Haemostatic and genetic factors, associated with left atrial appendage thrombosis in patients with permanent atrial fibrillation

A. Rubanenko, Y. Shchukin, O. Tereshina, O. Rubanenko, Samara State Medical University, Samara, Russian Federation

Purpose: To evaluate haemostatic and genetic factors associated with thrombus formation in left atrial appendage (LAA) in patients with permanent atrial fibrillation.

Methods: Studied were 240 patients with permanent atrial fibrillation (mean age 62.5±8.9 years). All the patients were divided into two groups: 1 group comprised 110 patients with LAA thrombosis and 2 group - 130 patients without LAA thrombosis according to transesophageal echocardiography. We evaluated haemostatic indicators such as thrombin activatable fibrinolysis inhibitor (TAI), soluble fibrin monomer complexes, antithrombin, fibrinogen and also genetic polymorphisms of cytochrome P-450 2C9, vitamin K epoxide reductase complex subunit 1 (VKORC1) C1173T and 4G allele of PAI-1 are associated with LAA thrombosis in patients with permanent atrial fibrillation.

Results: In patients with LAA thrombosis mean TAI level was 17.6% higher (p=0.005) than in patients without LAA thrombosis. Patients of the 1 group had CC genotype of VKORC1 30% more frequently (p=0.006) and allele 4G of PAI-1 21% more frequently (p=0.001) than patients of the 2 group. The odds ratio for LAA thrombus in patients with TAI levels more than 256% was 3.1 (95% CI: 1.5–6.9, p=0.006), with CC genotype of VKORC1 C1173T - 2.3 (95% CI: 1.2–5.3, p=0.01) and with 4G allele of PAI-1 – 3.5 (95% CI 1.6–8.5, p=0.02).

Conclusion: TAI levels more than 256%, the presence of CC genotype of VKORC1 C1173T and 4G allele of PAI-1 are associated with LAA thrombosis in patients with permanent atrial fibrillation.

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Effective safety of apixaban versus warfarin among high-risk subgroups of non-valvular atrial fibrillation patients: a propensity score matched analysis


4Pfizer, Inc., New York, United States of America; 5Pfizer, Inc, Groton, CT, USA; 6University of Hong Kong, Kowloon, Hong Kong; 7Guy’s and St Thomas’ Foundation, Department of Hospital Medicine, New Orleans, United States of America; 1Bristol-Myers Squibb Company, Lawrence, NJ, United States of America; 2STatinMED Research, Ann Arbor, MI, United States of America; 3Pfizer, Inc., New York, United States of America; 4Pfizer, Inc, Groton, CT, United States of America; 5University of Birmingham, Institute of Cardiovascular Sciences, Birmingham, United Kingdom

Background: In the ARISTOTLE trial, apixaban demonstrated reduction in both stroke/systemic embolism (SE) and major bleeding compared to warfarin among non-valvular atrial fibrillation (NVAF) patients, and such results were consistent across all high-risk subgroups of patients. However, a lack of evidence about the effectiveness and safety of apixaban in routine clinical practice among those high-risk subgroups.

Purpose: To compare the incidences of stroke/SE and major bleeding between apixaban and warfarin among NVAF patients stratified by age, CHA2DS2-VASc score, HAS-BLED score, congestive heart failure (CHF), coronary artery disease (CAD), and peripheral artery disease (PAD).

Methods: A retrospective cohort study was conducted using four US claims databases (Optum, MarketScan, PharMetrics, and Humana) of >163 million commercial and Medicare plan beneficiaries. NVAF patients aged ≥18 years who initiated apixaban or warfarin from January 1, 2013 to September 30, 2015 were included. In each database, 1:1 propensity score matching (PSM) was used to balance age, gender, region, baseline comorbidities, and comedinations. After PSM within each database, the resulting patient records were pooled. Cox proportional hazards models were used to estimate the hazard ratios of stroke/SE and major bleeding (identified using the first listed diagnosis of inpatient claims) within 1 year of therapy initiation for each subgroup. The statistical significance of the interaction between treatment and the specific subgroup(s) was evaluated.

