

Assessment of the safety using age adjusted D-dimer to rule out venous thromboembolism in a Swedish Emergency Department

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Introduction

In diagnosing venous thromboembolism (VTE) age adjusted D-dimer (AADD) has been shown to reduce false positives without significantly impacting sensitivity compared to the conventional cut-off value (CCD)¹⁻⁴. However, D-dimer tests are not standardized and AADD has not been studied in a Scandinavian setting.

Methods

All adult patient visits to the Emergency Department (ED) at Helsingborg Hospital between 2010-2014 who had an ECG and a D-dimer performed on clinical indications were included. Patients with headache as presenting complaint were excluded. All cases of VTE were radiologically verified. Using Medirox® D-dimer assay, CCD (<0,25 mg/L) results were compared to a AADD cut-off (<0,25 mg/L for patients <50 years of age and <[Age]/200 mg/L for patients >50 years of age).

Results

A total of 5020 Emergency department visits (4630 individual patients) were included. VTE was diagnosed in 198 cases. For a discharge diagnosis of VTE the CCD had a sensitivity of 96,0 % (95 % CI 92,2-98,2) and specificity of 74,7 % (95 % CI 74,7-75,9). Respectively AADD had a sensitivity of 91,9 % (95 % CI 87,2-95,3) and a specificity of 80,5 (95 % CI 79,3-81,6).

AADD reduced the cases with positive D-dimer without VTE (false positives) from 1215 to 939 compared to CCD. VTE cases with negative D-dimer (false negatives) increased from 8 to 16 cases.

Conclusion

In our setting AADD would have decreased the false positive tests by 5,5 % at the cost of a small, but not negligible increase in false negative tests and decrease in sensitivity.

References

1. Douma, R. A. et al. *Potential of an age adjusted D-dimer cut-off value to improve the exclusion of pulmonary embolism in older patients: a retrospective analysis of three large cohorts.* *BMJ* **340**, c1475 (2010).
2. Flores, J. et al. *Clinical usefulness and safety of an age-adjusted D-dimer cutoff levels to exclude pulmonary embolism: a retrospective analysis.* *Intern. Emerg. Med.* (2015). doi:10.1007/s11739-015-1306-5
3. Schouten, H. J. et al. *Diagnostic accuracy of conventional or age adjusted D-dimer cut-off values in older patients with suspected venous thromboembolism: systematic review and meta-analysis.* *BMJ* **346**, (2013).
4. Righini, M. et al. *Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study.* *JAMA* **311**, 1117–1124 (2014).

Table 1. Baseline characteristics and statistical comparison

	CDD ¹	Percent or 95 % CI	AADD ²	Percent or 95 % CI
ED visits ³	5002		5002	
Men	2196	43,90%	2196	
Women	2806	56,10%	2806	
Mean age	19,51		19,51	
Median age	20		20	
Age <50	2322	46,40%	2322	
Age 51-60	747	14,95%	747	
Age 61-70	867	17,35%	867	
Age 71-80	611	12,21%	611	
Age >80	455	9,09%	455	
VTE ⁴	198	3,96%	198	3,96%
Positive D-D	1405	28,13%	1121	22,45%
Negative D-D	3597	71,91%	3881	77,59%
True Positive	190	3,84%	182	3,68%
False Negative	8	0,16%	16	0,32%
False Positive	1215	24,29%	939	18,77%
True Negative	3589	71,75%	3865	77,27%
Sensitivity	95,96%	92,19 - 98,24 %	91,92%	87,21 - 95,31 %
Specificity	74,71%	74,71 - 75,93 %	80,45%	79,30 - 81,57 %
Positive LR ⁵	3,79	3,59 - 4,01	4,70	4,38 - 5,05
Negative LR ⁵	0,05	0,03 - 0,11	0,09	0,10

- 1.) Conventional D-dimer cutoff 2.) Age adjusted D-dimer cutoff 3.) Emergency department
4.) Venous thromboembolism 5.) Likelihood ratio

How was the age adjusted D-dimer cut-off value calculated?

