

Cost-minimization analysis of venous thromboembolism diagnosis: Comparison of standalone imaging with a strategy incorporating D-dimer for exclusion of venous thromboembolism

Karan Verma MSc, MBA¹ | Cristina Legnani PhD² | Gualtiero Palareti MD³

¹Instrumentation Laboratory, Bedford, MA, USA

²Angiology and Blood Coagulation, University Hospital of Bologna, Bologna, Italy

³Cardiovascular Diseases, University of Bologna, Bologna, Italy

Correspondence

Karan Verma, Instrumentation Laboratory, Bedford, MA, USA.

Email: kverma@ilww.com

Summary

Background: The burden of healthcare costs has substantially risen in the last few decades. One possible contributing factor to this increase are the diagnostic approaches for venous thromboembolism (VTE) using only imaging to exclude a diagnosis of VTE.

Objective: To demonstrate cost minimization in the diagnosis of VTE by comparing standalone imaging (computed tomography pulmonary angiography and compression ultrasonography) to a published VTE diagnostic strategy incorporating assessment of pre-test probability and D-dimer testing.

Methods: We retrospectively reviewed data from a multicenter diagnostic accuracy study of a D-dimer reagent where consecutive outpatients (n=747) with suspected VTE, including both pulmonary embolism (n=346) and deep venous thrombosis (n=401) were evaluated. By applying a VTE diagnostic strategy and using the proportion of patients that were diagnosed as VTE-negative (n=137 for PE; n=120 for DVT), we developed a cost calculator to compare the average diagnostic test cost per suspected VTE patient, both before and after the implementation of the VTE diagnostic strategy.

Results: Implementation of the VTE diagnostic strategy reduced the average diagnostic test cost for a suspected PE patient by 38% and for a suspected DVT patient by 24%. Assuming the proportion of VTE suspected patients to be 30% PE and 70% DVT, the weighted average reduction in the diagnostic test cost per suspected VTE patient was 32%.

Conclusion: Implementation of a VTE diagnostic strategy can allow hospitals to reduce costs without compromising patient safety.

KEYWORDS

costs and cost analysis, D-dimer, deep vein thrombosis, pulmonary embolism, venous thromboembolism

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2017 The Authors. Research and Practice in Thrombosis and Haemostasis published by Wiley Periodicals, Inc on behalf of International Society on Thrombosis and Haemostasis.

Essentials

- A venous thromboembolism (VTE) diagnostic strategy is economical compared to imaging alone.
- Applied a VTE diagnostic strategy to a D-dimer multicenter study for cost-minimization analysis.
- Average diagnostic test costs for patients were significantly lower with a diagnostic strategy.
- Implementation of a VTE diagnostic strategy reduces the diagnostic costs for a hospital.

1 | INTRODUCTION

The cost of healthcare is growing at an unsustainable rate worldwide. As a result, reimbursement agencies like the Centers for Medicare & Medicaid Services (CMS) in the United States (US) are pushing hospitals to reduce costs. Cardiovascular disease is one of the leading contributors to cost¹ with venous thromboembolism (VTE), comprised of deep venous thrombosis (DVT) and pulmonary embolism (PE), being the third most common cardiovascular disease in the world.² Despite a high prevalence, VTE has a relatively high rate of underdiagnosis. An undiagnosed DVT can evolve to a PE,³ which can be fatal if left untreated. Therefore, as the detection of VTE is vital for patient survival, it has often led to the overutilization of imaging tests, thereby straining limited hospital resources.

Considering the prevalence of VTE in suspected patients is 10-20%,^{2,4} the majority of imaging can be avoided with the implementation of a diagnostic strategy for VTE. This VTE diagnostic strategy does not entirely replace imaging, but instead complements it with clinical prediction models and D-dimer assays. Even though diagnostic strategies for VTE have existed for over a decade,^{5,6} implementation in clinical practice is reportedly low.⁷ The lack of adoption of these diagnostic strategies is directly associated with increased hospital costs for VTE diagnosis.

