Vascular and Endovascular Surgery
45(1) 22-27

DOI: 10.1177/1538574410385873
http://ves.sagepub.com
SAGE

The Current State of Practice in the Diagnosis of Venous Thromboembolism at an Academic Medical Center

Jung-Ah Lee, PhD[1], and Brenda K. Zierler, PhD[2,3,4]

Abstract

Evidence-based guidelines for the diagnosis of venous thromboembolism (VTE) have been recommended, yet the adoption of such guidelines into daily practice is unknown. The purpose of this study was to describe the current practices in the diagnosis of VTE. Medical records of 1161 adult patients who underwent lower extremity venous duplex scans (VDS), chest computerized tomographic (CT) angiography, or ventilation and perfusion (V/Q) scans during a 6-month period were retrospectively reviewed in an academic medical center. Patients who were first diagnosed by CT or V/Q scan still underwent a VDS. Nine patients at high risk had incomplete CT scans, yet no further tests were performed. Five pregnant patients had CT scans as the initial test instead of being screened with VDS or V/Q scanning. Inappropriate use of imaging tests was documented. The recommended guidelines of using clinical probability and D-dimer as the initial screening tests for VTE diagnosis were underused.

Keywords

venous thromboembolism diagnosis, D-dimer, venous duplex scan, chest computerized tomographic angiography, ventilation and perfusion scan

Introduction

Venous thromboembolism (VTE) manifests as deep vein thrombosis (DVT) and pulmonary embolism (PE). Venous thromboembolism is a major health care concern in the United States because it affects approximately 600 000 new patients each year.[1] Approximately 1% of all hospitalized patients are diagnosed with PE, and PE is considered to be responsible for 10% of all inpatient deaths.[2-4] The mortality associated with untreated PE ranges from 5%[5] to 35%.[6,7] The appropriate and timely diagnosis of VTE could decrease the mortality rates from undiagnosed, misdiagnosed, delayed, or untreated VTE. Individual health care institutions as well as governmental agencies have made the prevention, diagnosis, and treatment of VTE a high priority in patient safety.[8] However, the diagnosis of VTE is challenging since signs and symptoms of VTE are nonspecific.[9] The need for an accurate diagnosis of VTE is essential because untreated PE is potentially fatal and the anticoagulation therapy for VTE can produce significant complications, including bleeding or death.

There are various diagnostic strategies available for VTE. In a typical clinical setting, most suspected VTE patients typically undergo 1 of the 2 tests to rule out DVT or PE: (1)bilateral venous duplex scans (VDS) of the lower extremity to rule out DVT or (2) a chest computed tomographic (CT) angiography, called a spiral or helical CT, to rule out PE. However, currently recommended VTE diagnostic algorithms combine clinical assessment of VTE probability either using a clinically validated standard tool (eg, Wells score, Geneva score) or empirically by an expert physician, D-dimer testing, and objective imaging tests (eg, VDS, ventilation and perfusion (V/Q) scan, a spiral CT scan, or a pulmonary angiography). Effectiveness of this algorithms have been validated in the diagnosis of acute VTE by multicenter prospective outcomes studies.[10-13] Despite the availability of a variety of noninvasive imaging modalities, each has its own limitations based on accuracy, cost, expertise, and availability, thereby making it difficult for providers to choose the most cost-effective diagnostic strategy for VTE.[14]

The purpose of this study was to describe the current practice in the diagnosis of VTE for patients with suspected VTE at an academic medical center prior to implementing an educational intervention using a Web-based VTE Safety Toolkit.

