Author's response to reviews

Title: Bleeding from gastrointestinal angioectasias is not related to bleeding disorders - a case control study

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Author's response to reviews: see over
Dear editor,

Thank you for your letter indicating interest in our manuscript "Bleeding from gastrointestinal angioectasias is not related to bleeding disorders- a case control study"

We have carefully assessed the valuable criticism raised by the reviewers and made alterations/additions in line with the comments. It is our impression that the scientific strength of the paper has been improved following those changes, and we now hope you will find the manuscript suitable for publication in BMC Gastroenterology

Here follows a point-to-point response to the criticism expressed by the reviewers:

**Reviewer 1:**

1. Aims and primary goal were here described by the reviewer.
2. The reviewer is correct that different platelet dysfunctions may cause an increased bleeding tendency in our patients. However, our aim was focused on AVWS and therefore specific tests involved VWF parameters. We did perform the unspecific bleeding time test, as indicated in the Methods section, but more platelet-specific tests were not included in this study. None of the patients showed any other clinical signs of platelet dysfunction.
3. In the study group all patients had anemia at the time for bleeding and 15 of 23 patients received blood transfusions. The numbers of transfusions were two or more and this has been added in the text. Unfortunately it was not possible to find out the exact number of transfusions given in some of the cases.
4. The control group was suggested to be increased to a minimum of fifty to have a better statistical comparison. This is a good point and something to bear in mind when setting up studies in the future.
5. The discussion has been re-written as suggested.
6. Four new references recently written and covering the relevant field has been added [12,13,14,26].

**Reviewer 2:**

1. All patients in both the study group and the control group were enrolled retrospectively using the register of patients at our hospital. They were all enrolled at the same period of time (march 2006) and tested within three months. The design of the study has now been better described in the Methods section. We agree that it would have been better if the blood sampling was performed at the time for the
bleeding episode but this could not be arranged in this study. Also we were seeking a chronic bleeding tendency that ought to possible to detect even afterwards.

2. More specific data about the methods for VWF-activities and VWF-multimers as asked for are added in the Methods section.

3. More specific data about the VWF-multimer test used is added in the Methods section.

4. A new table has been added showing the parameters found in the four cases of either loss of high molecular weight multimers or prolonged bleeding time.

5. The discussion has been rewritten to ensure that no statement is based on non-published data. We agree that there is no specific data published of the role of VWF in angioectasias. However there are solid data confirming the importance of high molecular weight VWF’s role in maintaining hemostasis under conditions of high shear stress [Sugimoto et al, Blood 2003;101:915-20]. Since these conditions also can be found in angioectasias, we find the theory of the importance of VWF in maintaining hemostasis in angioectasias [Warketin et al, Transfus Med Rev 2003;4:272-86] both interesting and plausible.

6. MINOR POINTS: All VWF abbreviations now have capital letters.

The study was approved by the Swedish Ethics Committee in Stockholm (Regionala Etikprövningsnämnden - EPN, chairman Ulla Erlandsson, Box 289, S-171 77 Stockholm)

Yours sincerely

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