



## RECOMMENDED ARTICLE OF THE MONTH

### Comment on “Outpatient versus inpatient treatment for patients with acute pulmonary embolism: an international, open-label, randomised, non-inferiority trial”

**Outpatient versus inpatient treatment for patients with acute pulmonary embolism: an international, open-label, randomised, non-inferiority trial.**

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## Abstract

**Background:** Although practice guidelines recommend outpatient care for selected, haemodynamically stable patients with pulmonary embolism, most treatment is presently inpatient based. We aimed to assess non-inferiority of outpatient care compared with inpatient care.

**Methods:** We undertook an open-label, randomised non-inferiority trial at 19 emergency departments in Switzerland, France, Belgium, and the USA. We randomly assigned patients with acute, symptomatic pulmonary embolism and a low risk of death (pulmonary embolism severity index risk classes I or II) with a computer-generated randomisation sequence (blocks of 2-4) in a 1:1 ratio to initial outpatient (ie, discharged from hospital  $\leq 24$  h after randomisation) or inpatient treatment with subcutaneous enoxaparin ( $\geq 5$  days) followed by oral anticoagulation ( $\geq 90$  days). The primary outcome was symptomatic, recurrent venous thromboembolism within 90 days; safety outcomes included major bleeding within 14 or 90 days and mortality within 90 days. We used a non-inferiority margin of 4% for a difference between inpatient and outpatient groups. We included all enrolled patients in the primary analysis, excluding those lost to follow-up. This trial is registered with ClinicalTrials.gov, number NCT00425542.

**Findings:** Between February, 2007, and June, 2010, we enrolled 344 eligible patients. In the primary analysis, one (0.6%) of 171 outpatients developed recurrent venous thromboembolism within 90 days compared with none of 168 inpatients (95% upper confidence limit [UCL] 2.7%;  $p=0.011$ ). Only one (0.6%) patient in each treatment group died within 90 days (95% UCL 2.1%;  $p=0.005$ ), and two (1.2%) of 171 outpatients and no inpatients had major bleeding within 14 days (95% UCL 3.6%;  $p=0.031$ ). By 90 days, three (1.8%) outpatients but no inpatients had developed major bleeding (95% UCL 4.5%;  $p=0.086$ ). Mean length of stay was 0.5 days (SD 1.0) for outpatients and 3.9 days (SD 3.1) for inpatients.

**Interpretation:** In selected low-risk patients with pulmonary embolism, outpatient care can safely and effectively be used in place of inpatient care.

## Comment

The 2008 guidelines on the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC) classify pulmonary embolism (PE) patients in three groups according to the severity of PE: high-risk patients with a PE-related early mortality risk  $>15\%$ ; intermediate-risk patients with mortality risk between 3 and 15%; and low-risk patients with a mortality risk of less than 1%.<sup>1</sup>

The low-risk subgroup includes hemodynamically stable patients without evidence of right ventricular dysfunction or myocardial injury.

The same guidelines also recognize that routinely collected clinical and laboratory data may also have prognostic implications in acute PE when integrated into a weighted score. Such a score, also accounting for the pre-existing condition and the patient’s comorbidities, can be of help when considering early discharge and ambulatory treatment of patients with otherwise low-risk PE.

Some severity indexes have in fact been prospectively validated and enable risk stratification and identification of low-risk patients.<sup>2,3</sup>

Despite these facts, most PE patients are still treated in-hospital even when they present a low risk of PE-related complications.

In recent years, however, several authors have published results on the safety of early discharge and ambulatory treatment of low-risk PE patients, and systematic reviews of these results were also published.<sup>4,5</sup>

The work by Aujesky D et al., published in July 2011 in the *Lancet*, constitutes an important landmark in this issue. This international, open-label, randomized non-inferiority trial clearly shows that the number of thromboembolic events and hemorrhagic complications was very small in a group of low-risk patients and not significantly different between the subgroups (ambulatory and in-hospital).<sup>6</sup>

This study also supports the recommendation for early discharge of low-risk PE patients.

Proper clarification on the correct use of anticoagulant drugs in ambulatory patients could minimize the number of hemorrhagic events related to this therapy.

Reduction of hospital length of stay in this subgroup of PE patients appears a safe, rational and attainable goal to be considered by attending physicians.

### Conflicts of interest

The author has no conflicts of interest to declare.

### References

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