[1] Program in Nursing Science, College of Health Sciences, University of California, Irvine, CA, USA
[2] Department of Biobehavioral Nursing and Health Systems, School of Nursing, University of Washington, Seattle, WA, USA
[3] Department of Surgery, Vascular Division, Department of Medical Education and Biomedical Informatics, School of Medicine, University of Washington, Seattle, WA, USA
[4] Department of Health Services, School of Public Health, University of Washington, Seattle, WA

Corresponding Author:
Jung-Ah Lee, University of California, Irvine, College of Health Sciences, Program in Nursing Science, Irvine Hall 205B, Irvine, CA 92697, USA
Email: jungahl@uci.edu

Methods

This study is a part of a larger pre/post study funded by the Agency for Healthcare Research and Quality (AHRQ) Partners in Patient Safety grant. The parent study was designed to evaluate the effectiveness of 2 interventions: (1) a VTE Safety Toolkit and (2) an on-line provider training module on VTE prophylaxis. The VTE Safety Toolkit consists of evidence-based clinical algorithms for the prevention, diagnosis, and management of acute DVT and PE. The goal of the intervention study is to evaluate the effectiveness of the tools and products of a systems-supported VTE Safety Toolkit on improving clinical and system outcomes for patients at risk for or diagnosed with VTE. This substudy will describe the diagnostic strategies used for patients with suspected VTE prior to the implementation of the interventions.

The sample consists of 1161 consecutive inpatients and outpatients referred for a VDS, a spiral CT, or V/Q scan for a suspected VTE at an academic medical center during the period of October 2005 to March 2006. All patients aged 18 years and older who underwent VDS, CT, or V/Q scans for suspected VTE were included in this study. The medical records were retrospectively reviewed to document patient demographics, diagnostic strategies to rule out DVT and PE, indications for the imaging studies, signs and symptoms, and VTE risk factors at the time of the objective testing. Seven outpatients who underwent VDS but had no medical information available were excluded in the analysis.

Objective diagnostic testing for DVT or PE diagnosis included D-dimer assay, lower extremity VDS, chest CT scan, and V/Q scan. Pulmonary angiography (PA) was not included for PE diagnostic procedures because PA is currently only performed for therapeutic purposes such as catheter embolectomy or catheter-directed thrombolysis. D-Dimer assays measured within 2 days prior to an objective imaging test (VDS, CT, or V/Q scan) were considered as a screening test. Rapid quantitative immunoturbido-metric D-Dimer assays and 64 multislice CT scanners were used in this institution. A positive result for this particular assay was noted when the level of the quantitative D-Dimer was greater than 0.4 μg/mL.[15]

Acute DVT was diagnosed by a comprehensive VDS by registered vascular technologists in an Intersocietal Commission for the Accreditation of Vascular Laboratories (ICAVL) accredited laboratory. Venous duplex scanning has been used as the standard objective test for DVT diagnosis. The criteria used to diagnose acute DVT included incompressibility of the vein walls, the presence of intraluminal thrombus, loss of spontaneous and phasic Doppler flow signals, and abnormal blood flow augmentation with vein compression. A positive study for PE was noted when thrombi were detected by spiral CT or V/Q scanning (positive yield and high probability for PE, respectively). In this study, pulmonary and venous angiograms were not reviewed, since they are only used for therapeutic purposes in this institution.

Risk factors for VTE reviewed in this study included prior DVT/PE, active cancer with ongoing chemo or radiation therapy and palliative therapy, major surgery within 4 weeks, cardiac diseases, immobilization due to paralysis, limb trauma, hormone therapy including either hormone replacement therapy or oral contraceptives, pregnancy or postpartum, morbid obesity (body mass index [BMI] $\geq$ 40), prolonged travel ($\geq$ 6 hours), inherited or acquired thrombophilia, and a family history of VTE.

Data were analyzed using SPSS 15 for Windows. Descriptive statistical methods were used to describe patient demographic characteristics, signs and symptoms of VTE, VTE risk factors, and diagnostic management. The chi-square (χ^2) tests were performed to analyze categorical variables and Student *t* tests were performed for continuous variables. The Institutional Review Board of this institution approved this study.

Results

Table 1 shows the patient characteristics and risk factors for VTE. A total of 1161 consecutive patients underwent diagnostic testing to rule out VTE. Among those, 817 (70%) patients were suspected for DVT and 504 (43%) patients were suspected for PE. The majority of patients were females and Caucasians. The mean age was 56 years in patients with VDS and 53 years in patients who underwent lung scanning. The median length of hospital stay was 10 days in inpatients with suspected DVT and 6 days in inpatients with suspected PE. The majority of patients diagnosed with VTE were inpatients. Approximately 10% of patients (34 of 357) who were referred from outpatient clinics or emergency room had DVT diagnosed, while 18% (81 of 460) of inpatients were diagnosed with DVT.

