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Routine Use of Low Molecular Weight Heparin DVT Prophylaxis Following Certain Foot and Ankle Surgeries: A Cost Effectiveness Analysis

Richmond Robinson, DPM, AACFAS^a, Craig Wirt, PhD^b, Carolina Barbosa, PharmD, PhD^c, Arezou Amidi, DPM^d, Shirley Chen, BS^e, Robert Joseph, DPM, PhD, FACFAS^f, and Adam Fleischer, DPM, MPH, FACFAS^g

^aAssistant Professor, Department of Medicine and Radiology, Scholl College of Podiatric Medicine at Rosalind Franklin University of Medicine and Science. 3333 Green Bay Road, North Chicago, IL 60064. United States. richmond.robinson@rosalindfranklin.edu.

^bPodiatry Student, Scholl College of Podiatric Medicine at Rosalind Franklin University of Medicine and Science. 3333 Green Bay Road, North Chicago, IL 60064. United States. timothy.wirt@my.rfums.org

^cHealth Economist, RTI International. 230 West Monroe St. #2100. Chicago, IL 60606. United States. cbarbosa@rti.org

^dPGY3, Advocate Illinois Masonic Medical Center Podiatric Residency Program. 836 W Wellington Ave, Chicago, IL 60657. United States. arezou.amidi@gmail.com

^ePodiatry Student, Scholl College of Podiatric Medicine at Rosalind Franklin University of Medicine and Science. 3333 Green Bay Road, North Chicago, IL 60064. United States. shirley.chen@my.rfums.org

^fChairman, Department of Medicine and Radiology, Scholl College of Podiatric Medicine at Rosalind Franklin University of Medicine and Science. 3333 Green Bay Road, North Chicago, IL 60064. United States. robert.joseph@rosalindfranklin.edu

^gAssociate Professor, Department of Medicine and Radiology, Scholl College of Podiatric Medicine at Rosalind Franklin University of Medicine and Science. 3333 Green Bay Road, North Chicago, IL 60064. United States. adam.fleischer@rosalindfranklin.edu

Abstract

The purpose of this study was to determine whether certain foot/ankle surgeries would benefit from routine use of low molecular weight heparin (LMWH) as postoperative DVT prophylaxis. We conducted a formal cost-effectiveness analysis using a decision analytic tree to explore the healthcare costs and health outcomes associated with a scenario of no prophylaxis and a scenario of routine LMWH prophylaxis for 4 weeks. The two scenarios were compared for five procedures:

Corresponding Author: Richmond Robinson, DPM, AACFAS, richmond.robinson@rosalindfranklin.edu.

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1) Achilles tendon repair (ATR), 2) total ankle arthroplasty (TAA), 3) hallux valgus surgery (HVS), 4) hindfoot arthrodesis (HA), and 5) ankle fracture surgery (AFS). Outcomes assessed included short and long-term costs, quality-adjusted life-years (QALYs), and incremental cost per QALY gained. Costs were evaluated from the healthcare system perspective and expressed in US dollars at a 2015 price base. In the short-term, routine prophylaxis was always associated with greater costs compared to no prophylaxis. For ATR, TAA, HA and AFS, prophylaxis was associated with slightly better health outcomes; however, the gain in QALYs was minimal compared to the cost of prophylaxis (ICER was well above \$50,000/QALY threshold). For HVS, prophylaxis was associated with both worse health outcomes and greater costs. In the long-term, routine prophylaxis was always associated with worse health outcomes and either cost more (HA, AFS, HVS) or saved very little (ATR, TAA). We conclude that policies encouraging routine use of LMWH following foot/ankle surgery are unlikely to be cost-effective. Decisions to perform prophylaxis should be made on a case-by-case basis and emphasize individual patient risk factors.

Level of Clinical Evidence: 2, Economic and Decision Analysis

Keywords

cost-effectiveness; QALY; cost; DVT; LMWH; prophylaxis; foot and ankle surgery

Introduction

Venous thromboembolic disease (VTED), which includes deep venous thrombosis (DVT), affects 300,000 to 600,000 people and is the proximate cause of more than 60,000 deaths each year in the United States (1). Surgery is a recognized risk factor for VTED (2–7); however, the incidence following foot and ankle surgery is considerably lower than what is reported in other areas of the body (8–12). Low molecular weight heparin (LMWH), for example, is routinely prescribed following hip and knee replacement surgery (13), yet its use varies widely among providers following foot and ankle surgery (14,15). Recommendations from several prominent foot and ankle societies have recently suggested that routine chemical prophylaxis is not warranted when caring for foot/ankle disorders that require immobilization. They instead recommend that patients be risk stratified by their provider and have a VTED prevention plan (which may or may not include use of LMWH) tailored to their individual risk level (13,16,17). Because it is well known that the rate of VTED varies greatly after foot/ankle surgery (e.g., the rate of distal, asymptomatic DVT varies anywhere from 2% with hallux valgus surgery (18) to much as 36% after Achilles tendon surgery (19)), we postulated that, like hip and knee replacement surgery, the decision to provide chemical prophylaxis, from a strictly cost-effectiveness perspective, may be entirely explained by the type of foot/ankle surgery being performed, regardless of patient-specific factors (e.g., medications, comorbidities, personal history, etc.). (Figure 1)

