Reply to Reviewer's Comments

1. Minor English revision is required. Per es: "It can be noted that major GI bleeding during hospitalization when the patient was referred for another reason to emergency, as well as intentional overdoses of antithrombotics, were excluded." Difficult to comprehend. "…between January 1, 2013 and December 31, 2015 to the emergency department…" "…191 with upper GI symptoms and 192 with lower GI symptoms, because investigations yielded negative results (174 patients) or because of no investigations were performed (209 patients)."

We agree with reviewer's comment; the sentences have been rephrased as follows:

Of note, we excluded (i) patients who had major GI bleeding during hospitalization whereas they were referred to emergency for another reason, and (ii) patients referred for intentional overdoses of antithrombotics.

We studied all consecutive adult patients admitted in two tertiary care hospitals between January 1, 2013 and December 31, 2015 for major gastrointestinal (GI) bleeding.

No cause of bleeding was identified for 383 patients (35.5%), because investigations yielded negative results (174 patients) or because of no investigations were performed (209 patients). Those patients had upper GI symptoms (191 patients) or with lower GI symptoms (192 patients).

2. It would be useful to report the total number of GI bleedings during the study period (including patients not receiving antithrombotic therapy), in order to calculate the rate of GI bleedings in patients receiving antithrombotic therapy.

Unfortunately, only patients with GI bleeding and exposed to antithrombotic therapy were identified and included in the database. In addition, we also selected patients with major bleeding.

On the other hand, in order to calculate the rate of GI bleedings in patients receiving antithrombotic therapy, we should build a cohort of patients exposed to antithrombotic therapy, then identify those who experienced bleeding. This was the aim of another study recently published.

Bouget J, Balusson F, Maignan M, et al. Major bleeding risk associated with oral anticoagulant in real clinical practice. A multicentre 3-year period population based prospective cohort study. Br J Clin Pharmacol. 2020;1–11. https://doi.org/10.1111/bcp.14362

3." Few patients required surgery or embolization." The word "few" is vague. A number should be reported.

We agree with reviewer's comment; the sentences have been rephrased as follows:

In the "Upper GI bleeding management" paragraph:

Thirty patients required surgery and 2 an embolization.

In the "Lower GI bleeding management" paragraph:

Forty-one patients required surgery and fourteen an embolization.

4. Moreover, as the purpose of this study was to "To describe clinical characteristics, bleeding locations, management and in-hospital mortality related to these events.", the authors should also assess whether a specific antithrombotic therapy was correlated with failed endoscopy requiring surgery or embolization.

174 patients had failed endoscopy (i.e., endoscopy with a negative result) and none of those patients had either surgery or embolization.

5. How many patients with symptoms of lower GI bleeding (hematochezia) were diagnosed to have upper GI bleeding?

Among 504 patients with symptoms of lower GI bleeding (hematochezia) 55 (11%) were diagnosed to have upper GI bleeding.

6. The limitations of the study are not clearly mentioned and should be more clearly summarized in the end of the discussion section.

We added the following sentences in the end of the discussion section:

Our study was restricted to two tertiary care hospitals. We required extensive clinical data, and a trade-off had to be made between the number of participating centers and feasibility. We focused on major bleeding, and lastly we provided here only descriptive statistics.

Reply to Editor's comments

1. The authors need to provide the language certificate of L'AURACOISE.

A certificate is provided.

2. I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

The Agency did not provide an individual (per study) approval document.

The list of all approved and granted studies could be found at the following website:

https://solidarites-sante.gouv.fr/systeme-de-sante-et-medico-social/recherche-et-innovation/l-innovation-et-la-recherche-clinique/appels-a-projets/article/les-projets-retenus#PHRC

The number is 12-009-0243 / PHRCN-2012.

We provided the grant review form.

3. I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

4. I found the authors did not add the PMID and DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

5. I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text.

The “article highlights” section was written as follows:

1. We observed a high rate of identification of causative bleeding lesions.

2. There was a higher proportion of direct oral anticoagulant use among patients with lower GI locations than among those with upper GI lesion locations.

3. Dual antiplatelet regimen was more frequently encountered among patients with gastro-duodenal ulcers.

4. Our data did not support differences in management and outcomes across the various antithrombotics.

5. In-hospital mortality was low.