The CDD cut-off value and value used for patients <50 years of age in the AADD group
< 0,25 mg/L

Age adjusted cutoff value for patients >50 years of age suggested by Douma et al¹
< 10 x [Age of the patient] µg/L

Modification for D-dimer units measured: age adjusted cutoff value for patients >50 years of age

$$\lt \frac{[\text{Age}] \times 10}{2} \mu\text{g/L} = \lt \frac{[\text{Age}]}{200} \text{mg/L}$$

Fig 1. How the age adjusted D-dimer cut-off value was modified from the original formula suggested d by Douma et al¹ to accommodate for differences in units measured and expressed.

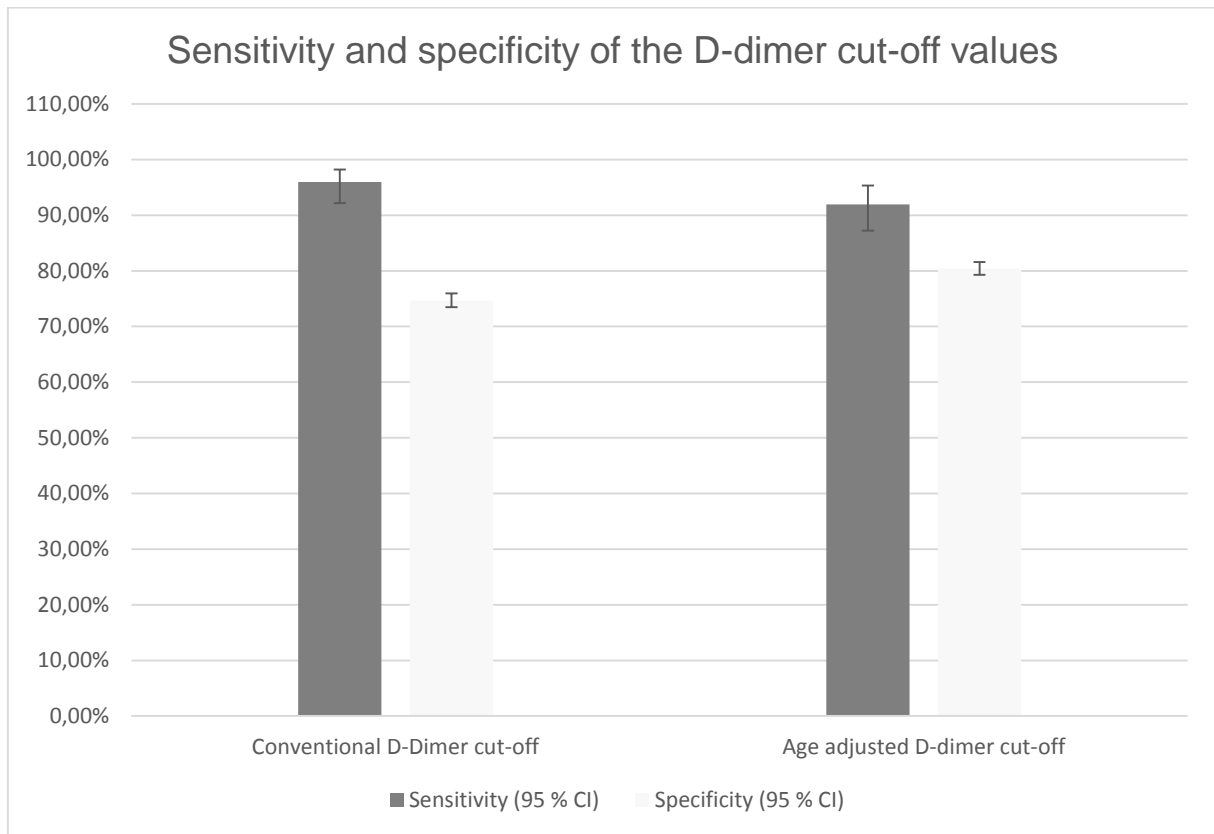


Fig 2. Sensitivity and specificity of the two cut-off values compared

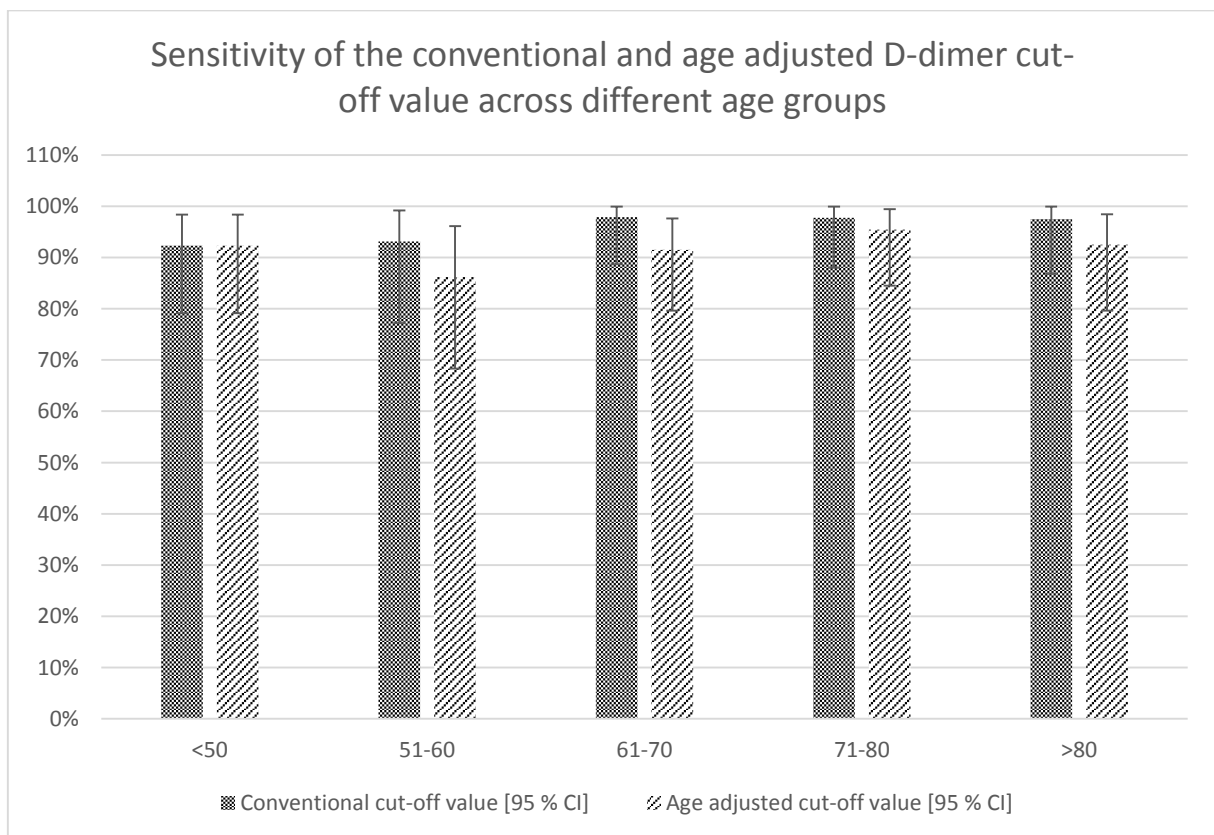


Fig. 3 Sensitivity of the conventional and age adjusted cut-off value across age groups

