

# Cost Analysis of Diagnosis and Treatment of Venous Thromboembolism in Total Knee Replacement Patients

Hadi Alizadeh Siuki<sup>1</sup>, Nikta Shobeiri<sup>2</sup>, Amin Adel<sup>3</sup>, Asma Rashki Kemmak<sup>4\*</sup>

<sup>1</sup>Health Sciences Research Center, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.

<sup>2</sup>Department of Pharmaceutical Control, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

<sup>3</sup>Social Determinants of Health Research Center, Social Health Research Institute, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.

<sup>4</sup>Health Sciences Research Center, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.

\* Corresponding Author: Asma Rashki Kemmak, Health Sciences Research Center, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran. Email: A.raashki@gmail.com

Received 2025 February 28; Accepted 2025 July 20.

## Abstract

**Background:** Venous thromboembolism (VTE) is a condition that occurs when a blood clot forms in a vein. It includes deep vein thrombosis (DVT) and pulmonary embolism (PE). VTE treatment incurs substantial costs, and it is predicted that the economic burden of this disease on society will continue to rise both domestically and globally. This study aimed to analyze the costs associated with the diagnosis and treatment of VTE in patients undergoing total knee replacement in order to identify major cost drivers and provide insights for more efficient healthcare management.

**Methods:** An incidence-based approach was used in this cross-sectional descriptive study to perform the cost analysis of diagnosis and treatment of VTE in total knee replacement patients in Iran in 2023. To this end, direct costs were calculated based on the bottom-up costing approach.

**Results:** The average direct medical cost per patient was \$1742.65. The average direct non-medical cost per patient was estimated at \$604.75. Notably, 44% of these costs are associated with patient companionship, while 33% are attributed to transportation costs.

**Conclusion:** With the elderly population on the rise in our country, the need for knee joint replacement surgeries is on an upward trajectory as well. However, it is associated with the risk of developing VTE, which can be severe and life-threatening. Moreover, patients who develop VTE after major orthopedic surgeries tend to have considerably longer hospital stays, placing a strain on hospital resources and finances.

**Keywords:** Cost Analysis; Direct Medical Cost; Direct Non-Medical Cost; Venous Thromboembolism

## 1. Background

Non-communicable diseases have emerged as the foremost cause of mortality and disease burden worldwide. In 2000, 60% of global fatalities were attributed to non-communicable diseases, with an anticipated increase to 73% by 2024. Consequently, there is a pressing need to prioritize the prevention of the disease in developing countries, a key initiative spearheaded by the World Health Organization (1).

Venous thromboembolism (VTE) is a formidable vascular disease, superseded only by coronary artery disease and stroke, with a lifetime incidence rate of approximately 2-5% (2). Although this condition is widely recognized, it is still fraught with grave complications and substantial mortality rates (3). Furthermore, although largely preventable, VTE remains a leading cause of death in hospitals (4).

VTE includes deep vein thrombosis (DVT) and pulmonary embolism (PE) (5). DVT is a condition that occurs when a blood clot forms in a vein, usually in the lower leg, thigh, or pelvis. The clot can break loose and travel through the bloodstream to the lungs. Less than 10% of VTE cases occur in areas other than the internal limb (6).

This disease affects 1-3 in 1000 individuals every year in developed countries and is regarded as one of the reasons

for cardiovascular death, alongside heart attacks and strokes (7).

The annual global incidence of VTE is approximately 10 million cases. In Europe, an estimated 100 to 200 cases of VTE occur annually per 100000 people (8). However, research in the Netherlands indicates that VTE mortality may be even higher, with 16000 to 20000 cases of DVT and 15000 to 20000 cases of PE reported each year (9). Moreover, the aging population is believed to increase the incidence of VTE, posing a significant public health challenge. In England, VTE-related hospitalization reportedly involves over 32000 individuals each year, with similar figures observed in Australia (30000) (10). The United States experiences a high incidence of VTE, more than 540000 cases annually (11).

