Cost-Effectiveness of Venous Thromboembolism Prophylaxis With a New Mobile Device After Total Hip Arthroplasty

Cost-effectiveness Writing Committee*

Abstract: Recent comparison (SAFE study) of a mobile, synchronized compression device and low-molecular-weight heparin for prophylaxis of venous thromboembolism showed similar efficacy but significant differences in major bleeding. A model was constructed to evaluate any difference in cost-effectiveness between the 2 therapies incorporating rates and probabilities of major bleeding from the SAFE study with published costs for treating those adverse events. Evaluation of the cost-effectiveness of each therapy was performed and applied to hypothetical patient populations representative of annual health system volume. The model showed a cost-effectiveness advantage of the compression device resulting in a savings of more than $3.69 million in a 10 000-patient cohort. The result was primarily driven by a decrease in the amount of major bleeding, which requires significant health care resources to treat. **Keywords:** thrombosis, thromboprophylaxis, venous thromboembolism, pulmonary embolism, arthroplasty, cost-effectiveness, mobile synchronized compression.

The Deficit Reduction Act of 2005 required the Centers for Medicare and Medicaid Services (CMS) to identify conditions that (*a*) are high cost or high volume or both, (b) result in the assignment of a case to a diagnosis-related group (DRG) that has a higher payment when present as a secondary diagnosis, and (c) could reasonably have been prevented through the application of evidence-based guidelines. On July 31, 2008, CMS identified deep venous thrombosis (DVT)/pulmonary embolism (PE) as one of those conditions, which resulted in payment implications from CMS since October 1, 2008. National quality guidelines for hospitals such as the Joint Commission and the Surgical Care Improvement Project also recognize readmission for venous thromboembolism (VTE) as a hospital-acquired condition resulting in a negative impact on a hospital's quality ratings, which results in loss of reimbursement from third-party payers [1,2].

Patients who have undergone major orthopedic surgery such as total hip arthroplasty (THA) are at an increased risk for VTE that includes the formation of DVT and/or PE. Venous thromboembolism is classically associated with existence of 1 or more of the following inducible events: venous stasis, increased coagulability, or vessel wall trauma. Total hip arthroplasty causes patients to experience both vessel wall trauma in surgery and decreased venous flow velocity and pulsatility due to decreased mobility during the recovery/rehabilitation period. The most frequent reason patients are readmitted to the hospital after major orthopedic surgery of the lower extremity is VTE [3]. It has been established that detectable DVT may occur in up to 25% of patients during the first 6 weeks postdischarge from the hospital [4-6]. Venous thromboembolism can also lead to significant long-term morbidity including recurrent thrombosis, postthrombotic syndrome, and mortality in many cases of PE.

Guidelines from both the American College of Chest Physicians and the American Association of Orthopedic Surgeons recommend specific strategies to prevent VTE

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[7,8]. A variety of pharmacologic and mechanical treatment modalities are available to mitigate the risk of VTE. Chemoprophylaxis introduces additional risks such as bleeding, hematoma, rehospitalization, increased risk of surgical wound infection, and, rarely, heparin-induced thrombocytopenia (HIT). An effective, nonpharmacologic approach to VTE prophylaxis is, therefore, highly desirable. Mechanical compression devices are thought to prevent clot formation by increasing the lower limb venous blood flow velocity and pulsatility, causing the release of endothelial-derived relaxing factors [9] and urokinase [10-12]. Hospital-based compression devices, although commonly available, are associated with additional perceived disadvantages: interference with ambulation, difficulty of application, challenging for the elderly to use, and tend to be bulky and uncomfortable. Devices that deliver a higher peak venous velocity achieve it through rapid inflation of the compression sleeve by using an air compression chamber in the pump unit. The rapid inflation can create an uncomfortable impact sensation on the patient's leg, discouraging the use of the device [13,14]. An improved mechanical compression device that reduces patient discomfort yet maintains inpatient and, specifically, outpatient efficacy would have potential to provide optimal outcomes of decreased thrombosis and avoidance of bleeding.

Recently, the outcome of the mobile compression device (MCD) (Continuous Enhanced Circulation Therapy plus Synchronized Flow Technology [Medical Compression Systems, Or-Akiva, Israel]) compared with low-molecular-weight heparin (LMWH) (enoxaparin sodium [Lovenox; Sanofi-Aventis, Bridgewater, NJ]) for VTE prophylaxis in patients with THA (the SAFE study, NCT00358735) was reported [12].