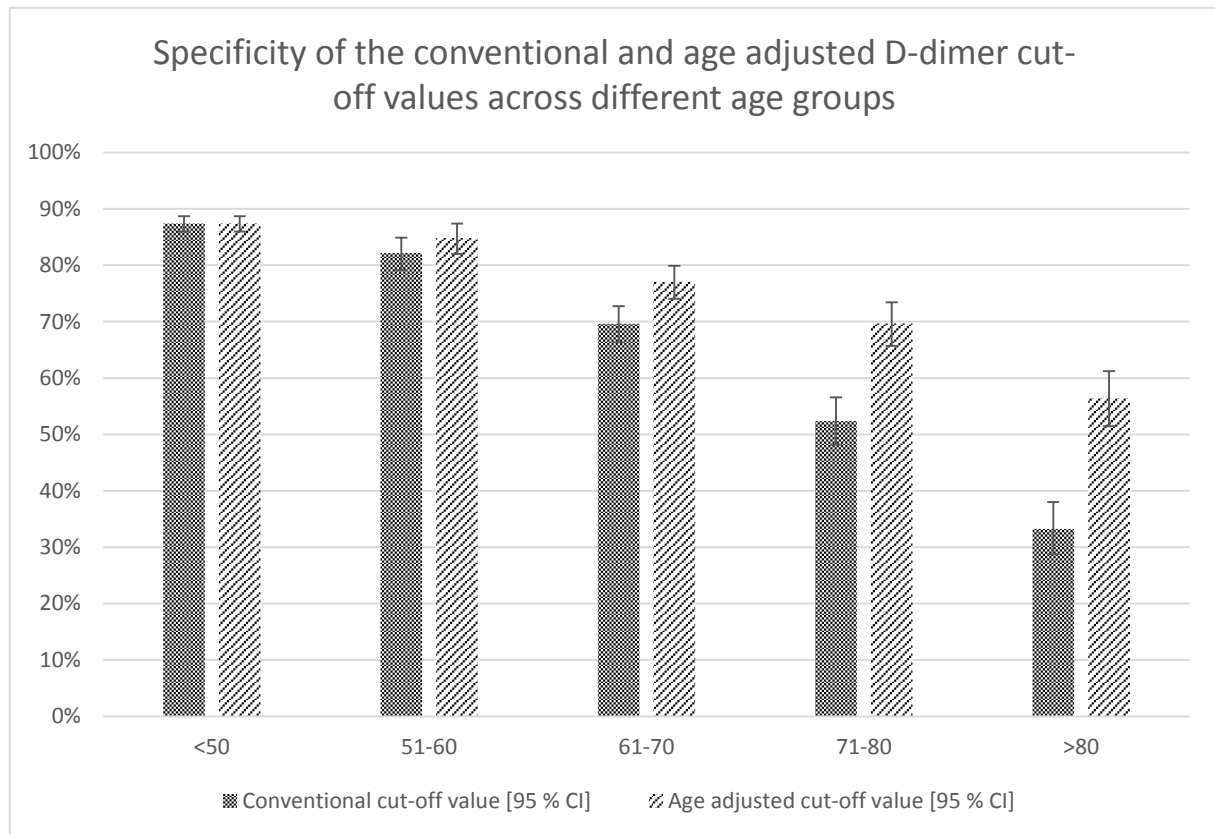


Fig. 4 Specificity of the conventional and age adjusted cut-off values across age groups

Table 2. Characteristics of patients with a false negative D-dimer

	CDD ¹	%	AADD ²	%
False negative D-dimer (% of total)	8	0,16%	16	0,32%
Mean age	59		65	
Women	5	63%	8	50%
Men	3	38%	8	50%
Pulmonary Embolism	6	75%	12	75%
Deep venous thrombosis	2	25%	4	25%
Wells score for DVT³ >2	1	13%	1	6%
Wells score for PE⁴ >4	3	38%	6	38%
Diagnosed with VQ⁵ scan	3	38%	4	25%
Symptom duration >7 days	3	38%	5	31%
APC⁶ resistance	1	13%	2	13%

Conventional D-dimer 2.) Age adjusted D-dimer 3.) Deep venous thrombosis 4.) Pulmonary embolism 5.) ventilation perfusion scan 6.) Activated protein C resistance

Comment: One patient present in both the CDD and AADD group had an arm vein thrombosis associated with a port-a-cath.