Author's response to reviews

Title: Interobserver reliability of echocardiography for prognostication of normotensive patients with pulmonary embolism

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Author's response to reviews: see over
Dear Editor:

We are grateful to the Editors and Reviewers of the Journal for this thorough review of our manuscript. Your detailed, constructive comments and suggestions help us improve the interpretation of our results and can, hopefully, also be translated into a better management of patients with pulmonary embolism (PE). On the pages that follow, we are addressing the Editors’ and Reviewers’ comments and concerns one by one, also providing additional data where requested. We look forward to your response.

On behalf of the authors
Sincerely yours,
David Jiménez, MD, PhD, FCCP
Reviewer #1

C1. The flow chart of patients should be included (patients that were excluded: number and why).

R1. For the original PROTECT cohort (n = 848), study staff screened 999 consecutive patients with acute PE for eligibility. Haemodynamic instability excluded 42 (4.2%) patients from participation. Of the remaining 957 hemodynamically stable patients, the study excluded 6.8% (65 of 957 patients) because they did not have a technically adequate MDCT (n = 28; 2.9%) or a transthoracic echocardiogram (n = 37; 3.9%). Other reasons for exclusion included unavailability for follow-up (n = 23) and refusal to give informed consent (n = 21). The study enrolled the remaining eligible 848 patients (416 men and 432 women). This information is cited in another manuscript, and this manuscript cites that publication (Jiménez D, Lobo JL, Monreal M, et al. Prognostic significance of multidetector computed tomography in normotensive patients with pulmonary embolism: results of the PROTECT study. Thorax 2014; 69: 109-115).

For this substudy of the first 75 eligible patients in the PROTECT study (n = 848), investigators excluded a small proportion of patients because they did not have adequately recorded echocardiographic data required for analyses (2/75; 2.7%; 95% CI, 0% to 6.3%). No statistically significant difference was observed between included and excluded patients regarding demographics, medical history, and clinical presentation. We added this information to the Results section of the manuscript.

C2. The clinical characteristics of the study population should also be included.

R2. Done, as suggested by the reviewer (see new Table 1).

C3. Moreover, as interobserver reliability has been analyzed in this study, it is
also important to 1) include the grade of quality of the echocardiographic studies (echocardiographic windows), as well as 2) the experience of physicians that performed the studies.


2) Trained and certified local cardiologists, blinded to the patient’s clinical data and laboratory test results, performed and interpreted each echocardiogram. We added this information to the Results section of the manuscript.
Reviewer #2

C1. Only some of the parameters that are commonly analyzed in the assessment of RV function in patients with suspected PE were included in the analysis, while other such as McConnell's sign, 2D FAC septal morphology and S' of the tricuspid annulus were omitted. For example, S' is easy to measure, reliable and reproducible. Therefore, authors should explain why these parameters were excluded from the analysis.

R1. This study only assessed interobserver reliability for those echocardiographic parameters commonly used to define right ventricular dysfunction in patients with acute PE. The authors agree with the reviewer that the requested information would be nice to have available for the reader. However, the PROTECT study protocol did not require this information to be systematically collected, and it was not collected by the PROTECT group. Thus, the study cannot report such information. The authors feel that this limitation does not significantly detract from the study. We added this issue to the limitations section of the Discussion: “We were not able to assess the interobserver reproducibility of systolic pulmonary pressure and other echocardiographic criteria for RV dysfunction (e.g., systolic excursion velocity of the tricuspid annulus)”.

C2. In the abstract (paragraph results, first 2 lines 1 and 2), there is probably a mistake: “the two observers had fair agreement (k=0.45) for RV enlargement and good agreement (k=0.65) for RV enlargement”. This paragraph must be corrected.

R2. We thank the reviewer for the attention to detail. We have clarified it in the Abstract: “The two observers had fair agreement (k=0.45) for RV enlargement assessed by the RV diameter, and good agreement (k=0.65) for RV enlargement assessed by the RV/LV diameter ratio”.
Thank you again for the opportunity to revise our manuscript. We think that the excellent reviewer suggestions and the associated revisions have substantially improved the quality of the manuscript, and we hope that the editorial staff and reviewers deem it suitable for publication. We look forward to your response.

On behalf of the authors
Sincerely yours,
David Jiménez, MD, PhD