The study randomized 410 patients who had a THA to receive prophylaxis with a MCD or LMWH for 10 days postoperatively. The compression device was initiated intraoperatively, and patients could also receive 81 mg of aspirin daily after surgery. The addition of 81 mg of aspirin daily had no impact on either efficacy or safety. The LMWH was started 12 to 24 hours postsurgery. All patients underwent bilateral lower-extremity duplex ultrasound to screen for DVT after 10 to 12 days, and any symptoms of PE were evaluated with spiral computed tomography lung scans. The study showed that MCD was not different from LMWH with regard to the occurrence of DVT (4.0% MCD vs 4.0% LMWH) and PE (1% MCD vs 1% LMWH); however, there was significantly less major bleeding in the compression-treated group (0% MCD vs 5.6% LMWH, $P = .0004$). Having shown that both prophylaxis treatments were comparably effective, the unanswered question is whether there is a difference in the cost-effectiveness between the 2 treatments. Therefore, a model was designed to investigate the cost-effectiveness of MCD compared with LMWH.

Materials and Methods

A model was designed based on the rates of VTE and bleeding from the SAFE study. The model included a decision tree analysis to measure the cost-effectiveness of MCD compared with LMWH (enoxaparin) in terms of cost per adverse event and the results applied to hypothetical 1000- and 10 000-patient cohorts. This cost-effectiveness analysis is adapted from a similar model previously described by McGarry et al [15].

To conduct the analysis, a software package designed for health outcomes research (TreeAge Pro Healthcare; TreeAge Software, Inc, Williamstown, Massachusetts) was used to compute the terminal branches of the decision tree values and create the cost analysis. The decision analysis allows the disaggregation of the possible events according to probability of influence on the final outcome, which is the total cost of care resulting from the method of VTE prophylaxis chosen. The mean expected value of each possible chain of events is calculated incorporating the probability of uncertain results (eg, DVT and bleeding) and identifies the course of action that will minimize costs. The decision tree was populated with adverse event probabilities from the SAFE study (major bleeding, minor bleeding, DVT, PE) and treatment costs from published literature and is depicted in Figure. The model estimation involved assigning probability estimates to each of the model's chance nodes and cost estimates to each pathway. Probabilities and data sources are summarized in Tables 1 and 2.

The model's cost parameters included (1) study medications and ancillary resources, (2) laboratory procedures, (3) hospital inpatient days, (4) physician inpatient visits, and (5) physician office/outpatient visits. The cost estimates and their respective formulas can be found in Table 3; available online at www.arthroplastyjournal.org. Drug costs were estimated by using the average wholesale prices published in the *Red Book* [16]. Cost estimates associated with the supplies used to administer drugs were obtained from published data (see Table 3; available online at www.arthroplastyjournal.org). The costs of laboratory procedures for monitoring anticoagulation therapy were estimated using data from the CMS. Costs for physician visits (inpatient or outpatient) were estimated using the Medicare Resource-Based Relative Value Scale Payment rates [17]. Cost of compression therapy was calculated from the manufacturer for the compression device based on the average lease price given to health systems. The average daily inpatient cost due to adverse drug reactions and VTE was estimated by dividing the unadjusted payment by the average length of stay for the diagnosis (DRG) [18]. The cost of treating major bleeding was calculated based on reimbursement rates for extended hospital stay and cost of transfusion reported by Shander et al [19]. The primary focus was based on costs incurred within 30 days of hospital

