A Cost-effectiveness Analysis of Diagnostic Algorithms of Deep Vein Thrombosis at the Emergency Department

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Keywords

D-dimer; Deep Vein Thrombosis; Cost-effectiveness

Abbreviations

Contrast venography (CV)

Compression Ultrasonography (CUS)

Deep Vein Thrombosis (DVT)

Pre-Test Probability (PTP)

Pulmonary Embolism (PE)

Venous Thromboembolism (VTE)

Abstract

Introduction: Suspected cases of deep vein thrombosis are common at emergency departments and they often require extensive and costly diagnostic testing. The objective of this study was to evaluate whether a diagnostic algorithm based upon pre-test probability and D-dimer in diagnosing deep vein thrombosis may be cost-effective from a societal perspective in a Swedish setting.

Material and Methods: The cost-effectiveness of two alternative diagnostic algorithms were calculated using decision analysis. An algorithm which out ruled deep vein thrombosis among low probability patients with negative D-dimer was compared to a traditional algorithm including compression ultrasonography and/or contrast venography for all patients. For sensitivity analysis, a third reversed algorithm, where D-dimer was followed by pre-test probability, was analyzed. Estimates of probabilities were obtained from a prospective management study, including 357 outpatients with clinical suspicion of deep vein thrombosis. Direct costs were estimated using prices from Scania, Sweden. Indirect costs were estimated using time spent at the local emergency department and gross average wages in Sweden.

Results: The total cost of the pre-test probability and D-dimer algorithm was estimated to €406 per patient and the traditional algorithm was estimated to €581 per patient. Reversing the order of the score and test resulted in an estimate of €421 per patient.

Conclusion: At no significant difference in diagnostic efficacy the algorithm based upon pre-test probability and D-dimer was cost-effective, while the reversed algorithm and diagnostic imaging for all patients were not.

Introduction

Suspected cases of deep vein thrombosis (DVT) are common at emergency departments and they often require extensive and costly diagnostic testing [1-3]. Clinical studies and meta analyses show that algorithms based upon Pre-Test Probability (PTP) assessment and D-dimer safely rule out venous thromboembolism (VTE) when the PTP for the disease is assessed as low and D-dimer is negative [1-3]. By these means DVT is ruled out in 30–50% of outpatients with suspected DVT and safely obviates the need for further diagnostic testing [4,5].

At times of economic constraint, the demand for effective use of scarce resources in the health sector may be more present than ever. New technologies often involve increased benefits to patients, but at a higher cost. Other new technologies are instead developed to achieve the same goal, but at a lower cost. Since few of patients with suspected DVT actually have the disease [6,7] the need for compression ultrasonography (CUS) and/or contrast venography (CV) could be obviated among a large number of patients. The implementation of an algorithm based upon PTP and D-dimer thus implies great cost savings at emergency departments. Earlier studies evaluating algorithms based upon PTP and D-dimer have mainly considered health care costs [8-11]. This study also includes the cost of waiting time at the emergency department, which is an important part of the societal costs from the patient's perspective.

The objective of this study was to evaluate whether a diagnostic algorithm based upon PTP and D-dimer in diagnosing DVT may be cost-effective compared to a traditional algorithm including CUS and/or CV for all patients, using Swedish data. The evaluation was made from a societal perspective.

Methods

Study Design

A decision analysis model was applied to evaluate the cost-effectiveness of two alternative diagnostic algorithms for DVT. The first algorithm is based upon PTP and D-dimer. Figure 1a illustrates the different possible pathways in the algorithm. DVT was excluded for patients with low PTP and a negative D-dimer in the PTP±D-dimer algorithm, while patients with high PTP or positive D-dimer continued with CUS and/or CV. The second algorithm (figure

1b), which has been used traditionally, involved diagnostic imaging for all patients. The mutually exclusive pathways were results of prior decisions and probabilities of different events. The expected cost for the algorithm was determined by the sum of the costs weighted by the probabilities of events for the particular pathway. Total costs were the sum of direct health care costs and indirect costs measured by patient time spent in the emergency department. To see the potential total cost to society, these costs were enlarged to the regional and the national level. For sensitivity analysis, a third algorithm was analyzed (Figure 1c), where the order of D-dimer and pre-test probability were reversed compared to the first algorithm.

