ERJ Express. Published on June 13, 2007 as doi: 10.1183/09031936.00140506

EARLY DISCHARGE OF PATIENTS WITH PULMONARY EMBOLISM: A TWO-PHASE OBSERVATIONAL STUDY

1. Dr CWH Davies
Consultant Physician
Royal Berkshire Hospital NHS Trust
London Road
Reading
RG1 5AN

Email: Chris.Davies@royalberkshire.nhs.uk
Fax: 0044 (0)118 322 8525

2. Dr J Wimperis
Consultant Haematologist
Norfolk and Norwich Healthcare NHS Trust
3. Dr ES Green
Consultant Haematologist
Swindon and Marlborough NHS Trust
4. Dr K Pendry
Consultant Haematologist
Wrightington, Wigan and Leigh NHS Trust
5. Dr J Killen
Consultant Physician
Gateshead Health NHS Trust
6. Dr I Mehdi
Consultant Physician
Milton Keynes General NHS Trust
7. Dr C Tiplady
Consultant Haematologist
Northumbria Healthcare NHS Trust
8. Dr P Kesteven
Consultant Haematologist
Newcastle upon Tyne Hospitals NHS Trust
9. Dr P Rose
Consultant Haematologist
University Hospitals Coventry and Warwickshire NHS Trust
10 Dr W Oldfield
Consultant Physician
St Mary's NHS Trust

Key Words
Pulmonary embolism
Low molecular weight heparin
Warfarin
Early Discharge
Home supervision

Total word count Abstract 200 Paper 3,330

ERJ resubmission
April 2007

Abstract

This study assessed whether patients with pulmonary embolism (PE) could be managed as outpatients (OP) after early discharge from hospital using low molecular weight heparin (LMWH) instead of remaining as inpatients until achieving effective oral anticoagulation.

Phase 1 identified criteria for safe discharge of selected patients and phase 2 treated a cohort of low-risk patients with PE as OP with tinzaparin using existing deep vein thrombosis (DVT) services. In phase 1, 127/225 (56.4%) patients were considered unsuitable for OP management. Reasons included: admission for another medical reason; additional monitoring or requirement for oxygen; bleeding disorders; previous PE/further PE whilst on warfarin; co-existing major DVT; likelihood of poor compliance; significant immobility; pregnancy.

In phase 2, 157 patients with PE received OP anticoagulation. There were no deaths, bleeding or recurrent thromboembolic events during acute treatment with LMWH. Median length of hospital stay was 1.0 (range 1 to 4) day. Median of 5.0 (range 1 to 42) bed days were saved per patient.

Patients were highly satisfied with OP management. 144 (96.6%) indicated they would prefer treatment as OP for a subsequent PE. Early discharge and OP management of PE appears safe and acceptable in selected low-risk patients and can be implemented using existing outpatient DVT services.

Introduction:

Pulmonary embolism (PE) is a major cause of admission to hospital with an incidence of approximately 23 per 100,000 population[1,2]. As PE and deep vein thrombosis (DVT) often co-exist as venous thromboembolism (VTE), many patients presenting with symptomatic DVT will have asymptomatic pulmonary emboli and vice versa[3-6]. The management of VTE is now well established with an initial period of treatment with subcutaneous low molecular weight heparin (LMWH) followed by a variable period of oral anticoagulation. As some LMWHs may be administered as a once-daily subcutaneous injection and does not require coagulation monitoring, most patients with confirmed DVT now receive outpatient anticoagulation organised by teams of specialist nurses[7-11]. As PE is part of the same disease process, it may be possible to extend outpatient management to selected low risk patients, in contrast to the current situation where the vast majority of patients remain as inpatients until oral anticoagulation is established.

To date no randomised studies have been published comparing ambulatory versus inpatient management of PE. Five small prospective studies[12-16] and several retrospective studies[17-20] have reported outcomes of outpatient management and indicate that treatment is safe in selected individuals. The British Thoracic Society (BTS) guidelines for the management of suspected PE acknowledge some patients might be treated out of hospital and recommend that the current organisation for outpatient management of DVT should be extended to include stable patients with PE[21]; however the guideline provides no criteria to help develop this service.

