

Peer Review File

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Review Comments A:

The subject is interesting because artificial intelligence applied to medical data is still current. The objective is clear. The manuscript is well written. However, I have a few comments to make:

- Avoid the use of abbreviations in the summary such as (ESR)
- Line 80: the second inclusion criteria is not clear
- Line 109: only patients with abdominal surgery at the time of diagnosis were included, why not also include patients operated for complicated Crohn's disease during follow-up.
- Upper gastro-intestinal location at 59.5% seems very high

Response to Reviewer A

Comment 1: Avoid the use of abbreviations in the summary such as (ESR).

Reply 1: Thank you for your comment. We had revised the abbreviations.

Changes in the text: See page 2, line 16-17. (“ESR” changed to “erythrocyte sedimentation rate”, “CRP” changed to “C-reactive protein”, “MCV” changed to “mean corpuscular volume”)

Comment 2: -Line 80: the second inclusion criteria is not clear.

Reply 2: Thank you for your comment. Our description was unclear, we had revised it.

Changes in the text: See page 4, line 54-55. (“patients had complete laboratory indicators including D-dimer at the time of admission” changed to “patients had complete laboratory indicators including D-dimer at the time of admission”)

Comment 3: -Line 109: only patients with abdominal surgery at the time of diagnosis were included, why not also include patients operated for complicated Crohn's disease during follow-up.

Reply 3: Thank you for your comment. In our study design, our aim was to classify prothrombotic state Crohn's disease on the basis of D-dimer levels. Because of the false positive of D-dimer after operation, we only collected CD patients diagnosed by surgery. The result of it may be more reasonable.

Changes in the text: -.

Comment 4: -Upper gastro-intestinal location at 59.5% seems very high.

Reply 4: Thank you for your comment.

In our study, We documented a relatively higher rate of upper gastro-intestinal phenotypes (59.5%) compared to other studies (PMID: 29899757, 15472528, 21825896). This discrepancy could be attributed to the larger cohort used in our study compared to previous studies on Asian populations (PMID: 29899757, 15472528, 21825896), as well as the improvement in imaging techniques for the upper gastric tract over the years. A recent prospective study showed that combining small bowel capsule endoscopy and MRE altered the original Montreal classification in 64% CD patients (PMID: 26748404). We established our diagnosis and classification based on gastroscopy, computed tomography enterography or magnetic resonance enterography, double-balloon enteroscopy or capsule endoscopy and colonoscopy.

Changes in the text: -.

Review Comments B:

The major methodological shortcoming of this manuscript is the use of D-dimer level as a surrogate for a "prothrombotic state". Among patients with inflammatory bowel disease (and among all patients with any chronic or acute inflammatory process) elevated D-dimer is just as likely to represent increased inflammation as it is to represent a prothrombotic process (i.e. D-dimer is a non-specific acute phase reactant). Further, even if D-dimer level were to be a specific and accurate measure of latent thrombotic tendency, it would still not be a clinically relevant outcome (the truly clinically relevant outcome in such a study would be rate of thrombotic events). If the authors are able to reassess and reanalyze this cohort (or a related cohort) with incident thrombotic events as the primary outcome rather than D-dimer level, it may have some clinical relevance.

Reply: Thank you for your comment.

D-dimer is very sensitive, and has been identified as a sensitive and significant indicator for prothrombotic state in CD patients in our Expert consensus.

The aim of our study was to use other indicators to predict the prothrombotic state in patients with Crohn's disease. It is different between prothrombotic state and thrombotic event. It may be too late, if clinician wait until CD patients have had a thrombotic event. Although prothrombotic state does not always evolve into a thrombotic event, the significance of it should not be ignored.

We believed that the prediction of this state could help clinicians to make individual therapy to CD patients. Once clinicians can identify patients with prethrombotic

state in the early stage, A targeted treatment intervention can be taken for such patients to avoid the risk of subsequent thrombosis.

Changes in the text: -