CLINICAL RESEARCH STUDY

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# A Prognostic Score to Identify Low-risk Outpatients with Acute Deep Vein Thrombosis in the Lower Limbs

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## ABSTRACT

**BACKGROUND:** No prior studies have identified which patients with deep vein thrombosis in the lower limbs are at a low risk for adverse events within the first week of therapy.

**METHODS:** We used data from the Registro Informatizado de la Enfermedad TromboEmbólica (RIETE) to identify patients at low risk for the composite outcome of pulmonary embolism, major bleeding, or death within the first week. We built a prognostic score and compared it with the decision to treat patients at home.

**RESULTS:** As of December 2013, 15,280 outpatients with deep vein thrombosis had been enrolled. Overall, 5164 patients (34%) were treated at home. Of these, 12 (0.23%) had pulmonary embolism, 8 (0.15%) bled, and 4 (0.08%) died. On multivariable analysis, chronic heart failure, recent immobility, recent bleeding, cancer, renal insufficiency, and abnormal platelet count independently predicted the risk for the composite outcome. Among 11,430 patients (75%) considered to be at low risk, 15 (0.13%) suffered pulmonary embolism, 22 (0.19%) bled, and 8 (0.07%) died. The C-statistic was 0.61 (95% confidence interval [CI], 0.57-0.65) for the decision to treat patients at home and 0.76 (95% CI, 0.72-0.79) for the score ($P = .003$). Net reclassification improvement was 41% ($P < .001$). Integrated discrimination improvement was 0.034 for the score and 0.015 for the clinical decision ($P < .001$).

**CONCLUSIONS:** Using 6 easily available variables, we identified outpatients with deep vein thrombosis at low risk for adverse events within the first week. These data may help to safely treat more patients at home. This score, however, should be validated.

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**KEYWORDS:** Anticoagulant therapy; Deep venous thrombosis; Home; Hospital; Outcome

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Current guidelines of antithrombotic therapy recommend that outpatients with deep vein thrombosis and adequate home circumstances be treated with anticoagulant therapy at home rather than in a hospital.[1] However, in a recent study using data from the Registro Informatizado de la Enfermedad TromboEmbólica (RIETE),[2] <50% of patients had been treated at home, thus suggesting that many physicians are still concerned about the risks of home therapy. The proportion has increased progressively over time, but still in 2012, 1 in every 2 patients was initially treated in a hospital, as also shown in another study.[3] Certainly, even with adequate anticoagulation, some patients with deep vein thrombosis may develop pulmonary embolism, major bleeding, or even die. Unfortunately, there is little evidence that could help identify ideal candidates for home therapy.

RIETE is an ongoing, international (Spain, France, Italy, Israel, Germany, Switzerland, Republic of Macedonia and Brazil), multicenter, prospective registry of consecutive patients presenting with symptomatic acute venous thromboembolism. It started in Spain in 2001, and some years later the database was translated into English aimed to expand the Registry to other countries, ultimately allowing physicians worldwide to use the database to select the most appropriate therapy for their patients. Data from this registry have been used to evaluate outcomes after acute venous thromboembolism, such as the frequency of recurrences, major bleeding, and mortality, and risk factors for such outcomes.[4-7] In the current analysis, we tried to identify characteristics associated with the composite outcome of symptomatic pulmonary embolism, major bleeding, or death within the first 7 days of therapy. Then, we generated a prognostic score to identify patients at low risk. Finally, we applied the C-statistics, net reclassification improvement, and integrated discrimination improvement to assess the incremental prognostic value of the score compared with the clinical decision to treat patients at home.

**CLINICAL SIGNIFICANCE**

- Using 6 easily available variables (chronic heart failure, recent immobility, recent bleeding, active cancer, renal insufficiency, and abnormal platelet count), we identified deep vein thrombosis (DVT) patients at low risk to develop pulmonary embolism, major bleeding, or death within the first week of therapy.
- These data may help to safely treat more DVT patients at home.
- This prognostic score needs to be validated.

## METHODS

Consecutive outpatients with symptomatic acute deep vein thrombosis of the lower limbs confirmed by objective tests (compression ultrasonography or contrast venography) were enrolled in RIETE. Patients were excluded if they were currently participating in a therapeutic clinical trial with a blinded therapy. All patients (or their relatives) provided written or oral consent for participation in the registry, in accordance with local ethics committee requirements.

In the RIETE registry, participating physicians ensured that eligible patients were enrolled consecutively. Data were recorded onto a computer-based case report form at each participating hospital and submitted to a centralized coordinating center through a secure Web site. The study coordinating center assigned patients with a unique identification number to maintain patient confidentiality and was responsible for all data management. Data quality was regularly monitored electronically, including checks to detect inconsistencies or errors, which were resolved by contacting the local coordinators. Data quality also was monitored by periodic visits to participating hospitals by contract research organizations that compared medical records with the submitted data.

### Study Design

For this study, only outpatients with acute deep vein thrombosis in the lower limbs, with no respiratory symptoms suggesting pulmonary embolism, were considered. Home therapy was considered when patients spent <24 hours in the hospital from their arrival in the Emergency Unit. The major outcome was the composite outcome of symptomatic, objectively confirmed pulmonary embolism, major bleeding, or death within the first 7 days. Secondary outcomes were the development of fatal pulmonary embolism or fatal bleeding within the first week. Fatal pulmonary embolism, in the absence of autopsy, was defined as any death appearing within 10 days of a confirmed diagnosis of pulmonary embolism, in the absence of any alternative cause of death. Fatal bleeding was defined as any death occurring within 10 days of a major bleeding episode, in the absence of an alternative cause of death. Major bleeding was defined as an overt bleed that required a transfusion of 2 or more units of blood, was retroperitoneal, spinal, or intracranial, or was fatal.

### Baseline Variables

The following parameters were recorded when the qualifying episode of deep vein thrombosis was diagnosed: patient's sex, age, and body weight; presence of coexisting conditions such as chronic heart or lung disease; recent (<30 days before the thrombotic event) major bleeding; presence of risk factors for deep vein thrombosis, including active cancer (defined as newly diagnosed cancer or cancer that is being treated [ie, with surgery, chemotherapy, radiotherapy, hormonal or supportive therapy]); recent immobilization (defined as nonsurgical patients who were confined to bed with bathroom