Data

The probabilities used in the analysis were derived from a clinical management study [12] where 357 outpatients with a suspected first episode of DVT were prospectively recruited. PTP was estimated by the emergency physician using Wells score [13,14]. Enrollment was possible 24h/day 7d /week and occurred immediately on arrival to the emergency department by the emergency physician on duty. If categorized as having a low pre-test probability, real time D-dimer (Auto Dimer ® (Biopool ® International Umeå, Sweden), cut off 250 ng/mL) was analyzed and if negative, DVT was considered ruled out. The remaining patients proceeded to CV and/or CUS. The primary outcome was recurrent VTE during 3 month follow up. One out of 110 patients, in the low probability-negative D-dimer cohort, developed DVT (distal) during follow up. PTP followed by D-dimer safely ruled out DVT in about 30% of patients with a suspected first episode of DVT. As recently shown in a meta-analysis [2], this outcome was consistent with other similar clinical studies. Table 1 shows patients characteristics.

Estimates of time patients spent at the hospital were based on estimates from the emergency department at the Lund university hospital (low probability patients with negative D-dimer, 3h 50 min, high probability patients or positive D-dimer, 8h, and CV/ CUS alone without D-dimer determination, 7h) [Personal communication Dr J L Elf].

Distributions between the different methods of diagnostic imaging in the CUS/CV alone algorithm were estimates about hospital practice of diagnosing DVT before PTP and D-dimer was an available option [15]. These estimates were in accordance with previous research [16].

Previous studies have shown that the incidence of DVT is between 48/100.000 and 160/100.000 in the population [17-20]. The prevalence of patients with actual DVT in the group of suspected cases of DVT at the emergency department was 23.5% [12]. The number of suspected cases of DVT in the county Scania, with 1.2 million inhabitants, was thus estimated to reach 2400 - 8200 cases each year. In Sweden, with 9.2 million inhabitants, the number of suspected cases of DVT was estimated to reach 19.000 – 63.000 cases each year. A previous study have reported 40.000 suspected cases of DVT in Sweden in a year [16].

Valuation of costs

All costs are in 2008 Euros (€1= SEK 9,6055). Direct costs were estimated using the pricelist from Southern Regional Health Care Committee [21] (D-dimer €16, CUS €157, CV €461). To ensure that prices used reflected full costs of the algorithms, prices between health care regions were used. Indirect costs occurred when patients spent time at the hospital instead of working, or as a loss of leisure time. We used the human capital approach to value time as loss of production [22]. For patients in working age, productivity loss was estimated by using gross average wage including payroll tax (38.8% [23]) in Sweden 2007. For patients assumed to be retired (aged 65 and older) lost leisure time was estimated by assuming a 35% value of the gross average wage, following previous research [24, 25]. We used age specific probabilities when estimating the indirect cost, as suspected DVT is more likely among elderly patients.

Outcome

Based on previous results [26] we assumed that the alternative diagnostic algorithms did not differ significantly in terms of diagnostic efficacy. In this analysis all cases of DVT were assumed to be detected. As a consequence, risks and costs associated with a false negative diagnosis, such as DVT developing to pulmonary embolism (PE) or post-phlebitic syndrome, or a false positive diagnosis, such as the cost due to side effects of over-treatment of anticoagulation therapy, were not included.

Sensitivity analysis

It has been reported from clinical practice that D-dimer is commonly analysed before the PTP assessment, for both low and high probability patients. A sensitivity analysis was therefore performed in which the order of D-dimer and PTP was reversed (Figure 1c). This reversed algorithm resulted in D-dimer tests for both high and low risk patients. The time spent at the hospital was assumed to be one hour shorter for the reversed algorithm, as a nurse could perform the D-dimer test and get the result before the patient meets with the physician.

Because of parameter uncertainty, D-dimer analysis and proportion of low and high probability patient groups were varied in one-way sensitivity analyses based on assumptions made in a previous study [15]. Prices were varied from a decrease of 50% to an increase of 50%. Time spent at the hospital was varied likewise, due to differences in procedures between hospitals and over time.

Results

The expected total cost for using the PTP±D-dimer algorithm was €406 per patient, where the direct and indirect costs were €311 and €95 respectively. The CV/CUS algorithm was estimated to €581 per patient, where the direct and indirect costs were €471 and €110 respectively. The PTP±D-dimer algorithm is therefore cost-effective. These results are presented in Table 2.

The potential regional cost of the algorithm which involves a PTP±D-dimer was estimated to a total cost of €1- €3.3 million for the county of Scania based on our estimate of 2400-8200 cases per year. The CV/CUS algorithm was estimated to €1.4-4.7 million.