In 2006, the overall prevalence of VTE in the US was 422 per 100000 people and it is estimated to reach 567 per 100000 people in 2050 (10). In Iran, the prevalence of DVT has been reported to be 25% in patients with femur and knee fractures without pharmaceutical prophylaxis and 1.9% with pharmaceutical prophylaxis (11). Additionally, the annual average prevalence of DVT among adult patients exposed to the risk of this disease is reported to be about 130 to 395 cases per 1000 patients in Iran (12).

In the last 30 years, numerous cost-of-illness studies



have been carried out to analyze the economic burden of diseases on society. These studies are integral in shaping public health policies and treatment regulations as they highlight the profound impact of diseases on well-being of society. Cost-of-illness studies aim to determine the overall costs and challenges faced by healthcare systems when addressing particular diseases (13).

VTE treatment incurs substantial costs, and it is predicted that the economic burden of this disease on society will continue to rise both domestically and globally. It is imperative to have a comprehensive understanding of the costs involved in managing any medical condition to help policymakers make informed decisions about prioritizing healthcare policies for prevention and treatment, thus ensuring optimum utilization of resources. These cost analysis studies can also provide valuable insights into determining which treatment procedures will effectively reduce the burden of disease.

## 2. Materials and Methods

The analysis was based on a bottom-up costing approach from the perspective of the health system. The data were meticulously described using means and standard deviations and analyzed using SPSS version 11.0. The inclusion criteria encompassed patients whose treatment information is comprehensively documented at all stages, as well as patients who have experienced VTE following knee replacement surgery. Patients who did not develop VTE and those who were either unable or unwilling to respond to the inquiries of the study were excluded from the study. Additionally, certain patients, such as children, as well as individuals whose treatment details were not recorded in the information system or whose treatment period was prematurely terminated due to death or referral, were excluded from the research due to their adherence to a distinct treatment protocol.

The analysis of costs was conducted using the bottom-up approach, incorporating all costs incurred by the hospital for the treatment of VTE. In the bottom-up approach, the average cost per patient is first calculated and then multiplied by the total number of patients. To calculate the cost per patient, various components of the cost are identified and the cost generated is measured for each component. For example, to calculate the total cost of patients' travel, the average number of trips per patient is multiplied by the average cost of each trip and then multiplied by the total number of patients. Given the insured status of patients, the majority of these costs are typically covered by medical insurance providers. The statistical population of this retrospective-descriptive analysis included 300 patients diagnosed with VTE who were admitted to the hospitals affiliated with Tehran University of Medical Sciences.

Data related to direct medical costs were collected from hospitalization and outpatient medical records. Direct medical costs include costs of physician visits, surgeries, hospitalization, diagnostic procedures, and

paraclinical (laboratory) measures. The required data to calculate non-medical direct costs were collected using a questionnaire. In order to assess the scientific credibility of the questionnaire, content validity was utilized and it was validated by experts in medical universities. The questionnaire was pilot-tested among a group of patients to identify and address any concerns. Additionally, in-person or telephone interviews were conducted with patients and their caregivers to accurately assess incurred costs, including travel and home care costs. These measures were taken to ensure the accuracy and reliability of the data collected.

This study calculated and evaluated costs from the perspective of the health system. Hence, all costs incurred in disease management were taken into account, irrespective of the payer, whether it is the patient, insurance, or healthcare system. However, the study focused solely on evaluating direct healthcare costs and indirect healthcare costs.

Demographics and types of costs were described using mean and standard deviation (SD) and analyzed using SPSS version 11.

## 3. Results

A total of 300 subjects were analyzed. The subjects were categorized into 3 groups (n=100): hemorrhage, DVT, and PE. Table 1 represents the demographics of the subjects in the study groups.

Among these individuals, 62% were married and 38% were single. Additionally, 26% had no education, 45% had a high school diploma or less, and 24% had a bachelor's degree or higher. Additionally, most individuals had social security insurance. Among these individuals, 65%

**Table 1.** Socio-economic and Demographic Characterizations of Patients

Variable	Frequency (%)
Average age	61
Gender	59% Female 41% Male
Marital status	62% Married 38% Single 26% Illiterate
Literacy	45% Diploma or lower 24% Bachelor's degree and above 65% Unemployed
Employment status	29% Retired 3% Farmer 3% Other 61% Social security
Health insurance	23% Health care 16% Other insurance Bleeding: 9 days
Average length of stay	DVT: 10 days PE: 9 days

were unemployed, 29% were retired, and 3% were farmers. The average income of these individuals was 17291000 Rials. The average length of hospital stay was 9 days for patients with bleeding, 10 days for those with DVT, and 9 days for individuals with PE. The average age of the patients was 66.