Diagnostic Procedures for DVT

The incidence of DVT in patients who underwent VDS was 14% (115 of 817) and the incidence of PE was 18.5% (93 of 504) in patients who underwent either spiral CT or V/Q scanning. Thirty patients were diagnosed with both DVT and PE during the 6-month study period. The most common risk factor for VTE was surgery in patients suspected with DVT ($P < .05$) and cardiac disease in patients suspected with PE ($P < .05$). Table 2 describes the incidence of DVT by indication in patients who were referred to the vascular laboratory to rule out DVT by VDS. Approximately 70% (567 of 817) of patients who underwent VDS were symptomatic and among those 14% (78 of 567) had a positive study for DVT. About a quarter of patients (188 of 817) underwent VDS to look for a source of PE and among those 21% (39 of 188) were diagnosed with DVT; half of these patients (91 of 188) presented with both leg and lung symptoms. Approximately 12% (100 of 817) of patients had VDS for surveillance purposes and among those 13% (13 of 100) had DVT, which was similar to the incidence of DVT in the symptomatic patients (14%). About 80% of patients who underwent VDS for surveillance had one or more VTE risk factors.

Table 1. Demographic Information and Risk Factors in Patients With Suspected VTE

Patient Characteristics	Patients With Suspected DVT	Patients With Suspected PE
Patients, n (%)	817	504
Mean age (y)	56 ± 16.7	53 ± 17.1
Median length of hospital stay	10 days	6 days
Gender (female)	433 (53.0%)[a]	273 (54.2%)
Race (Caucasian)	697 (85.3%)	405 (73.6%)[a]
Inpatient status[b]	461 (56.4%)[a]	313 (68.0%)
Incidence of DVT	115 (14.1%)	–
Incidence of PE	–	93 (18.5%)
VTE Risk factors		
Previous VTE	143 (17.5%)[a]	76 (15.1%)[a]
Active malignancy	122 (14.9%)[a]	85 (16.9%)[a]
Surgery within 4 weeks	235 (28.8%)[a]	128 (25.4%)
Cardiac diseases	216 (26.4%)	140 (27.8%)[a]
Limb trauma	42 (5.1%)	6 (1.2%)
Hormonal therapy	53 (6.5%)	18 (3.6%)
Pregnant or postpartum	24 (2.9%)	8 (1.6%)
Morbid obesity[c]	51 (6.2%)	25 (5.0%)
Prolonged travel (>6 hours)	24 (2.9%)	17 (3.4%)
Inherited or acquired thrombophilia	31 (3.8%)	22 (4.4%)
Family history of VTE	23 (2.8%)	10 (2.0%)
Immobilization due to paralysis	25 (3.1%)	14 (2.8%)

Abbreviations: DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.
[a] $P < .05$.
[b] Inpatient status was at the time of the diagnostic testing obtained.
[c] Morbid obesity defined as body mass index ≥ 40.

Table 2. Deep Vein Thrombosis DVT Incidence by Indication for Referral for VDS

	No (%)[a]	DVT Incidence (%)
Rule-out acute DVT Patients with symptomatic legs (swelling, pain)	567 (70)	78 (14)
Look for a source of PE Patients with dyspnea, chest pain, fever	188 (23)	39 (21)[b]
Surveillance Patients with asymptomatic legs	100 (12)	13 (13)

Abbreviations: PE, pulmonary embolism; VDS, venous duplex scans.
[a] The numbers are not mutually exclusive because some patients had both leg and lung symptoms.
[b] $P < .001$.

Table 3. Pulmonary Embolism (PE) Incidence by Diagnostic Test

	No (%)[a]	PE Incidence (%)
CT scan	437/504 (87)	88 (20)[b]
V/Q scan	77/504 (15)	6 (8)
Venous duplex scan	124/504 (25)	52 (42)[c]

Abbreviations: CT, spiral computer tomographic angiography; V/Q, ventilation and perfusion lung scan; PE, pulmonary embolism.
[a] The numbers are not mutually exclusive because some patients had both CT and V/Q scans.
[b] $P < .001$.
[c] The patients with venous duplex scan had PE diagnosis by either CT or V/Q scan.