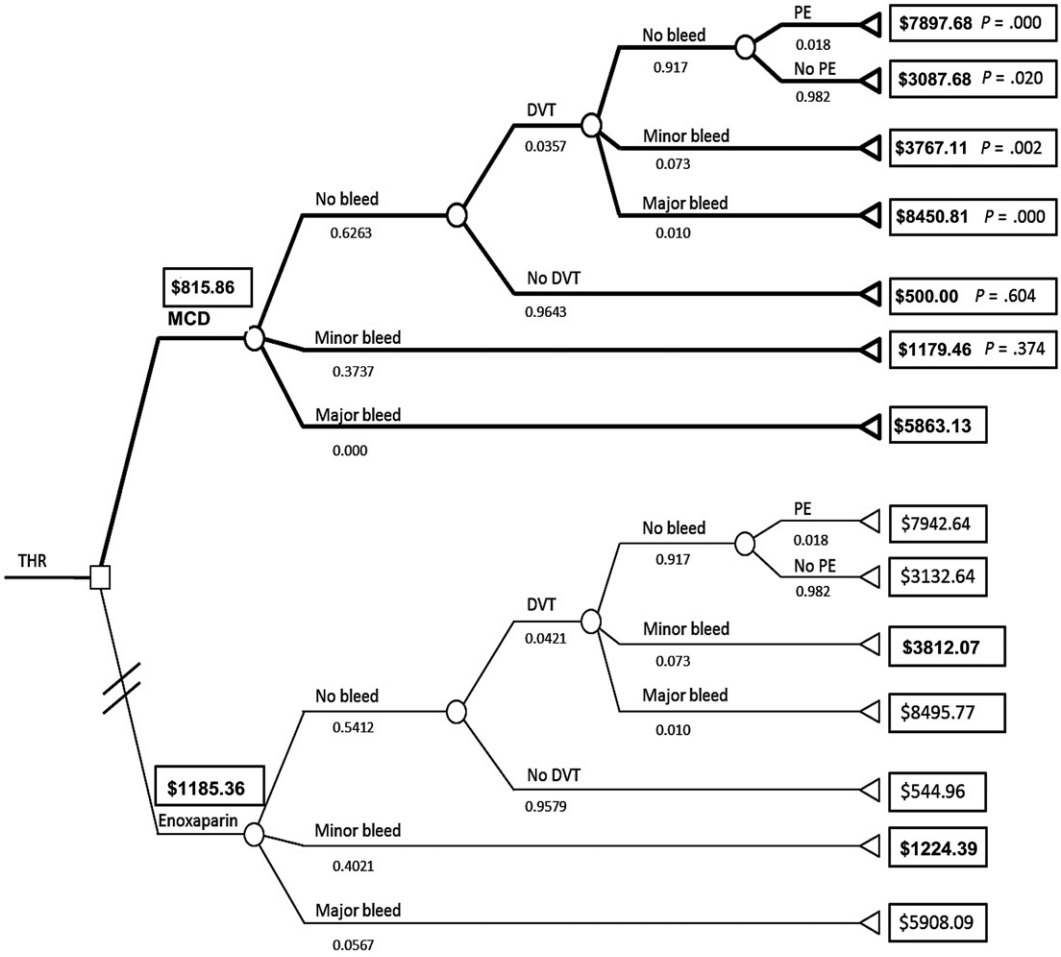

Fig. Decision tree model probabilities and results.

admission. All costs were measured in 2010 US dollars; where necessary, costs were updated to 2010 using the Consumer Price Index. Because of the brief time horizon of the model, discounting was not required.

Results

The model assumptions included (1) that the rate of compliance was equivalent for both treatments and the patient outcomes in the SAFE study and other published references would be reproducible in clinical practice; (2) the length of therapy would be the same as described by Colwell et al [12] in the SAFE study for each therapy (10 days for compression and 10 days for LMWH); and (3) the dose of enoxaparin was the same as that used in the SAFE study and commonly used in the United States, specifically, 30 mg every 12 hours starting 12 to 24 hours postsurgery until discharge, then 40 mg once daily, for a total of 10 days.

The cost total in the model included the probability and cost of the individual uncertain events of DVT, PE, and minor and major bleeding. The model showed that VTE prophylaxis with MCD would have an average cost

Table 1. SAFE Trial: Safety and Efficacy Results

	MCD (n = 198), n (%)	Enoxaparin (n = 194), n (%)	*P*
Safety Results			
Minor bleeding	74 (0.3737)	78 (0.4021)	.319
Major bleeding	0	11 (0.0567)	.0004
	MCD (n = 196)	Enoxaparin (n = 190)	*P**
Efficacy Results			
DVT	8 (0.0408)	8 (0.0421)	*
PE	2 (0.0102)	2 (0.0105)	*

* *P* value for VTE = .953.

Table 2. Decision Tree Base-Case Probabilities for the MCD and Enoxaparin

Model Parameter	MCD	Enoxaparin	Source
Efficacy and safety of prophylaxis			
P{DVT}	.036	.042	Colwell et al [12]
P{bleed}	.374	.459	Colwell et al [12]
Consequences of adverse events			
P{major bleed|bleed}	.000	.124	Colwell et al [12]
Efficacy and safety of DVT treatment			
P{bleed|DVT tx}	.083	.083	Dolovich et al [23], Merli [1]
P{PE|DVT tx, DVT}	.018	.018	Dolovich et al [23], Merli [1]

Abbreviation: P, probability.

advantage of $369.50 per patient (Figure). The cost differential in a hypothetical 1000-patient cohort would be $369 502, and in a 10 000-patient cohort, it would be $3 695 027.