This two-phase study identified patients at low-risk of adverse outcome from management of PE, and assessed the acceptability of early discharge, and subsequently validated a set of exclusion criteria for early discharge management using LMWH in a prospective cohort of patients with confirmed PE.

Methods:

Phase 1

Phase 1 was a prospective multi-centre cohort study performed in 5 centres within the UK (Royal Berkshire Hospital NHS Trust, Reading; Swindon and Marlborough NHS Trust, Wrightington, Wigan and Leigh NHS Trust, Norfolk and Norwich Healthcare NHS Trust, NHS Lothian – University Hospitals Division) over a 12 month period commencing August 2001. Multicentre and Local Research and Ethics Committees approved the study protocol.

Patients

All patients over the age of 18 years admitted with symptoms and/or signs of possible pulmonary embolism were included. Anonymous demographic and clinical data were collected on each subject at admission. A positive diagnosis of PE was based on investigations including ventilation/perfusion (V/Q) or perfusion (Q) scans, CT pulmonary angiography (CTPA), or lower limb imaging (venography or ultrasound) when patient had symptoms compatible with a PE and evidence of DVT. If PE was confirmed, patients commenced warfarin according to local anticoagulation protocols and remained in hospital in all centres until oral anticoagulation was adequate (International

Normalised Ratio INR target range 2-3) and LMWH had been discontinued. For each patient diagnosed with PE, the clinician responsible for patient care was asked about the theoretical suitability of the patient for inclusion in an early discharge protocol. At this stage there was no suggested exclusion list and the physicians gave the reason themselves. For each patient deemed unsuitable for outpatient management, the clinician recorded the indication(s) for exclusion. This information was only collected on patients with confirmed PE and at the time diagnosis was confirmed. None of the patients were managed as outpatients or actually given early discharge.

Follow-up and outcome

Patients' outcome was assessed at the end of acute LMWH treatment and 3 months after commencing anticoagulation. Outcome measures included: 1) early bleeding complications (during acute inpatient anticoagulation with LMWH), 2) later bleeding complications (i.e. on oral anticoagulants), 3) thromboembolic complications (with objective confirmation), 4) mortality at 3 months (cause of death was taken from the death certificate entry and this was clarified by the lead clinician at the relevant site where possible). Bleeding was classified as minor or major. Major bleeds were defined as overt bleeding causing a fall in haemoglobin of more than 2g/dL, requirement for transfusion of 2 or more units of blood, retroperitoneal or intracranial bleeding or bleeding into a major prosthetic joint[22].

Phase 2

Phase 2 was a prospective multi-centre cohort study to validate the criteria for exclusion derived from phase 1 in order to assess safety and acceptability of

early discharge and outpatient treatment. Patients were recruited from 10 centres between October 2003 to February 2006. Centres were invited to participate based on established nurse-led outpatient DVT services. Multicentre and Local Research and Ethics Committees approved the study protocol.

Objectives

The primary objective was to estimate the incidence of major bleeding complications, thromboembolic complications and death, in a cohort of patients treated for PE using tinzaparin in an early discharge protocol at the end of the acute phase of treatment.

The secondary objectives were to a) estimate the incidence of major bleeding complications, thromboembolic complications and death, in a cohort of patients treated for PE using tinzaparin in an early discharge protocol during the 3 month period following confirmation of a PE, b) to estimate the number of bed days that could be saved by discharging the appropriate patient groups to receive early outpatient treatment, and c) to assess patient satisfaction with early discharge and treatment out of hospital.

Patients

Inclusion criteria

Patients were identified as soon possible after admission by the local study team and considered for early discharge once objective testing confirmed the diagnosis of PE. To be eligible for early discharge diagnosis of PE had to be confirmed within 72 hours of initial assessment. PE was defined as 1) clinical

features of PE plus high probability V/Q or Q scan, 2) clinical features of PE plus positive CT pulmonary angiogram, or 3) clinical features of PE plus confirmed DVT by any imaging technique. All patients had to be age 18 years or over and provide informed consent.