Cost-effectiveness analyses (CEAs) are useful tools for determining which, of two or more competing strategies, would be the best allocation of resources. In a CEA, health effects can be measured in natural units of outcome (e.g., number of deaths) or the value individuals place on their health (e.g., quality adjusted life years [QALYs]). QALYs estimate a patient's health related quality of life and their length of life in a less than perfect state of health. QALYs are useful for determining the cost-effectiveness of competing strategies as they act

as a common measure of health benefits, while accounting for such things as mortality and morbidity. Specifically, cost per QALY estimates allow a comparison between different health care interventions that compete for the same pool of resources (20,21). No study has focused on the costs and health effects of VTED prophylaxis with LMWH after foot and ankle surgery. In this study, we conducted a CEA to assess whether routine prophylaxis with LMWH after certain types of foot and ankle surgery was a good use of resources, irrespective of patient factors.

Methods

Overview

A decision tree model following a cohort approach was built in TreeAge Pro Healthcare 2014 (TreeAge Software, Inc, Williamstown, MA). The model was used to conduct a CEA that compared the costs and outcomes of implementing LMWH as a form of chemical DVT prophylaxis versus the strategy of implementing no prophylaxis following foot and ankle surgery. The two strategies, prophylaxis with LMWH vs. no prophylaxis, were compared in five different surgical scenarios: Achilles tendon repair (ATR), total ankle arthroplasty (TAA), hallux valgus surgery (HVS), hindfoot arthrodesis (HA), and ankle fracture surgery (AFS).

For each surgical scenario, the two strategies were compared in terms of two outcomes: incremental health care costs and incremental quality-adjusted life years (QALYs). The two outcomes were combined in the form of incremental cost-effectiveness ratios (ICERs). We calculated short- and long-term results, where short-term results considered 1-year outcomes and long-term results considered lifetime outcomes. Costs were evaluated from the healthcare system perspective and expressed in 2015 US dollars. For the long-term analysis, future costs and QALYs were discounted at a 3% annual rate in accordance with recommendations provided by the U.S. Public Health Service and consistent with other CEAs.

Decision tree model

Structure—The decision tree model is presented in Figure 2. Patients receiving no prophylaxis had several health effects including: no event, asymptomatic DVT, symptomatic DVT, or PE. In the case of an asymptomatic DVT our model allowed for two likely outcomes: resolution or mild post thrombotic syndrome (PTS). In the case of symptomatic DVT, there were five potential outcomes: resolution, PTS, major hemorrhage, recurrent DVT, or subsequent PE. A patient with PTS may have developed either the mild or severe form of PTS after symptomatic DVT. A patient with major hemorrhage either died or their condition resolved. Following a recurrent DVT, patients either resolved their condition or experienced a major hemorrhage due to treatment. Following a subsequent PE, patients died, developed chronic pulmonary hypertension, had a major hemorrhage due to treatment, or resolved with treatment. In the prophylactic strategy, in addition to the conditions following no prophylaxis, patients were also at risk of major hemorrhage and symptomatic heparin-induced thrombocytopenia (HIT) due to prophylaxis with LMWH. Patients undergoing any of those two conditions either resolved due to treatment or died.

Surgical scenarios and events—We selected several surgeries that are known to be associated with increased VTED risk (i.e., ATS, AFS, HA, TAA) (16,17,22) and also a common foot surgery (HVS) to model. We considered only outcomes/events that received frequent enough attention in the literature to be able to calculate summary probabilities. Although less commonly reported, we also considered the costs and health effects associated with PTS. PTS may develop following DVT and those affected may present for treatment of leg pain and swelling (23). PTS may affect 20% to 50% of patients diagnosed with a DVT and the clinical manifestations can occur within 2 years of the inciting event (24). For those living with PTS, especially the severe form of disease, it can lead to a diminished quality of life (25). The severe form of PTS typically includes venous leg ulcers which substantially increase treatment costs and may affect 5% to 10% of patients with PTS (23,24). In this analysis we chose to consider both mild and severe forms of PTS.