The national potential expenditure of the PTP±D-dimer algorithm in Sweden was estimated to €7.7 –25.6 million per year based on our estimates of 19.000-63.000 cases per year, using cost in Scania as approximates for local costs. The CV/CUS algorithm was estimated to €11 – 36.6 million at the national level.

Sensitivity analysis

If the order of PTP and D-dimer was reversed, D-dimer followed by PTP, the total average cost was estimated to €421 per patient, where the direct and indirect costs were €332 and €89 respectively.

Table 2 shows how sensitive the direct costs are to an increase or decrease of the direct costs with 50% and how sensitive indirect cost are to an increase or decrease of 50% in time spent at hospital. The PTP±D-dimer algorithm remains cost-effective, but the difference to the reversed algorithm decreases as direct cost decreases.

The cost of the PTP±D-dimer algorithm was sensitive to the number of patients in the population who has negative D-dimer as well as low probability. Table 2 shows how the result was affected if 80% of the patients had negative D-dimer, instead of 69% and if the number of patients with low probability would be 35% instead of 45%. The PTP±D-dimer algorithm remains cost-effective compared to the reversed algorithm and the CV/CUS algorithm, which is not affected by the share of patients with negative D-dimer or low probability.

Discussion

The expected cost per patient of using the PTP±D-dimer algorithm was €406 and the cost of the traditional CV/CUS algorithm was 43 % higher. The PTP±D-dimer algorithm is thus cost saving for the health care sector and for patients. At no differences in diagnostic efficacy [26], the PTP±D-dimer algorithm may be considered a dominant strategy, i.e. giving the same result at a lower price. The reduction in cost is mainly due to the possibility to avoid costly and time-consuming CV and/or CUS among patients with low probability and negative D-dimer. Furthermore, the cost-effective algorithm contains the benefit of patient’s preference of an immediate diagnosis and of avoiding the inconvenience of CV, an invasive method associated with a small but significant risk of complications, among low probability patients.

This cost-effectiveness analysis was based on a management study made in clinical practice [12] and available published data. Sensitivity analysis was performed for important variables because of uncertainty. The main result did not change although these variables were varied in different scenarios; the algorithm including PTP followed by D-dimer remains the cost-effective algorithm.

Goodacre and colleagues [8] analyzed various different strategies in an UK setting, which in accordance with our study, showed that diagnostic imaging for all patients is not cost-effective. Humphreys and colleagues [10] performed a similar analysis in the case of acute PE comparing two algorithms, with the result that PTP score and D-dimer was less costly than a standard algorithm involving diagnostic imaging. Ten Cate- Hoek and colleagues [11] recently showed in a cost-effectiveness analysis that an algorithm based on PTP D-dimer was cost-effective in a primary care setting. Hence, previous research is consistent with our results that the PTP±D-dimer algorithm is both safe and cost-effective.

Our model entails the simplifying assumption that all cases of DVT are detected even though one patient in the low probability-negative D-dimer cohort developed DVT (distal) during follow up in the clinical management study [12]. Previous research suggests that the algorithms do not differ substantially in efficacy [26].

Waiting time was clearly an important component in the cost of the alternative algorithms. By including productivity loss, one assumes that the community loses employed labor. Indirect costs may have been overestimated if loss of production was compensated by unemployed labor, colleagues or by the patient at a later point [27] or underestimated as informal care (e.g. the time family members spend accompanying a patient) was not included in the analysis. We used information from estimates of expected waiting time and we carried out a sensitivity analysis of these estimates. The estimates used here were assumed to reflect current practice in Swedish emergency departments.

Differences between algorithms become more evident, even though they should be interpreted carefully, when enlarged to the regional and national level. Our estimates of suspected cases of DVT were based on literature [12, 17-20] and it was in agreement with a survey on the extent of diagnostic imaging of DVT made in Sweden from 2002 [16]. Based upon our estimates the county of Scania would decrease expenditures with €0.4 – 1.4 million per year depending on the incidence rate, moving from the traditional algorithm to the PTP±D-dimer based algorithm. On the national level, savings were estimated to € 3.3 - 11 million per year, by implementing the PTP±D-dimer algorithm instead of the traditional algorithm.

The limitations of this study are that direct costs and waiting times at the emergency departments can vary in different settings and over time. Furthermore, the incidence of DVT can vary between countries [17-20] and cohorts of patients. Our analysis is based on available published research, which explains the wide interval of potential cost on the regional and national level.

