Apixaban Length-Of-Stay Pulmonary Embolism study - Hospital Admissions (ALPHA-PE), Final results

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Introduction

- Patients presenting with venous thromboembolism (VTE), including pulmonary emboli (PEs), in the UK have historically been treated in hospital with warfarin.
- Direct oral anticoagulants (DOACs) have more recently been introduced.
- Patients treated with DOACs instead of warfarin require less frequent blood test monitoring and also benefit from standardised dosing and quicker onset of action.
- These patients are also at reduced risk of major bleeding compared with patients who received warfarin[1].
- A database study in England found that after the introduction of apixaban (a DOAC), patients experienced shorter hospital length of stay (LOS) to treat acute PE[2].
- However, there remains limited evidence from routine clinical practice on the clinical impact of apixaban, especially in terms of LOS[3-5].
- **Study objective: This study of real-world UK clinical practice compared LOS in patients initiated on anticoagulation for acute PE before and after licensing of apixaban.**
- **Primary study hypothesis: LOS has decreased since the introduction of apixaban.**

Methods

- ALPHA-PE was a multicentre, retrospective, observational study using medical record review.
- Data were collected at five UK hospital sites: Birmingham, Glasgow, Northumbria, Oxford and Sunderland.
- Sites with a preference for prescribing apixaban over other DOACs for the treatment of acute PE were selected. Sites that ran a dedicated ambulatory PE service at any time during the study period were excluded.
- The study included adult patients (≥18 years) who presented with acute PE and were initiated on anticoagulation (parenteral anticoagulation and warfarin, or apixaban) during the hospital admission, and were in receipt of anticoagulation on discharge.
- A before and after study design was used, with two cohorts:
  - **Cohort 1** (before licensing of apixaban): comprised of eligible patients admitted from 01 January 2013 to 30 June 2013.
  - **Cohort 2** (after licensing of apixaban): comprised of eligible patients admitted from 01 January 2017 to 30 June 2017.
- Data were analysed descriptively and inferentially. Statistical inferences were obtained from linear mixed models.

Table 1: Baseline demographics and patient characteristics in cohort 1 compared with cohort 2

	Cohort 1 (n = 269)	Cohort 2 (n = 269)	P-value
Demographics			
Age (years), mean (SD)	66.83 (17.53)	64.20 (15.88)	0.069
Gender (male), n (%)	120 (44.61)	138 (51.30)	0.262
Smoking status [current/former], n (%)	110 (40.89)	116 (43.12)	0.690
Height (m), mean (SD)	1.67 (0.11)	1.68 (0.11)	0.173
Weight (kg), mean (SD)	82.90 (21.48)	86.15 (21.86)	0.143
BMI (kg/m^2), mean (SD)	29.69 (7.07)	29.73 (7.00)	0.956
Clinical measurements			
SBP (mmHg), mean (SD)	133.56 (23.58)	135.19 (21.54)	0.408
DBP (mmHg), mean (SD)	76.80 (15.31)	79.21 (13.43)	0.057
Heart rate (beats per minute), mean (SD)	94.47 (21.98)	90.81 (19.51)	0.045
Respiration rate (breaths per minute), mean (SD)	20.19 (5.63)	19.51 (4.34)	0.126
Temperature (°C), mean (SD)	36.59 (0.69)	36.57 (0.57)	0.731
O_2 saturation (%), mean (SD)	94.67 (5.98)	94.59 (4.73)	0.868
Serum creatinine (µmol/L), mean (SD)	93.68 (39.77)	86.03 (24.14)	0.008
CrCl (Cockcroft-Gault [mL/min]), mean (SD)	84.06 (46.11)	91.42 (38.71)	0.092
eGFR (mL/min/1.73m^2), mean (SD)	72.53 (25.95)	78.18 (22.83)	0.008
PE diagnosis, n (%)			
CTPA	251 (93.31)	265 (98.51)	0.538
CT	<5	0 (0.00)	0.317
D-dimer, n (%)			
Positive	192 (97.96)	220 (98.21)	1.000
Negative	<5	<5	
Discharge status, n (%)			
Dead	6 (2.23)	0 (0.00)	0.014
Risk scores, n (%)			
Wells PE score			
Low risk (<2)	125 (53.19)	83 (44.62)	0.197
Moderate risk (≥2 and <6)	82 (34.89)	74 (39.78)	
High risk (≥6)	28 (11.91)	29 (15.59)	
sPESI score			
Low risk (0)	100 (40.65)	128 (50.00)	0.044
High risk (≥1)	146 (59.35)	128 (50.00)	
PESI score			
Very or low risk (≤85)	164 (74.89)	213 (84.52)	<0.001
Intermediate risk (>85 and ≤105)	10 (4.57)	22 (8.73)	
High risk (>105 and ≤125)	19 (8.68)	10 (3.97)	
Very high risk (>125)	26 (11.87)	7 (2.78)	
Provoked/unprovoked PE, n (%)			
Unprovoked	177 (69.41)	180 (70.87)	0.794
Provoked	78 (30.59)	74 (29.13)	
Anticoagulation, n (%) *			
Parenteral anticoagulation	40 (14.87)	20 (7.43)	<0.001
Warfarin	214 (79.55)	14 (5.20)	
Apixaban	0 (0.00)	194 (72.12)	
Rivaroxaban	8 (2.97)	41 (15.24)	
Dabigatran etexilate	<5	0 (0.00)	
Concomitant medications, n (%)			
Platelet aggregate inhibitors	21 (7.81)	17 (6.32)	0.516
IVC filter	<5	5 (1.86)	0.103

