



# Home Treatment of Pulmonary Embolism in the Era of Novel Oral Anticoagulants

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## ABSTRACT

**BACKGROUND:** Outpatient therapy of patients with acute pulmonary embolism has been shown to be safe in carefully selected patients. Problems related to the injection of low-molecular-weight heparin at home can be overcome by use of novel oral anticoagulants. The purpose of this investigation is to assess the prevalence of home treatment in the era of novel oral anticoagulants.

**METHODS:** This was a retrospective cohort study of patients aged  $\geq 18$  years with acute pulmonary embolism seen in 5 emergency departments from January 2013 to December 2014.

**RESULTS:** Pulmonary embolism was diagnosed in 983 patients. Among these, 237 were considered ineligible for home treatment because of instability or hypoxia. Home treatment was selected for 13 of 746 (1.7%) patients who were potentially eligible. Anticoagulant treatment for those treated at home was low-molecular-weight heparin or warfarin in 9 (69.2%) and novel oral anticoagulants in 4 (30.8%). Hospitalization was chosen for 733 of 746 (98.3%). Discharge in  $\leq 2$  days was in 119 patients (16.2%). Treatment of these patients was low-molecular-weight heparin or warfarin in 76 (63.9%), novel oral anticoagulants in 34 (28.6%), and in 9 (7.6%), anticoagulants were not given because of metastatic cancer or treatment was not known.

**CONCLUSION:** Even in the era of novel oral anticoagulants, the vast majority of patients with acute pulmonary embolism were hospitalized, and only a small proportion were discharged in  $\leq 2$  days. Although home treatment has been found to be safe in carefully selected patients, and scoring systems have been derived to identify those at low risk of adverse events, home treatment was infrequently selected.

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**KEYWORDS:** Home treatment; Oral anticoagulants; Pulmonary embolism; Venous thromboembolism

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Pulmonary embolism traditionally has been perceived as a serious condition requiring hospitalization, and established attitudes can be hard to change.<sup>1</sup> Randomized trials,<sup>2,3</sup> systematic reviews,<sup>4-7</sup> and meta-analysis<sup>8</sup> showed that

outpatient therapy of acute pulmonary embolism is safe in low-risk, carefully selected compliant patients who have access to outpatient care if necessary. Investigations of outpatient treatment of acute pulmonary embolism have been reported since 2000.<sup>9</sup> Review identified 1374 patients with pulmonary embolism who were treated entirely as outpatients,<sup>2,9-21</sup> 102 who were hospitalized  $\leq 24$  hours,<sup>2,10,17</sup> and 297 patients were treated either at home or after  $\leq 24$  hours hospitalization.<sup>22</sup> Among these patients, death from pulmonary embolism occurred in 0.06% and nonfatal recurrent pulmonary embolism occurred in 1.5%. Fatal bleeding occurred in 0.11% and nonfatal major bleeding occurred in 1.5%. All patients treated entirely at

**Funding:** None.

**Conflict of Interest:** None.

**Authorship:** All authors had access to the data and a role in writing the manuscript.

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home or after early discharge were considered to be at low risk of dying from pulmonary embolism and low risk of bleeding. Typical exclusions were patients in shock, those who required oxygen, parenteral treatment for pain, and those with concomitant medical conditions. Most of these patients (1713) were treated with low-molecular-weight heparin followed by warfarin.<sup>2,9-20,22</sup>

Rivaroxaban was used in one investigation of 30 patients.<sup>21</sup> A possible hesitancy in the use of home treatment may relate to logistic problems. Problems related to the injection of low-molecular-weight heparin at home can be overcome by the use of novel oral anticoagulants. The oral factor Xa inhibitors rivaroxaban and apixaban were approved for treatment of deep venous thrombosis and pulmonary embolism by the US Food and Drug Administration on November 2, 2012 and August 21, 2014, respectively.<sup>23,24</sup> Whether the availability of novel oral anticoagulants has resulted in physicians selecting home treatment for patients with pulmonary embolism is not known. The purpose of this investigation is to assess the prevalence of home treatment of acute pulmonary embolism in the era of novel oral anticoagulants.