Diagnostic Procedures for PE

The majority of patients who were suspected of having PE underwent spiral CT (437 of 504, 87%) rather than VQ scanning. The incidence of PE was 20% in those with CT scan and 8% in those with V/Q scan (Table 3). In addition to undergoing lung scanning for possible PE, 25% of these patients (124 of 504) underwent VDS and among those 29% (36 of 124) were diagnosed with DVT and 45% (52 of 124) were diagnosed with PE by lung scanning. Table 4 describes various PE diagnostic strategies used in this institution. The CT alone strategy was used most frequently to rule out PE in 65% patients with suspected PE. Approximately 25% of patients underwent both a lung scan and lower limb VDS. Sixty-three patients had VDS only to look for the source of symptomatic PE; 6 were diagnosed with DVT and 57 had a negative examination with no further lung imaging tests performed.

Incomplete or Indeterminate Studies

Fourteen patients had incomplete CT scanning due to reasons such as inadequate contrast opacification, respiratory motion artifact (especially in elderly patients), or obesity (obese patients too heavy for CT table). Twelve patients with incomplete CT scans did not have further objective testing, while 2 patients with indeterminate CT results underwent subsequent V/Q scan or VDS to rule out PE. Of 12 patients, 9 who had incomplete CT scans had 1 or more VTE risk factors. Among 3 patients with intermediate V/Q scan results (or indeterminate), subsequent studies demonstrated 1 positive result using CT scan and 2 negative VDS scans. Approximately 82% (63 of 77) of V/Q studies resulted in a low clinical probability for PE and half (31 of the 63 patients) had no further objective imaging tests. Four patients had subsequent CT scans and the remaining 28 patients had VDS within 7 days of symptoms. Five patients with low clinical probability on V/Q scan had abnormal D-dimer testing, but they had no further imaging tests.

D-Dimer Measurement as a Screening Test in Outpatients. D-dimer testing was performed prior to objective imaging tests in patients who presented to outpatient clinics or to the emergency room (Table 5). Approximately 14% of patients who underwent VDS were initially screened using D-dimer testing, while a greater number (42%) of patients who underwent CT had D-dimer tests and 23% of patients who underwent V/Q scans had D-dimer tests.

Table 4. Various Strategies for PE Diagnosis Work-Up

	Number of Patients (%)	PE Diagnosis	DVT Diagnosis	Both DVT and PE Diagnosis
1. CT scan alone	328/504 (65)	37	–	–
2. CT and Duplex scan	99 (20)	47	29	25
3. V/Q scan alone	48 (10)	3	–	–
4. V/Q and Duplex scan	24 (5)	5	7	4
5. CT scan and V/Q scan	4 (0.8)	1	–	
6. Duplex scan, V/Q and CT scan	1 (0.2)	0	0	0

Abbreviations: DVT, deep vein thrombosis; PE, pulmonary embolism; CT, spiral computer tomographic angiography; V/Q, ventilation and perfusion lung scan.

Table 5. D-Dimer Tests as a Screening Test Prior to an Imaging Test in Outpatients[a]

	Venous Duplex Scan (n = 357)	CT Scan (n = 164)	V/Q Scan (n = 31)
D-Dimer test performed in outpatients prior to a scan	50/357 (14%)	69/164 (42%)	7/31 (23%)
Outpatients without VTE risk factors	128/357 (36%)	64/164 (39%)	14/31 (45%)
D-Dimer test performed in outpatients without any VTE risk factors	20/128 (16%)	40/64 (63%)	3/14 (21%)

Abbreviations: VTE, venous thromboembolism; CT, spiral computer tomographic angiography; V/Q, ventilation and perfusion lung scan.
[a] Outpatient status was when a patient underwent an objective imaging test.

