Can you age adjust the SIUH D-dimer for appropriate patients with suspected PE?

Bottom Line Up Top: You can age adjust both D-dimer assays for appropriate patients with suspected pulmonary embolism.

Link to age adjusted Calculator for both assays: MD Calc

Clinical Scenario: An 81-year-old female PMHx HTN, DM, remote history of breast cancer who presents to the ED with shortness for the past 2 days. She denies any recent fever, chills, or sick contacts. Patient has no history of DVT or PE. On exam, VS unremarkable except for a heart rate of 105. The resident identifies the patient as low-risk for PE via Wells score and orders a D-dimer. The attending is upset that the resident sent the test without telling them because "it's always positive" but lets the resident ride it out. The D-dimer comes back "high" from the lab at 270 ng/mL. The resident asks the attending if we could age-adjust the D-dimer and end the workup for PE.

What Your Gut Says: You can age adjust the D-dimer assay that other hospitals have, which have a cut off of 0.5 µ/mL or 500 ng/mL, but cannot be used in D-dimers with cutoffs of 230 µg/mL. Maybe in a different life or different hospital system this would work.

Background: D-dimer is a protein fragment found in the blood after a blood clot is broken down. This test is highly sensitive and can be used to "rule out" appropriate patients for Venous Thromboembolism (VTE). However, specificity is low, leading to a high number of false-positives and can increase the CTPA rate. D-dimer levels increase with age further reducing the specificity of the test in patients over 50. Most labs, and thus the vast majority of published studies, report D-dimer in fibrinogen equivalent units (FEUs). The common cutoff for this test is 500 ng/ml. Some laboratories use assays that report D-dimer units (DDU) where the cutoff is commonly set at 230 ng/ml. Thus, roughly 2 FEUs are equal to 1 DDU.

What The Evidence Says:

The Age-Adjusted D-dimer

There is strong evidence that we can safely use the age-adjusted D-dimer for appropriate patients for work up for VTE. Numerous studies have shown that using an age adjusted D-dimer could improve the specificity of the test while preserving its sensitivity. A summary of studies looking at the conventional D-dimer against the age-adjusted D-dimer was done by Wolf et al. showing comparable sensitivities for the conventional and age-adjusted values:

Study	Class	Age Adjusted D-dimer cutoff (μg/L)	Conventional Sensitivity (%; 95% CI)	Age Adjusted Sensitivity (%; 95% CI)
Righini et al	II	Age×10†	NR	NR
Flores et al	II	Age×10†	100 (94-100)	100 (94-100)
van Es et al	II	Age×10†	99 (99-100)	99 (98-99)
van Es et al	III	Age×10†	NR	NR
Gupta et al	III	Age×10†	100 (94-100)	97 (90-100)
Friz et al	III	Age×10†	100 (97-100)	98 (94-100)
Jaconelli et al	III	Age×5‡	95 (86-99)	95 (86-99)
Sharp et al	III	Age×10†	98 (96-99)	93 (90-95)
Douma et al	III	Age×10†	NR	NR
Douma et al	III	Age×10†	NR	NR
Sharp et al	III	1,000†	98 (96-99)	84 (81-87)
Friz et al	III	1,000†	100 (97-100)	96 (91-99)
Kline et al	III	1,000†	94 (88-97)	92 (86-96)

The 230 D-dimer Assay:

Though less studied than the FEU assay, there is growing evidence that the DDU assay can also be age-adjusted for appropriate VTE patients. All of the available data supports this approach:

- **Jaconeli et al:** Can an age-adjusted D-dimer level be adopted in managing venous thromboembolism in the emergency department? A retrospective cohort study

- Parks et al: Investigation of age-adjusted D-dimer using an uncommon assay

- Gutovitz et al: A Tale of Two D-Dimers: Comparison of Two Assay Methods to Evaluate Deep Vein Thrombosis or Pulmonary Embolism

- Dutton et al: Can the use of an age-adjusted D-dimer cut-off value help in our diagnosis of suspected pulmonary embolism?

This practice is supported by the ACEP guidelines on VTE:

ACEP guidelines: Level B Evidence

In patients older than 50 years deemed to be low or intermediate risk for acute PE, clinicians may use a negative age-adjusted D-dimer* result to exclude the diagnosis of PE. For highly sensitive D-dimer assays using fibrin equivalent units (FEU) use a cutoff of age×10 µg/L; for highly sensitive D-dimer assays using D-dimer units (DDU), use a cutoff of age×5 µg/L.

Bottom Line: The available evidence supports the use of an age-adjusted D-dimer, with either assay (FEUs or DDUs), to rule out VTE in patients that are low risk by Wells criteria. The use of the age-adjusted D-dimers decreases the number of PE studies needed in the Emergency Department and does not significantly increase false negatives. Choose the appropriate assay when age-adjusting this test.

Bonus Pearls: The 230 µg/mL D-dimer Reference Card

Age	Age Adjusted D-dimer (µg/L) DDU Assay
55	275
60	300
65	325
70	350
75	375
80	400
85	425
90	450
95	475
100	500

Read More

CORE EM: Age Adjusted D-dimer

REBEL EM: The YEARS Study – Simplified Diagnostic Approach to PE

REBEL EM: The Pragmatic Combination of YEARS Score and Age-Adjusted D-Dimer

References

American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Thromboembolic Disease:; Wolf SJ, Hahn SA, Nentwich LM, Raja AS, Silvers SM, Brown MD. Clinical Policy: Critical Issues in the Evaluation and Management of Adult Patients Presenting to the Emergency Department With Suspected Acute Venous Thromboembolic Disease. Ann Emerg Med. 2018 May;71(5):e59-e109. Doi: 10.1016/j.annemergmed.2018.03.006. PMID: 29681319.

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