The difference in cost of therapy was primarily driven by the cost of major bleeding, which has a significantly greater probability when chemoprophylaxis was used. In the SAFE study, there were 11 of 194 cases of major bleeding in the enoxaparin group compared with 0 of 198 in the compression group ($P = .0004$). Major bleeding leads to extended hospital stays; increased physician, nursing, and pharmacy care; additional laboratory costs; and blood transfusions. In our analysis, the incremental cost to treat a major bleeding event was calculated to be $5363.13. Similarly, minor bleeding was slightly more prevalent in the chemoprophylaxis arm of the decision tree.

Discussion

Our analysis shows that mobile, synchronized mechanical compression after major orthopedic surgery of the lower extremity is associated with significant cost savings of $369.50 per patient. It is estimated that there are more than 234 000 THAs each year in the United States [20], which would result in per-annum savings of more than 86 million dollars. In addition, there are approximately 500 000 THAs that may also benefit from VTE prophylaxis with compression [20].

A large amount of data exist regarding the increased risk of VTE after major orthopedic surgery of the lower extremity. Improvements in chemoprophylactic therapy over the past 20 years have diminished the risk of bleeding, although any anticoagulant use introduces some risk of bleeding. Efforts to improve patient outcomes and, more recently, avoidance of reimbursement penalties have led to a larger percentage of patients receiving prophylaxis for VTE in the hospital. Routine use of anticoagulants for VTE prophylaxis after major orthopedic surgery of the lower extremity, though, is not widely endorsed by many orthopedic surgeons as demonstrated in the recent American Association of Orthopedic Surgeons guidelines for prophylaxis against symptomatic PE after THA [8]. Major bleeding is detrimental for patient recovery because it significantly increases the amount of time for recovery and healing and puts patients at risk for additional surgery, hematoma, infection, and death.

The use of compression also prevents exposure to heparin and the possibility of HIT. Published reports of the incidence and costs to treat the incremental cost of asymptomatic HIT are $733.75, and for symptomatic HIT, it was $14 058.01 [15-18,21-24]. Heparin-induced thrombocytopenia is a rare but costly adverse effect of heparin-based VTE prophylaxis after major orthopedic surgery, and those incremental costs could be avoided with the appropriate use of mechanical compression. Because HIT is extremely uncommon with the short-term use of LMWH, the additional cost of HIT was not used in the model.

The significant cost savings potential observed in our model by using mobile compression would have an impact on both patient and societal costs of major orthopedic surgery of the lower extremity. Our study cannot directly compare the use of warfarin against the MCD because we did not use warfarin in the SAFE study. Aspirin was used as an adjunct to the MCD in approximately 50% of the patients. Recent cost-effectiveness of VTE, as reported by Kapoor et al [25] in a review article, indicated that an incremental cost-effectiveness ratio would be $1700 per VTE avoided for 4-week warfarin compared with aspirin and $1300 for 4 weeks of LMWH compared with aspirin. Kapoor et al found that the incremental cost-effectiveness ratio for LMWH was $2000 per VTE avoided compared with warfarin. To make LMWH cost competitive with the MCD, the overall initial cost would have to be decreased by approximately $400 per patient. This still does not take into account the cost of the bleeding that occurs after pharmacologic prophylaxis. We recognize that the true costs of VTE and bleeding events after major orthopedic surgery may not be fully appreciated. At the same time, we are comfortable that our results do not overstate the cost savings of using the MCD because similar analyses of other prophylaxis regimens have produced higher costs of a VTE or major bleeding event [26].

Recent policy changes in the US health care system are likely to reinforce the US government as the major buyer for health care services, which will have greater exposure to the costs of more than 734 000 hip and knee surgical procedures each year. The cost of the MCD used in the hospital is considered part of the hospital cost and paid for by insurance or Medicare Part A; outpatient cost is presently paid for by the patient or the insurance company. Outpatient use of the MCD is currently under review for Medicare Part B coverage. A worst-case scenario is that the outpatient charge would be the responsibility of the patient. Decreased health care resource use in treating major bleeding and the rare complication of HIT would also contribute to efficiency gains and cost savings that were not captured by the model.