In the short run, the PTP±D-dimer algorithm may not be considered as cost-saving for hospitals that currently have excess capacity of diagnostic imaging. The excess capacity will favor patients who are waiting for CV or CUS in the short run, since the demand for such diagnostic methods have decreased. However, in the longer term the reduction of investment costs in equipment and education of staff, associated with diagnostic imaging, is likely to make the PTP±D-dimer algorithm cost-effective.

The reversed algorithm was shown to be suboptimal as the direct costs increased when D-dimer is used for all patients; not only low probability patients. Indirect costs savings made by allowing a nurse to take the D-dimer test before the patient meets with the physician, was not enough to compensate for the increase in direct cost.

D-dimer is only to be applied if the physician is convinced that DVT is a diagnostic possibility. If the D-dimer test is used as a screening test, the reversed algorithm increases the risk of physicians to suspect more patients for DVT, as a positive D-dimer can depend on many other factors then DVT, and the positive predictive value is low. Indiscriminate use of D-dimer may result in many unnecessary diagnostic imaging tests and thus at a higher costs.

Conclusion

The findings of this economic evaluation support the implementation of an algorithm which involves PTP followed by a D-dimer test. If implemented in the this way, the diagnostic algorithm implies better use of resources for the health care sector as well as the society as a whole, compared to a traditional algorithm which involves diagnostic imaging for all patients.

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Conflict of interest statement

There are no conflicts of interest declared from the authors.

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Legends to figures and tables

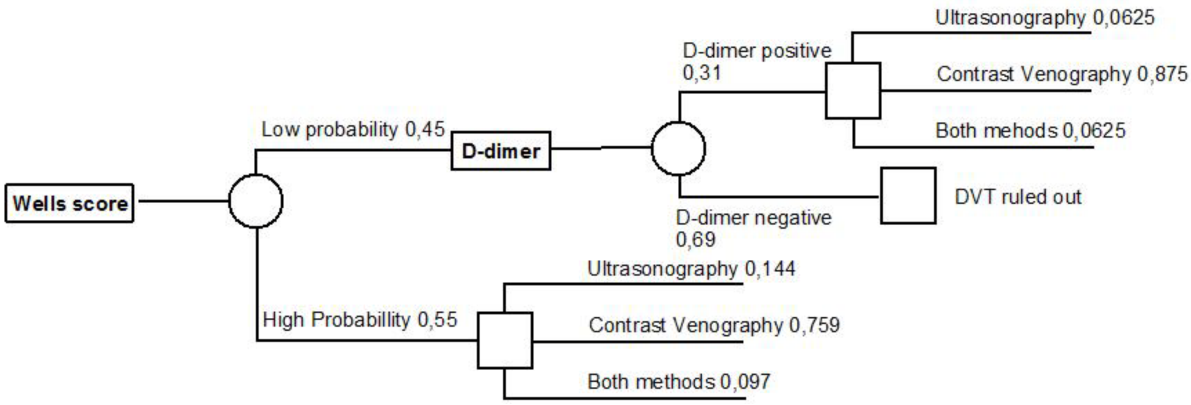
Figure 1a The PTP±D-dimer algorithm. Probabilities were based on a prospective management study made by Elf and collegues [12].

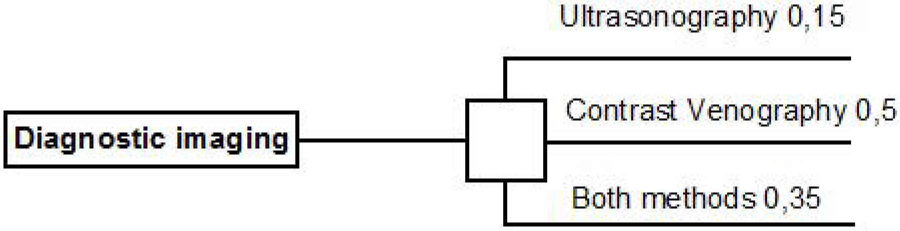
Figure 1b The traditional (CUS/CV) algorithm. Probabilities were estimated made by National Board of Health and Welfare [15].

