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Home Treatment Compared to Initial Hospitalization in Normotensive Patients with Acute Pulmonary Embolism in the Netherlands: A Cost Analysis

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Abstract

Background Venous thromboembolism constitutes substantial health care costs amounting to approximately 60 million euros per year in the Netherlands. Compared with initial hospitalization, home treatment of pulmonary embolism (PE) is associated with a cost reduction. An accurate estimation of cost savings per patient treated at home is currently lacking.

Aim The aim of this study was to compare health care utilization and costs during the first 3 months after a PE diagnosis in patients who are treated at home versus those who are initially hospitalized.

Methods Patient-level data of the YEARS cohort study, including 383 normotensive patients diagnosed with PE, were used to estimate the proportion of patients treated at home, mean hospitalization duration in those who were hospitalized, and rates of PE-related readmissions and complications. To correct for baseline differences within the two groups, regression analyses was performed. The primary outcome was the average total health care costs during a 3-month follow-up period for patients initially treated at home or in hospital.

Keywords
- costs
- home treatment
- hospitalization
- pulmonary embolism

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Results Mean hospitalization duration for the initial treatment was 0.69 days for those treated initially at home ($n = 181$) and 4.3 days for those initially treated in hospital ($n = 202$). Total average costs per hospitalized patient were €3,209 and €1,512 per patient treated at home. The adjusted mean difference was €1,483 (95% confidence interval: €1,181–1,784).

Conclusion Home treatment of hemodynamically stable patients with acute PE was associated with an estimated net cost reduction of €1,483 per patient. This difference underlines the advantage of triage-based home treatment of these patients.

Introduction

Venous thromboembolism (VTE), consisting of pulmonary embolism (PE) and deep vein thrombosis (DVT), constitutes a major global health issue. It represents the third leading cause of vascular disease with nearly 10 million annual cases worldwide.[1–3] Therefore, the yearly economic burden of VTE is substantial. In the Netherlands, costs of VTE-related medical care in 2015 amounted to nearly 60 million euros, not including the costs of VTE-associated intensive care admissions, which accounted for another 8 million euros.[4]

Home treatment of VTE is associated with improvement of quality of life and prevention of hospital overcrowding. Moreover, the potential reduction of health care costs is a frequently suggested argument in favor of home treatment compared with initial hospitalization.[5,6] For DVT, the strategy to treat patients at home has been widely accepted since the introduction of low-molecular-weight heparins (LMWHs).[7,8] For PE, there has been a change over the last decade, as the safety and feasibility of home treatment have been shown in several large trials.[9–16] With the recent introduction of direct oral anticoagulants (DOACs) that have a better safety profile than conventional anticoagulants,[17] the threshold to treat a PE patient at home has been further lowered.[18] A reduced length of stay and resultant decrease in total hospital costs in patients treated with a DOAC has already been demonstrated.[19–21] An accurate estimation of cost saving per patient when choosing for home treatment is currently however still lacking.

We therefore aimed to evaluate the health care utilization and medical costs of home treatment compared with initial hospitalization in the treatment of acute PE in the setting of Dutch clinical practice.

Methods

Patient Selection

This was a posthoc analysis of the YEARS study, performed in 12 academic and nonacademic centers across the Netherlands.[22] For the present analysis, data of all normotensive outpatients who were diagnosed with acute PE and in whom home treatment may have been considered were studied, reflecting daily practice circumstances. The YEARS study was a prospective, multicenter, diagnostic management study between October 2013 and July 2015 in the Netherlands that aimed to validate the safety and efficacy of the YEARS algorithm in the diagnostic management of suspected PE.[22] Patient-level data from the YEARS study were used to estimate the mean hospitalization duration of patients with confirmed PE, as well as the rates of PE-related scheduled and unscheduled readmissions. Further, we extracted details of home treatment and discharge from the original patient charts. Lastly, demographic data of PE patients in the YEARS cohort were used to adjust the health economic model for baseline characteristics and to estimate pharmaceutical costs.

Study Objectives and Outcomes

The primary aim of this study was to compare health care utilization and costs of normotensive PE patients treated at home to those treated initially in hospital. The primary outcome of this analysis was the amount of average total health care costs during a 3-month follow-up period.