Since there can be no compromise on patient safety while cutting costs, hospitals often look for answers by performing cost-minimization analysis, which evaluates 2 established and equally efficacious medical procedures that have the same objective, but differ in their cost burden. This is different than the commonly used cost-effectiveness analysis, which is used to compare relative costs and outcomes in nonmonetary units, such as Quality Adjusted Life Years (QALY). In this study, we report the results of a cost-minimization analysis for the diagnosis of VTE in which standalone imaging is compared to a VTE diagnostic strategy using assay performance data from a previously published multicenter study that evaluated a highly sensitive D-dimer assay.⁸

2 | MATERIALS AND METHODS**2.1 | Study data**

The cost-minimization analysis (CMA) was conducted retrospectively using the data obtained from the multicenter evaluation of HemosIL D-Dimer HS 500 (Instrumentation Laboratory, Bedford, MA, USA).⁸ The study protocol was designed as a management study to evaluate diagnostic accuracy of a specific D-dimer assay, which required a 3-month follow-up to confirm exclusion of VTE. The patient

evaluations were conducted in emergency rooms or outpatient clinics at 4 teaching hospitals on consecutive outpatients (>16 years of age) with suspected VTE. A total of 747 outpatients suspected of VTE (346 for PE, 401 for DVT) were enrolled in the study between January 2006 and January 2008 (Table 1). The plasma samples from all 747 patients were initially evaluated using the center's routine D-dimer assays, but samples were frozen and tested using HemosIL D-Dimer HS 500 at each participant center from February to May 2008.⁸

2.2 | Imaging tests for VTE

There are multiple imaging tests available for the detection of VTE, with computed tomography pulmonary angiography (CTPA) preferred for PE,⁴ and compression ultrasonography (CUS) for DVT.⁹ To maintain the simplicity of the cost calculator we utilized the costs associated with CTPA and CUS as examples in this study.

2.3 | Clinical prediction models

To quantify the pretest probability (PTP) of VTE in suspected patients during the multicenter study, the Wells Model (PE¹⁰ and DVT³) was utilized by the treating physician, at the time of the suspected VTE patient evaluation. The Wells Model classifies patients with suspected DVT and PE as "low," "moderate," and "high" risk. The VTE diagnostic strategy used in the multicenter study is depicted in Figure 1A; however, because the study was designed as a diagnostic accuracy study rather than be representative of clinical practice, we retrospectively applied the Clinical & Laboratory Standards Institute (CLSI) VTE diagnostic strategy (Figure 1B),¹¹ which is similar to the recommendation by other professional organizations such as the American College of

TABLE 1 Proportion calculations from multicenter study data

Proportion category	PE suspected patients		DVT suspected patients	
Total suspected VTE patients	346		401	
Suspected VTE patients with Low/Moderate PTP	322	93%	322	80%
Suspected VTE patients with Low/Moderate PTP & Negative D-dimer	137	40%	120	30%

VTE, venous thromboembolism; PTP, pretest probability; PE, pulmonary embolism; DVT, deep venous thrombosis.

