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Advocating prudent D-dimer testing: constructive perspectives and comments on 'How we manage a high D-dimer'

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Dear editor,

We read with great interest the narrative review, "How we manage a high D-dimer", authored by Massimo Franchini and colleagues and published in a recent issue of Haematologica[1]. This review offers didactic and informative content, and although we generally agree with the perspectives and recommendations presented, we would like to address two specific issues that are vital to good clinical practice: the correct understanding of the properties of diagnostic tests; and the need for reduction of unnecessary test ordering.

Regarding the first issue, the review mentions the intrinsically low Positive Predictive Value (PPV) of D-dimer testing. It is essential to clarify that PPV is not an intrinsic characteristic of the test. Rather, PPV is determined by the interaction between the pre-test probability and the test's positive likelihood ratio[2,3]. Therefore, even a test like D-dimer, which has a low positive likelihood ratio[4], can exhibit a high PPV if applied in a setting with a very high pre-test probability.

Regarding the second issue, the review highlights that among the main causes of elevated D-dimer levels are ubiquitous physiological conditions such as aging, pregnancy, and physical activity. It also states that D-dimer testing has limited clinical utility in the random asymptomatic ambulatory patient and appropriately suggests that it should only be ordered in specific clinical situations. Yet, it also asserts that an elevated D-Dimer ordered in the random asymptomatic ambulatory patient cannot be ignored and warrants further consideration and proposes an algorithm for management of these patients. In our opinion, this approach legitimizes the inappropriate ordering of the test and shifts the focus away from what truly should be good clinical practice: the use of a diagnostic test as a complement to sound clinical reasoning. This applies not only to D-dimer, but also for other tests inappropriately ordered as routine in asymptomatic individuals, such as high-sensitivity troponin[5] and the ANA test[6]. These tests should be reserved for instances of clinical suspicion due to the extremely high rates of false positives in the context of low pre-test probability, which can lead to further unnecessary tests, invasive procedures with iatrogenic risk, increased costs to healthcare system, and anxiety for the patient. We reinforce the need for a rational patient selection **before**

ordering the diagnostic test, rather than seeking an unlikely diagnosis afterwards motivated by inappropriate test ordering[7].

For these reasons, we suggest that instead of recommending an evaluation algorithm for elevated D-dimer tests in asymptomatic ambulatory individuals, the focus should shift back towards avoiding unnecessary medical tests. Such efforts could better educate healthcare professionals on the rational ordering of these tests, ensuring effective and appropriate use based on solid clinical reasoning and specific patient contexts.

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