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Clinical Paper

Age adjusted D-dimer in the Belfast Health and Social Care Trust: A retrospective study

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ABSTRACT

D-dimers combined with clinical pre-test probability (PTP) scores are used to determine the likelihood of a venous thromboembolic event (VTE). It is recognised that with advancing age, d-dimer values increase, leading to a cohort of patients with a d-dimer above the standard cut-off of 500μg/L. A recent systemic review, examined the accuracy of an age-adjusted D-dimer in those aged > 50 years with a low clinical risk of a VTE. This showed an increase in specificity without loss of sensitivity. Our study, aimed to examine a population of patients, who between 2011 and 2014 underwent ultrasound Doppler studies of lower limbs. By applying a corresponding age-adjusted D-dimer, we determined the sensitivity and specificity and compared this to use of conventional D-dimer.

INTRODUCTION

D-dimers are fibrin degradation products which result from plasmin activated fibrinolysis. Their presence suggests activation of the coagulation system.[1] D-dimers are used in conjunction with clinical pre-test probability (PTP) scores to determine the likelihood of a venous thromboembolic event (VTE).[2] A commonly used pre-test probability scoring system is the Wells' Score.[3] The Wells' score is used in ambulatory patients and calculates the likelihood of VTE, such as deep venous thrombosis or pulmonary embolism. This practice is supported by NICE guidelines on diagnosing VTE.[4] If the PTP score is low, a corresponding negative D-dimer rules out the need for imaging, as the likelihood of a VTE is low. If however, the D-dimer is elevated, then ultrasound Doppler imaging is required.[4] It is recognised that D-dimers increase with advancing age, leading to a high proportion of patients with d-dimers above the standard cut off value of 500μg/L with no underlying VTE.[5,6]

A recent systematic review assessed the accuracy of age adjusted D-dimer in those >50 years of age with a low PTP for a VTE event. It suggested there was an increased specificity without loss of sensitivity of age-adjusted D-dimer versus conventional D-dimer.[7] This would infer benefit in using age adjusted d-dimer in determining which patients require ultrasound Doppler. An age-adjusted D-dimer is calculated based on age (years) x10μg/L.

Lapner et al published evidence refuting the role of age-adjusted D-dimer, suggesting that the increased specificity is a result of a non-specific increase in the average D-dimer threshold used to exclude VTE.[8]

In our study, we aimed to assess the potential role of age adjusted d-dimer, its reliability and the potential impact it could have on both the patient journey and radiology services within the Belfast trust. If evidence supported age-adjusted D-dimer, it could potentially reduce the number of ultrasound Doppler requests, resulting in time and resource savings.

METHODS AND MATERIALS

The radiology department of the Royal Victoria Hospital provided data on all ultrasound Doppler of lower limbs performed in the department between 2011 and 2014. This included both inpatients and those attending A&E (either self-presentation or referral from primary care).

A search was then conducted through hospital laboratory records for the corresponding d-dimer result. This left us with a cohort of 350 patients, aged >50 years, with a recorded d-dimer who underwent Doppler ultrasound imaging of lower limbs. Using this data, we calculated the sensitivity and specificity using age-adjusted d-dimer versus conventional D-dimer in four different age categories; 51-60 years, 61-70 years, 71-80 years and > 80 years of age. A cohort of patients aged less than 50 years were also included as a comparator group.

PTP was not consistently recorded in inpatient records or on radiology requests to allow for any reliable, accurate statistical information to be calculated from this.

RESULTS

Demographics of the group are detailed in Table.1

Specificity of conventional D-dimer is known to be between

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Table1.

Patient Demographics

Patient Demographics			
Age Group (years)	Total	Male	Female
51-60	69	37	32
61-70	85	42	43
71-80	107	69	38
>80	89	60	29

49-67% in those less than 50 years and anything between 0-18% in those over 80 years.[7] The specificity of age-adjusted d-dimer in our cohort was higher than that of conventional d-dimer in all age groups recorded. The sensitivity was maintained above 75% in all categories with use of age-adjusted d-dimer. These figures are shown in Table.2.

Table2.

Specificity and Sensitivity of age-adjusted and conventional D-dimer

Age Group (years)	Specificity (%)		Sensitivity (%)	
	Age-adjusted	Conventional	Age-adjusted	Conventional
<50	N/A	41	N/A	68.8
51-60	39	23	92	92
61-70	33.8	23	80	80
71-80	32	16.5	78.6	100
>80	36.4	8.1	80	100

N/A – Not applicable

Hypothetically, if those with a low PTP had a corresponding negative age-adjusted D-dimer, application of age-adjusted d-dimer cut-off value could have prevented 59 (16.6%) inappropriate Dopplers in our cohort.

With use of age-adjusted D-dimer across the whole cohort, there were 14 false negatives. Of these, four Dopplers revealed non-occlusive clot in keeping with an old VTE and not an acute episode, reducing this to 10 false negatives. Of these ten episodes, only five had a corresponding PTP recorded. Three patients had low risk scores while the remaining two had scores suggesting high likelihood of DVT. It is difficult to draw conclusions from this data due to its limited nature.

DISCUSSION

Our findings are in keeping with those of Schouten et al; the use of an age-adjusted d-dimer cut-off value of age (years) x 10μg/L, increases the specificity of the test, when used in conjunction with a low risk PTP score. Patient care could be improved with a reduction in the number of unnecessary tests and time spent at hospital. Unnecessary low molecular weight heparin administration whilst awaiting diagnostic imaging would not be required, again improving the patient experience

Sensitivity was maintained in the 51-60 and 61-70 age groups, but there was a reduction in sensitivity in the older age groups when compared to conventional d-dimer group. Our small numbers may have contributed to this. Those with a high PTP, a Well's Score of two or more, do not require a D-dimer if imaging is performed within four hours.[4] It could be inferred that those high risk of a VTE as per their PTP score would not have had a D-dimer performed and therefore would not be in our cohort of patients

The false negative results are notable, the consequences of not diagnosing a new VTE having the potential to be fatal. To examine the false negative cohort within this study requires access to the PTP which unfortunately is not available for informative conclusions to be made. In line with recommendations regarding interpretation of PTP, it should only be those patients considered low risk for VTE that should have had a D-dimer performed.

One of the study's strengths is the standardised calculation of the D-dimer, using the Innovance latex assay, as part of the standard operating procedure in our laboratory. The main limitations of this study are its small numbers and that this was a retrospective study. The lack of data on the pre-test probability scores reduces the reliability of the results.

CONCLUSION

Age-adjusted D-dimer is more specific for those with a low risk pre-test probability for VTE, when aged > 50 years. Sensitivity in our cohort was reduced which may be the result of small numbers and the retrospective nature of the data. Although the results are similar to those of Schouten et al, they do not support the role of age-adjusted D-dimer, as increased specificity with age-adjusted D-dimer is secondary to increased over-all average D-dimer threshold, as proven by Lapner et al.[8] Further studies are necessary to optimise the diagnostic role of the D-dimer in VTE.

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