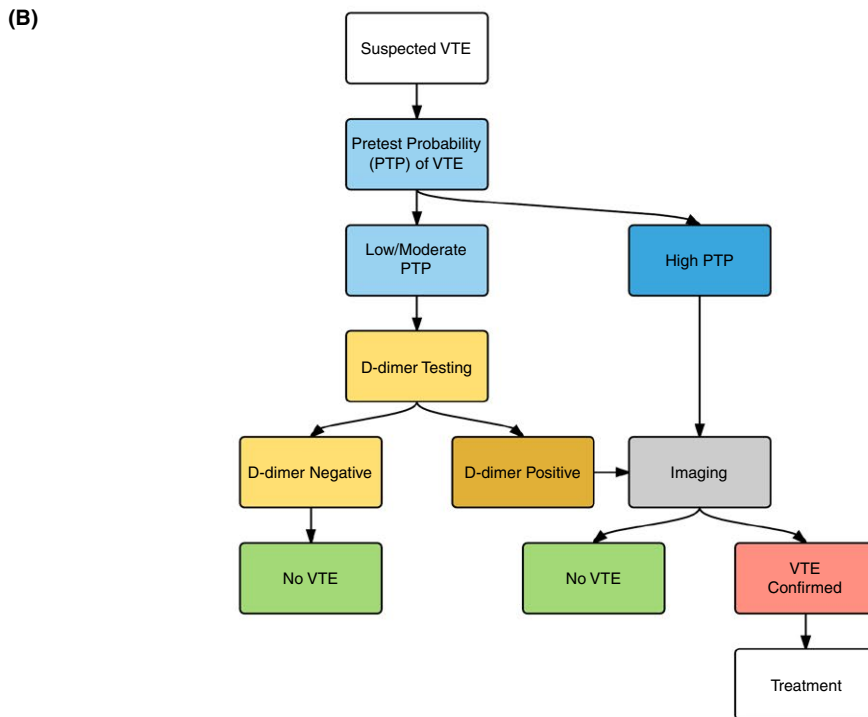
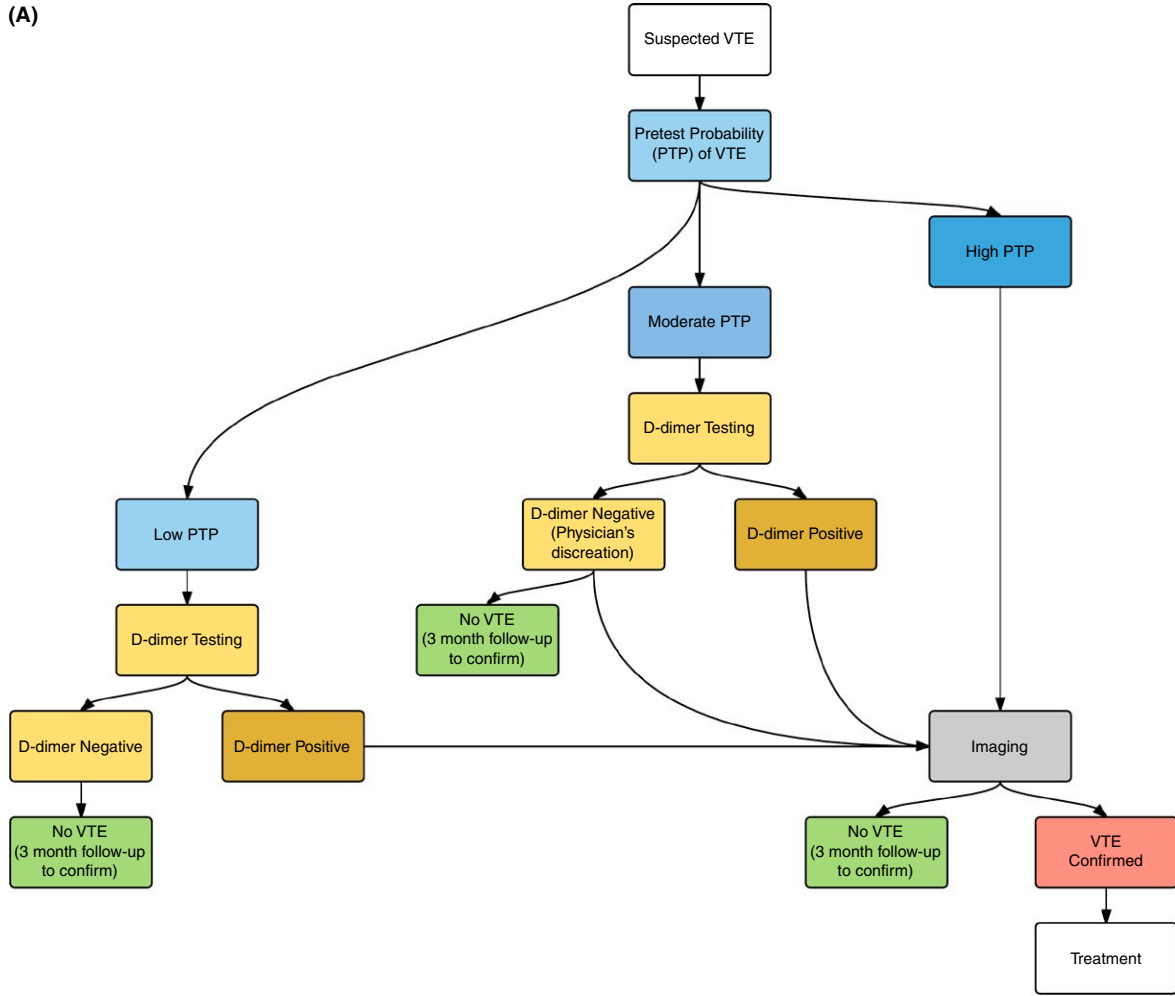


FIGURE 1 (A) VTE diagnostic strategy utilized in the multicenter study. (B) VTE diagnostic strategy recommended by CLSI

Chest Physicians,⁹ British Thoracic Society,⁵ and British Committee for Standards in Haematology.⁶ Using this strategy, all high risk patients (24 for PE, 79 for DVT) would have been sent straight to imaging, whereas all “low” and “moderate” risk patients (322 for PE, 322 for DVT) would have had D-dimer testing performed initially (Table 1).

