et al. describes a new, quantitative model for the pathomechanism of ascites in portal hypertension. The authors explain in detail the two common theories of evolving ascites, the underfill and the overflow theory. They conclude that the mechanism of developing ascites is only poorly understood beside both theories.

Furthermore, they remark that the pathophysiology of the known plasma-ascitic gradient of albumin is also poorly understood.

The manuscript is structured in three sections. In section III, a new quantitative physical model describing ascites accumulation is discussed.

It is a very interesting and new attempt to explain the pathomechanism of ascites.

However, there are some comments:

1) One main pathomechanism is the activation of the RAAS in portal hypertension. Please discuss this mechanism more detailed.

1) On page 14 (E), SAAG as differential diagnostic marker between different causes of ascites is discussed. “A SAAG of > 1.1 gm% is ... indicative of portal hypertension (either cirrhotic or cardiac ascites).” The authors should explain the pathophysiology of cardiac ascites in comparison to cirrhotic ascites. Portal hypertension is not the common cause for cardiac ascites.

2) Please give references for a) “…administration of spironolactone or furosemid decreases P(HVPG) by about 20%” and b) decrease in cardiac output with corresponding fall in hepatic blood flow and P(HVPG) in the main text..

3) On page 17, the authors explain that clonidine produces a significant decrease in P (HVPG).

Please explain the effect in more detail and add references.

It is not common that clonidine is used for treatment of varices. The authors should comment on this and add references in the main text (not only in the attachment).

5) The authors should also discuss the effect of terlipressin and vasopressin-2 antagonists in the treatment of ascites in the main text.
Minor comments:
1) Page 8, line 22 (section II, A.): please change ascetic in ascitic (or contrariwise)
2) typing error: Page 20, 2 mmHg instead of 2 mm

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I do not have anything to declare.