Discussion

The purpose of this study was to describe the current practices in the diagnosis of VTE prior to the implementation of evidence-based educational interventions. We identified underuse of evidence-based screening tests and overuse of objective imaging tests. There appeared to be no standard approach for the diagnosis of DVT or PE. Some patients received multiple objective imaging tests, even after an initial diagnosis of VTE was found. Other patients received only 1 imaging test when a second confirmatory test was indicated. The cost and effectiveness of the various strategies for the diagnosis of PE will be described in a subsequent paper. The results from this study have provided data on overuse and underuse of diagnostic tests. Educational interventions for standardizing the diagnostic approach for VTE will be implemented and evaluated to determine changes in practice.

Diagnostic Procedures of DVT

Lower extremity VDS was the test of choice used in patients with suspected DVT. The incidence of DVT was approximately 14% in this study, which is similar to that of the literature.[16] To improve the appropriate use of VDS in outpatients, including emergency room settings, D-dimer measurements have been shown to be effective in safely ruling out DVT in patients who present with a low clinical probability and negative D-dimer without VDS.[17-20]

Fowl and his colleagues reviewed the use of venous duplex ultrasound as a screening tool for acute DVT[21] and reported that the high percentage of normal studies indicated that there were inappropriate referrals for the test. They also reported the refusal of third-party payers who retrospectively reviewed all diagnostic studies to pay for these normal studies, as they believed that the tests were not indicated. Moreover, Medicare guidelines have mandated that medical directors of vascular laboratories be held legally liable for ensuring that venous scans are ordered for appropriate indications, otherwise they might be regarded as inappropriate scans and Medicare can refuse to reimburse for the unnecessary studies.[21] In this study, about 10% of patients who underwent VDS did so for surveillance. Those patients had asymptomatic legs but had VTE risk factors such as recent surgery, active cancer, previous DVT, known hypercoagulable state, or bed rest for >3days. Therefore, it is important to document indications for VDS to improve the appropriate use of VDS with the benefit of being adequately reimbursed.[16,22]

Diagnostic Procedures of PE

A spiral CT scan is currently the test of choice in the diagnosis of PE, replacing V/Q scanning,[9,23,24] which is consistent with current practice at this institution. In this study, a majority of emergency room patients who presented with pleuritic chest pain or shortness of breath and underwent a spiral CT scan had normal examinations, similar to the majority of outpatients that were found to have normal or very low clinical probability of PE by V/Q scanning. To reduce such normal studies in outpatients who are unlikely to have VTE, all outpatients including patients from emergency room settings should be evaluated using a combination of the clinical probability assessment and D-dimer tests prior to further objective imaging tests.[12]

The use of complete VDS, bilaterally from proximal to distal lower extremity, prior to lung imaging testing in patients with suspected PE is recommended to be cost-effective.[25,26] However, in this study, some VDS were performed in patients without leg symptoms who had already had a normal CT or V/Q scan. In addition, 57 patients who underwent VDS to look for a source of symptomatic PE had normal VDS, yet they did not have further lung imaging tests, which is now recommended.[26,27]

Inappropriate Use of VTE Diagnostic Testing

Integrated approaches to the diagnosis of VTE have been recommended.[9,11,19,28-30] Patients with a low clinical probability

and a normal D-dimer could safely rule out PE without further imaging tests (such as VDS, CT scan, or V/Q scan).[9] Those integrated strategies would be safer, more convenient, and cost-effective in the care of patients suspected of VTE.[9] However, in this study, diagnostic tests deemed to be unnecessary or inappropriate were documented. Four examples of inappropriate use can be described: (1) symptomatic PE patients who were first diagnosed by CT or V/Q scan, still underwent a VDS to look for the source of the PE. If a DVT is diagnosed by VDS or a PE is diagnosed by lung scanning, anticoagulation therapy should be initiated and further investigation to exclude PE may not be necessary[30]; (2) 9 patients at high risk for PE had incomplete CT scans, yet no further tests were performed to rule out PE or DVT; (3) D-dimer tests were underused as a screening test in low-risk outpatients prior to ordering more expensive diagnostic imaging studies; objective imaging tests were directly performed in low-risk patients who were less likely to have VTE, which is not considered cost-effective[26]; and (4) 5 pregnant patients had CT scans for suspected PE as the initial diagnostic test instead of being screened with VDS or V/Q scanning. For special cases, such as pregnant women or patients with allergies to contrast dye, the investigators of the Prospective Investigation of Pulmonary Embolism Diagnosis II[24] study recommended that a CT scan be preceded by a combination of clinical assessment and D-dimer first, followed by VDS and or pulmonary scintigraphy before resorting to a CT scan. There was no institutional or department-specific standard approach to VTE diagnosis used in this institution.