In conclusion, consideration and modeling of the costs associated with VTE prophylaxis in the SAFE study show a significant cost advantage for the use of the MCD compared with LMWH in major orthopedic surgery of the lower extremity. Before wide acceptance by the orthopedic community, an efficacy study conducted at 10 medical centers show the rate of VTE with numbers adequate to establish noninferiority or superiority for the MCD.

Appendix

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References

1. Merli G. Improving venous thromboembolism performance: a comprehensive guide for physicians and hospitalists. Hosp Pract (Minneap) 2010;38:7.
2. Hospital-Acquired Conditions (HAC) in Acute Inpatient Prospective Payment System (IPPS) Hospitals Department of Health and Human Services. 2010 http://www.cms.gov/HospitalAcqCond/downloads/HACFactsheet.pdf. Accessed on 10/17/2011.
3. Pellegrini Jr VD, Sharrock NE, Paiement GD, et al. Venous thromboembolic disease after total hip and knee arthroplasty: current perspectives in a regulated environment. Instr Course Lect 2008;57:637.
4. Scurr JH, Coleridge-Smith PD, Hasty JH. Deep venous thrombosis: a continuing problem. BMJ 1988;297:28.
5. Trowbridge A, Boese CK, Woodruff B, et al. Incidence of posthospitalization proximal deep venous thrombosis after total hip arthroplasty. A pilot study. Clin Orthop Relat Res 1994;203.
6. Tremaine MD, Choroszy CJ, Gordon GH, et al. Diagnosis of deep venous thrombosis by compression ultrasound in knee arthroplasty patients. J Arthroplasty 1992;7:187.
7. Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008;133(6 Suppl):381S.
8. Johanson NA, Lachiewicz PF, Lieberman JR, et al. Prevention of symptomatic pulmonary embolism in patients undergoing total hip or knee arthroplasty. J Am Acad Orthop Surg 2009;17:183.
9. Vanhoutte PM, Boulanger CM, Mombouli JV. Endothelium-derived relaxing factors and converting enzyme inhibition. Am J Cardiol 1995;76:3E.
10. Allenby F, Boardman L, Pflug JJ, et al. Effects of external pneumatic intermittent compression on fibrinolysis in man. Lancet 1973;2:1412.
11. DiGiovanni CW, Restrepo A, Gonzalez Della Valle AG, et al. The safety and efficacy of intraoperative heparin in total hip arthroplasty. Clin Orthop Relat Res 2000;178.
12. Colwell Jr CW, Froimson MI, Mont MA, et al. Thrombosis prevention after total hip arthroplasty: a prospective, randomized trial comparing a mobile compression device with low-molecular-weight heparin. J Bone Joint Surg Am 2010;92:527.
13. Westrich GH, Jhon PH, Sanchez PM. Compliance in using a pneumatic compression device after total knee arthroplasty. Am J Orthop (Belle Mead NJ) 2003;32:135.
14. Lachiewicz PF, Kelley SS, Haden LR. Two mechanical devices for prophylaxis of thromboembolism after total knee arthroplasty. A prospective, randomised study. J Bone Joint Surg Br 2004;86:1137.
15. McGarry LJ, Thompson D, Weinstein MC, et al. Cost effectiveness of thromboprophylaxis with a low-molecular-weight heparin versus unfractionated heparin in acutely ill medical inpatients. Am J Manag Care 2004;10:632.
16. PDR Network L. Red Book—pharmacy's fundamental reference. Montvale, NJ: Thomson Reuters (Healthcare) Inc; 2010.
17. Medicare RBRVS – The physician's guide: American Medical Association, 2010.
18. Ingenix. DRG expert—a comprehensive guidebook to the DRG classification system. In: Ingenix, ed.: Ingenix. 2010.
19. Shander A, Hofmann A, Ozawa S, et al. Activity-based costs of blood transfusions in surgical patients at four hospitals. Transfusion 2009;50:753.
20. The burden of musculoskeletal disease in the United States. In: The burden of musculoskeletal disease in the United States. American Academy of Orthopaedic Surgeons. 2008.
21. Warkentin TE, Greinacher A, Koster A, et al. Treatment and prevention of heparin-induced thrombocytopenia: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008;133(6 Suppl):340S.
22. Greinacher A. Heparin-induced thrombocytopenia–pathogenesis and treatment. Thromb Haemost 1999;82(Suppl 1):148.
23. Dolovich LR, Ginsberg JS, Douketis JD, et al. A meta-analysis comparing low-molecular-weight heparins with unfractionated heparin in the treatment of venous thromboembolism: examining some unanswered questions regarding location of treatment, product type, and dosing frequency. Arch Intern Med 2000;160:181.
24. Gould MK, Dembitzer AD, Sanders GD, et al. Low-molecular-weight heparins compared with unfractionated heparin for treatment of acute deep venous thrombosis. A cost-effectiveness analysis. Ann Intern Med 1999;130:789.
25. Kapoor A, Chuang W, Radhakrishnan N, et al. Cost effectiveness of venous thromboembolism pharmacological prophylaxis in total hip and knee replacement: a systematic review. Pharmacoeconomics 2010;28.
26. Shorr AF, Sarnes MW, Peeples PJ, et al. Comparison of cost, effectiveness, and safety of injectable anticoagulants used for thromboprophylaxis after orthopedic surgery. Am J Health Syst Pharm 2007;64:2349.