## METHODS

This was a retrospective cohort study of patients aged  $\geq 18$  years with acute pulmonary embolism seen in 5 emergency departments from January 2013 to December 2014. Collaborating sites were McLaren Oakland Hospital, Pontiac, Mich.; Summa Akron City Hospital, Akron, Ohio; St. Mary Mercy Hospital, Livonia, Mich.; University of Toledo, Medical Center of Ohio, Toledo, Ohio; and Sparrow Hospital, Lansing, Mich. The medical records of patients aged 18 years or older with pulmonary embolism seen on the emergency service were manually reviewed. These records were identified by searching for patients discharged from the emergency service with International Classification of Diseases, Ninth Edition, Clinical Modification code 415.1. Comorbid conditions were largely those identified by the Charlson Index.<sup>25</sup> This investigation was approved by the Institutional Review Boards of each of the participating centers.

## RESULTS

Pulmonary embolism was diagnosed in the emergency departments January 2013-December 2014 in 983 patients. Among these, 80 were hypotensive (systolic blood pressure  $< 90$  mm Hg), on vasopressors, or on ventilator support. In addition, 157 had an arterial oxygen saturation of  $\leq 90\%$ .

These patients were considered ineligible for home treatment, and therefore, excluded. There remained 746 patients who were potentially eligible for home treatment of pulmonary embolism. The diagnosis of pulmonary embolism was made by computed tomographic angiography in 695, ventilation-perfusion lung scan in 37, positive venous ultrasound with clinical findings of pulmonary embolism in 5, and in 9 the method of diagnosis was not stated.

Home treatment was chosen for 13 of 746 (1.7%) stable patients with pulmonary embolism who were not hypoxic. Anticoagulant treatment for those treated at home was low-molecular-weight heparin or warfarin (or both) in 9 (69.2%) and novel oral anticoagulants in 4 (30.8%). Patients treated at home were aged  $56 \pm 17$  years (mean  $\pm$  standard deviation); 8 (61.5%) were male. Among those treated at home, 10 had no comorbid conditions and 3 had cancer. Two

(15.4%) were considered at high risk of bleeding. One patient was dyspneic at rest.

Hospitalization was chosen for 733 of 746 (98.3%). Patients treated in the hospital were aged  $59 \pm 18$  years; 340 (46.4%) were male. No comorbid conditions were present in 319 of 733 (43.5%). Comorbid conditions in hospitalized patients are shown in the **Table**. A high risk of bleeding was assessed in 128 of 733 (17.5%). Dyspnea at rest was present in 260 of 733 (35.5%).

Discharge in  $\leq 2$  days was in 119 of 733 patients (16.2%). The length of stay of hospitalized patients is shown

### CLINICAL SIGNIFICANCE

- Even in the era of novel oral anticoagulants, the vast majority of patients with acute pulmonary embolism were hospitalized.
- Only a small proportion of hospitalized patients with pulmonary embolism were discharged in  $\leq 2$  days.
- Novel oral anticoagulants were administered to less than one-third of patients with pulmonary embolism treated entirely at home or discharged early.

**Table** Comorbid Conditions in 733 Hospitalized Patients with Pulmonary Embolism

Comorbid Condition	Number (%)
Heart failure	21 (2.9)
History of myocardial infarction	7 (1.0)
Peripheral vascular disease	25 (3.4)
Cerebrovascular disease	40 (5.5)
Dementia	33 (4.5)
Chronic obstructive pulmonary disease	79 (10.8)
Rheumatologic disease	30 (4.1)
Ulcer disease	12 (1.5)
Acute or chronic liver disease	8 (1.1)
Diabetes mellitus	118 (16.1)
Hemiplegia and hemiparesis	5 (4.1)
Moderate or severe renal disease	37 (5.0)
Any neoplasms, leukemia, lymphoma	161 (22.0)
Metastatic cancer	53 (7.2)

Patients may have had more than one comorbid condition.

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