2.4 | D-dimer assays

D-dimer assays are commonly used in the exclusion of VTE. Using the data from the multicenter study, 137 of suspected PE and 120 of suspected DVT patients with low or moderate PTP were also negative for HemosIL D-Dimer HS 500 (<500 ng/mL Fibrinogen Equivalent Units [FEU]). These patients were followed three-months later and demonstrated no symptoms of VTE, accounting for a 100% negative predictive value (NPV) (95% CI: 98.6-100%) and 100% sensitivity (95% CI: 95.9-100%) of HemosIL D-Dimer HS 500 in conjunction with a PTP score.⁸

2.5 | Cost-minimization analysis

Using the CLSI recommended VTE diagnostic strategy (Figure 1B), two scenarios were created for developing the cost calculator (Table 2), where the final output was the average diagnostic test cost per suspected VTE patient both before and after the implementation of the VTE diagnostic strategy. In the before scenario, all suspected VTE patients were sent to imaging whereas in the after scenario, only suspected patients that had high PTP or were not excluded by D-dimer testing were referred for imaging.

The cost inputs for imaging and D-dimer tests were obtained from published literature.^{12,13} All monetary amounts used for calculators are reported in US dollars. The average diagnostic test cost per suspected VTE patient in the before scenario was calculated by multiplying 100%, assuming all suspected VTE patients went for imaging, with the imaging costs of CTPA (\$648)¹² and CUS (\$184)¹³ for PE and DVT, respectively. In the after scenario, the average diagnostic test cost per suspected VTE patient was calculated using weighted averages of the proportion of patients that had low and moderate PTP and went for D-dimer testing (\$14),¹² and the proportion of suspected VTE patients that were not excluded after the D-dimer test and went for imaging (Table 1).

3 | RESULTS AND DISCUSSION

With the implementation of a VTE Diagnostic Strategy such as the recommendation from CLSI, the total diagnostic test cost per suspected patient was reduced from \$648 to \$404 (38% reduction) for PE, and from \$184 to \$140 (24% reduction) for DVT (Table 2). Assuming the proportion of suspected PE and DVT patients as 30% and 70%, respectively,¹⁴ the weighted average savings per suspected VTE patient was approximately \$104 (32% reduction). Therefore, if a hospital evaluates approximately 5000 suspected VTE patients per year, the incorporation of a VTE Diagnostic Strategy yields a cumulative annual savings of \$518 695.

The objective of CMA is to compare two equally efficacious medical procedures that differ in their cost burden. For this purpose, we

TABLE 2 Cost calculator demonstrating the cost-minimization analysis

Tests	PE	DVT	VTE
Cost: D-dimer	\$14	\$14	
Cost of PE imaging: eg CTPA	\$648		
Cost of DVT imaging: eg CUS		\$184	
VTE prevalence distribution	30%	70%	100%
<i>Before using a VTE Diagnostic Strategy</i>			
Suspected patients using D-dimer tests (Low/Moderate PTP)	0%	0%	
Suspected patients excluded (Low/Moderate PTP & negative D-dimer)	0%	0%	
Suspected patients using imaging tests	100%	100%	
Total diagnostic test cost per suspected VTE patient (Before)	\$648	\$184	\$323
<i>After using a VTE diagnostic strategy</i>			
Suspected patients using D-dimer tests (Low/Moderate PTP)	93%	80%	
Suspected patients excluded (Low/Moderate PTP & negative D-dimer)	40%	30%	
Suspected patients using imaging tests	60%	70%	
Total diagnostic test cost per suspected VTE patient (After)	\$404	\$140	\$219
Average savings per suspected VTE patient when a VTE diagnostic strategy is applied	\$244	\$44	\$104
Cost reduction	38%	24%	32%
Assuming 5000 suspected VTE Patients/Hospital/Year	1500	3500	5000
Total savings	\$365 324	\$153 372	\$518 695

PE, pulmonary embolism; CTPA, computed tomography pulmonary angiography; DVT, deep venous thrombosis; CUS, compression ultrasonography; VTE, venous thromboembolism; PTP, pretest probability.

chose a study that demonstrated no false negative results because if a false negative D-dimer result was identified, a CMA could not have been performed, as the cost of a false negative is assumed to be very high.

Therefore, the implementation of a VTE Diagnostic Strategy incorporating D-dimer testing provides an opportunity for hospitals to effectively reduce the diagnostic test costs for suspected VTE patients without compromising patient safety. In addition to cost savings, patients also benefit by saving the time required for imaging and avoiding unnecessary and potentially harmful radiation.

