# Overall Effectiveness of Rivaroxaban in Patients with Pulmonary Embolism

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## ABSTRACT

**Purpose:** Due to limited evidence on the impact of rivaroxaban in clinical practice, we compared the effectiveness of rivaroxaban versus standard of care (SOC) among patients in the Veterans Health Administration.

**Methods:** Adult patients with continuous enrollment in a health plan with medical and pharmacy benefits for ≥12 months before and ≥3 months after an inpatient diagnosis of pulmonary embolism (PE) between October 1, 2011, and June 30, 2015, and a prescription claim for an anticoagulant during the index hospitalization, were included. SOC drugs were low-molecular-weight heparin, unfractionated heparin, and warfarin. Propensity score matching was used in comparing PE-related outcomes (recurrent venous thromboembolism, major bleeding, and death), hospital-acquired complications (HACs), health care resource utilization, and costs among patients receiving SOC versus rivaroxaban. We defined *net clinical benefit* as 1 minus the combined rate of PE-related outcomes and HACs.

**Findings:** Among 6746 patients with PE, 208 received rivaroxaban, 4641 received SOC and 1897 received other anticoagulants. Most (95%) were male; 22% were black. After 1:3 propensity score matching, there were 203 rivaroxaban and 609 SOC patients. During the 90-day follow-up, rivaroxaban users had similar rates of PE-related outcomes, but fewer had experienced at least 1 HAC (10.3% vs 15.9%; $P = 0.0506$), resulting in better net clinical benefit (82.8% vs 71.1%; $P = 0.001$). Rivaroxaban users had fewer outpatient visits per patient (17.0 vs 19.9; $P = 0.0005$), a similar rehospitalization rate (0.2 vs 0.3; $P = 0.084$), lesser inpatient costs (US $3501 vs $6189; $P < 0.0001$), lesser inpatient costs and lesser total costs ($10,545 vs $14,192; $P = 0.0002$). When the sample was limited to patients with low-risk PE, we found similar patterns.

**Implications:** Patients with PE prescribed rivaroxaban had similar PE-related outcomes, but fewer HACs and lesser total costs, than did patients on SOC. (*Clin Ther*. 2017;39:1426–1436) 

**Key words:** cost burden, hospital-acquired complications, pulmonary embolism, rivaroxaban.

## INTRODUCTION

Pulmonary embolism (PE) is a pulmonary vascular emergency, with an occlusion of the pulmonary artery by a thrombus that requires urgent intervention.[1] It is the third-most common cause of cardiovascular-related death, involved in 300,000 deaths in the United States each year.[2,3] The annual incidence rate of PE is 1.0 per 1000 people, and it increases with age.[4] The mortality rate in patients with untreated acute PE is as high as 30%, whereas the death rate in patients with diagnosed and treated PE is 8%.[5] The economic burden of PE is also substantial, with the

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estimated cost of an initial PE episode ranging from $13,000 to $31,300 per year.[6]

Historically, the standard of care (SOC) in most patients with PE included the administration of low-molecular-weight heparin (LMWH) bridged to the vitamin K antagonist warfarin.[7–9] Although this treatment approach is effective, it has several limitations, including the need for parenteral administration (LMWH), frequent laboratory monitoring, and dose adjustments and the risks for multiple drug–drug and drug–food interactions.[7] Rivaroxaban, a fixed-dose oral direct factor Xa inhibitor, was approved by the US Food and Drug Administration in 2012 for use in the treatment of PE and has been shown to be well tolerated and noninferior to SOC in previous clinical trials.[8] Its use does not require laboratory monitoring, it has no known food interactions, and it has been associated with fewer drug interactions compared with SOC drugs.[9] Additionally, the median hospital length of stay (LOS) was significantly shorter in patients receiving rivaroxaban than in patients receiving SOC therapy.[10,11] A reduction in hospital LOS can potentially reduce the economic burden in patients with PE.[6,12] Results from previous randomized controlled trials have been reported; however, evidence from clinical practice on the impact of rivaroxaban among patients with PE is limited. Therefore, we compared the effectiveness of rivaroxaban versus SOC among patients with PE in a Veterans Health Administration (VHA) population.

## PATIENTS AND METHODS

### Data Source

This longitudinal, retrospective, matched-cohort study assessed data from claims dated October 1, 2010, to September 30, 2015, from the VHA population. The VHA is the largest integrated health care system in the United States, providing care for veterans across the country. According to estimates from the US Department of Veterans Affairs (VA), the system includes 162 VA hospitals, 137 long-term-care facilities, 43 domiciliaries, >850 community and facility-based clinics, 14,800 doctors, 61,000 nurses, and 5 million patients.[13]

Electronic health-related data collected within the VHA's national Medical Statistical Analysis System Dataset and Decision Support System were evaluated, including patients' medical, pharmacy, laboratory, and VHA health plan enrollment information.[14] These data included hospital and outpatient diagnoses (recorded using the *International Classification of Diseases, 9th Revision*—Clinical Modification [ICD-9-CM] codes), procedures (recorded using ICD-9 procedural codes and Current Procedural Terminology codes), laboratory results, and dispensed medication. The *date of death,* if any, was determined using the VA Vital Status file, which ascertains mortality using the Social Security Death master file, Medicare Vital Status files, and VA Beneficiary Identification and Records Locator subsystem.

### Study Population

Patients were included in the study if they were 18 years of age or older, had at least 1 inpatient diagnosis of PE (ICD-9-CM code 415.1, 415.11, or 415.19) during the observation period, had received an anticoagulant (unfractionated heparin, LMWH, warfarin, or a novel oral anticoagulant) during the index hospitalization, and were continuously enrolled in a health plan with medical and pharmacy benefits for at least 12 months prior to the index hospitalization discharge, including the hospital stay (*baseline period*) until 3 months after the index date or until death, whichever occurred first (*follow-up period*). The first PE diagnosis date during the identification period was considered the *initial diagnosis date,* and the discharge date was designated as the *index date*. Patients who were administered subcutaneous heparin during the hospital stay were not included. Patients with a claim containing a code for PE or any anticoagulant, dated prior to the initial diagnosis date, were excluded.

Eligible patients with PE were stratified, using the simplified PE Stratification Index criteria, as having low-risk PE (LRPE) or high-risk PE. In the simplified PE Stratification Index, selected variables of the original score are included (age, history of cancer, history of chronic cardiopulmonary disease, heart rate, systemic blood pressure, and oxygen saturation level). Patients scoring 0 points are considered at low risk. Patients with PE or LRPE were further stratified, based on the prescription claim for an anticoagulant on the index date, into rivaroxaban and SOC cohorts. SOC drugs included LMWH and/or unfractionated heparin along with warfarin. Patients in the SOC cohort did not have a claim for rivaroxaban during the index hospitalization.