#### *Direct Medical Costs*

To accurately diagnose VTE, specific diagnostic measures are taken prior to any therapeutic intervention. These measures include specialist visits, radiology, Doppler ultrasonography, CT scans, MRI, laboratory tests, ECGs, and echocardiography. Tables 2 and 3 represent the costs of diagnosis and treatment of VTE based on the type of intervention and treatment service within the public sector. The cost of each service is based on the tariff rate set by the Ministry of Health, Treatment, and Medical Education.

As shown in Table 2, the highest cost incurred in the surgery section and operating room was attributed to medications and consumables (45%), followed by surgeons (35%). Table 3 indicates the diagnostic costs of VTE, which primarily include costs for medical consultations, radiological tests, Doppler ultrasounds, CT scans, MRI scans, laboratory tests, ECG, and echocardiography. Radiology, ECG, and MRI scans were the least costly services.

#### *Direct Non-medical Cost*

Table 4 details non-medical direct costs. As shown, 44% of these costs are associated with patient companionship, while 33% are attributed to transportation costs.

#### **4. Discussion**

This study aimed to conduct a comprehensive cost analysis

**Table 2. Treatment Costs of VTE per Patient**

Service	Cost (\$)	Percent	SD
Consultation	52.13	3	18.7
Surgeon	532.82	35	45.2
Anesthesia	76.07	5	10.1
Operating room	174.13	12	12.3
Medication and consumables	674.38	45	26.3

**Table 3. Diagnostic Costs of VTE per Patient**

Service	Cost (\$)	SD	Percent
Physician visit	58.44	13.02	25
Radiology	6.13	2.5	3
Doppler ultrasound	22.82	5.1	10
CT scans	24.31	2.8	10
MRI	5.21	1.2	2
Laboratory	73.31	13.4	32
ECG	5.81	1.7	3
Echocardiography	37.08	14.2	16

on the diagnosis and treatment of VTE in Iran. As the first and groundbreaking cost analysis study on the disease in the country in 2022, the required data were collected from diverse sources such as hospital records, surveys, and the HIS system, in addition to phone interviews with patients and/or companions. The interviews with families of patients were subject to bias. Besides, the failure of some patients to disclose the exact details of their costs made it quite challenging to accurately calculate the cost. Hence, the calculated costs may be lower than the actual costs.

This study revealed that approximately 46% of the overall costs of treatment are associated with surgical procedures. The treatment options for patients with this medical condition include anti-coagulation agents or thrombolysis therapy, which can be administered intravenously or through catheterization, while advanced surgical interventions, such as embolectomy, are usually considered the ultimate solution after the failure of other treatments (14). Consequently, surgeon and surgical charges could burden patients with the highest costs incurred, compromising the quality of care.

Moreover, the greatest cost following surgery cost was attributed to medication and consumables. The use of pain-free techniques that required more expensive consumables, such as intrathecal pumps (also known as pain relief pumps), epidural sets, and surgical threads of high-end brands, as well as lengthy hospitalization periods, accounted for the increased costs in consumables observed both in the ward and operating room (15).

The increase in medication costs can be attributed to the use of newly developed oral anticoagulants for treating VTE. These anticoagulants have fewer side effects, including bleeding, which encourages patients to use them more frequently. However, since these medications are new, they are more expensive (16).

Various studies have been carried out to examine the expenditures involved in treating VTE. One of these studies concentrated on the cost associated with the treatment of VTE after orthopedic surgery. The research revealed that the overall cost of medical care given during the first 6 months of post-hospital discharge amounted to \$3500 (17). Dobesh (18) reported that the total cost of treatment for DVT patients was \$10804. In contrast, among patients with PE, the cost of this treatment amounted to \$16644.