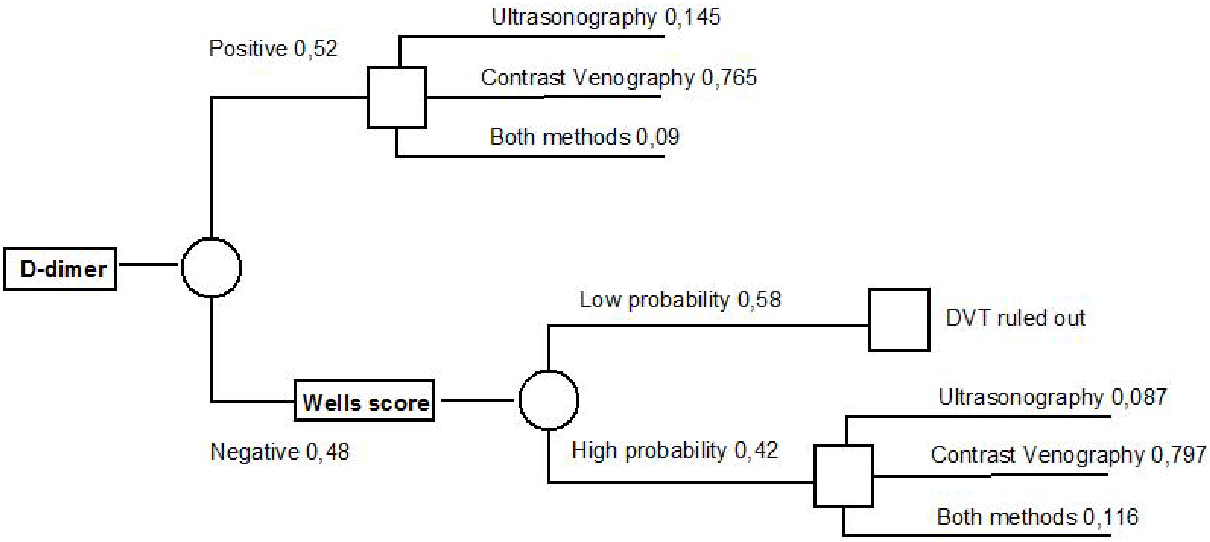
Figure 1c The reversed algorithm, where D-dimer is followed by PTP. Estimates were derived from the prospective management study made by Elf and colleagues [12].

Table 1 Patients characteristics (Summary) [12]

Table 2 Results of direct, indirect and for the sensitivity analysis. Total costs of alternative algorithms are in bold type. € = Euro and PTP = Pretest probability


Wells score
Low probability 0,45
D-dimer
D-dimer positive 0,31
Ultrasonography 0,0625
Contrast Venography 0,875
Both mehods 0,0625
D-dimer negative 0,69
DVT ruled out
High Probabillity 0,55
Ultrasonography 0,144
Contrast Venography 0,759
Both methods 0,097


Diagnostic imaging
Ultrasonography 0,15
Contrast Venography 0,5
Both methods 0,35



D-dimer
Positive 0,52
Ultrasonography 0,145
Contrast Venography 0,765
Both methods 0,09
Negative 0,48
Wells score
Low probability 0,58
DVT ruled out
High probability 0,42
Ultrasonography 0,087
Contrast Venography 0,797
Both methods 0,116

	All patients (n=357)	Patients with DVT (n=84)	Patients without DVT (n=273)
Low probability	159 (45%)	14 (17%)	145 (53%)
Intermed/high probability	198 (55%)	70 (83%)	128 (47%)
Age (median)	62 (33, 82)*	67 (32, 83)	60 (33, 81)
Men	138 (39%)	34 (40%)	104 (38%)
Heredity	62 (17%)	16 (19%)	46 (17%)
Smoking	66 (18%)	12 (14%)	54 (20%)
BMI	26 (21,33)*	26 (20, 33)	26 (22, 33)
* Median (10th, 90th percentiles).			

Main Results			Sensitivity Analysis					
			Direct cost Decrease 50%	Indirect cost Increase 50%	Indirect cost Decrease 50%	Indirect cost Increase 50%	Negative D-dimer 80%	Low PTP 35%
PTP and D-dimer	Direct cost	€311	€156	€467	€311	€311	€289	€338
	Indirect cost	€95	€95	€95	€48	€143	€94	€100
	Total cost	**€406**	**€251**	**€562**	**€359**	**€454**	**€383**	**€438**
CV/CUS	Direct cost	€471	€235	€706	€471	€471		
	Indirect cost	€110	€110	€110	€55	€165		
	Total cost	**€581**	**€345**	**€816**	**€526**	**€636**		
Reversed order	Direct cost	€332	€167	€500	€332	€332	€313	€438
	Indirect cost	€89	€89	€89	€45	€134	€80	€99
	Total cost	**€421**	**€256**	**€589**	**€377**	**€466**	**€393**	**€537**