Data inputs and assumptions

The decision tree model base case parameters and sources are summarized in Tables 1 and 2. The rates and probability of each health effect (tree node) were derived from the available literature. Summary estimates were used when more than one source was available. Direct costs were derived from the published literature, drug manuals, and the Centers for Medicare and Medicaid. All costs were adjusted to reflect US dollar 2015 rates. Costs associated with each health effect included both diagnostic costs and treatment costs (e.g., outpatient and inpatient costs, pharmacological treatment, and disease management).

In this analysis we assumed maximal benefit and least harm with LMWH use. As such we assumed that both the asymptomatic and symptomatic DVT rate would be reduced by 0.51 with LMWH use, and the PE rate would be reduced to 0 (26). Similarly, we assumed the fewest possible side effects resulting from LMWH use, using the lowest reported rates of HIT and major hemorrhage from the literature, and we did not consider the negative health effects and costs associated with minor hemorrhage (i.e., minor hemorrhage rate = 0).

For the long-term analysis, our base case assumption for ATR, AFS, and HVS was a 45 year old female. This was based on the approximate age and gender of patients typically undergoing these surgeries (8,11,27,28). Similarly the base case assumption we used for TAA and HA was a 60 year old female (8,29). Although some procedures (e.g., ATR, TAA) did not demonstrate a clear gender predilection, we chose a female patient for each scenario as women have longer lives than men. We rationalized that if providing prophylaxis is not cost-effective in preventing the long-term complications of VTED over the lifetime of a female patient, it would not be cost-effective for a male patient with a shorter life either. Other than age and gender (which was required for long-term cost estimates and utilities), no other patient factors (e.g., personal history of VTED, oral contraceptive use, etc.) were considered in the analysis. This was done to ensure that we answer our primary question of whether surgery alone can drive the decision to use LMWH or not. Duration of prophylaxis with LMWH varied in the literature with few clear guidelines. Prophylaxis in this analysis consisted of enoxaparin 40 mg once daily for 4 weeks postoperatively to allow for a period of immobilization. For resolution of first symptomatic DVT, we assumed treatment with enoxaparin x 7 days at 80 mg twice daily followed by subsequent use of Coumadin for 3

months (30). For a second symptomatic DVT we assumed treatment with enoxaparin 80 mg twice daily followed by Coumadin for 6 months, although there is less clarity for the approach to treatment of recurrent VTED and indefinite anticoagulation may be performed (31).

Utilities for health events were used to calculate QALYs. Utilities are weights representing quality of life on a standard 0 to 1 scale. While the short-term analysis considers 1-year costs and utilities, the long-term analysis considers lifetime costs and utilities to account for chronic conditions associated with the development of VTED. To calculate life expectancy, the long-term analysis assumed a 45 year old female cohort for ATR, AFS and HVS; and a 60-year-old female cohort for TAA and HA. For the long-term analysis, only chronic pulmonary hypertension was found to have a long-term impact on utilities estimates. The long-term management of severe PTS, mild PTS and chronic pulmonary hypertension was considered in the calculation of lifetime costs.

Analysis outcomes

Expected health outcomes were the number of QALYs and costs associated with each strategy. To calculate the QALYs associated with each strategy, utilities were attached to each health event and multiplied by the probability of each event, by “rolling back” the decision tree. Performing the calculation for each node and working from the last decision in the sequence to the first constituted “rolling back” the decision tree. The total cost of each strategy was calculated by associating a cost to each health event and multiplying the probability of each event by the associated cost, again by “rolling back” the decision tree.

Cost-effectiveness analysis

Incremental cost-effectiveness ratios (ICERs) were estimated. The ICER represents the additional cost to achieve one additional QALY and is computed by dividing the difference in total costs by the difference in total QALYs associated with each strategy. The preferred strategy is determined by comparing the ICER to what decision makers are willing to pay for an additional QALY. A strategy is considered cost-effective if the ICER is not more than the decision maker’s intrinsic valuation for an additional QALY (20,21). No consensus has been reached on decision makers’ willingness to pay in the United States, although a \$50,000/QALY benchmark has been used in several studies (32,33).