Definitions

Acute PE was defined as intraluminal filling defects of the subsegmental or more proximal pulmonary arteries confirmed by computed tomography pulmonary angiography (CTPA).[23] Home treatment was defined as hospital discharge within 24 hours after diagnosis of VTE. A PE-related readmission was defined as any scheduled or unscheduled visit to the outpatient clinic, emergency room, or readmission in hospital due to PE-related complications, such as thoracic pain, dyspnea, major bleeding, clinically relevant nonmajor bleeding, or (suspected) recurrent VTE.

Medical costs are reported in euros at price level 2018 (updated using the general consumer price index, if necessary) and include pharmaceutical, radiological, and hospital costs. These reference prices are designed to reflect realistic costs and to standardize health-economic evaluations in the Netherlands.

Pharmaceutical Costs

For the calculation of medication costs in the 3-month period following the PE diagnosis, we included the costs of the medication itself (including value-added tax) and an additional €6 pharmacy delivery costs per regular delivery.[24] Deductibles were not included in this analysis as they have to be paid by the patients themselves and are the same for both the in-hospital- and outpatient-treated patients. Because no individual data on types of anticoagulant were available, data on anticoagulant use were obtained from IQVIA's Real-World Data Longitudinal Prescription database

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(LRx, Amsterdam, The Netherlands). From anonymous patient prescription records, data on basic patient characteristics, dispensing (e.g., pharmacy, prescription date and duration), medication (e.g., generic and brand name, dosage, dosing regimen), and prescriber information were collected. The database covers approximately 75% of all prescriptions dispensed in the Netherlands, represented by both retail pharmacies and dispensing general practitioners. The price per day of apixaban use was €4.49 for the first 7 days and €2.25 thereafter. For rivaroxaban the price per day was €4.71 for the first 21 days and €2.35 thereafter. The price per day of dabigatran and edoxaban were €2.44, with a recommended prior 5 day use of LMWH. For the cost of vitamin K antagonists (VKAs), we included €0.09 per day, plus a 7-day run-in period with LMWH. The price of LMWH was based on the price of nadroparin, the most used LMWH in the Netherlands.[25] We used the price per day of €10.34, for a 0.8 mL 19,000 IE/mL syringe, closest to the recommend 171 IE/mL per kilogram for an average weight of 86 kg, derived as mean weight from the YEARS study cohort.[22]

Additional costs when carrying out VKA controls were obtained from annual reports of the Dutch thrombosis service and included the average annual costs for diagnostics and treatment in a primary care setting. For the patients with VTE, the yearly average additional cost was €333, corresponding with a 3-month cost of €83. We conservatively assumed no cost difference for treatment options and monitoring of VKA when initial therapy was started in a clinical setting or at home.[26]

Radiological Costs

The costs of radiological imaging were set at € 183 and € 43 per CTPA and chest X-ray, respectively.[27,28] Every PE patient in the YEARS study was diagnosed with CTPA. X-ray testing had been performed in 86% of all patients diagnosed with PE in the initial diagnostic assessment.[29]

Laboratory Costs

Laboratory costs were obtained by the price level 2018 (updated using the general consumer price index, if necessary) and were derived from laboratory analysis of the 12 academic and nonacademic centers and included costs for complete blood count, kidney function, liver function, electrolytes, inflammatory markers, and D-dimer.

Hospital Costs

Hospital days, outpatient visits, and emergency visits were valued in accordance with the reference prices from the Dutch guidelines for economic evaluations in health care at €495, €95, and €269, respectively. This includes costs for administration, specialist time, and nursing care.[27,28] Estimated hospital costs did not include intensive care unit care, since patients with high-risk PE were not included in the YEARS study and these patients cannot be treated at home. Total hospital costs were based on the average costs per hospital day multiplied by the length of stay, as diagnosis-related group-based reimbursement systems in the Dutch health care setting have to the substantiated with interventions and days of admission to reach to the total amount of costs.

The proportion of patients who needed an unscheduled visit to the ER or outpatient clinical ward was obtained from a posthoc analysis of the YEARS study.[30] If patients were readmitted, we assumed a mean readmission duration of 5.0 days, obtained from previous publications.[31] The price per day for a readmission was assumed equal to the initial hospitalization. To calculate the number of planned outpatient clinic visits, we used the hospitals' protocol for VTE management for patients after home treatment or initial hospitalization. As detailed data were lacking, we could not take visits to the general practitioner into account.