Exclusion criteria for outpatient treatment

Patients were excluded from early discharge if they: 1) required admission for another medical reason (e.g. significant respiratory and/or cardiovascular disease and/or treatment for active malignancy), 2) required additional monitoring such as ECG monitoring or administration of any form of oxygen therapy for hypoxemia or administration of any intravenous drugs including analgesia, 3) history of previous PE or further PE developing whilst currently on anticoagulation treatment, 4) had co-existing major DVT (high segment femoral and above) confirmed by radiological imaging, 5) bleeding disorders or active bleeding, 6) pregnancy, 7) likelihood of poor compliance or difficulty ensuring appropriate follow-up, including complex elderly patients, infirm, significant immobility, geographic inaccessibility, history of non-compliance, IV drug abuser, 8) patient preference.

Once recruited into the study patients either attended hospital for daily LMWH injections and INR monitoring, or had these administered in Primary Care according to the local ambulatory DVT service. All patients received an information leaflet about the study and anticoagulation and were instructed to report any symptoms or signs of VTE and/or bleeding. A 24-hour emergency telephone number was provided. Patients receiving LMWH for 7 or more days had a full blood count to assess possible heparin induced thrombocytopenia.

When patients did not attend for the daily injection or were not contactable the GP was contacted by telephone.

Follow up

At the completion of LMWH treatment (the 'acute treatment phase') all patients were reviewed by the specialist nurses' co-ordinating care. The patient was asked to complete a satisfaction score. This asked how satisfied they were with the management of this PE using a visual analogue score, zero indicating poor satisfaction and 10 indicating total satisfaction. Patients were also asked whether they would prefer to receive treatment for a subsequent PE as an inpatient or outpatient.

Further outpatient follow up occurred for all patients at 3 months from study entry to establish any subsequent complications during the 'late treatment phase' whilst on oral anticoagulation. Outcomes measures were as described for phase 1. Any patients who did not attend the 3-month follow-up were contacted directly by telephone and where necessary their GP was contacted to establish end-points.

Treatment Protocols (both phase 1 and 2)

On admission patients were initially commenced on subcutaneous tinzaparin 175 IU/kg once daily (Innohep®, LEO Pharma). If PE was confirmed warfarin was commenced and tinzaparin was discontinued when a therapeutic INR (target range 2-3) was achieved.

Statistical Methods

For both phases of the study the number of complications was described for the acute and late treatment periods using the number and percentage of patients for each outcome (thromboembolic event, minor bleed, major bleed and mortality, readmission to hospital in phase 2). Duration of hospital stay and length of treatment with LMWH are shown as median (with 95% confidence intervals). For phase 2 the treatment duration of tinzaparin after discharge was used as a surrogate measure of the bed days saved. The patient satisfaction score and patient preference are presented as the number and percentage of patients with each score or category, respectively.

Results

Phase 1

Subjects

In phase 1 of the study, 643 patients presented with suspected PE, 225 (35.0%) were diagnosed and subsequently treated for PE (age deleted here) (109 (48.4%) male). Pulmonary embolism was diagnosed by V/Q scan in 161/225 (71.6%) and Q scan in 11/225 (4.9%), CTPA scanning in 45/225 (20.0%), and by lower limb ultrasound in 8/225 (3.6%). Median time to diagnosis was 2.0 (range 0 to 15; 95% CI for median 1 to 2) days. These patients received a median of 7.0 (range 1 to 26) days tinzaparin and had a median in-patient stay of 7.0 (range 0 to 77) days. Complete three month follow up data were available in 202/225 (89.8%) of PE treated subjects.

Suitability for early discharge

Of the 225 patients, 98 (43.6%) were considered suitable for outpatient management at the time of diagnosis, including 85 (42.1%) of 202 patients with 3 month follow up data. The median age of the patients in phase 1 considered suitable for early discharge was 59 (range 19 to 91) years. For the remaining 127 patients considered unsuitable, 5 categories of exclusion reasons for remaining in hospital for treatment were given (table 1).

