

Dear Editor,

We submit a revised version of our invited editorial titled “New guidelines for the diagnosis and management of pulmonary embolism: key changes”, Manuscript ID 55098, for consideration for publication in the World Journal of Cardiology. We thank the Reviewers for their comments, which improved our manuscript. We modified our review accordingly. All changes are shown in red in the revised text. This is an invited editorial and the invited manuscript ID is 00036318.

Response to Reviewers' comments:

Reviewer's code: 03645171

In this editorial the authors discuss the basic changes between the recent Pulmonary embolism guidelines and the previous ones.

Major comments: 1. To facilitate the reader to identify the key changes between the last guidelines and the previous ones a summary table is needed.

We added a summary table.

Minor comments: 1. In the Core tip the authors used the acronym PE without mentioning previously Pulmonary embolism (PE)

We added the meaning of the acronym.

2. in the CHANGES IN THE DIAGNOSIS OF PULMONARY EMBOLISM is not clear how the age-adjusted cut -off level of D-dimers is calculated and how to use it.

We now mention “Based on the new ESC guidelines, instead of a fixed-cut off level of D-dimers (500 ng/mL), an age-adjusted cut-off level of D-dimers should be considered to exclude PE in patients with low or intermediate clinical possibility for PE and in those where PE is unlikely. The age-adjusted cut -off level of D-dimers is calculated by multiplying the age of the patient by 10 (for patients older than 50 years). Thus, in a 60-year-old patient who has a low or intermediate clinical possibility for PE or who is unlikely to have PE, D-dimers levels < 600 ng/mL (i.e. age * 10) instead of D-dimers levels < 500 ng/mL (i.e. the fixed-cut off level) excludes PE. On the other hand, in a 40-year-old patient who has a low or intermediate clinical possibility for PE or who is unlikely to have PE, the fixed-cut off D-dimers level of < 500 ng/mL should be used, since the patient is younger than 50 years.”

3. in CHANGES IN RISK ASSESSMENT OF PULMONARY EMBOLISM provide the definition of haemodynamic instability, please.

We now provide the definition of haemodynamic instability “More specifically, haemodynamic instability is defined as a) cardiac arrest i.e. need for cardiopulmonary resuscitation or b) obstructive shock i.e. systolic blood pressure (SBP) < 90 mmHg (or need for vasopressors to achieve SBP ≥ 90 mmHg) despite adequate filling status and end-organ hypoperfusion

(altered mental status, cold/clammy skin, oliguria/anuria or increased serum lactate) or c) persistent hypotension i.e. SBP < 90 mmHg or SBP drop \geq 40 mmHg, lasting > 15 min and not caused by new-onset arrhythmia, hypovolemia or sepsis."

Reviewer's code: 03552376

The manuscript is well written and acceptable for publication.

We thank this Reviewer for these positive comments.

Reviewer's code: 02465908

I read with interest the paper entitled "New guidelines for the diagnosis and management of pulmonary embolism: key changes".

We thank this Reviewer for her/his interest in our paper.

I have only a minor point to discuss. I would suggest authors to write a paragraph or a flow chart for emergency rooms doctors, those that are the first line in diagnosing this condition.

We added a flow chart.

Moreover, please check the paragraph entitled "Changes in the treatment of pulmonary embolism", the word in the fourth line "hrombolysis" should be corrected with "thrombolysis".

We made this correction.

We look forward to your decision.

Best regards,

Konstantinos Tziomalos, MD, PhD

Associate Professor of Internal Medicine

Medical School, Aristotle University of Thessaloniki, Greece