

We would like to express our sincere thanks to the reviewers for the constructive and positive comments. We have addressed the comments raised by the reviewers, and the amendments are highlighted in yellow in the revised manuscript.

Reviewer #1:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** This study aimed to develop and externally validate a nomogram for prediction of transmural bowel infarction (TBI) in patients with acute superior mesenteric venous thrombosis, and the nomogram achieved an optimal prediction of TBI. This is an interesting study; however, I have the following questions and comments.

(1) The optimal cutoff value of the Nomo-score was determined to be 90. According to your nomogram as shown in Figure 2A, the score 90 means that one of three factors (DVT history, rebound tenderness, and decreased bowel wall enhancement) is positive. Is this correct? If this is correct, it is much easier to remember the risk factors for TBI, as compared to the score, and you emphasize these clinical factors in the text.

(2) As you mentioned in the section of discussion, evaluation of decreased bowel wall enhancement on enhanced CT was influenced by interpretation of

each radiologist, which may vary among them. Did you examine the association between the length of decreased bowel wall enhancement and transmural bowel infarction?

Response: (1) Thanks for your comments. Yes, the score 90 means that one of three factors (DVT history, rebound tenderness, and decreased bowel wall enhancement) is positive. We can easily remember these risk factors. However, using the nomogram we can calculate the exact probability of progression to transmural bowel infarction. In order to provide a more accurate calculation of predictions than drawing lines on the nomogram, we added the scoring system in Supplementary Table 1 (presented as follows) in the revised manuscript. Besides, we have also added **“The scoring system is shown in Supplementary Table 1, which can be used for a more accurate calculation of predictions than drawing lines on the nomogram”** in the revised manuscript (page 14, paragraph 1).

(2) Since it is hard to assess the length of decreased bowel wall enhancement quantitatively on CT image, we did not examine the association between the length of decreased bowel wall enhancement and transmural bowel infarction. But we think further high-level evidence are needed to clarify this issue. Thus, we have added **“In addition, since it is hard to assess the length of decreased bowel wall enhancement quantitatively on CT image, we did not examine the association between this factor and TBI. Further high-level evidence are needed to clarify this issue”** as a limitation in the Discussion section of the

**Supplementary Table 1** Point assignment and prognostic score for the nomogram.

Previous history of DVT	Points	Rebound tenderness	Points
No	0	No	0
Yes	90	Yes	100
Decreased bowel wall enhancement	Points	Serum lactate levels	Points
No	0	$\leq 2$ mmol/L	0
Yes	94	$> 2$ mmol/L	59
Total Points	Probability of transmural bowel infarction		
21	0.1		
62	0.3		
89	0.3		
112	0.4		
132	0.5		
153	0.6		
175	0.7		
202	0.8		
243	0.9		

Reviewer #2:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** In this paper the authors aim to develop and externally validate a nomogram for prediction of transmural bowel infarction (TBI) in patients with acute superior mesenteric venous thrombosis (SMVT).

The authors conclude that the nomogram achieved an optimal prediction of

TBI in patients with AMI. Using the model, the risk for an individual patient inclined to TBI can be assessed and this can lead to a rational therapeutic choice.

#### Minor Revisions

A) MATERIALS AND METHODS section Patients, Page 8 lines 15 16: Two senior radiologists reviewed all CT images. The authors should define what the k concordance of the two senior radiologists was and in the statistical section indicate that is used the k concordance. I suggest to anticipate the statistical analysis section after the outcomes section and so to anticipate the lines 1-4 of the current page 12 and then do follow the current sections Data collection, Construction of the nomogram, Performance of the nomogram, Clinical use assessment.

Response: Thanks for your kind suggestion. We have added **“K statistics was used to evaluate the concordance between the two radiologists, and any disagreements were resolved by discussion” in the revised manuscript (page 8, paragraph 2)**. Besides, we have placed the **statistical analysis section** after the outcomes section as per your suggestion.

B) Some of the variables mentioned in table 1 do not seem to me with a Gaussian distribution, the authors if it is true what I suppose, should evaluate and verify and in this case they should report the variables as median (min-max) or median and IQR. They should also indicate in the statistical analysis section how the variables are described.

Response: As suggested, we have added **“Continuous variables were**

presented as median (interquartile range [IQR]), and were compared between the training and validation cohort using Mann-Whitney U test or t-test as appropriate. Categorical variables were reported as whole numbers and proportions, and were compared by the  $\chi^2$  test or Fisher exact test where appropriate" in the statistical analysis section (page 10, paragraph 2), and revised the continuous variables as median (IQR) in the Table 1.

C) The authors should indicate which statistical tests were used in table 1 in the statistical analysis section and according to whether the distribution is Gaussian or non-Gaussian use the appropriate tests.