Table 1: Phase 1 - Reasons given for non-suitability for early discharge (n=127 patients)

Reason	Number (percentage of total number of reasons)
Patient requires admission for additional monitoring, administration of any form of oxygen therapy and/or hypoxemia or for another medical reason (e.g. significant respiratory and/or cardiovascular disease and/or treatment for active malignancy) requiring admission	70 (43.2%)
Likelihood of poor compliance or difficulty ensuring appropriate follow-up, including complex elderly patients, infirm, significant immobility, geographic inaccessibility, history of non-compliance, IV drug abuser	47 (29.0%)
History of previous PE or further PE and currently on treatment	12 (7.4%)
Co-existing major DVT (high segment femoral and above)	8 (4.9%)
Others (e.g. bleeding disorders or active bleeding, pregnancy)	25 (15.4%)

Outcomes

During the 'acute treatment phase' there were no deaths, thromboembolic events or major bleeding events (table 2). There was 1/225 (0.4%) minor bleeding event (a small cutaneous haematoma). During the 3 months follow up during oral anticoagulation (table 2), there were 9/202 (4.5%) deaths, 10/202 (5.0%) bleeding events (6 major and 4 minor) and 6/202 (3.0%) thromboembolic events. Deaths were due to carcinomatosis (n=5; including 1 patient with an additional reason of ischaemic heart disease, PE and DVT), haemorrhagic stroke (n=2), pneumonia (n=1) and PE (n=1). Late phase thromboembolic complications were due to PE (n=2), DVT (n=2), both PE and DVT (n=1) and non fatal stroke (n=1).

Table 2: Outcome data – Phase 1 (225 patients with 3 month follow up data available on 202 patients)

At the end of the acute LMWH treatment phase			
Outcome	All suspected PEs **(n=225)**	Patients considered suitable for early discharge (n=98)	Patients not considered suitable for early discharge (n=127)
Recurrent thromboembolic complications			
Thromboembolic event	0 (0%) 95%CI: 0.0 to 1.6%	0 (0%) 95%CI: 0.0 to 3.7%	0 (0%) 95%CI: 0.0 to 2.9%
Bleeding complications			
Minor bleed	1(0.4%) 95%CI: 0.0 to 2.5%	0 (0%) 95%CI: 0.0 to 3.7%	1 (0.8%) 95%CI: 0.0 to 4.3%
Major bleed	0 (0%) 95%CI: 0.0 to 1.6%	0 (0%) 95%CI: 0.0 to 3.7%	0 (0%) 95%CI: 0.0 to 2.9%
Mortality			
Deaths	0 (0%) 95%CI: 0.0 to 1.6%	0 (0%) 95%CI: 0.0 to 3.7%	0 (0%) 95%CI: 0.0 to 2.9%
At 3 months after commencing treatment for PE			
Outcome	All suspected PEs **(n=202)**	Patients considered suitable for early discharge (n=85)	Patients not considered suitable for early discharge (n=117)
Recurrent thromboembolic complications			
Thromboembolic event	6 (3.0%) 95%CI: 1.1 to 6.4%	2 (2.4%) 95%CI: 0.3 to 8.2%	4 (3.4%) 95%CI: 0.9 to 8.5%
Bleeding complications			
Minor bleed	4 (2.0%) 95%CI: 0.5 to 5.0%	3 (3.5%) 95%CI: 0.7 to 10.0%	1 (0.9%) 95%CI: 0.0 to 4.7%
Major bleed	6 (3.0%) 95%CI: 1.1 to 6.4%	3 (3.5%) 95%CI: 0.7 to 10.0%	3 (2.6%) 95%CI: 0.5 to 7.3%
Mortality			
Deaths	9 (4.5%) 95%CI: 2.1 to 8.3%	3 (3.5%) 95%CI: 0.7 to 10.0%	6 (5.1%) 95%CI: 1.9 to 10.8%

Phase 2

Subjects

157 patients with confirmed PE were entered: median age 58 (range 18-85) years and 86 (54.8%) male. The 3-month follow up was completed by 156 patients. Pulmonary embolism was diagnosed by V/Q in 85 (54.1%) and Q scans in 2 (1.3%), CTPA scanning in 65 (41.4%) and by lower limb ultrasound in 5 (3.2%). The median time to diagnosis was 1.0 (range 0 to 3; 95% CI of the median 0 to 1) days. The median length of hospital stay was 1.0 (range 0 to 3 days) distributed as 0-24 hours: 91 (58.0%), 24-48 hours 33 (21.0%), 48-72 hours 33 (21.0%). Patients received a median 7 (range 3-46) days of tinzaparin. The median number of days treated as an outpatient with tinzaparin was 5 (range 1-42) days. The total number of days treated as outpatients (bed days saved) for all patients was 990 days.