* Six patients died during their hospital stay and were excluded from analyses. One patient received dabigatran etexilate and was excluded from analyses.
BMI: body mass index; CrCl: creatine clearance; CT: computerised tomography; CTPA: computerised tomography pulmonary angiogram; DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate; IVC: inferior vena cava; O_2: oxygen; PE: pulmonary embolism; PESI: pulmonary embolism severity index; SD: standard deviation; sPESI: simplified pulmonary embolism severity index; SBP: systolic blood pressure; VQ: ventilation-perfusion.

Results

- Final analyses included 538 patients (cohort 1: n=269; cohort 2: n=269).
- Patients in cohorts 1 and 2 were comparable in age (mean age 66.9 years versus 64.2 years), gender (51.30% male versus 44.61%) and other demographic and clinical characteristics at baseline (**Table 1**).
- In cohort 1, 40.65% of patients were classified as low risk according to simplified Pulmonary Embolism Severity Index (sPESI) risk scores and 59.35% as high risk. By comparison, patients in cohort 2 were equal divided between low and high risk classifications (50.00% in each group).
- As prespecified, most patients in cohort 1 were anticoagulated with warfarin (79.55%), whereas most patients in cohort 2 received apixaban (72.12%).

Length of stay

- The mean (±SD) LOS for all patients in cohort 1 was 7.43 (±9.39) days, compared with 4.64 (±7.31) days in cohort 2.
- The difference in LOS between the two cohorts represents a 2.79-day reduction in mean LOS (p<0.005) (**Figure 1A**).
- In patients who received warfarin, mean (±SD) LOS was similar in cohorts 1 (n=214) and 2 (n=14), at 7.31 days (± 8.10) and 7.21 days (± 5.96), respectively. Patients who received apixaban in cohort 2 (n=194) had mean LOS of 4.48 days (± 7.80) (**Figure 1B**).
- Patients treated with apixaban had shorter LOS irrespective of sPESI score. Among patients at low risk according to sPESI, those on apixaban had shorter mean LOS of -2.0 days compared with patients on warfarin (p<0.005) (**Figure 1C**).

