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Response to: *Predilection to Pursue Pulmonary Embolism in Young Females*

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The authors read the letter by Akhter, *et al.* with great interest. We agree that there is a compelling need to continue to investigate disparities in testing for pulmonary embolism (PE) by patient sex. As noted by Akhter, *et al.*, females comprise a majority of enrollees in nearly all large PE diagnostic studies in North America and Europe, most of which use "suspicion for PE" as the principal inclusion criterion.[1–4] This fact is surprising because the overall age-adjusted PE incidence is higher in males than females and males have a nearly 3-fold higher risk of recurrent PE compared to females.[5–7] There is one notable exception in that females have a slightly higher incidence than males in young adulthood but this trend is likely due to peripartum and estrogen related venous thromboembolism and is reversed among older patients. Large emergency department (ED) datasets - including the National Emergency Department Sample (NEDS) with over 10 million visits – find the incidence of PE to be approximately equal by patient sex.[8]

We agree with Dr. Akhter's assertion that emergency physicians (EPs) appear apt to test young females for PE more often than clinically similar men, but this hypothesis has not been proven. Our group is studying this question of whether clinical decisions are influenced by a gendered heuristic in which EPs believe that the risk of PE in female patients is greater than that of matched males. Several PE risk factors (e.g., exogenous estrogen; third-trimester pregnancy; postpartum status) are associated with female sex, and physicians may unconsciously perceive that this risk applies to all female patients, regardless of pregnancy or estrogen status. Another consideration is the clinical history. Perhaps there is something systematically different about the way that women and men describe their symptoms that influences the decision to test. A final consideration relates to laboratory testing: a smaller proportion of females than males have PE excluded by D-dimer, and mean D-dimer levels appear to be higher in premenopausal females than age-matched males.[9–11] D-dimer is also influenced by exogeneous estrogen.[11] As with all clinical decisions, we suspect a combination of these factors contribute to the observed differences in testing by patient sex.

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Regardless of the reason, we would argue that *too many* females are being placed on the PE workup pathway, not *too few* males, given the exquisitely low yield in our study (3.1% female, 5.3% male).[12]

When working with trainees, we frequently cite a flow chart from the EMCrit Project blog that begins with "Do you think this could be a PE? No really, do you?!"[13] Although sarcastic in tone, this question highlights the idea that many patients (particularly young patients) are at such low risk that PE testing should only be pursued after careful consideration, and certainly with the use of clinical decision support tools (e.g., Wells, PERC) whenever possible. In very low risk groups, PE is so rare that positive test results are likely to be false positive, in which case we may be doing harm by testing. This principle of Bayesian inference is often challenging to learners, and we encourage clinical educators to incorporate this important information about PE epidemiology into their teaching about who should even be tested for PE. Lest the pendulum swing too far, we acknowledge that over testing is not the only problem but hope that future research on sex differences in PE diagnostics will examine strategies to reduce low-yield testing.

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