Outcomes

There were no deaths, thromboembolic events or bleeding events during the acute treatment phase (table 3). Three patients required readmission due to complications unrelated to PE (1 anxiety episode, 1 pneumonia, 1 asymptomatic high INR) during the acute treatment phase. During the late treatment phase (3 month follow-up) there were 3 (1.9%) deaths (1 abdominal bleed/sepsis due to neutropenia 25 days post acute phase, 1 cancer oesophagus with bronchopneumonia 35 days post acute phase, 1 cancer/cardiac failure 43 days post acute phase), 1 minor rectal bleed 80 days post acute phase and no thromboembolic events.

Table 3: Phase 2 outcome data from patients with confirmed PE treated as outpatients

At the end of the acute LMWH treatment phase (n=157)	
Outcome	Number (percentage)
Recurrent thromboembolic complications	
Thromboembolic event	0 (0%) 95%CI: 0.0 to 2.3%
Bleeding complications	
Minor bleed	0 (0%) 95%CI: 0.0 to 2.3%
Major bleed	0 (0%) 95%CI: 0.0 to 2.3%
Mortality	
Deaths	0 (0%) 95%CI: 0.0 to 2.3%
Readmission to hospital	
Related	0 (0%)
Unrelated	3 (1.9%)
At 3 months after commencing treatment for PE (n=156)	
Outcome	Number (percentage)
Recurrent thromboembolic complications	
Thromboembolic event	0 (0%) 95%CI: 0.0 to 2.3%
Bleeding complications	
Minor bleed	1 (0.6%) 95%CI: 0.0 to 3.5%
Major bleed	0 (0%) 95%CI: 0.0 to 2.3%
Mortality	
Deaths	3 (1.9%) 95%CI: 0.4 to 5.5%

Patient satisfaction

124/157 (79.0%) completed the satisfaction score (table 4). Eighty-one (65.3%) patients gave a score of 10 indicating the majority of patients were highly satisfied with OP management. Of 149/157 (94.9%) of patients expressing a preference, 144/149 (96.6%) patients indicated that they would prefer to receive treatment for a subsequent PE as an outpatient.

Table 4: Phase 2 - Patient satisfaction at end of the acute LMWH treatment phase

Patient satisfaction scores 0-10 (n=124)	
Score	Number (percentage)
0-4	0 (0%)
5-7	9 (7.3%)
8	19 (15.3%)
9	15 (12.1%)
10	81 (65.3%)
Mean	9.28 (SD 1.2)
Median	10 (95% CI 9.07-9.49)
Patient preference (n=149)	
Inpatient management	5 (3.4%)
Outpatient management	144 (96.6%)

Note: 33 patients did not complete the patient satisfaction score and 8 patients did not complete the preference for treatment question.

Discussion

This two-phase study has derived a series of exclusion criteria for early discharge management of PE and prospectively shown that selected patients with PE can be safely managed with outpatient anticoagulation using tinzaparin with a consequent reduction in hospital stay of approximately 5 days per patient. Outpatient treatment after early discharge was highly acceptable to patients and using once-daily tinzaparin required no significant laboratory monitoring. There were no significant complications or deaths in the acute treatment phase with LMWH when traditionally patients have been kept in hospital. The results from Phase 1 suggest that early discharge and outpatient anticoagulation may be suitable for nearly half of all patients with confirmed PE. A major strength of this study is that we have demonstrated that it is relatively straightforward to implement an ambulatory PE service where there are existing nurse-led DVT services with established local procedures for outpatient DVT treatment, thereby with minimal cost implications. The variety of centres that participated involving both district general and regional teaching hospitals also implies that this approach is widely applicable and not restricted to specialist centres.

Whilst performing this study, we have been aware of apprehension from medical colleagues about the safety of outpatient PE management. This concern is similar to the development of outpatient DVT management seen a decade ago and may have influenced the ability to enter all suitable patients with PE into this study. The initial outpatient DVT studies were interpreted with caution but further studies confirmed both the safety and acceptability of