Results: A total of 38,470 PSM-matched pairs of warfarin-apixaban patients (14,563 pairs from MarketScan, 7,683 pairs from PharMetrics, 7,894 pairs from Optum, and 8,330 pairs from Humana) were included in the study with a mean follow-up length of 6 months. After PSM, the baseline characteristics were balanced with a mean age of 71 years (SD=12), mean CHA2DS2-VASc score of 3.0 (SD=1.7), and mean HAS-BLED score of 2.6 (SD=1.3). Analyses stratified by age, CHA2DS2-VASc score, HAS-BLED score, CHF, CAD, and PAD all show consistent results of lower risk of stroke/SE and major bleeding associated with apixaban compared to warfarin treatment (Figure). No significant interaction was found in any subgroup analysis except for the interaction between treatment and CHA2DS2-VASc score strata in the analysis of major bleeding. Apixaban patients had a significantly lower risk of major bleeding compared to warfarin across all CHA2DS2-VASc score strata, with a slightly greater reduction among patients with CHA2DS2-VASc score ≥1.5–6.9, p=0.006, with CC genotype of VKORC1 C1173T - 2.3 (95% CI: 1.2–5.3, p=0.01) and with 4G allele of PAI-1 – 3.5 (95% CI 1.6–8.5, p=0.02).

Conclusions: In this “real-world” study pooling four large US databases, apixaban initiation was associated with a lower risk of stroke/SE and major bleeding among high-risk subgroups of patients with NVAF.

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Anticoagulation in atrial fibrillation and risk of myocardial infarction: choice of treatment matters

C.-J. Y. Lee1, A. N. Bondes2, N. Carlson3, J. B. Olsen4, J. L. Pällgaard5, G. H. Glisason2, C. T. Pedersen1, M. L. Hansen6, D. Aalborg University, Science Health and Technology, Aalborg, Denmark; 2Gentofte University Hospital, Cardiology, Copenhagen, Denmark; 3Holbaek Hospital, Internal Medicine, Holbaek, Denmark; 4Roskilde Hospital, Cardiology, Roskilde, Denmark

Introduction: In addition to the increased risk of thromboembolic stroke, patients with atrial fibrillation (AF) also have an increased risk of developing myocardial infarction (MI). Both randomized clinical trials and meta-analyses have been inconclusive regarding the increased risk of MI with the use of non-vitamin K antagonist oral anticoagulants (NOAC). Using the Danish nationwide registries we can provide insights of the MI risk associated with NOACs in a “real-life” cohort.

Purpose: To investigate the risk of first time MI in patients with atrial fibrillation using one of the following NOACs: rivaroxaban, apixaban, and dabigatran compared with vitamin K antagonist (VKA).

Methods: Subjects with non-valvular AF without prior coronary artery disease were included between 2011 and 2016 by using the Danish nationwide registries. The study cohort was divided into four separate groups according to prescriptions of rivaroxaban, apixaban, dabigatran, or VKA. The associated risk of first-time MI, in a one year follow-up, was estimated as both absolute risk using incidence rates per 100 person years and as relative risks using multivariable adjusted Cox regression analyses.

Results: The study cohort included 19,061 oral anticoagulant naive patients with AF, where 6,200 (33%) were prescribed VKA, 4,339 (23%) apixaban, 5,039 (26%) dabigatran, and 3,483 (18%) rivaroxaban. The median age was 62, 74, 70, and 72 years in the four groups, respectively. During the study period, a total of 303 MIs were diagnosed, where 167 occurred within one year after the prescription of oral anticoagulation therapy. The incidence rates per 100 person years were 1.22 (0.96–1.55) for VKA, 0.78 (0.53–1.14) for apixaban, 1.06 (0.80–1.40) for dabigatran, and 0.87 (0.58–1.30) for rivaroxaban. The adjusted hazard rates (95% confidence intervals) were 0.74 (0.70–0.78) for apixaban, 0.80 (0.76–0.83) for dabigatran, and 0.87 (0.82–0.91) for rivaroxaban compared to VKA (see figure 1).

Conclusion: For oral anticoagulation naive patients with AF, NOACs were associated with a lower risk of first-time MI compared to vitamin K antagonist therapy during the first year of anticoagulative therapy. Of the NOACs, apixaban was associated with a lower risk of MI than dabigatran or rivaroxaban.