Appendix

Table 3. Base-Case Cost Estimates

Cost Item	Estimate (US$)	Notes
10 d of prophylaxis		
MCD	500.00	Lease: $50/d for a mean of 10 d per the study
Enoxaparin	544.96	Average wholesale price of $36.09 for 40-mg prefilled syringe* times 8 doses plus average wholesale price of $27.07 for 30-mg prefilled syringe* times 4 doses, plus $12.33 in pharmacy and nursing costs assumed per administration for a mean of 10 d per the study
Adverse events		
Minor bleed	679.43	Assume 1 additional hospital day ($679.43) based on average reimbursement per day for deep vein thrombophlebitis (DRG 295) †
Major bleed	5363.13	Assume 5 additional hospital days ($3397.15), 5 additional physician inpatient visits ($271.10), total cost of 2 units of blood transfusion ($1521.64), § CBC ($55.70) (CPT 85025), ‖ and 2 additional outpatient visits ($117.54): established patient, moderate complexity (CPT 99214) ‡
Cost of diagnosis and treatment		
DVT	2587.68	Diagnosis: assume 1 additional physician inpatient visit ($54.22) plus ultrasound ($189.36) (CPT 93970) ‡ Treatment: assume 2/3 of patients treated inpatient [including 5 d of therapy with 1 mg/kg enoxaparin twice a day for patient weighing 75 kg ($722.52), 2 additional hospital days ($1358.86), 5 additional physician inpatient visits ($271.11), 5 physician office/outpatient visits ($293.85), 6 mo of warfarin therapy including daily 5-mg warfarin ($0.59)* and weekly prothrombin time tests ($5.62) (CPT 85610) ‖] and 1/3 treated outpatient (including 5 d of enoxaparin therapy [$722.52], 5 additional physician office/outpatient visits ($293.85), and 6 mo of warfarin therapy including daily 5-mg warfarin ($0.59)* and weekly prothrombin time tests ($5.62) (CPT 85610) ‖
PE	4810.00	Diagnosis: assume 1 additional physician inpatient visit ($54.22) plus CT scan ($238.47) (CPT 71260) ‡ or V/Q scan ($116.11) (CPT 78584)‡ Treatment: assume 5 additional days in the hospital ($3397.15), 5 physician inpatient visits ($271.11), 5 d of UFH therapy (including 30 000 U/d UFH [$21.00], a dextrose 5% 500 mL [$14.88], IV catheter [$4.88], ¶ tubing [$1.60], ¶ pump [$5.21], ¶ phlebotomy [$3.00], partial thromboplastin time monitoring [$8.60]), 5 additional office/outpatient visits ($373.30), and 6 mo of warfarin therapy including daily 5-mg warfarin ($0.59)* and weekly prothrombin time tests ($5.62) (CPT 85610) ‖

Abbreviations: CBC, complete blood count; IV, intravenous; V/Q, ventilation and perfusion scan; UFH, unfractionated heparin.

* Red Book 2010.

† DRG Guidebook 2010.

‡ RBRVS 2010.

§ Shander et al [19].

‖ Clinical Diagnostic Laboratory Fee Schedule 2010.

¶ Costs provided by Gould et al [24] were converted to fiscal year 2010 dollar using medical care component of the Consumer Price Index from the Bureau of Labor Statistics.