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Title: Prognostic impact of body mass index on in-hospital bleeding complications after ST-segment elevation myocardial infarction

Authors: Delphine Ingremeau, Sylvain Grall, Florine Valliet, Laurent Desprets, Fabrice Prunier, Alain Furber and L Biere

We would like to thank the editorial board for giving us the opportunity to resubmit our paper.

Please find below the answers to all issues raised by reviewers.

Reviewer #1:

1. The title reflects the main hypothesis of the manuscript. 2. The abstract summarizes and reflects the work described in the manuscript. 3. The keywords are quite sufficient. 4. The manuscript adequately describes the background, present status and significance of the study. 5. The methods were adequately detailed. 6. The research objectives were achieved by the experiments of this study.

7. The discussion was not adequate, and the following points need to be more highlighted to improve the discussion:

A. Few details are needed about the possible influence of obesity on the pharmacokinetic features of the anticoagulants used by the targeted patients???

Indeed, pharmacokinetic of anticoagulants may be driven by body composition, notably the content of lean body mass compared to fat body mass. Pharmacokinetic data for dose management being obtained in normal-weight individuals, obese patients may be exposed to supra-therapeutic dose.

Nevertheless, our study included a low number of class ≥ 2 obese patients (20%), so that this specificity may not have contributed to our results, even though anticoagulant therapies were given per kg of body mass (see supplementary file for institutional antithrombotic protocol).

As guidelines-recommended, antiplatelets therapy were administrated at the same dose for every patient with little concern (except for PRASUGREL) about body weight. By doing so, we may have virtually overdose normal weight patients compared to overweight and more patients. Nevertheless, there is no data about tailoring antiplatelet dose in thin patients.

The manuscript have been modified as required by the reviewer (page 9 line 18-4).

B. There is no suggestion or recommendation on how this finding can improve the clinical practice for the aim of reducing bleeding in non-obese subjects!!!! Accordingly, the discussion part needs to be improved with adequate reference citation.

The following paragraph has been added to the discussion (page 9 line 25-6):

"In the present study, we showed the prognostic impact of in-hospital bleeding events. Special concerns should be given in the management of antithrombotic therapies, including following drug requirements, early stop of anticoagulant after effective angioplasty 1, avoiding multiple switch for anticoagulant 2, and encouraging low-risk strategies when invasive management is uncertain 3. Even though the benefits of newer antiplatelet therapy is unquestionable in term of prevention of stent thrombosis, a switch to clopidogrel – as soon as one month after angioplasty - may lower bleeding events 4."

1. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimský P, Collet J-P, Kristensen SD, Aboyans V, Baumbach A, Bugiardini R, Coman IM, Delgado V, Fitzsimons D, Gaemperli O, Gershlick AH, Gielen S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2017;
2. Feldman DN, Wang TY, Chen AY, Swaminathan RV, Kim LK, Wong SC, Minutello RM, Bergman G, Singh HS, Madias C. In-Hospital Bleeding Outcomes of Myocardial Infarction in the Era of Warfarin and Direct Oral Anticoagulants for Atrial Fibrillation in the United States: A Report From the National Cardiovascular Data Registry Acute Coronary Treatment and Intervention Outcomes Network Registry. *J Am Heart Assoc* 2019;**8**.
3. Yusuf S, Mehta SR, Chrolavicius S, Afzal R, Pogue J, Granger CB, Budaj A, Peters RJG, Bassand J-P, Wallentin L, Joyner C, Fox KAA, OASIS-6 Trial Group. Effects of fondaparinux on mortality and reinfarction in patients with acute ST-segment elevation myocardial infarction: the OASIS-6 randomized trial. *JAMA* 2006;**295**:1519–1530.
4. Cuisset T, Deharo P, Quilici J, Johnson TW, Deffarges S, Bassez C, Bonnet G, Fourcade L, Mouret JP, Lambert M, Verdier V, Morange PE, Alessi MC, Bonnet JL. Benefit of switching dual antiplatelet therapy after acute coronary syndrome: the TOPIC (timing of platelet inhibition after acute coronary syndrome) randomized study. *Eur Heart J* 2017;**38**:3070–3078.

8. The data are well presented. 9. The statistical evaluation is adequate.

Reviewer #2:

Authors discussed an interesting topic about the BMI paradox in STEMI patients. In the present study, authors summarized normal weight (BMI < 25 kg/m²) per se did not impact on one-year CV mortality but increased the effect of bleeding on mortality. They present a hypothesis of the obesity paradox, with in-hospital bleeding in BMI ≥ 25 kg/m² patients related to lower impact on one-year mortality after STEMI. The manuscript has delivered important clinical message and should be of great interest to the readers.

Although needs extensive language corrections before being published, this article could have been improved by minor revisions.

The manuscript have been reviewed for English editing.

Reviewer #3:

The study group report on the prevalence and prognosis of in-hospital and one year follow-up bleeding events in relation to BMI after ST-segment elevation myocardial infarction Major findings are that normal weight patients presented a higher rate of bleeding complications and a lower survival rate after STEMI and multivariate analysis provided causal relationships.

Comment

The first sentence in the Conclusion drawn at the end of the body text needs clarification as it is seemingly pointing to the multivariate findings. In this context, a higher prevalence should be considered: The novelty of this report was the evidence of lower prevalence and a poorer prognostic impact of bleeding complications in normal weight patients

We thank the reviewer for his comment, and modified the manuscript as required, by modifying the conclusion and highlighting the difference in the prevalence of bleeding and prognosis. We agree the multivariate findings are only hints to explain this observation.

Table 1: statistics for multivessel disease should be reassessed.

Indeed this statistic was skewed by mistake, as multivessel disease was wrongly coded (1:monotroncular, 2: bitroncular, 3: tritroncular). We preferred to distinguish monotroncular from pluritroncular patients. Indeed the p value was not significant. This has been changed in the manuscript (table 1).

Spelling Table I: phophokinase, phosphokinase

The spelling was modified in the manuscript.