Atrial fibrillation (AF) causes substantial morbidity and is associated with a 1.5- to 1.9-fold mortality risk in both genders across a wide range of ages (1). Therapy of choice for AF is anticoagulation with the objective to reduce the risk of [embolic] stroke without causing major bleedings. For a long time, Warfarin had been the only drug approved for the prevention of stroke in patients with AF.

Dabigatran is one of three new oral anticoagulants and has been associated with lower rates of stroke than Warfarin in trials of AF (2). However, large-scale evaluations in clinical practice were limited. Just recently a retrospective cohort study on claims data was published (3) and provided first insights in usual care settings (See figure 1).

**OBJECTIVES**

Our study intended to replicate findings of a recently published retrospective cohort study on data identified from hospital claims (FDA Sentinel program) to answer the following questions:

- Can the results of the FDA-Sentinel study comparing Warfarin and Dabigatran be replicated with electronic medical records (EMR)?
- Are there any flaws which the use of EMR can add as compared to a mainly claims-based real-world study?

**METHODS**

Data Source: We used TriNetX, a global health research network with the ability to perform real-time analyses on EMRs of 43 million patients, predominantly in the US (numbers as of January 2018). The network contained 1,007,340 patients with AF (ICD10 code I48), of which 88,000 started on Warfarin or Dabigatran between Nov. 2010 and May 2014 (the time frame of the Sentinel study (S3)).

Patient Cohorts and Definition: Non-rheumatic cardiac valve diseases, kidney transplant status, and end stage renal disease were excluded, which left a total of 49,610 patients (Warfarin: 42,130; Dabigatran: 7480).

Outcomes:
- **Cardiovascular Event:** Myocardial Infarction (ICD10 code I21) or Stroke (ICD10 code I63).
- **Major Bleeding:** Any of a series of 23 different ICD10 codes representing intracranial, pericardial, esophageal, gastrointestinal, opharyngeal-nasal, or respiratory bleeding or internal hemorrhage.

**RESULTS**

- Mean age in the Dabigatran group was 72 years with 34% female patients versus 76 years and 41% in the Warfarin group, respectively, which does not represent a clinically relevant difference in this context.
- Mean INR in the Dabigatran group was 1.37 units, compared to 1.85 units in the Warfarin group, which supports the appropriate selection and reasonable compliance within the cohorts, especially quality of Warfarin anticoagulation (See figure 3).
- 170 (2.27%) patients experienced a major bleeding event under Dabigatran, compared to 5,250 (12.46%) with Warfarin.
- 930 (12.2%) patients experienced a cardiovascular event under Dabigatran, compared to 6,705 (15.9%) with Warfarin.
- For myocardial infarction as component of the CV event, the respective numbers were 320 (4.3%) and 2,620 (6.2%), respectively.

**DISCUSSION**

- INR levels in the Warfarin group showed an overall satisfactory anticoagulation in the Warfarin group. Dabigatran patients had significantly fewer bleeding events and significantly fewer cardiovascular events than patients with Warfarin.
- A previously reported signal of potentially higher rates of myocardial infarctions under Dabigatran (S3) could not be verified in this data set.

**LIMITATIONS**

- We did not calculate exposure by person-years. Continuous exposure to the respective anticoagulants was assumed.
- The Dabigatran cohort was slightly younger and had slightly less cardiovascular pre-existing conditions. Ideally, this would have been addressed by censoring or by matching (e.g., propensity score). However, as a real-world study, this shows the current actual use of the two products which includes not only the mechanism of action of the molecule in isolation, but also the prescribing behavior, the medication compliance, the patient population and their concomitant risk factors.

**CONCLUSIONS**

- The frequency of bleeding events and of CV events (STEMI or stroke) was lower in the Dabigatran group than in the Warfarin group.
- This real-world study conducted on EMRs of large unselected populations in real practice could confirm the results of randomized clinical trials and of an FDA sponsored, mainly claims-based national surveillance system.
- The access to laboratory values, by using EMR rather than claims data, added value for internal validation, i.e., coagulation parameters.

**REFERENCES**