Apixaban Major Bleeding in Atrial Fibrillation: Patient Characteristics, Management, and Outcomes

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INTRODUCTION

- Apixaban is an oral direct factor Xa inhibitor FDA-approved for stroke prophylaxis and systemic embolism prevention in patients with non-valvular atrial fibrillation
- Apixaban has a favorable safety profile in ARISTOTLE trial compared to warfarin with a reduction in major bleeding, intracranial hemorrhage and all-cause mortality[1]
- Limited data are available which evaluate the safety of apixaban in clinical practice where use occurs in a population more broad than that studied and with less-structured follow-up
- Apixaban was associated with nearly 500 hemorrhage adverse events that were reported to the FDA in 2014[2]

OBJECTIVES

- To assess characteristics, management and outcomes in patients with atrial fibrillation who experience a major bleeding event while taking apixaban
- To identify opportunities for improving apixaban safety at our institution

METHODS

- Institutional Review Board approved
- Retrospective cohort study (electronic chart review)
- Timeframe: January 1, 2013 – June 30, 2015
- Patients with atrial fibrillation taking apixaban who experienced a major bleeding event will be assessed for inclusion using the following steps:
    1. Identification of apixaban use through an electronic medical record system search
    2. From the apixaban use list, identification of patients with ICD-9 codes for hemorrhage, atrial fibrillation with or without transfusion (not required for intracranial hemorrhage patients)
    3. Additional cases identified using an internal adverse event reporting system
    4. Identify patients with a major bleed (based on International Society on Thrombosis and Haemostasis criteria) and a temporal relationship to apixaban use
- Systematic data collection will occur on those with a major bleed: patient characteristics, management of bleed, and outcomes will be assessed and reported using descriptive statistics

Figure 1. Data Collection

Patient Characteristics

- Patient demographics
- Drug interactions
- Renal function
- Apixaban dose adjustment
- Medication reconciliation
- Anticoagulant transition
- Co-morbid conditions
- Bleed and stroke risk assessment scoring systems
- Bleed site/type
- Continued anticoagulation while bleeding

Management of Bleed

- Diagnostic tests
- PRBCs
- FFP
- Vitamin K
- FEIBA®
- Kcentra®
- NovoSeven®
- Surgical intervention
- Procedural intervention
- Change in anticoagulation regimen

Outcomes

- Post-bleed hospital length of stay
- Post-bleed ICU length of stay
- Transition to hospice or palliative care
- In-hospital mortality
- 30-day mortality
- Inpatient thrombotic event
- Thrombotic event within 30 days
- Status of anticoagulation therapy

PRELIMINARY RESULTS*

***Data Collection Ongoing**

Table 1. Patient Demographics	n=7
Male, n (%)	5 (71.4)
Age (years), mean ± SD	81.5 ± 3.9
Weight, mean ± SD	87.4 ± 16.2
Creatinine clearance (mL/min), mean ± SD	47.9 ± 13.9
Heart Valve Replacement, n (%)	2 (28.6)
HAS-BLED, median (IQR)	3 (1.5)
$HEMORR_2HAGES$, median (IQR)	5 (3)
$CHADS_2$, median (IQR)	3 (1.5)
CHA_2DS_2-VASc, median (IQR)	4 (1.5)
Apixaban use ≤ 3 months, n (%)	4 (57.1)
Bleed prior to admission, n (%)	5 (71.4)
Bleed while inpatient, n (%)	2 (28.6)

Table 2. Select Patient Characteristics, n = 7	%
Chronic kidney disease	42.9
Acute kidney injury at time of bleed	28.6
Anemia	57.1
Hypertension	85.7
Malignancy	28.6
Fall risk	28.6
Congestive heart failure/left ventricular dysfunction	42.9
Diabetes mellitus	42.9
Peptic ulcer disease	42.9
Continued anticoagulation while bleeding	14.3
Antiplatelet therapy	57.1
Dual antiplatelet-therapy	28.6
Inappropriate apixaban dose	14.3

Figure 2. Major Bleed Type/Site (n=7)

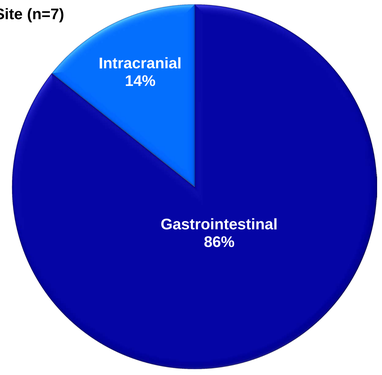

Figure 3. Patient Identification Breakdown

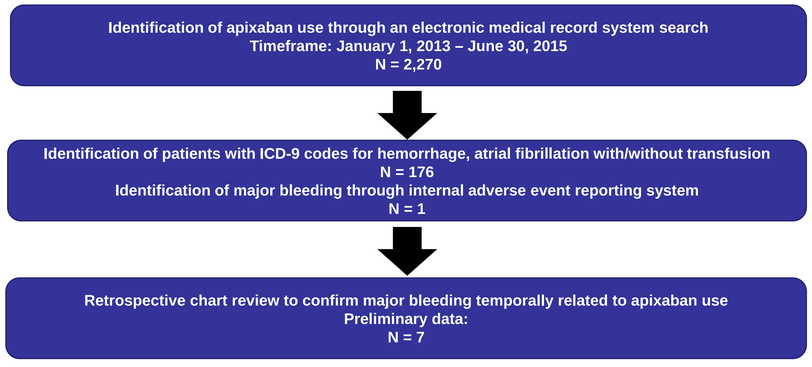

Figure 4. Diagnosis and Management of Bleed

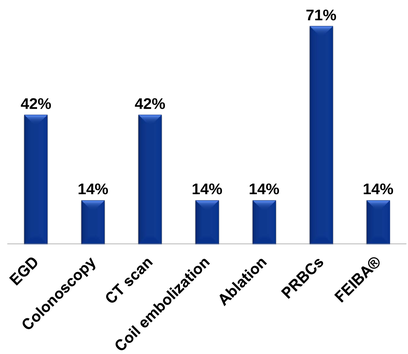

Table 3. Outcomes	n=7
Post-bleed hospital length of stay (days), mean ± SD	6.7 ± 9.4
Post-bleed ICU length of stay (days), mean ± SD	9.1 ± 12.7
Transition to palliative/hospice care, n (%)	2 (28.6)
Thrombotic event while anticoagulation on hold , %	1 (14.3)
Anticoagulation held at discharge (out of 5 patients) , n (%)	3 (60)
In-hospital mortality, n (%)	0 (0)
30-day mortality, n (%)	2 (28.6)

DISCUSSION

- Seven out of twelve patients screened thus far were included in the study, suggesting an approximate 50% rule-in rate from our screening criteria
- Patients who experienced a major bleed were often male, older, had hypertension, anemia, and moderate bleeding risk scores
- Most patients bled prior to admission
- Gastrointestinal bleeding was the most common bleed site
- Concurrent antiplatelet therapy occurred in more than 50% of patients
- PRBCs were the most commonly used method of bleed management
- One patient suffered a thrombotic event (bilateral lower extremity deep vein thrombosis) while apixaban was held
- The 30-day mortality was 28.6%

DISCLOSURE

Authors of this presentation do not have any disclosures to report regarding financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter presented.

REFERENCES

1. Granger CB, Alexander JH, McMurray JJ, et al. ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011 Sep 15;365(11):981-92.
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