outpatient DVT management allowing up to 91% of patients to be managed without admission[10,11,14,23]. As a significant proportion of patients with DVT will also have silent PE (as defined by high probability V/Q scan)[3-6], it is likely that many patients who receive outpatient treatment for DVT have also had outpatient treatment of PE. Mortality and morbidity from PE is highest in those presenting with features of massive PE and in those with other established risk factors for mortality including co-morbidity from cancer, chronic cardiovascular and respiratory disease, right ventricular dysfunction on echocardiography[24] and elevation of cardiac troponin[25], brain natruretic peptide (BNP) and/or NT proBNP[26,27]. However, mortality for other PE patients on adequate anticoagulation is actually low (<2%), with the risk of mortality within the first 7 days less than 1%[7,28]. Echocardiography and biochemical predictive tests were not measured routinely as part of this study as neither was routinely available in these centres at the time the study commenced. This is a major limitation to the study and should be considered in future studies attempting to stratify risk associated with the outpatient treatment of PE.

Previous smaller studies have also identified subgroups of PE patients who appear to be suitable for safe outpatient management of PE. Wells *et al*[14] treated 34 patients with PE and assessed both home care nursing and patient administration of dalteparin, and found this acceptable and safe with few complications of therapy. The same group have published their experience of a further 108 subjects with PE treated as outpatients using the following criteria; 1) a medical condition which necessitated admission to hospital for another reason, 2) active bleeding or high risk of bleeding, 3) haemodynamic

instability, 4) pain requiring parenteral narcotics, 5) requirement for oxygen therapy to maintain saturation greater than 90%, 6) age less than 18 years, 7) likelihood of poor compliance[12]. Phase 1 of our study derived similar criteria for exclusion to safe outpatient PE management which were used in phase 2. As with the Kovacs study[12], some of the criteria we used are relatively subjective such as the need for admission for another medical condition, the need for additional monitoring or treatments, and estimates of poor compliance. In our study we did not define a specific level of oxygen required to maintain oxygen saturation and instead excluded anyone where the managing clinician felt the patient required ongoing oxygen therapy for dyspnoea and/or hypoxemia. The study by Kovacs *et al* had a much higher incidence of complications than our study, which may reflect different patient selection despite the similar exclusion criteria and could be due to interobserver variability of the application of these criteria. This potential for bias has not been formally assessed in either study. Recurrent VTE is also a risk factor for mortality, up to 26% in one case series[29] and so patients developing recurrent PE were excluded in our study to ensure that only the safest patients were considered for outpatient treatment. It may be unnecessary to exclude these patients in future treatment protocols. In the Canadian studies[12,14] support was provided with daily telephone contact by a research nurse, access to a 24 hour telephone helpline and follow up clinics at 1 week, 1 month and 3 months. A similar level of support should be possible in centres wishing to implement outpatient anticoagulation of PE using existing DVT nurse led services and on call medical staff.

Although phase 1 of the study was able to capture all suspected and subsequently confirmed patients with PE, we know this was not achieved in consecutive patients in all centres in phase 2, which is a weakness of the study. Where possible all potential patients with PE were notified by medical staff from the different teams caring for these patients and by liaison with radiological staff. To accelerate the patient pathway and optimise the benefits of days saved in hospital, one of our criteria for inclusion in phase 2 was that the diagnosis and subsequent discharge had to be made within 72 hours of admission; hence the length of stay for phase 2 was influenced by this criterion. Recruitment is likely to be easier with dedicated, specialised staff (e.g. research staff, clinical nurse specialists) and where all patients are reviewed for potential early discharge. A similar study by Beer *et al*[13] highlighted this difficulty, where 150 (60%) of 255 patients with PE were excluded from outpatient treatment by predefined criteria and another 57 (22%) were not treated due to admission at the weekend – only 16.8% were eventually managed as outpatients. In both phases of this study we ensured patients had a confirmed PE before being selected for early discharge. Phase 1 suggested this approach may lead to early discharge of 47% of subjects with PE, although the proportion suitable for immediate discharge may in fact be smaller if the diagnosis is confirmed more rapidly as some patients may not be clinically stable at presentation. The next step in managing patients with PE will be to consider avoiding admission altogether in those predicted to be at low risk from adverse outcome. Only one small series has addressed this area[30]. In this study 50 highly selected patients with suspected PE attending an emergency department in Canada received one dose of dalteparin and were then discharged overnight with further investigations

arranged as an outpatient. There were no adverse events relating to treatment or complications whilst at home overnight.

