The use of age-dependent D-dimer cut-off values to exclude deep vein thrombosis. *Reply to* "Using an age-dependent D-dimer cut-off value increases the number of older patients in whom deep vein thrombosis can be safely excluded". Haematologica 2012;97(10):1507-13

Following on from recent studies which suggest in patients over 50 years of age an age-dependent D-dimer cut off of 'age multiplied by 10', in conjunction with a non-high clinical probability, can be used to safely exclude pulmonary embolism (PE),[1-3] we read with interest the application of the same age-dependent D-dimer cut off to the exclusion of deep vein thrombosis (DVT) by Douma *et al.*[4] Their retrospective analysis of a number of different patient cohorts found incorporation of this higher D-dimer cut off was associated with only a minimal increase in diagnostic failure rate compared to the conventional cut off of 500 μg/L (0.8% *vs.* 0.7%), a finding replicated in the recent data of Schouten *et al.*[5]

We analyzed our data covering 6,599 consecutive patient episodes (individual patients may have had more than one attendance) in the out-patient DVT clinic (i.e. patients with a suspected lower limb proximal DVT not requiring hospital admission) from 2007 to 2011 to evaluate what proportion of patient management would have differed had an age-dependent D-dimer cut off been used and what the diagnostic failure rate would have been. In this cohort, 826 (12.5%) had DVT proven on a proximal compression ultrasound. As shown in Figure 1, our diagnostic algorithm for the investigation of suspected lower limb proximal DVT includes two points at which the D-dimer (STA-Liatest) may be measured.

Point 1: patients with an 'unlikely' clinical probability score (Wells score ≤1);[6]

Point 2: patients with a 'likely' clinical probability score (Wells score ≥2)[6] and a negative first lower limb proximal compression ultrasound.

Patients who have already received low molecular weight heparin are ineligible for D-dimer testing.

Using an age-dependent D-dimer cut off at Point 1, 89 additional patients (1.3% of total patient cohort) would have been discharged without radiological investigation, 2 of whom did have DVT demonstrated on proximal compression ultrasound giving a diagnostic failure rate of 0.03% (for total patient cohort). Using the same age-dependent D-dimer cut off at Point 2, 342 patients would not have undergone a second proximal compression ultrasound (5.2% of total patient cohort), one of whom had DVT demonstrated on the second scan giving a diagnostic failure rate of 0.015% (for total patient cohort). Therefore, if an age-dependent D-dimer cut off had been implemented in our cohort it would have resulted in 431 fewer scans being performed at the expense of failing to diagnose 3 DVTs in 6,599 patients, increasing the diagnostic failure rate by 0.045%, a rate similar to that observed by Douma *et al.*[4] Sixty-five percent of the scans 'avoided' using an age-dependent cut off would have involved patients over 70 years of age. This both correlates with the findings of Douma *et al.*[4] and reflects the observation that the D-dimer increases in a continuum with age,[7] supporting the use of a coefficient to correct for age rather than a fixed higher cut off.[8]

Although compression ultrasound is a non-invasive test with few complications for the patient, it requires hospital attendance, is only available in normal working hours, and incurs a cost of £60 per procedure (UK National Health Service reference cost). This retrospective analysis of our data suggests an age-dependent D-dimer cut off could be safely implemented, which would have meant an additional 1.5% of patients would not

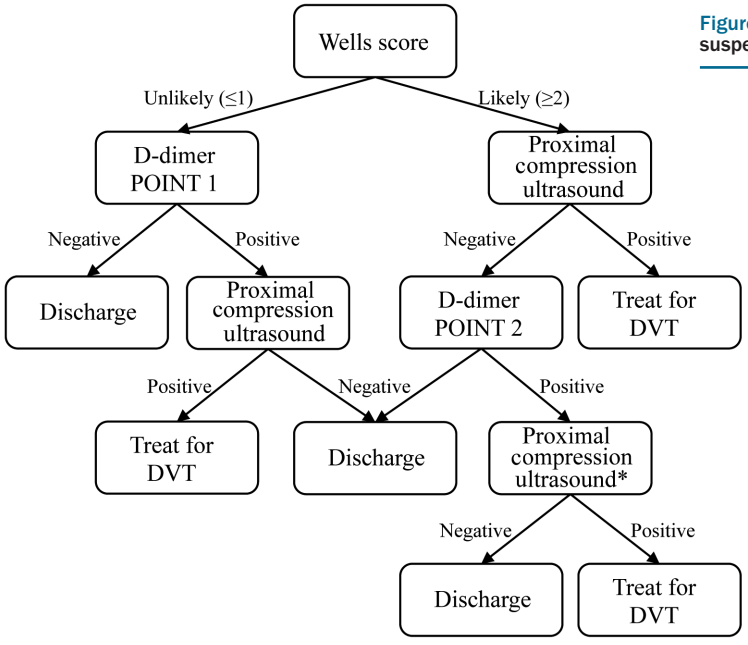

Figure 1. Diagnostic algorithm for the investigation of suspected lower limb proximal DVT.

*Repeat proximal compression ultrasound is undertaken 6-8 days after the initial negative scan.

need any diagnostic imaging, and an additional 5.2% would not need to return to hospital for a repeat compression ultrasound. This is of particular relevance with very elderly patients for whom hospital visits present a number of logistical problems.

As with all studies evaluating an age-dependent D-dimer cut off in the diagnosis of venous thromboembolism, the major limitation of our data is the retrospective nature of the analysis; prospective validation of the age-dependent cut off is needed before it can be confidently implemented into clinical practice. Nevertheless, our data suggest an age-dependent D-dimer cut off could be safely used to decide whether to scan patients (in conjunction with clinical probability scores) and is associated with a very low diagnostic failure rate (<0.05%).

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