A study led by Spyropoulos and Lin found that

**Table 4. Direct Non-Medical Costs of Venous Thromboembolism in 2022**

Cost type	Cost per patient (\$)	Percent
Patient companionship	268.21	44%
Transportation	202.12	33%
Home care	89.10	15%
Time	45.32	7%
Total	604.75	100%

diagnosing DVT and PE can lead to substantial healthcare costs. The average total annual payment for the healthcare system was \$10804 for DVT and \$16644 for PE, taking into account the cost of initial diagnosis. Furthermore, the additional annual cost for secondary diagnoses was \$7594 for DVT and \$13018 for PE. The average cost of hospital readmission due to DVT was approximately \$11862, whereas for PE, it was \$14722. Interestingly, our study revealed that the monetary burden on patients associated with hospitalization and treatment was lower in comparison to that of diagnostic procedures (19).

Vekeman et al demonstrated that the healthcare costs of patients with VTE-related conditions remain high even 3 months after knee joint replacement. Specifically, the study revealed an average expenditure of \$2729 per patient per month (20).

It is important to recognize the limitations of this study. The data extracted from hospital systems may be incomplete or contain inaccuracies concerning procedures, diagnoses, or costs. A weakness of this study was the lack of access to data on the indirect costs of VTE, such as reduced work productivity and quality of life, as well as direct medical costs. Generating evidence for policymakers to prevent VTE among knee replacement patients was one of the strengths of this study.

## 5. Conclusion

With the elderly population on the rise in our country, the need for knee joint replacement surgeries is on an upward trajectory as well. However, it is associated with the risk of developing VTE, which can be severe and life-threatening. Moreover, patients who develop clinical VTE after major orthopedic surgeries tend to have considerably longer hospital stays, leading to a strain on hospital resources and finances.

## Authors' Contribution

Conceptualization: Asma Rashki Kemmak.

Data curation: Amin Adel.

Formal analysis: Hadi Alizadeh Siuki.

Funding acquisition: Asma Rashki Kemmak.

Investigation: Nikta Shobeiri, Amin Adel.

Methodology: Nikta Shobeiri, Hadi Alizadeh Siuki.

Project administration: Asma Rashki Kemmak.

Resources: Asma Rashki Kemmak.

Software: Amin Adel.

Supervision: Asma Rashki Kemmak.

Validation: Nikta Shobeiri, Asma Rashki Kemmak.

Visualization: Amin Adel.

Writing-original draft: Hadi Alizadeh Siuki, Nikta Shobeiri.

Writing-review & editing: Asma Rashki Kemmak.

## Competing Interests

The authors declare that they have no conflict of interests.

## Data Availability Statement

Not applicable.

## Ethical Approval

This study was approved by the Ethics Committee of Iran University of Medical Sciences (Ethical Code: IR.IUMS.REC.1398.534).

## Funding

No funding was obtained for this study.