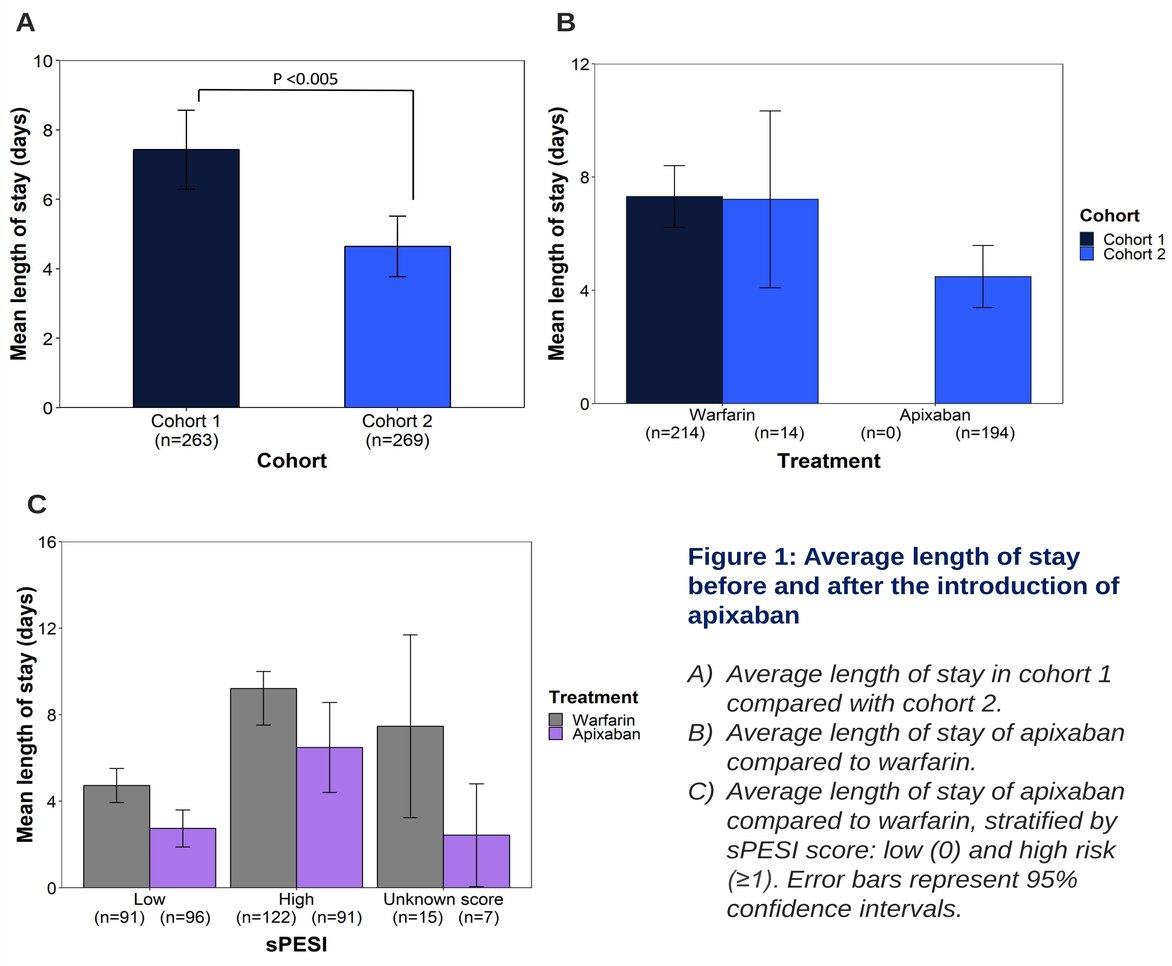

Figure 1: Average length of stay before and after the introduction of apixaban

A) Average length of stay in cohort 1 compared with cohort 2.
B) Average length of stay of apixaban compared to warfarin.
C) Average length of stay of apixaban compared to warfarin, stratified by sPESI score: low (0) and high risk (≥1). Error bars represent 95% confidence intervals.

Conclusions

- Use of apixaban to treat acute PE was associated with reduced length of stay compared with warfarin, with a reduction of 2.79 days.
- Across different risk stratifications (sPESI), apixaban was associated with shorter mean hospital LOS compared with warfarin, especially in low risk patients.
- This study was conducted across five geographically dispersed UK secondary care sites. However, the generalisability of the findings to the wider PE patient population and other care settings is unknown.
- Shorter hospital stays reduce the burden to patients and may also benefit local healthcare services and the NHS in potential savings on scarce resources.

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