

**Title:** Incidence and Causes of Rivaroxaban Related Major Bleeding in a Tertiary Care Hospital

**Category:** Prevention

### **Abstract**

Introduction: Direct oral anticoagulants (DOACS), such as Rivaroxaban, are new emerging group of medications for their use in stroke prophylaxis in patients with Non-valvular atrial fibrillation (NVAf) and in Deep venous thrombosis/Pulmonary embolism treatment or prevention.

Clinical trials have shown that rivaroxaban is a safe and effective alternative to the conventional Warfarin therapy in the studied indications. Furthermore, they represented a convenient option with their fixed dosing and the lack of specific and frequent monitoring parameters.

However variabilities in patient's demographics and characteristics and conflicting rates of adverse events may warrant further investigation of the safety profile of Rivaroxaban in the daily practice

Objectives:

- To evaluate the incidence of rivaroxaban-related-complications, primarily major bleeding.
- To further investigate the possible underlying causes for the development of rivaroxaban related complications in a tertiary care facility.

Endpoints:

- **Primary**
  - Rate of Rivaroxaban-associated major Bleeding events - as defined by International Society of Thrombosis and Haemostasis (ISTH).
- **Secondary**
  - Rate of any Rivaroxaban-associated non-major bleeding events (Defined as any bleeding event not meeting the criteria for a major bleeding).
  - Rate of any other Rivaroxaban associated complications.
  - Possible contributing factors for complication occurrence.

Methods:

- **Study design:** Single Center, Retrospective chart review.
- **Sample size:** 250 patients randomly selected.
- **Statistical analysis:**
  - Descriptive analysis using frequency distribution, mean and standard deviation was performed for all categorical and continuous variables respectively.
  - Analysis of association between risk factors, possible causes and bleeding was performed using Pearson Chi-Square test and Fisher's exact test.
  - **Figure 1. Inclusion and Exclusion criteria**

### Inclusion Criteria

All patients who were prescribed Rivaroxaban between May 2013- December 2016

### Exclusion Criteria

Patients prescribed rivaroxaban for thromboprophylaxis post hip or knee replacement

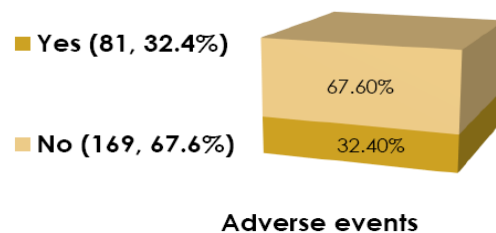
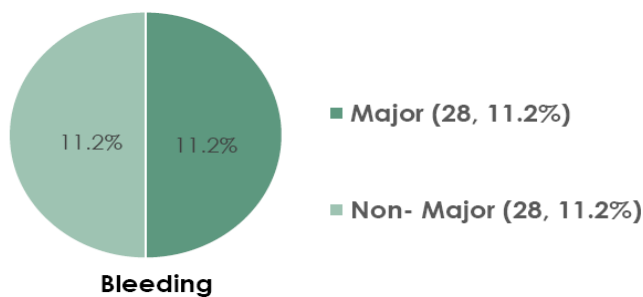
**Table 1. Patient Demographics and Baseline Characteristics (n=250)**

#### Indications n (%)

Stroke Prophylaxis in NVAF	136 (64.5%)
CHA2DS2-VASc (Mean $\pm$ St Dev)	4.1 $\pm$ 1.7
Mean HAS-BLED (Mean $\pm$ St Dev)	1.88 $\pm$ 1.
DVT/PE treatment	28 (13.3%)
DVT/PE prevention of recurrence	47 (22.3%)
Prior Anticoagulation Therapy n (%)	151 (60.6%)

### Results:

#### Rate of bleeding and other adverse events

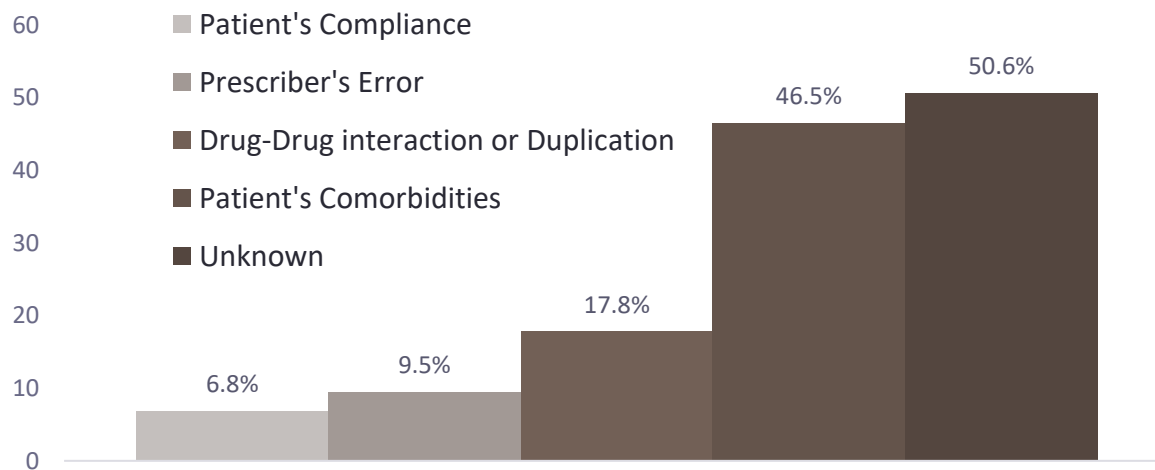


## Association between comorbidities and bleeding

**Table 2. Information about Bleeding (n=56)**

Risk factor	Bleeding		P Value	Odds Ratio (95%CI)
	n	%		
Anemia	20	37	0.002	2.8 (1.4 - 5.4)
Myocardial Infarction	10	18.5	0.002	3.822 (1.5 - 9.5)
Known Coagulopathy	8	14.8	0.845	1.09 (0.46 - 2.5)
History of bleeding	9	16.7	0.001	7.6 (2.4 - 23.8)
Peptic Ulcer history	5	9.3	0.012	4.8 (1.3 -18.9)
Active Cancer	10	18.5	0.039	2.39 (1.02 - 5.5)

**Figure 3. Possible underlying causes for Complications**



**Conclusion:**

- Study results indicate an increased rate of rivaroxaban related major bleeding, compared to published international data (11.3 vs. 6%). These findings warrant further investigation on a larger scale of patients with multiple comorbidities.
- Several factors may have contributed to the increased incidence of bleeding including patient's comorbidities and drug-interactions as well as prescriber errors.
- Emphasis on the role of pharmacists in providing proper counseling and ensuring correct dosing and adjustment, as well as investigating drug-drug or drug disease interactions may contribute to preventing complications and adverse events.
- **Limitations:** incidence rates (events per 100 patient-years) were not evaluated.