This study has limitations due to the study design, a descriptive study at a single institution, which provides the lowest methodological quality (descriptive reports-observational study).[31] However, this study was conducted to provide baseline data on the current practice in the diagnosis of VTE prior to the implementation of evidenced-based diagnostic algorithms for DVT and PE.

In summary, this study evaluating the current practice in the diagnosis of VTE identified inappropriate use of imaging tests and underuse of D-dimer measurement and clinical probability assessment as a screening test prior to imaging tests. The parent intervention study (VTE Safety Toolkit) that includes the implementation of DVT/PE diagnostic algorithms will improve VTE diagnostic testing. Dissemination of the intervention has begun and continued within the academic medical center and diffusion of the intervention to other health care institutions have taken via the AHRQ.

Acknowledgment

We would like to acknowledge R. Eugene Zierler, MD, for the review of this manuscript.

Declaration of Conflicting Interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

This project was supported by grant number 1 U18 HS015898 from the Agency for Healthcare Research and Quality Partnerships in Patient Safety (Principal Investigator: Brenda K. Zierler, PhD).

References

1. Srivastava SD, Eagleton MJ, Greenfield LJ. Diagnosis of pulmonary embolism with various imaging modalities. *Semin Vasc Surg*. 2004;17(2):173-180.
2. Sandler DA, Martin JF. Autopsy proven pulmonary embolism in hospital patients: are we detecting enough deep vein thrombosis? *J R Soc Med*. 1989;82(4):203-205.
3. Lindblad B, Eriksson A, Bergqvist D. Autopsy-verified pulmonary embolism in a surgical department: analysis of the period from 1951 to 1988. *Br J Surg*. 1991;78(7):849-852.
4. Stein PD, Henry JW. Prevalence of acute pulmonary embolism among patients in a general hospital and at autopsy. *Chest*. 1995;108(4):978-981.
5. Stein PD, Henry JW, Relyea B. Untreated patients with pulmonary embolism. Outcome, clinical, and laboratory assessment. *Chest*. 1995;107(4):931-935.
6. Dalen JE. Pulmonary embolism: what have we learned since Virchow? Natural history, pathophysiology, and diagnosis. *Chest*. 2002;122(4):1440-1456.
7. Iles S. Clot burden and comorbidity in natural history of untreated pulmonary thromboembolism: autopsy data in the trial by Barritt and Jordan. *Chest*. 2003;124(3):1178; author reply-9.
8. Anaya DA, Nathens AB. Thrombosis and coagulation: deep vein thrombosis and pulmonary embolism prophylaxis. *Surg Clin North Am*. 2005;85(6):1163-1177, ix-x.
9. Wells PS. Integrated strategies for the diagnosis of venous thromboembolism. *J Thromb Haemost*. 2007;5(suppl 1):41-50.
10. Ghanima W, Almaas V, Aballi S, et al. Management of suspected pulmonary embolism (PE) by D-dimer and multi-slice computed tomography in outpatients: an outcome study. *J Thromb Haemost*. 2005;3(9):1926-1932.
11. Parent F, Maitre S, Meyer G, et al. Diagnostic value of D-dimer in patients with suspected pulmonary embolism: results from a multicentre outcome study. *Thromb Res*. 2007; 120(2):195-200.
12. Perrier A, Roy PM, Aujesky D, et al. Diagnosing pulmonary embolism in outpatients with clinical assessment, D-dimer measurement, venous ultrasound, and helical computed tomography: a multicenter management study. *Am J Med*. 2004;116(5): 291-299.
13. van Belle A, Buller HR, Huisman MV, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. *JAMA*. 2006;295(2):172-179.
14. Quiroz R, Schoepf UJ. CT pulmonary angiography for acute pulmonary embolism: cost-effectiveness analysis and review of the literature. *Semin Roentgenol*. 2005;40(1):20-24.
15. Schutgens RE, Haas FJ, Gerritsen WB, van der Horst F, Nieuwenhuis HK, Biesma DH. The usefulness of five D-dimer