## References

- Shams M, Samavat T, Hojatzadeh A, Afkhami A, Mahdavi A, Bashti S, et al. Ways of Prevention and Control of Cardiovascular Diseases. Tehran: Press Javan; 2013. [Persian].
- Aslan A, Khorami R, Rezaei J, Godarzi M, Abbasi Dolatabadi Z. Drug updates for prevention and treatment of venous thromboembolism in orthopedic surgeries. *Iranian Journal of Cardiovascular Nursing*. 2017;6(2):66-73. [Persian].
- Beckman MG, Abe K, Barnes K, Bartman B, Brady PJ, Hooper WC. Strategies and partnerships toward prevention of healthcare-associated venous thromboembolism. *J Hosp Med*. 2016;11 Suppl 2:S5-7. doi: 10.1002/jhm.2659.
- Le Sage S, McGee M, Emed JD. Knowledge of venous thromboembolism (VTE) prevention among hospitalized patients. *J Vasc Nurs*. 2008;26(4):109-17. doi: 10.1016/j.jvn.2008.09.005.
- Diamantopoulos A, Lees M, Wells PS, Forster F, Ananthapavan J, McDonald H. Cost-effectiveness of rivaroxaban versus enoxaparin for the prevention of postsurgical venous thromboembolism in Canada. *Thromb Haemost*. 2010;104(4):760-70. doi: 10.1160/th10-01-0071.
- Glynn RJ, Rosner B. Comparison of risk factors for the competing risks of coronary heart disease, stroke, and venous thromboembolism. *Am J Epidemiol*. 2005;162(10):975-82. doi: 10.1093/aje/kwi309.
- Jha AK, Larizgoitia I, Audera-Lopez C, Prasopa-Plaizier N, Waters H, Bates DW. The global burden of unsafe medical care: analytic modelling of observational studies. *BMJ Qual Saf*. 2013;22(10):809-15. doi: 10.1136/bmjqqs-2012-001748.
- Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galie N, et al. Corrigendum to: 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J*. 2015;36(39):2666. doi: 10.1093/eurheartj/ehv131.
- Heisen M, Treur MJ, Heemstra HE, Giesen EB, Postma MJ. Cost-effectiveness analysis of rivaroxaban for treatment and secondary prevention of venous thromboembolism in the Netherlands. *J Med Econ*. 2017;20(8):813-24. doi: 10.1080/13696998.2017.1331912.
- House of Commons Health Committee. The Prevention of Venous Thromboembolism in Hospitalised Patients. London: The Stationery Office; 2005.
- Centers for Disease Control and Prevention (CDC). Venous thromboembolism in adult hospitalizations - United States, 2007-2009. *MMWR Morb Mortal Wkly Rep*. 2012;61(22):401-4.
- Sharif-Kashani B, Mohebi-Nejad A, Abooturabi SM. Estimated prevalence of venous thromboembolism in Iran: prophylaxis still an unmet challenge. *Tanaffos*. 2015;14(1):27-33.
- Jefferson T, Demicheli V, Mugford M, Baranpourian F. Economic Evaluation of Health Care Services. Tehran: Higher Institute for Social Research. 2007.
- Abutorabi A, Haj Ahmadi M, Bagheri Faradonbeh S, Rashki Kemmak A, Alipour V. Cost-effectiveness rivaroxaban versus enoxaparin for prevention of venous thromboembolism after knee replacement surgery in Iran. *Med J Islam Repub Iran*. 2023;37:20. doi: 10.47176/mjiri.37.20.
- Aghazadeh S, Nemati M, Sharif Nia E, Hamishehkar H. The cost benefit of drugs and medical consumables in common global gynecological surgeries of two educational-therapeutic hospitals of Tabriz city. *J Mod Med Info Sci*. 2017;3(2):49-55.
- Lefebvre P, Coleman CI, Bookhart BK, Wang ST, Mody SH, Tran KN, et al. Cost-effectiveness of rivaroxaban compared with enoxaparin plus a

vitamin K antagonist for the treatment of venous thromboembolism. *J Med Econ.* 2014;17(1):52-64. doi: 10.3111/13696998.2013.858634.

- 17. Nutescu EA, Shorr AF, Farrelly E, Horblyuk R, Happe LE, Franklin M. Burden of deep vein thrombosis in the outpatient setting following major orthopedic surgery. *Ann Pharmacother.* 2008;42(9):1216-21. doi: 10.1345/aph.1L135.
- 18. Dobesh PP. Economic burden of venous thromboembolism in hospitalized patients. *Pharmacotherapy.* 2009;29(8):943-53. doi: 10.1592/phco.29.8.943.
- 19. Spyropoulos AC, Lin J. Direct medical costs of venous thromboembolism and subsequent hospital readmission rates: an administrative claims analysis from 30 managed care organizations. *J Manag Care Pharm.* 2007;13(6):475-86. doi: 10.18553/jmcp.2007.13.6.475.
- 20. Vekeman F, LaMori JC, Laliberté F, Nutescu E, Duh MS, Bookhart BK, et al. Risks and cost burden of venous thromboembolism and bleeding for patients undergoing total hip or knee replacement in a managed-care population. *J Med Econ.* 2011;14(3):324-34. doi: 10.3111/13696998.2011.578698.