

Reviewer 02454978:

(1) Generally well-written introduction. The rationale for this review has been clearly stated.

Response: We thank the reviewer for their positive comments

(2) Page 9, Statistical analysis,

To my understanding, the choice of using either fixed- or random- effect(s) model is dependent on whether the included studies were functionally identical, in terms of characteristics, or methodology etc. I feel that this should be stated (with references provided) at the outset. This is primarily because it probably doesn't make sense for the authors to choose random-effects model, even before knowing whether their included studies were going to be identical? It would also be good if the authors could provide some references with regards to the use of DerSimonian and Laird effects model, Cochran's Q statistics and I^2 index.

Response: We have stated this and provided requested references (page 10).

(3) Page 12, PVT and Mortality,

Just checking if the funnel plot to assess the relationship between reported effect variance and the reported studys' odds ratio was used on a post-hoc basis? This is because such intent was not stated earlier on in page 9, "Statistical analysis" section. Secondly, I am not sure if it makes any sense in showing a funnel plot with only three (3) data points. How do we judge the symmetry, in order to ascertain the presence or absence of any publication bias?

Response: We have added a sentence in the statistical analysis section to comment on the post-hoc funnel plot we created (page 10). We agree that the inclusion of only 3 studies limits the systematic assessment for publication bias and have provided commentary on this in the discussion section (page 16).

(4) Page 13, The authors attempted to pool OR results for secondary outcomes (i.e. effects of PVT on ascites development). However, they did not state whether fixed- or random-effects model was used.

Response: We used random effects modeling and have clarified this (page 14).

(5) Page 15,

I feel that the authors need to elaborate a little more about the limitations. For example, the high level of heterogeneity presented in Figure 4 (PVT and ascites) may limit interpretation, and this may be due to the small number of included studies.

Response: We agree that heterogeneity is present and is a limiting feature to our study. We have provided commentary on this (page 16) and also in the conclusions statement (page 17)

(6) For Figure 1, I suggest stating specifically the number of studies (including citations) which were excluded. For example, "Different primary endpoint (n=2)^[xx,xx]", "No comparison group (n=1)^[xx]" etc.

Response: We feel this figure is appropriate the way that it is presented and have not made any adjustments.

(7) It would be good to concatenate Table 1 and Table 2.

Response: We have elected to keep table 1 and table 2 separate given that they describe different characteristics, study level and patient level.

Reviewer: 02456377

COMMENTS TO THE AUTHORS:

The authors in this study provided us a systematic review about the relationship of portal vein thrombosis, mortality and hepatic decompensation in patients with cirrhosis. The results showed portal vein thrombosis appeared to increase mortality and ascites in cirrhosis patients, however, other markers of decompensation including gastroesophageal variceal bleeding or hepatic encephalopathy should be needed more trials.

The manuscript is well organized and is written in a fluent style. There are some suggestions that remain to be considered.

1. The Figure1-4 should be provided figure legends, so as to elucidate the results more clearly. In addition, the figures should be uploaded in the format of JPEG, TIFF,

Response: We agree and have provided figure legends for each included figure in our paper.

2. In this study, the authors only enrolled the patients with cirrhosis, the patients with liver cancer or patients with other liver diseases were not taken into account. So, whether portal vein thrombosis was related to the mortality and ascites in liver cancers patients? Or, portal vein thrombosis appeared to increase mortality and ascites specifically in cirrhosis patients and was no relationship with other liver diseases?

Response: We chose to exclude patients only with cirrhosis to provide the most rigorous study population in order to be able to draw the most homogenous conclusions. Including patients with neoplastic associated portal vein thrombosis would introduce significant bias and heterogeneity. Furthermore, non-cirrhotic portal vein thrombosis typically occurs in the absence of chronic liver disease and is usually present in the setting of systemic disease leading to a clotting predilection (e.g. JAK-2 mutation or anti-phospholipid antibody syndrome or Sweet syndrome to name a few) and this population is an entirely different phenotype so we chose to exclude these patients as well.

3. In Conclusions section, the authors mentioned that "More trials with a direct comparison group are needed". The authors should briefly discuss how to do further investigation and predict the prospect of possible results.

Response: We have expanded this section (page 17) and would propose prospective, randomized study of either portal vein thrombosis prevention or treatment in a placebo controlled manner with a direct comparator group as the

study design of choice utilizing heparin based or new direct acting oral anticoagulation therapy.

Reviewer: 02453616

COMMENTS TO THE AUTHORS:

The authors used a-priori determined criteria to select 3 datasets out of the originally identified 226 studies. The criteria appear to be reasonable according to the scope of the current investigation, although it is a dramatic reduction of sample size after filtering by the criteria, causing the authors to conclude that they were unable to generalize their results due to the relatively small number of included studies.

There are two questions coming out of this, considering whether the applied criteria are too stringent and whether it is necessary to be so stringent:

1. One of the criteria used was "if PVT was found in non-cirrhotic patients with portal hypertension: If now we consider expanding the analysis cohort, can't we just remove only the non-cirrhotic patients and keep the cirrhotic patients for analysis if they are present in the study? What is the problem of doing this?"

Response: While we agree that removing the non-cirrhotic patients would expand the included study number and thus increase the overall patient population for calculation of pooled measures of effect, the logistics of doing so do not allow for this as most studies do not delineate which individual patients with non-cirrhotic portal hypertension experienced our outcomes of interest.

2. In the Background, the authors stated that "Others have argued that PVT does not affect clinically relevant outcomes" from the reference 11. This result is against the authors' observation. Interestingly this study was not included in the final 3 datasets the authors used. Why were they excluded? Why did reference 11 have the validity to make this claim and yet failed to pass the authors' criteria? If reference 11 did not have the validity to make the claim, or they have the validity but the data fell out of the scope of this manuscript, the authors should explain why, because it appears suspicious where the authors mentioned in the Introduction a study with an opposite conclusion to what the authors eventually make, and yet left it out of their meta-analysis in the end. It looks confusing.

Response: Reference 11 is a large multicenter multinational prospective series of 1,243 adult patients with cirrhosis without baseline PVT by Nery et al that while initially considered in full-text review, was excluded specifically because absolute numbers for mortality or individual types of hepatic decompensation were not provided; rather, univariate and multivariable analysis p-values were provided only and only a composite of hepatic decompensation was given in absolute number. We have acknowledged this in the results section on page 11 and again as a limitation on page 15-16.