Statistical Analysis

Total medical costs were calculated for each patient in the YEARS study cohort. For the presentation of the baseline characteristics, categorical data are presented as percentages or as proportion and continuous variables (as means with standard deviation [SD]). To compare average costs of home treatment to initial hospitalization, costs for the mean hospitalization duration were compared for both treatment modalities. In multivariate analysis we will provide the adjusted cost differences with a 95% confidence interval (CI) as well as adjusted *p*-values for significance. To correct for baseline differences within the two groups, regression analyses will be performed to estimate a proper estimation between those initially treated at home or after hospitalization. We also planned a sensitivity analysis restricted to those patients who were admitted but discharged after 2 and 3 days, respectively, as these are likely patients who are most comparable to those treated at home. SPSS version 25.0.0 (SPSS, IBM) was used to perform all analyses.

Results

Study Patients

Of all 383 normotensive patients diagnosed with PE, 181 (47%) were treated at home. Overall, the mean age was 59 years (SD: 17), 50% were females, and 12% had active malignancy at the time of diagnosis. Patients initially treated at home were younger with a mean age of 56 years versus 62 years in those initially hospitalized (mean difference: 6.9 years; 95% CI: 3.6–-10.2), and the prevalence of cardiopulmonary comorbidity was higher among those with initial hospitalization. Other baseline patient characteristics between those treated at home and initially hospitalized were comparable. Of note, relevant inter-hospital differences were observed in the proportion of patients treated initially at home with percentages ranging from 13 to 83%.

Health Care Utilization

All patients diagnosed with acute PE visited the emergency room at initial diagnosis and were subjected to laboratory testing and CTPA. The mean hospitalization duration of those treated at home was 0.69 days, whereas patients with initial hospitalization had a mean hospitalization duration of 4.3 days. The 3-month rate of total PE-associated unscheduled readmissions in patients treated at home was 9.7% versus 8.6% for initially hospitalized patients. Proportions for each

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type of unscheduled visit are shown in ►**Table 1**. As part of the hospitals' VTE management protocol, all patients who required in-hospital care were followed at the outpatient clinic two times at week 6 and after 3 months. For those with initial home treatment, an additional visit in the first 2 weeks after the index event was scheduled. The most frequent prescribed anticoagulant was rivaroxaban (56%), followed by apixaban and VKA (both 17%). Dabigatran and edoxaban were each prescribed in 5% of patients.

Health Care Costs

Initial costs for an emergency room visit with subsequent laboratorial costs were €269 and €35, respectively, independent of initial treatment modality. Average total radiological costs for each patient amounted to €220. An overview of the pharmaceutical costs are provided in ►**Table 2**. The average hospital admission cost per patient was € 342 for home treatment compared with the average cost per patient treated initially in hospital of € 2,148. Readmission costs were calculated separately for hospital readmissions, emergency room visits, or unscheduled visits to the outpatient clinic. An overview of these specific extra costs is summarized in ►**Table 2**. No relevant differences were found in total readmission costs for home treatment compared with initial hospitalization, for a mean difference of €34 (95% CI: € − 79 to €146).

Primary Outcome

Total average costs per hospitalized patient were €3,209 and €1,512 per patient treated at home. Thus, the crude average reduction per PE patient in a 3-month follow-up period was €1697 when selecting for home treatment. The adjusted mean difference was €1,483 (95% CI: €1,181–€1,784).

We also performed sensitivity analyses for those with a mean admission duration of 2 or 3 days, and still found considerable mean differences compared with home treatment: the adjusted mean differences were €414 (95% CI: €268–€560) and €1,115 (95% CI: €900–€1,330), respectively.

Table 1 Baseline characteristics and outcome for patients with acute pulmonary embolism of the YEARS study