Adverse outcome scores may help to predict the risk of adverse outcome from PE in treated patients. The Geneva score uses clinical parameters such as history of cancer, heart failure or VTE, hypotension and hypoxemia, but only looks at outcome after 3 months[31]. A recently reported 11 point score also accurately predicts 30-day mortality for patients with PE by classifying into 5 groups from very low risk to very high risk of death[32]. This score uses clinical parameters plus age, male sex and risk factors such as cardio-respiratory disease and cancer. It is likely that patients with the highest scores (higher risk of 30-day mortality) would also be selected by the criteria used in our phase 2 exclusion simply because they are more likely to require admission for additional treatment or monitoring and would be acutely unwell. However, these scores predicting 30-day and 3-month mortality are not likely to be clinically useful when trying to predict the safety of outpatient treatment during the acute phase with LMWH – the treatment phase currently performed as an inpatient. Ultimately these adverse outcome scores and the other criteria such as those derived in our study or by Kovacs et al[12] would need to be assessed as part of a large prospective randomised controlled trial using treatment-decision algorithms.

In summary, this prospective observational cohort study shows that highly selected patients with PE can be managed by early discharge from hospital once diagnosis has been confirmed. Using outpatient anticoagulation in these

patients was safe and highly acceptable to patients, and can be implemented in a centre with existing DVT services.

Acknowledgements

The following people were involved in the recruitment of patients and collection of data: D Heneghan; K Smith; L Binks ; S Rhodes; S Bond; S Gee; C Ashbrook-Raby; J Ross; Dr J Lordan; B Robinson: E Cheyne; R James; Professor D Bell; K Humphrey; E Fearnhead; K Peperell. The study was supported by a research grant from LEO Pharma to pH Associates to conduct the project. pH Associates have been involved in the design of the study and provided assistance with data collation and reporting.

References

1. Keely MA. Overview of the diagnosis of pulmonary embolism. In: Hull RD, Raskob GE, Pineo GF, eds. *Venous thromboembolism: An evidence based atlas*. 1996;155-167.

2. Anderson FA, Wheeler HB, Goldberg RJ, et al. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism. The Worcester DVT Study. *Arch.Intern.Med.* 1991;151(5):933-938.

3. Wells PS, Ginsburg JS, Anderson DR, et al. Use of a clinical model for safe management of patients with suspected pulmonary embolism. *Ann.Intern.Med.* 1998;129:997-1005.

4. American Thoracic Society. The diagnostic approach to acute venous thromboembolism. *Am.J.Respir.Crit.Care Med.* 1999;160:1043-1066.

5. Huisman MV, Buller HR, Ten Cate JW, et al. Unexpected high prevalence of silent pulmonary embolism in patients with deep venous thrombosis. *Chest* 1989;95(3):498-502.

6. Meignan M, Rosso J, Gauthier H, et al. Systematic lung scans reveal a high frequency of silent pulmonary embolism in patients with proximal deep venous thrombosis. *Arch.Intern.Med.* 2000;160(2):145-146Charbonnier B.

7. Simmonneau G, Sors H, Charbonnier B. A comparison of low molecular weight heparin with unfractionated heparin for acute pulmonary embolism. *N.Engl.J.Med.* 1997;337:663-669.

8. Levine M, Gent M, Hirsh J, et al. A comparison of low-molecular-weight heparin administered primarily at home with unfractionated heparin administered in the hospital for proximal deep-vein thrombosis. *N.Engl.J.Med.* 1996;334(11):677-681.

9. Koopman MM, Prandoni P, Piovella F, et al. Treatment of venous thrombosis with intravenous unfractionated heparin administered in the hospital as compared with subcutaneous low-molecular-weight heparin administered at home. The Tasman Study Group. *N.Engl.J.Med.* 1996;334(11):682-687.

10. Rose P, Bell D, Green ES, et al. The outcome of ambulatory DVT management using a multidisciplinary approach. *Clin Lab Haematol* 2001;**23(5)**:301-306.

11. Gould MK, Dembitzer AD, Doyle RL, Hastie TJ, Garber AM. Low-molecular-weight heparins compared with unfractionated heparin for treatment of acute deep venous thrombosis. A meta-analysis of randomized, controlled trials. *Ann.Intern.Med.* 1999;130(10) :800-809.