Sensitivity analysis

One-way sensitivity analyses were conducted to estimate the impact on the cost-effectiveness results of changing key parameters individually. The sensitivity analysis tested a range of values for all cost and utility parameters, and four selected probabilities: the probability of death from hemorrhage, the probability of death from HIT, the probability of hemorrhage due to prophylaxis and the probability of HIT due to prophylaxis. Those four probabilities were selected because they were the probabilities where a higher impact of prophylaxis with LMWH would be expected. Variations to costs were taken from values reported in the literature and, when not available in the literature the sensitivity analysis used a 20% variation from the base case. For utilities, upper and lower values of the range were informed by the 95% confidence interval or the interquartile range reported in the study

where the base case value was taken from. Sensitivity analysis on the probabilities selected considered the double of the base case for upper value, and zero probability for lower value.

Results

Short-term analysis

The results from the short-term analysis can be found in Table 3.

ATR: When compared to not performing prophylaxis, prophylaxis with LMWH cost on average \$745 more and was associated with small QALY gains (0.002). This resulted in an ICER of \$329,656 which is well above the commonly accepted \$50,000/QALY threshold. Therefore, for ATR the low incremental QALY gained associated with prophylaxis did not justify the additional cost and prophylaxis with LMWH was not a cost-effective use of resources.

TAA: When compared to not performing prophylaxis, prophylaxis with LMWH cost on average \$664 more and was associated with small QALY gains (0.003). This resulted in an ICER of \$249,669 which is well above the \$50,000/QALY threshold. Therefore, for TAA the low incremental QALY gained associated with prophylaxis did not justify the additional cost and prophylaxis with LMWH was not a cost-effective use of resources.

HVS: When compared to not performing prophylaxis, prophylaxis with LMWH cost on average \$1,045 more and was associated with a small QALY loss. Therefore, for HVS an ICER was not computed because no prophylaxis dominated prophylaxis, and prophylaxis with LMWH was not a cost-effective use of resources.

HA: When compared to not performing prophylaxis, prophylaxis with LMWH cost on average \$1,020 more and was associated with very small QALY gains. This resulted in an ICER of \$76,778,968 which is well above the \$50,000/QALY threshold. Therefore, HA prophylaxis with LMWH was not a cost-effective use of resources.

AFS: When compared to not performing prophylaxis, prophylaxis with LMWH cost on average \$906 more and was associated with small QALY gains (0.002). This resulted in an ICER of \$425,082 which is well above the \$50,000/QALY threshold. Therefore, for AFS the low incremental QALY gained associated with prophylaxis did not justify the additional cost, and prophylaxis with LMWH was not a cost-effective use of resources.

Long-term analysis

The results of the long-term (or lifetime) analysis can be found in Table 4.

ATR: Prophylaxis with LMWH was associated with slightly lower long-term costs, where not performing prophylaxis cost \$126 more over the lifetime of the individual. However, not providing LMWH prophylaxis was associated with significantly higher QALY (0.94). For ATR, not performing prophylaxis was therefore very cost-effective, the ICER was \$134.

TAA: Prophylaxis with LMWH was associated with slightly lower long-term costs, where not performing prophylaxis cost \$108 more. However, not performing prophylaxis was associated with significantly higher QALY (1.04). For TAA, not performing prophylaxis was therefore very cost-effective, the ICER was \$104.

HVS: When compared to not performing prophylaxis, prophylaxis with LMWH cost on average \$1,013 more and was associated with QALY losses (−0.05). Therefore, for HVS an ICER was not computed because no prophylaxis dominated prophylaxis, and prophylaxis with LMWH was not a cost-effective use of resources.

HA: When compared to not performing prophylaxis, prophylaxis with LMWH cost on average \$972 more and was associated with QALY losses (−0.33). Therefore, for HA an ICER was not computed because no prophylaxis dominated prophylaxis and prophylaxis with LMWH was not a cost-effective use of resources.

AFS: When compared to not performing prophylaxis, prophylaxis with LMWH cost on average \$271 more and was associated with QALY losses (−0.4). Therefore, for AFS an ICER was not computed because no prophylaxis dominated prophylaxis, and prophylaxis with LMWH was not a cost-effective use of resources.

Sensitivity analyses

In the short-term analysis for ATR and TAA, the only variable which impacted the results was the cost of LMWH. Holding all other variables constant, prophylaxis with LMWH after ATR and TAA would become a cost-effective use of resources when the cost of LMWH dropped below \$400. The results were robust to changes in the other variables. For AFS, similarly, the only variable with an impact on the results was the cost of prophylaxis with LMWH. Holding all other variables constant, for a cost of LMWH below \$100, prophylaxis with LMWH for AFS would be a cost-effective use of resources. The results were robust to changes in the other variables. For both HA and HVS, the short-term base case results were robust to sensitivity analyses. There were no circumstances under which prophylaxis was cost-effective for HA and HVS. For the long-term analysis the results were robust to all sensitivity analyses. There were no circumstances under which prophylaxis was cost-effective when long-term costs and effects were taken into account.