	Home treatment ($n = 181$)	Initial hospitalization ($n = 202$)
Demographics		
Age, mean (SD)	56 (16)	62 (16)
Male sex, no. (%)	92 (51)	96 (49)
Weight in kg, mean (SD)	85 (17)	86 (18)
Body mass index, mean (SD)	28 (5.4)	28 (5.3)
VTE risk factors		
COPD (%)	6 (3.3)	13 (6.6)
Heart failure (%)	2 (1.1)	6 (3.1)
Previous VTE, no. (%)	49 (27)	41 (21)
DVT	19 (11)	13 (6.6)
PE ± DVT	26 (14)	28 (14)
Estrogen use (%)	23 (13)	17 (8.7)
Active malignancy, no. (%)	20 (11)	26 (13)
Treatment		
Admission days, no. (%)		
0	56 (31)	
1	125 (69)	
2		62 (32)
3		51 (26)
4		21 (11)
5		23 (12)
6–28		38 (19)
> 28		1 (0.5)
Readmissions, no. (%)		
Outpatient visit	–	2 (1.0)
ER visit	9 (5.0)	7 (3.6)
Admission	9 (5.0)	9 (4.6)
Diagnostic imaging performed for suspected VTE recurrence, no. (%)	3 (1.7)	3 (1.5)
Major bleeding, no. (%)	4 (2.2)	4 (2.0)

Abbreviations: DVT, deep vein thrombosis; PE, pulmonary embolism; SD, standard deviation; VTE, venous thromboembolism.
Note: Data of admission days were 7 missing for seven patients.

Discussion

In this analysis, we estimated a €1,483 reduction per acute normotensive PE patient if they were treated at home, instead of initial hospitalization. The decrease in total costs was adjusted for relevant patient characteristics and mainly driven by the reduction in costs for hospital admission. No relevant differences were found in costs for pharmacological treatment and readmissions in patients with home treatment versus those with initial hospitalization.

Global growth in health care expenditure demands effective cost-containment policies to keep health care payable. Introducing home treatment of PE as standard of care is likely to result in considerable cost savings. For example, it is estimated that U.S. health care costs could be reduced by $1 billion per year if home treatment would have been applied properly.[32] These expenses reflect an U.S. perspective, with globally the highest health care costs and also with early hospital discharge initiated in the vast minority of all PE patients.[5] Our data support these U.S. data by showing that significant health care cost reductions can be realized by treating PE patients at home. Current evidence suggests that as much as 30 to 55% of patients with acute PE could be selected for home treatment, which could lead to a considerable global cost reduction.[32,33]

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Table 2 Average health care utilization and costs during a 3-month follow-up period, for patients initially treated at home or in hospital

Type of health care		Unit price	Home treatment		Hospitalization		Cost difference	Adjusted cost difference[a]	95% CI	*p*-Value adjusted
			Volume	Costs	Volume	Costs				
Initial ER visit		€269	1	€269	1	€269	–	–	–	–
Laboratory testing		€35	1	€35	1	€35	–	–	–	–
Radiological imaging	X-ray	€43	0.88	€38	0.88	€37.4	€0.03	€ 2.5	−0.7 to 5.7	0.13
	CTPA	€186	1	€186	1	€186	–	–	–	–
Room and board		€495	0.69	€342	4.34	€2,148	€ −1,806	€ −1,612	−1,900 to −1,324	< 0.001
Pharmacy		€228	1	€228	1	€228	–	–	–	–
PE-related readmission	Admission	€2,475	0.05	€124	0.046	€113	€11	€55	−55 to 164	0.33
	ER	€269	0.05	€13	0.036	€9	€4	€ −2.6	−15 to 10	0.68
	Outpatient visit	€ 95	–	0	0.01	€1	€1	€0.8	−2.4 to 0.78	0.31
Outpatient clinic		€ 95	3	€285	2	€190	€95	–	–	–
All costs				*€1,512*		*€3,209*	*€ −1,697*	*€ −1,483*	*€ −1,784 to −1,181*	*< 0.001*

Abbreviations: CI, confidence interval; CTPA, computed tomography pulmonary angiography; ER, emergency room; PE, pulmonary embolism.
Note: Definitions: Heart failure: a history of known heart failure requiring active treatment. Kidney injury: MDRD < 60 mL/min. Malignancy: active cancer was defined as a diagnosis of cancer that occurred within 6 months before the diagnosis of index VTE (excluding basal-cell or squamous-cell carcinoma of the skin), or any treatment for cancer within the previous 6 months, or recurrent or metastatic cancer. Tachycardia: heart rate > 100 beats/min.
[a]Adjusted for age, gender, COPD, heart failure, kidney injury, malignancy, tachycardia, and oxygen administration.