4 | LIMITATIONS

Cost-minimization analysis are based on assumptions that carry limitations. First, the savings listed in our study can only be achieved if a hospital appropriately applies the VTE diagnostic strategy. Second, the retrospective nature of this study limited us from utilizing an activity-based costing approach to the analysis, which would have demonstrated other direct and indirect costs; eg savings resulting from patients in the Emergency Department who were referred to imaging that resulted in an increase in their length of stay, costs resulting from patients who required additional imaging to confirm VTE, as well as costs associated with D-dimer test processing. This is where we hope the calculator model (Table 2) could be used for hospitals to input their local calculated costs, for diagnosis of PE and DVT, and visualize their customized savings. There are also limitations associated with imaging techniques, which we compared the VTE diagnostic strategy to in our study, as they do not give 100% NPV. Even for the VTE diagnostic strategy that demonstrated a 100% NPV using the multicenter data, the 95% CI lower limit is 98.6% so there is the possibility of a false negative result in a different study population. Finally, as the scope of this study was to perform the cost-minimization analysis, the case for VTE diagnostic strategy can be made stronger by performing cost-effectiveness and cost-utility analysis.

ACKNOWLEDGMENTS

The authors would like to thank Kerrie Jaskal, Anne Winkler, and Xavier Rubiralta for providing a critical review of the manuscript.

AUTHOR CONTRIBUTIONS

K. Verma designed the cost-minimization analysis and contributed as the technical writer during manuscript preparation. C. Legnani and G. Palareti provided clinical guidance with access to the multicenter data, and supported the writing of the manuscript.

RELATIONSHIP DISCLOSURE

All financial support for the design, interpretation, and reporting of the study was provided by Instrumentation Laboratory (IL). K. Verma

is an employee of IL, and C. Legnani and G. Palareti have received honoraria from IL.

REFERENCES

1. Tarride JE, Lim M, DesMeules M, et al. A review of the cost of cardiovascular disease. *Can J Cardiol*. 2009;25:e195–202.
2. Wells P, Anderson D. The diagnosis and treatment of venous thromboembolism. *Hematology Am Soc Hematol Educ Program*. 2013;2013:457–63.
3. Wells PS, Anderson DR, Rodger M, et al. Evaluation of D-Dimer in the diagnosis of suspected deep-vein thrombosis. *N Engl J Med*. 2003;349:1227–35.
4. Shujaat A, Shapiro JM, Eden E. Utilization of CT pulmonary angiography in suspected pulmonary embolism in a major urban emergency department. *Pulm Med*. 2013;2013:915213.
5. British Thoracic Society Standards of Care Committee Pulmonary Embolism Guideline Development Group. British Thoracic Society guidelines for the management of suspected acute pulmonary embolism. *Thorax*. 2003;58:470–83.
6. Keeling DM, Mackie IJ, Moody A, Watson HG; Haemostasis and Thrombosis Task Force of the British Committee for Standards in Haematology. The diagnosis of deep vein thrombosis in symptomatic outpatients and the potential for clinical assessment and D-dimer assays to reduce the need for diagnostic imaging. *Br J Haematol*. 2004;124:15–25.
7. Zhi M, Ding EL, Theisen-Toupal J, Whelan J, Arnaout R. The landscape of inappropriate laboratory testing: a 15-year meta-analysis. *PLoS ONE*. 2013;8:e78962.
8. Legnani C, Cini M, Scarvelis D, Toulon P, Wu JR, Palareti G. Multicenter evaluation of a new quantitative highly sensitive D-dimer assay, the HemosIL D-Dimer HS 500, in patients with clinically suspected venous thromboembolism. *Thromb Res*. 2010;125:398–401.
9. Bates SM, Jaeschke R, Stevens SM, et al. Diagnosis of DVT: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 suppl):e351S–418S.
10. Wells PS, Anderson DR, Rodger M, et al. Derivation of a simple clinical model to categorize patients' probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. *Thromb Haemost*. 2000;83:416–20.
11. CLSI. Quantitative D-dimer for the Exclusion of Venous Thromboembolic Disease; Approved Guideline. CLSI document H59-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2011.
12. Lee JA, Zierler BK, Liu CF, Chapko MK. Cost-effective diagnostic strategies in patients with a high, intermediate, or low clinical probability of pulmonary embolism. *Vasc Endovascular Surg*. 2011;45:113–21.
13. Righini M, Nendaz M, Le gal G, Bounameaux H, Perrier A. Influence of age on the cost-effectiveness of diagnostic strategies for suspected pulmonary embolism. *J Thromb Haemost*. 2007;5:1869–77.
14. Lippi G, Favaloro EJ, Cervellin G. A review of the value of D-dimer testing for prediction of recurrent venous thromboembolism with increasing age. *Semin Thromb Hemost*. 2014;40:634–9.

How to cite this article: Verma K, Legnani C, Palareti G. Cost-minimization analysis of venous thromboembolism diagnosis: comparison of standalone imaging with a strategy incorporating D-dimer for exclusion of venous thromboembolism. *Res Pract Thromb Haemost*. 2017;1:57–61. <https://doi.org/10.1002/rth2.12008>