Discussion

Like several recently published guidelines written primarily with the individual in mind (13,16,17,34), the results of our analysis which represent the healthcare system's perspective also discourage a strategy of routine LMWH prophylaxis after foot/ankle surgery. This was true in both the short and long-term analyses for all five surgeries. These findings should be of interest when developing broad clinical guidelines and algorithms that consider healthcare appropriation and cost containment with healthcare policy.

The short-term analysis showed that prophylaxis with LMWH was always associated with higher costs, which was mainly driven by the cost of prophylaxis. For ATR, TAA, HA and AFS prophylaxis was associated with slightly better health outcomes. However, the gain in

QALYs was too small to justify the additional investment on prophylaxis with LMWH. Therefore, for those four surgery scenarios, prophylaxis was not cost effective as the ICER was well above \$50K threshold. For HVS, in addition to being more costly, prophylaxis was associated with worse health outcomes and, therefore was dominated by not performing prophylaxis.

For HVS, when compared to no prophylaxis, prophylaxis was associated with a QALY loss because the reduction in the probability of DVT, and therefore of utility losses associated with DVT, was not large enough to overcome the utility loss associated with major hemorrhage and symptomatic HIT caused by prophylaxis with LMWH. This is related to extremely low probabilities of asymptomatic and symptomatic DVT following HVS. Similarly, for HA the very low probabilities of asymptomatic and symptomatic DVT following HA lead to practically undistinguishable QALY between prophylaxis and no prophylaxis. For ATR, TAA and AFS the utility loss associated with complications of LMWH prophylaxis was superseded by utility gains derived from a lower risk of DVT. However, the modest gains (as seen by an ICER for each of these 3 surgeries well above the \$50,000/QALY threshold) made routine use of LMWH an undesirable strategy from a cost-effectiveness perspective.

The long-term analysis showed that prophylaxis with LMWH was associated with worse health outcomes for the 5 surgical scenarios. For ATR and TAA, prophylaxis was associated with slightly lower long-term costs (< \$200 less per patient over lifetime). For HVS, HA and AFS prophylaxis cost more over the long-term.

In the long-term for both ATR and TAA, when compared to no prophylaxis, prophylaxis with LMWH showed a higher decrease in the costs which can be explained by a sufficient decrease in the probability of conditions that require long-term management (mild or severe PTS and pulmonary HTN) to justify the cost of prophylaxis. However, prophylaxis with LMWH was also associated with lower QALYs, mainly because the QALYs gained due a lower probability of conditions with a long-term impact on health utility (pulmonary HTN), did not overturn the QALYs lost associated with symptomatic HIT and major hemorrhage due to LMWH. For those two surgeries an ICER was computed because no prophylaxis was more expensive but also associated with better health outcomes. The low ICER associated with no LMWH prophylaxis (\$104 to \$126 per QALY) supports a strategy that does not routinely use LMWH for prophylaxis in ATR and TAA surgery.

For HVS, HA and AFS, prophylaxis with LMWH was more expensive than no prophylaxis over the lifetime because the lower costs associated with lower probabilities due to conditions that require long-term management (mild or severe PTS and pulmonary HTN) did not justify the added cost of prophylaxis. Prophylaxis with LMWH was associated with lower QALYs because the QALYs gained due to a lower probability of conditions with a long-term impact on health utility (pulmonary HTN), did not overturn the QALYs lost associated with symptomatic HIT and major hemorrhage due to LMWH.

The findings of this study, therefore, argue against the routine use of LMWH prophylaxis from a cost-effectiveness vantage point. Instead, we believe our findings highlight the

importance of risk stratification for individual patients based on their unique characteristics (e.g., personnel prior history of VTED, obesity, etc.) and postoperative course as opposed to performing prophylaxis solely based upon the type of foot and ankle surgery performed. This stance is consistent with the ACFAS Clinical Consensus Statement on risk and prevention of VTED and is consistent with other recent guidelines as well (13,16,17,34). While these guidelines were written primarily with the healthcare provider and individual patient in mind, our findings which focus on the health outcomes and economics of the healthcare system are actually quite complimentary and in support of this notion. Careful determination of the need for LMWH prophylaxis following foot and ankle surgery should be performed on a case-by-case basis.