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This is the first analysis focusing on costs in a detailed patient level with an accurate estimation of costs per patient. The validity and robustness of our model depends on the impact of uncertainties in key input variables. First of all, not all PE patients are candidates for home treatment. Even despite the fact that high-risk PE patients were not taken into account, not all patients who were admitted were candidates for home treatment, which is among others shown by relevant differences in baseline characteristics. These differences reflect the selection of PE patients by the Hestia criteria, selecting lower risk PE patients eligible for home treatment.[11] With regression analysis we performed a correction for relevant baseline characteristic differences, but we acknowledge that still some degree of residual confounding may be present. Comorbid conditions that may prolong the hospital stay, e.g., delirium, were not available in the original YEARS database, and could therefore have a potential effect on the cost difference between patients treated at home or in the hospital. Even so, we think that our present cost estimate is accurate. Moreover, the clear heterogenicity of initiated home treatment between hospitals (ranging from 13 to 83%) suggests the eligibility of home treatment in a considerable proportion of PE patients with current hospitalization, which is favorable to the validity of our analysis. Due to the design of our study, it was not possible to distinguish hospitalized patients who may have been candidates for home treatment from those who were not. Therefore, we performed sensitivity analysis for PE patients with a short hospitalization duration, in which still considerable cost savings were calculated.

Second, readmission costs did not include costs for the treatment of adverse events, i.e., major bleeding or recurrent VTE, which could underestimate the total readmission costs. However, adverse events occurred similarly in both groups and costs for readmission will largely be determined by the length of hospital admission, which was taken into account. Considering the comparable readmission rates between each initial treatment strategy, we think that our present cost estimate is reasonably accurate.

Third, we could not provide differences in pharmaceutical costs between patients treated initial in hospital or at home due to lack of detailed data on medication use. However, total pharmaceutical costs were relatively low compared with the other costs and potential excessive differences within this category between both initial treatment strategies are not expected. Therefore, we do not think no major changes in outcome for this analysis are expected.

Lastly, this analysis reflects on the Dutch health care setting. Cost estimates of hospitalization for VTE vary by country; for example, a study estimating costs per hospitalization for PE estimated the cost to be over $8,700 in the United States (where health care costs are generally highest globally) and over €3,400 in Italy and Belgium.[34] Therefore, the generalizability of this analysis remains to be proven. We have provided our cost analysis calculator in the ►**Supplementary Material** (available in the online version) to be adapted based on local circumstances elsewhere.

To our knowledge this is the first economic comparison for home treatment of PE patients in the current literature. Strengths of this analysis include the detailed estimation of costs per patient working toward total average costs. In contrast to most research studies on health care and health economics using ICD-10 (International Classification of Diseases, Tenth Revision) codes to select for patient eligibility, our database does not contain flaws caused by imperfect coding practice. Further, with patient data of both academic and nonacademic centers, including smaller and larger peripheral hospitals, we consider our results representative for a daily practice cohort in the Netherlands. Lastly, although these results must be interpreted within the framework and limitations of findings of the YEARS study, a management study with possible underrepresentation of high-risk subgroups, the YEARS algorithm was implemented as a standard diagnostic strategy in all participating hospitals. Therefore, we consider the YEARS study patients representative.

In conclusion, home treatment of hemodynamically stable patients with acute PE was estimated to result in a net cost reduction of €1,483. Although, this could be a slight overestimation of real cost difference, it certainly shows the potential for major cost savings on regional or national level, if patients eligible for home treatment for acute PE are not hospitalized. Of note, we only included direct medical costs in this analysis, and indirect medical costs (e.g., loss of productivity in hospitalized patients) would probably further increase the cost difference between patients treated initially in-hospital or as outpatient. With the safety and feasibility of home treatment already been proven in carefully selected patients with PE, this difference underlines the advantage of triage-based home treatment of these patients.

What is known about this topic?

- The introduction of DOAC treatment has resulted in decreased total hospital costs in PE patients.
- The safety and feasibility of home treatment in carefully selected patients with PE has already been proven.

What does this paper add?

- Home treatment of PE patients is associated with an estimated net cost reduction of €1.483 per patient compared with initial hospitalization.
- This difference underlines the advantage of triage-based home treatment of hemodynamically stable PE patients.

Author Contributions

All authors have contributed significantly to this manuscript and take responsibility for the analyses.

Conflict of Interest

F.K. reports research grants from Bayer, Bristol-Myers Squibb, Boehringer-Ingelheim, Daiichi-Sankyo, MSD, Actelion, the Dutch Heart Foundation, and the Netherlands Thrombosis Foundation, outside the

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