INTRODUCTION

- The management of venous thromboembolism (VTE) and the prevention of recurrent VTE consists of anticoagulation, primarily with vitamin K antagonists (VKAs), for at least 90 days after a VTE event.
- The main adverse effect of anticoagulation is bleeding; therefore, this study investigated the incidence of significant bleeding occurring in the following situations:
  - Primary care
  - Out of hospital
  - Within 90 days' posttreatment initiation with VKAs in patients with a first VTE.
- This study also investigated both established and potentially new predictors of significant bleeding in a large United Kingdom-based population of patients with VTE.

METHODS

- A cohort study was undertaken using the United Kingdom’s Clinical Practice Research Datalink, a primary care database containing the records of 5.1 million individuals from 401 primary care practices, plus additional data from hospitalizations and causes of death.
- Patients of any age and with a first incident VTE between January 2008 and March 2016 were identified based on an established algorithm:
  - Patients with VTE treated with VKAs within 60 days of first VTE were included in the cohort.
- Significant bleeding was defined as either major bleeding or clinically relevant non-major bleeding requiring hospital admission (CRNMB-H) in accordance with the International Society on Thrombosis and Haemostasis recommendations.
- Study analyses were performed using all data on the following:
  - Signs and symptoms
  - Investigations (including laboratory results)
  - Diagnostic methods
  - Therapies (including transfusions)
  - Discharge diagnoses and causes of death.
- Data were assessed for all potentially significant bleeding events, and were then reviewed, adjudicated, and categorized as major bleeding or CRNMB-H.
- Bleeding categories were then validated by 3 physicians experienced in the management of patients with VTE and who were blinded to any anticoagulant treatment:
  - All bleeding events that occurred in the hospital setting were excluded.
  - Patients were followed for 90 days from VKA treatment initiation.
- The association of various risk factors with major bleeding and also with CRNMB-H, and the strengths of those associations, were estimated from sub-hazard ratios derived from Fine and Gray regression models, with mortality as a competing risk and time-dependent covariates in each case.
- Models included recognized predictors for major bleeding and CRNMB-H before the diagnosis of VTE and a list of potential predictors during VKA treatment.

RESULTS

- 11 871 Patients were at risk of major bleeding and 11 760 of CRNMB-H (Figure 1):
  - Nearly half (49.5%) were men
  - The mean age (± standard deviation) was 62.4 (± 17.2) years
  - The mean body mass index was 28.9 ± 6.5 kg/m²
  - Deep vein thrombosis was present in 56.3% and pulmonary embolism in 43.7%
  - A past history of major bleeding was recorded in 3.6% and CRNMB-H in 31.6%
  - The mean Charlson score was 4.6 ± 3.2
  - Current, active cancer was reported in 7.6%.

- There were 45 acute major bleeding events requiring hospitalization and 146 CRNMB-H events in the first 90 days following commencement of VKA therapy.
- The sites for both major bleeding and CRNMB-H are shown in Table 1a and Table 1b, respectively. A significant fatality rate (27.6%) was observed for all major bleeds.
- The 90-day cumulative incidences of major bleeding and CRNMB-H were 0.4% and 1.3%, respectively.
- Incidence rates for each type of bleeding peaked in the first 2 weeks after the start of VKA therapy.
- Independent predictors for major bleeding included (Table 2) male sex, anemia within 6 months before first VTE, history of renal disease, and trauma during VKA treatment.
- Independent predictors for CRNMB-H (ratios with 95% CI) (Table 3) included male sex, history of CRNMB, active cancer, trauma during VKA treatment, and history of dementia.

CONCLUSIONS

- CRNMB-H occurred at least 3 times as often as major bleeding.
- Event rates were highest in the initial period following commencement of VKA therapy.
- Significant mortality occurred in relation to major bleeding.
- Assessment for, and awareness of, predictors prior to and during VKA treatment are needed to prevent significant bleeding events.
- Caution is warranted after commencing VKA treatment, particularly in patients with prevalent risk factors.

REFERENCES

5. Institute for Epidemiology, Statistics and Informatics GmbH; employment; University of Delaware School of Nursing Advisory Committee; membership on an entity’s board of directors or advisory committees.

DISCLOSURES

- Martinez: CSL Behring: research funding; Bayer AG: research funding; Bristol-Myers Squibb: research funding; Merck Pharma: research funding; Pfizer: consulting; honoraria; membership on an entity’s board of directors or advisory committees.
- Wallenhorst: Institute for Epidemiology, Statistics and Informatics GmbH; employment; Li: Bristol-Myers Squibb: employment; equity ownership; Wygan: Bristol-Myers Squibb: employment; equity ownership; University of Delaware School of Nursing Advisory Committee; membership on an entity’s board of directors or advisory committees.

Poster presented at: 59th Annual American Society of Hematology (ASH) meeting; December 9–12, 2017; Atlanta, GA.