It is important to consider the findings of this analysis within the context of its limitations. We purposely did not factor additional patient-specific risk factors into this analysis, and instead only a base case scenario (age and gender) for each surgery. This was done to see whether the surgery (and the circumstances surrounding the surgery) would be enough, in and of itself, to drive the decision to provide LMWH prophylaxis. It is important to recognize therefore that the findings of this CEA can only be generalized to the base case scenario which is essentially someone of moderate risk for VTED based on the average participant in the studies used to derive VTED event probabilities (Table 1). It is very likely that if we considered the base case to be an elderly patient presenting with a prior personal history of VTED and morbid obesity (high risk for VTED), we would have concluded that a strategy that favors routine LMWH is actually cost-effective for the health system for many of the surgeries we examined.

Another limitation in this work is that our results will not necessarily be generalizable to other forms of chemical prophylaxis. We chose to look at LMWH as this is currently the most widely used chemical agent for VTED prophylaxis in the US. However, newer agents that can be taken by mouth and do not require blood monitoring (e.g., apixaban, etc.) with lower potential risk for bleeding are becoming increasingly more available. Furthermore, our short-term conclusions were heavily dependent upon the cost of LMWH, and might change some if/when LMWH becomes less expensive. Our findings may also be less generalizable to health systems outside the US where the cost of LMWH therapy may be less. A similar study conducted in those systems may reach alternate conclusions.

Other limitations and considerations arise from the assumptions that were made. One such assumption is the length of VTED prophylaxis following surgery. Surgeons, for example, may choose to perform prophylaxis for their patient for a shorter or longer time period than the 4 weeks utilized in this analysis. This CEA also assumed maximal efficacy of LMWH for event probabilities not available in the literature. New evidence actually suggests LMWH may be less effective at preventing VTED after lower extremity injury/surgery than previously thought (35). This new evidence however only strengthens our conclusions, namely, that routine use of LMWH is not recommended after foot/ankle surgery.

Finally, our analysis considered only the direct healthcare costs associated with the two competing strategies, and did not factor in the effect of indirect costs.

In conclusion, assuming maximal efficacy and minimal harm with LMWH use, we did not find any foot/ankle surgical condition where routine prophylaxis would be preferred from the healthcare system standpoint. Unlike hip and knee replacement surgery, the decision to use LMWH prophylaxis should not be based solely on the type of foot/ankle surgery planned. Patient-specific risk factors (e.g., personal history of VTED, comorbidities, etc.) and/or prolonged ankle immobilization (16) will continue to drive the decision whether to provide chemical prophylaxis or not.

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Risk factors for venous thromboembolism disease during management of foot and ankle conditions

Patient Specific	Treatment Specific	Surgery/Injury Specific
Primary		
Personal history of VTED	Immobilization >4 wk	
Hypercoagulability		
Active/recent (<6 mo) cancer		
Secondary		
Advanced age (>60)*	Non-weightbearing	Achilles tendon rupture [‡]
Obesity (BMI >30)	Hospitalization	Ankle fracture [‡]
Family history of VTED	Bed rest	Total ankle replacement
OCP or HRT use [†]		Hindfoot arthrodesis
Varicose veins		General anesthesia
Diabetes mellitus or >1 comorbidity		
Severe foot/ankle injury		

Abbreviations: BMI, body mass index; HRT, hormone replacement therapy; OCP, oral contraceptive pill; VTED, venous thromboembolism disease (includes deep venous thrombosis or pulmonary embolism).

Figure 1.

Risk factors for DVT following foot and ankle surgery can be divided into one of three categories generally—patient specific, treatment specific and surgery specific. While none of the surgery-specific factors in the far right column identified in the recent ACFAS Clinical Consensus Statement rose to the level of a primary risk factor, the current study tested this assumption using direct costs and utilities as outcomes. Reprinted from Fleischer et al. (2015)¹⁶ with permission.

Figure 2.
Decision tree model.

Table 1 (A, B, & C) -

Model parameters: base case probabilities and their sources, and assumptions

1 A. Model Parameters Without Prophylaxis				
Variable	Reference	Base Case Probability	Variable Description	
Asymptomatic DVT			Asymptomatic DVT without LMWH prophylaxis following surgery	
ATR	19,36	0.247		
TAA	Estimate	0.259		0.076 (symptomatic DVT without LMWH prophylaxis) × 3.4 = 0.259
HVS	18,37	0.021		
HA	11	0.035		
AFS	38	0.3		
Symptomatic DVT			Symptomatic DVT without LMWH prophylaxis following surgery	
ATR	19,27,39–42	0.062		
TAA	8,43	0.076	Calculated by multiplying 43 (Barg et al., 2011) which routinely used LMWH by 1.96	
HVS	8,10,12	0.0001		
HA	8	0.0003		
AFS	38,44	0.026		
PE				PE without LMWH prophylaxis following surgery independent of DVT
ATR	19,27,36,39,42,45	0.004		
TAA	8	0.006		
HVS		0		
HA	8	0.0021		
AFS	8,44	0.0017		
1 B. Model Parameters With Prophylaxis				
Variable	Reference	Base Case Probability	Variable Description	
Asymptomatic DVT**			Asymptomatic DVT with LMWH prophylaxis following surgery	
ATR	0.51 reduction	0.126		
TAA	0.51 reduction	0.132		
HVS	0.51 reduction	0.01		
HA	0.51 reduction	0.018		
AFS	0.51 reduction	0.15		Symptomatic DVT with LMWH prophylaxis following surgery
Symptomatic DVT			Symptomatic DVT with LMWH prophylaxis following surgery	
ATR	0.51 reduction	.032		
TAA	43	0.039		
HVS	0.51 reduction	0.00005		
HA	0.51 reduction	0.00015		

