EVMS Emergency Medicine Journal Club

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**Citation:** Freund Y, Chauvin A, Jimenez S, et al. Effect of a Diagnostic Strategy Using an Elevated and Age-Adjusted D-Dimer Threshold on Thromboembolic Events in Emergency Department Patients With Suspected Pulmonary Embolism: A Randomized Clinical Trial. *JAMA.* 2021;326(21):2141–2149. doi:10.1001/jama.2021.20750

**Patient Population:** Adults from 16 EDs in France and 4 in Spain. 1271 patients qualified for final analysis, 648 in the intervention group and 623 in the control group. Mean age was 55 years (SD 19 years) and 58% were female.

**Methodology (*Study design)*:** Cluster-randomized, crossover, noninferiority trial in France and Spain. Each ED was “randomized to a sequence of periods: intervention (Modified Diagnostic Strategy: MODS) followed by control (usual care) or control followed by intervention”. There was one month of washout between the two periods. MODS protocol: if YEARS criteria were negative then the d-dimer level threshold was raised to 1000 ng/ml but if YEARS were positive then the d-dimer threshold remained at the usual age-adjusted level. PERC: age ≥50 years, pulse rate ≥100/min, arterial oxygen saturation <95%, unilateral leg swelling, hemoptysis, recent trauma or surgery, prior PE or deep venous thrombosis, and exogenous estrogen use. YEARS: clinical signs of DVT, hemoptysis, PE most likely. Inclusion criteria: acute onset or acute worsening of dyspnea, chest pain, syncope AND either low subjective probability (gestalt <15%) with positive PERC rule or intermediate subjective probability (gestalt 16-50%). Exclusion criteria: other obvious cause of PE, estimated physician gestalt >50% for suspected PE, low probability of PE determined by physician gestalt estimated <10% or negative PERC, acute severe presentation (respiratory distress, hypotension, SpO2 <90%), concurrent AC use, already diagnoses VTE, prisoners, pregnancy, no social security, participation in another trial, anticipated inability to follow up in three months.

**Primary Outcome:** Failure percentage of the diagnostic strategy, which was defined as a thromboembolic event at three months. This was determined via phone interview with patient at three months. PCP was contacted in patient could not be reached and death records were consulted if neither PCP nor patient could be reached. A research technician reviewed records for return visits.

**Secondary Outcome:** Use of advanced imaging studies, AC administration, ED LOS, hospital admission, all cased of re-admission at three months, all cause mortality at three months.

**Results:** 100 patients were diagnosed with PE, 54 in the intervention group and 46 in the control group, -0.8% 95% CI, -2.0% to 3.5%. There was one VTE at three months in the intervention group and five in the control group, which is a failure rate of 0.15% (95% CI, 0.00% to 0.86%) and 0.80% (95% CI, 0.26% to 1.86%) in the intervention and control groups, respectively.

Advanced chest imaging was performed in 221 patients in the intervention group and 275 in the control group (difference, −9.6%; adjusted difference, −8.7% [95% CI, −13.8% to −3.5%]). The median ED length of stay was 6.0 hours (IQR, 4.0-8.0) vs 6.0 hours (IQR, 5.0-9.0) (adjusted difference, −1.6 hours [95% CI, −2.4 to −0.9]). The other secondary outcomes did not vary statistically. There were 5 deaths from unknown causes.

**Post Hoc Analysis:** There were “956 patients with a YEARS score of zero (515 in the intervention group and 441 in the control group). In a post hoc analysis limited to these patients, there were no missed PEs in the intervention group (failure rate, 0.00% [95% CI, 0.00% to 0.71%], below the noninferiority margin) and 3 missed PEs in the control group (failure rate, 0.68% [95% CI, 0.00% to 1.45%]). In this post hoc analysis, chest imaging was performed in 22.9% of patients in the intervention group vs 37.2% in the control group (absolute reduction, 14.3% [95% CI, 8.3% to 20.2%]).”

**Strengths:** This study looked at a challenging group of patients, those at moderate risk by physician gestalt and those at low risk by gestalt but PERC positive. Given that 80% of the patients were YEARS negative, the patients who were PERC positive were likely positive for reasons like age, prior PE/DVT, estrogen use as the other PERC criteria are more likely to encompass clinical signs and symptoms of DVT/PE. Additional strengths include that analysis was conducted on per-protocol population and this study demonstrated that using criteria that change d-dimer thresholds allows for reduced advanced imaging while not missing PEs.

**Limitations:**

Recruitment was impacted by COVID. ED physician blinding was not possible. Randomization occurred at the ED level and not the patient level, though this was controlled for by the crossover design. The patients were included by the clinicians, which means that some eligible patients may not have been included. The CI prevents validation of the safety of the YEARS criteria in the subgroup of patients that were YEARS negative but had d-dimer >1000 ng/mL. The primary outcome was missing for 37 patients, but sensitivity analysis to account for this did not change the results. Protocol deviations occurred in both arms, but though this was minimal and thought to be prevented by the washout period.

**My Clinical Bottom Line:** Applying the YEARS criteria and adjusted d-dimer thresholds to a clinically challenging group of patients (namely, those at low risk of PE but still PERC positive) resulted in a significant decrease in advanced chest imaging while not missing PE.