**Response:** We have added "Continuous variables were presented as median (interquartile range [IQR]), and were compared between the training and validation cohort using Mann-Whitney U test or t-test as appropriate. Categorical variables were reported as whole numbers and proportions, and were compared by the  $\chi^2$  test or Fisher exact test where appropriate" in the statistical analysis section (page 10, paragraph 2).

D) 12 patients with SMVT are excluded in table 1 and are not reported in the results

**Response:** We have added "After excluding 12 patient with chronic SMVT..." in the revised manuscript (page 12, paragraph 2).

E) In the results section page 13 section Characteristics of the study population the authors state: There were no differences...; actually some variables show significant differences, it is necessary that the authors verify or correct.

Response: We have changed this sentence as **“There were no differences in the clinicopathological characteristics between the two cohorts in most of the comparisons”** in the revised manuscript to make it more accurate (page 13, paragraph 4).

F) Results section: I am surprised that in a venous ischemia the D Dimer is not significantly increased. The authors use as cut off  $> 0.5\text{mg} / \text{L}$ , did they evaluate whether there are other cut-offs to which the D Dimer could be useful and statistically significant?

Response: In our study, the D-dimer in both the training (16.9, IQR 3.0-179.6) and validation cohorts (14.1, IQR 6.9-60.2) were significantly increased (Table 1). We just did not detect a significant difference between the transmural bowel infarction (TBI) group and reversible intestinal ischemia group, and this was not affected by the cut off value.

G) Liver Cirrhosis and therefore the consequent portal hypertension are considered risk factors in the literature, is it possible that the lack of significance at the multivariate analysis depend on the number of cases? If the answer is yes, the authors should report in the results how many patients with cirrhosis were in the series and report it in the discussion.

Response: In the univariate analysis of risk factors associated with transmural bowel infarction in the training cohort, the liver cirrhosis was associated with transmural bowel infarction. However, it was eliminated after the multivariate logistic regression. It might be due to the number of cases, but we deemed that the sample size is not a major reason. As suggested, we have added **“In the training cohort, 82 patients had a clinical history of liver cirrhosis, and 17**

(20.7%) cases developed TBI. In the validation cohort, 18.9% (7/37) of the patients with liver cirrhosis progressed to TBI finally” in the revised manuscript (page 13, paragraph 4).

H) Discussion seems to me to be studied in deep, however I suggest to shorten it because it is very long. I congratulate the authors for the captions to the figures very explicative and complete.

Response: Thanks for the suggestion. The discussion might be a little too long, because this issue is very important in clinical practice. We intended to provide profound evidence to guide clinical decision-making.

Reviewer #3:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** This study was conducted to stratify the risk of mesenteric venous thromboembolism (MVT) developing to bowel infarction by nomogram established from two independent retrospective cohorts. The incidence of acute abdomen or mesenteric ischemia caused by MVT itself was relatively low, however the mortality after developing intestinal gangrene was reportedly ranged high and mostly lethal. The training cohort was thoroughly examined by multiple logistic regression model and nomogram by four independent risk factor significantly predicted TBI in validation cohort.

Response: Thanks for your positive comments.

Reviewer #4:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** Very interesting paper. Outside of temperature did you assess other vital signs or change in signs like heart rate, respiration rate and blood pressure? Did you consider trying a lower value of c-reactive protein?

Response: We deemed that the vital signs such as heart rate, respiration rate and blood pressure might be affected significantly by the patients' basic characteristics. Therefore they were not considered for model construction. We used 50 mg/l as the cut off value of c-reactive protein, which is in accordance with previous study<sup>[1]</sup>. We used this value to be comparable with previous data. We think that this cut-off value is reasonable, for a lower value might not be specifically predicting TBI.

**Refence:**

1 Nuzzo A, Maggiori L, Ronot M, Becq A, Plessier A, Gault N, Joly F, Castier Y, Vilgrain V, Paugam C, Panis Y, Bouhnik Y, Cazals-Hatem D, Corcos O. Predictive Factors of Intestinal Necrosis in Acute Mesenteric Ischemia: Prospective Study from an Intestinal Stroke Center. The American journal of



gastroenterology 2017; 112: 597-605 [PMID: 28266590 DOI: 10.1038/ajg.2017.38]

Reviewer #5:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** The study deals with an interesting theme, concerning the prediction of transmural bowel infarction (TBI) in patients with acute mesenteric ischemia (AMI) due to superior mesenteric venous thrombosis (SMVT). The patients included in the study came from two distinct hospitals (multicenter study) and their number was considerable. The discussion section gave emphasis to the new contribution of the study in its field. The authors stated that they constructed and externally validated the nomogram to predict TBI in patients with acute SMVT, which gave novelty to the study. The limitations of the study were also described. The figures and tables are informative and aesthetically pleasing. Therefore, the manuscript presents sufficient quality to be published in this journal.

**Response:** Thanks for the positive comments.

**Again, we would like to express our sincere thanks to the experts for their constructive and positive comments, which are very important for improving the quality of our paper.**