1 A. Model Parameters Without Prophylaxis			
Variable	Reference	Base Case Probability	Variable Description
AFS	0.51 reduction and ref 27	0.013	
PE			PE with LMWH prophylaxis following surgery independent of DVT
ATR		0	
TAA	43	0	
HVS	10	0	
HA	10	0	
AFS	44	0	
1 C. Probabilities Not Specific to Surgery			
Variable	Reference	Base Case Probability	Variable Description
Mild PTS after asymptomatic DVT	46	0.078	
Mild PTS after symptomatic DVT	46	0.133	
Severe PTS after symptomatic DVT	47	0.081	
Hemorrhage after DVT management	48	0.02	
Hemorrhage after PE management	49	0.041	
Death after major hemorrhage [†]	48,50	0.148	
Recurrent DVT after symptomatic DVT	46,48	0.016	
Hemorrhage after recurrent DVT	48	0.013	Assumes pt would be treated with 6 months anticoagulation with LMWH and coumadin
PE after symptomatic DVT	48,50	0.018	In the immediate (12 mo) period
Pulmonary HTN after PE	47	0.013	
Death from PE	8,9	0.072	
Hemorrhage with LMWH prophylaxis [†]	26	0.0027	
HIT with LMWH [†]	50	0.0005	
Death from HIT [†]		0.098	

*** Assumes maximal efficacy of LMWH (reference rate $\times$ 0.51)

[†]Probabilities varied in the sensitivity analysis. Double of the base case value for upper and 0 for lower values were used.

ATR, Achilles Tendon Repair; TAA, Total ankle arthroplasty; HVS, hallux valgus surgery; HA, Hindfoot Arthrodesis; AFS Ankle Fracture Surgery

Table 2 -

Model parameters: base case costs and utilities and their sources, and assumptions

Variable	Reference	2015 Estimate Cost: Base Case [*]	Source for Upper & Lower Values	Range 2015 Cost [*]
Drug Cost				
LMWH		1000		0 – 1200
Warfarin	51	29/month		
Complication				
DVT	52,53 ^{††}	6,836	(53) & (52) - 20%	5,469 – 16,090
PE	53,54	24,787	(53) + 20% & (54)	10,149 – 29,774
Mild PTS [§]	52	1,510	(52) +/- 20%	1,208 – 1,812
Severe PTS [§]	52	6,870	(52) +/- 20%	5,496 – 8,244
Pulmonary HTN [§]	55	27,365	(55) +/- 20%	21,892 – 32,838
Recurrent DVT ^{**}	52,53 ^{††}	6,865	(53) & (52) - 20%	5,492 – 16,118
Event				
Hemorrhage (Resolution)	56	7,311	(56) +/- 20%	5,410 – 10,715
Hemorrhage (Death)	56	10,950	(56) +/- 20%	10,715 – 13,585
HIT	50,57	61,553	(57) + 20% & (50)	15,178 – 73,865
Utilities				
Health Utility of General Population	58	0.870		
QALY Severe PTS [#]	59	0.818	0.825	0.810
QALY Mild PTS ^{##}	59	0.853	0.868	0.837
QALY Pulm HTN	60	0.710	0.780	0.640
QALY Following PE Resolution [∞]	61	0.852	0.863	0.830
QALY Following DVT Resolution [∞]	61	0.856	0.866	0.837
QALY Following Hemorrhage Resolution ^{∞∞∞}	61	0.864	0.868	0.856
QALY Following HIT Resolution	Estimate [†]	0.852	0.866	0.837

Cost of LMWH represents the retail price of enoxaparin for 4 weeks of prophylaxis from: <http://www.goodrx.com/enoxaparin>

^{*} Costs are presented in 2015 U.S. dollars. Costs from studies using older costs were inflated using the rate appropriate for medical costs at each year from the medical component of the Bureau of Labor Statistics Consumer Price Index, medical component.