12. Kovacs MJ, Anderson D, Morrow B, Gray L, Touchie D, Wells PS. Outpatient treatment of pulmonary embolism with dalteparin. *Thromb Haemostas* 2000;**83**:209-211.

13. Beer JH, Burger M, Gretener S, Bernard-Bagattini S, Bounameaux H. Outpatient treatment of pulmonary embolism is feasible and safe in a substantial proportion of patients. *Journal of Thrombosis and Haemostasis.* 2003;1:186-187.

14. Wells PS, Kovacs MJ, Bormanis J, et al. Expanding eligibility for outpatient treatment of deep venous thrombosis and pulmonary embolism with low-molecular-weight heparin: a comparison of patient self-injection with homecare injection. *Arch.Intern.Med.* 2000;160(6):869-870.

15. Siragusa S, Arcara C, Malato A, et al. Home therapy for deep vein thrombosis and pulmonary embolism in cancer patients. *Annals of Oncology* 2005;16(supplement 4):136-139.

16. Bakehe M, Bitzen U, Olsson B, et al. Outpatient tinzaparin therapy in pulmonary embolism quantified with ventilation/perfusion scintigraphy. *Med Sci Monit* 2006;12(2):19-23.

17. Ong BS, Karr MA, Chan DKY, Frankel A, Shen Q. Management of pulmonary embolism in the home. *MJA.* 2005;183:239-242.

18. Dager WE, King JH, Branch JM, et al. Tinzaparin in outpatients with pulmonary embolism or deep vein thrombosis. *Ann Pharmacother* 2005;39:1182-1187.

19. Lim AY, Parr DG, Stableforth DE, Fellows M, Fontaine R, Fegan CD. Early discharge and home supervision of patients with pulmonary embolism treated with low-molecular weight heparin. *Eur J Intern Med* 2003;14(2):89-93.

20. Labas P, Ohradka B, Cambal M. Could deep vein thrombosis be safely treated at home. *Bratisl Lek Listy* 2001;102:458-461.

21. British Thoracic Society Standards of Care Committee Pulmonary Embolism Guideline Development Group. British Thoracic Society guidelines for the management of suspected acute pulmonary embolism. *Thorax* 2003;58:470-484.

22. Levine MN, Hirsh J, Landefeld S, Raskob G. Hemorrhagic complications of anticoagulant treatment. *Chest* 1992;102(4 Suppl):352S-363S.

23. Tillman DJ, Charland SL, Witt DM. Effectiveness and economic impact associated with a program for outpatient management of acute deep vein thrombosis in a group model health maintenance organization. *Arch.Intern.Med.* 2000;160(19):2926-2932.

24. Goldhaber SZ. Echocardiography in the management of pulmonary embolism. *Ann.Intern.Med.* 2002;136:691-700.

25. Konstantinides S, Geibel A, Olschewski M, Bloggs. Importance of cardiac troponins I and T in risk stratification of patients with acute pulmonary embolism. *Circulation* 2002;106:1263-1268.

26. Douketis JD. Prognosis in pulmonary embolism. *Current Opinion in Pulmonary Medicine* 2001;7(5):354-359.

27. Greco F, Porto I. Clinical usefulness of cardiac biomarkers in hemodynamically stable pulmonary embolism. *Journal of Thrombosis and Haemostasis.* 2006;4:550-551.

28. The Columbus Investigators. Low-Molecular-Weight Heparin in the Treatment of Patients with Venous Thromboembolism. *N.Engl.J.Med.* 1997;337(10):657-662.

29. Douketis JD, Kearon C, Bates S, Duku EK, Ginsberg JS. Risk of fatal pulmonary embolism in patients with treated venous thromboembolism. *JAMA* 1998;279(6):458-462.

30. Bauld DL, Kovacs MJ. Dalteparin in emergency patients to prevent admission prior to investigation for venous thromboembolism. *Am.J.Emerg.Med.* 1999;17:11-15.

31. Wicki J, Perrier A, Perneger TV, Bounameaux H. predicting adverse outcome in patients with acute pulmonary embolism: a risk score. *Thromb Haemostas* 2000;84:548-552.

32. Aujesky D, Obrosky DS, Stone RA, et al. Derivation and validation of a prognostic model for pulmonary embolism. *Am.J.Respir.Crit.Care Med.* 2005;172:1041-1046.