assays in the exclusion of deep venous thrombosis. *J Thromb Haemost*. 2003;1(5):976-981.
16. Zierler BK. Screening for acute DVT: optimal utilization of the vascular diagnostic laboratory. *Semin Vasc Surg*. 2001;14(3):206-214.
17. Engelhardt W, Palareti G, Legnani C, Gringel E. Comparative evaluation of D-dimer assays for exclusion of deep venous thrombosis in symptomatic outpatients. *Thromb Res*. 2003;112(1-2):25-32.
18. Michiels JJ, Gadisseur A, van der Planken M, et al. Screening for deep vein thrombosis and pulmonary embolism in outpatients with suspected DVT or PE by the sequential use of clinical score: a sensitive quantitative D-dimer test and noninvasive diagnostic tools. *Semin Vasc Med*. 2005;5(4):351-364.
19. Michiels JJ, Gadisseur A, Van Der Planken M, et al. A critical appraisal of non-invasive diagnosis and exclusion of deep vein thrombosis and pulmonary embolism in outpatients with suspected deep vein thrombosis or pulmonary embolism: how many tests do we need? *Int Angiol*. 2005;24(1):27-39.
20. Michiels JJ, Gadisseur A, van der Planken M, et al. Different accuracies of rapid enzyme-linked immunosorbent, turbidimetric, and agglutination D-dimer assays for thrombosis exclusion: impact on diagnostic work-ups of outpatients with suspected deep vein thrombosis and pulmonary embolism. *Semin Thromb Hemost*. 2006;32(7):678-693.
21. Fowl RJ, Strothman GB, Blebea J, Rosenthal GJ, Kempczinski RF. Inappropriate use of venous duplex scans: an analysis of indications and results. *J Vasc Surg*. 1996;23(5): 881-885; discussion 5-6.
22. Zierler BK, Meissner MH, Cain K, Strandness DE Jr. A survey of physicians' knowledge and management of venous thromboembolism. *Vasc Endovascular Surg*. 2002;36(5):367-375.
23. Ghaye B, Dondelinger RF. When to perform CTA in patients suspected of PE? *Eur Radiol*. 2008;18(3):500-509.
24. Stein PD, Woodard PK, Weg JG, et al. Diagnostic pathways in acute pulmonary embolism: recommendations of the PIOPED II investigators. *Am J Med*. 2006;119(12):1048-1055.
25. Elias A, Molinier L, Bauvin E, Elias M, Duru G, Colin C. Integrating complete lower limb venous ultrasound into diagnostic strategies for pulmonary embolism: a cost-effectiveness analysis. *Thromb Haemost*. 2004;91(1):205-207.
26. 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(9):1869-1877.
27. Perrier A, Nendaz MR, Sarasin FP, Howarth N, Bounameaux H. Cost-effectiveness analysis of diagnostic strategies for suspected pulmonary embolism including helical computed tomography. *Am J Respir Crit Care Med*. 2003; 167(1):39-44.
28. Arnason T, Wells PS, Forster AJ. Appropriateness of diagnostic strategies for evaluating suspected venous thromboembolism. *Thromb Haemost*. 2007;97(2):195-201.
29. Stein PD, Hull RD, Patel KC, et al. D-dimer for the exclusion of acute venous thrombosis and pulmonary embolism: a systematic review. *Ann Intern Med*. 2004;140(8):589-602.
30. Zierler BK. Ultrasonography and diagnosis of venous thromboembolism. *Circulation*. 2004;109(12 suppl 1):I9-I14.
31. Guyatt G, Gutterman D, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an American College of Chest Physicians Task Force. *Chest*. 2006;129(1):174-181.