Consumer price Index. U.S. Bureau of Labor Statistics Washington, DC . Available at <http://data.bls.gov/cgi-bin/surveymost>. Accessed August 3, 2015.

^{**} Cost of treatment for DVT + cost of treatment with Warfarin for 3 additional months

[§] Chronic condition: Apply cost to every year for remainder of the patient's life. Apply discounted rate after year 1

[†] Assumption: Average of mild PTS and PE resolution utilities

[‡]2010 Life Expectancy in 2010 for a 45 year old man and woman is 33.9 years and 37.7 years respectively (62)

Rationale for selecting female gender is life expectancy is longer for women.

^{††}Reference (53) did not specify price year, assumed 2004

[#]Utility reported in reference (59) was adjusted for US population normal value of 0.87 and recalculated for one year based on the duration of condition of 0.86 years reported in reference 52. Remaining years apply utility of 0.87.

^{##}Utility reported in reference (59) was adjusted for US population normal value of 0.87 and recalculated for one year. Remaining years apply utility of 0.87.

[∞]Calculated QALYs using US population norm of 0.87 using the time with the condition as reported in reference (61). 1 month with PE or DVT symptoms respectfully and calculated for 1 year. Remaining years apply utility of 0.87.

^{∞∞}Assuming the rate utilized is for GI hemorrhage. Calculated QALYs using US population norm of 0.87 using the time with the condition as reported in (61), 1 week with symptoms. QALY, Quality Adjusted Life Year; ATR, Achilles Tendon Repair; TAA, Total ankle arthroplasty; HVS, hallux valgus surgery; HA, Hindfoot Arthrodesis; AFS Ankle Fracture Surgery

Table 3 -

Base case estimates of short-term costs and QALYs, for each strategy and surgery, together with incremental analysis

SURGERY	STRATEGY	COST	INC COST	QALY	INC QALY	ICER
ATR	No Proph	\$575		0.8650		
	Proph LMWH	\$1,320	\$745	0.8670	0.0020	\$329,656
TAA	No Proph	\$713		0.8640		
	Proph LMWH	\$1,377	\$664	0.8670	0.0030	\$249,669
HVS	No Proph	\$6		0.8700		
	Proph LMWH	\$1,051	\$1,045	0.8690	-0.0000	Dominated
HA	No Proph	\$32		0.8690		
	Proph LMWH	\$1,052	\$1,020	0.8690	0.0000	\$76,778,968
AFS	No Proph	\$265		0.8650		
	Proph LMWH	\$1,171	\$906	0.8670	0.0020	\$425,082

INC, Incremental; QALY, Quality Adjusted Life Year, ICER, Incremental cost-effectiveness ratio; ATR, Achilles Tendon Repair; TAA, Total ankle arthroplasty; HVS, hallux valgus surgery; HA, Hindfoot Arthrodesis; AFS Ankle Fracture Surgery; Proph, Prophylaxis; Proph, Prophylaxis; LMWH, Low Molecular Weight Heparin. Costs in US dollars at a 2015 price base.

Table 4 -

Base case estimates of lifetime costs and QALYs, for each strategy and surgery, together with incremental analysis

SURGERY	STRATEGY	COST	INC COST	QALY	INC QALY	ICER
ATR	Proph LMWH	\$2,207		20.5440		
	No Proph	\$2,333	\$126	21.4840	0.9400	\$134
TAA	Proph LMWH	\$2,149		15.7020		
	No Proph	\$2,257	\$108	16.7380	1.0360	\$104
HVS	No Proph	\$65		20.4790		
	Proph LMWH	\$1,078	\$1,013	20.4290	−0.0500	Dominated
HA	No Proph	\$119		15.9300		
	Proph LMWH	\$1,090	\$972	15.5970	−0.3320	Dominated
AFS	No Proph	\$1,522		20.8780		
	Proph LMWH	\$1,793	\$271	20.4740	−0.4040	Dominated

INC, Incremental; QALY, Quality Adjusted Life Year, ICER, Incremental cost-effectiveness ratio; ATR, Achilles Tendon Repair; TAA, Total ankle arthroplasty; HVS, hallux valgus surgery; HA, Hindfoot Arthrodesis; AFS Ankle Fracture Surgery; Proph, Prophylaxis; LMWH, Low Molecular Weight Heparin. *Costs and QALYs are discounted at a 3% annual rate. Costs in US dollars at a 2015 price base. Base case assumes 45 year old female cohort for ATF, AFS, and HVS; and 60 year old female for TAA and HA.