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Comparison of P2Y12 inhibitors in atrial fibrillation patients treated by dual-antiplatelet therapy without oral anticoagulant after acute myocardial infarction with percutaneous coronary intervention

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Background: Oral anticoagulants (OACs) and dual anti-platelet therapy (DAPT) is needed to reduce thromboembolism and stent thrombosis in atrial fibrillation (AF) patients experiencing acute myocardial infarction (AMI) with percutaneous coronary intervention (PCI). Because of the increased risk of major bleeding, DAPT without warfarin is preferred to triple therapy (OACs and DAPT) in real world practice. We aimed to compare clinical outcomes among 3 different P2Y12 inhibitors in AF patients with DAPT after AMI with PCI.
Methods: A total of 18,841AMI patients enrolled in Korean AMI Registry (KAMIR) from Nov 2011 to Dec 2016, constituting 14,748 (80.6%) patients undergoing PCI and 1,708 (9.3%) patients presenting AF. We analyzed consecutive 740 AF patients who underwent PCI and survived at hospital discharge with DAPT. One-year clinical outcomes were compared among 3 different P2Y12 inhibitors (clopidogrel, n=500; ticagrelor, n=190; prasugrel, n=50). Primary efficacy end-point was defined as major adverse cardiac and cerebral events (MACCE), composed of death, recurrent MI, target vessel revascularization (TVR), and coronary artery bypass grafting (CABG), and new-onset stroke. Secondary end-point was the composite of death, new-onset stroke and MI.
Results: CHA2DS2-VASc score was higher in clopidogrel group (3.6±1.6 vs. 2.8±1.5 vs. 3.1±1.6, $p<0.001$). One-year mortality was higher in clopidogrel group (13.2% vs. 6.8% vs. 5.3%, p=0.029) without differences in the rate of one-year MI, TVR, CABG, and new-onset stroke among the 3 groups. There were no differences in the primary and secondary end-point between clopidogrel and ticagrelor. However, prasugrel significantly lowered mortality (13.2%, 5.3%, log-rank p=0.045), primary (14.4% vs. 6.0%, log-rank p=0.043) and secondary (13.0% vs. 4.0%, log-rank p=0.043) end-point compared with clopidogrel. Multivariate Cox-regression analysis demonstrated that prasugrel reduced primary (adjusted hazard ratio [HR] 0.40, 95% confidence interval [CI] 0.12–0.90, p=0.035) and secondary (adjusted HR 0.33, 95% CI 0.08–0.90, p=0.035) end-point compared with clopidogrel. Also, DAPT with prasugrel had similar events rate of primary and secondary end-point compared with triple therapy.
Conclusions: DAPT with prasugrel was associated with better clinical outcomes compared to DAPT with clopidogrel. Also, DAPT with prasugrel demonstrated similar clinical outcomes compared to triple therapy. Prasugrel might be best option if OACs is not indicated or available. Further clinical trials are warranted to prove comparative efficacy and safety among P2Y12 inhibitors in AF patients with DAPT after AMI with PCI.

P6076
Oral anticoagulants in patients with atrial fibrillation and non-mechanical heart valve disease

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Introduction: The role of non-vitamin K antagonist oral anticoagulants (NOAC) in patients with atrial fibrillation and valvular heart disease has not yet been thoroughly established outside patients with mechanical heart valves or mitral stenosis.
Aim: To describe patient characteristics of NOAC and vitamin K antagonist-treated patients with atrial fibrillation and valvular heart disease and to describe the temporal trends in initiation of NOAC and vitamin K antagonists in this patient population.
Method: Our study was based on the Danish nationwide administrative registries. From the 22nd of August 2011 to the 30th of June 2017, we identified all patients with atrial fibrillation and valvular heart disease, including bioprosthetic heart valves, aortic stenosis/insufficiency, mitral insufficiency, and aortic/mitral valve repair. Only patients initiating treatment with a NOAC (apixaban, rivaroxaban or dabigatran) or vitamin K antagonists were selected.
Results: A total of 4739 patients were included, of which 2292 (48.4%) were treated with vitamin K antagonist (55.4% males, median age 76.5 years; IQR 70–83) and 2447 (51.6%) were treated with the following NOACs: 990 (20.9%) with apixaban (45.4% males, median age 81 years; IQR 74–88), 700 (14.8%) with dabigatran (50.4% males, median age 78 years; IQR 71–84), and 757 (16.0%) with rivaroxaban (49.3% males, median age 80 years; IQR 72–87). Mean CHA2DS2-VASc score (SD) was for apixaban 3.9 (1.6), dabigatran 3.6 (1.6), rivaroxaban 3.7 (1.6) and vitamin K antagonist 3.5 (1.6). Mean HAS-BLED score (SD) was for apixaban 2.7 (1.6), dabigatran 2.6 (1.3), rivaroxaban 2.7 (1.2) and VKA 2.7 (1.2).
Temporal trends (Figure) showed an increase in the use of apixaban and rivaroxaban between 2011 and 2017. By June 2017 43.0%, 3.0%, 37.3%, 16.7%, of patients were initiated on apixaban, dabigatran, rivaroxaban and vitamin K antagonist, respectively.
Conclusion: Patients treated with apixaban were at the highest predicted risk of stroke and bleeding. Since the approval of the various NOACs, the use of

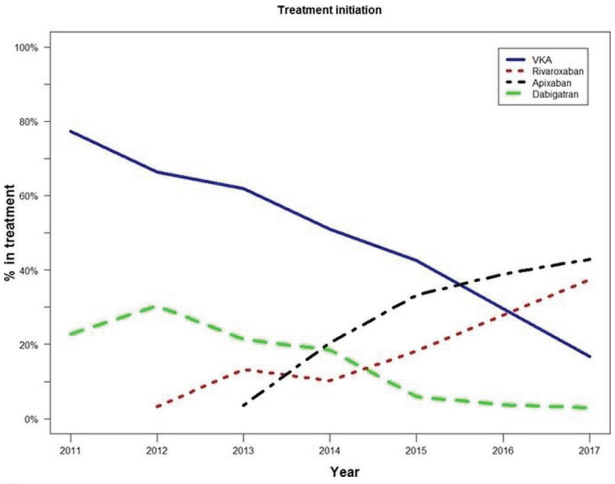

Figure 1

vitamin K antagonist has noticeably declined leaving apixaban and rivaroxaban as the preferred drugs for patients with atrial fibrillation and valvular heart disease. Whether these findings translate into altered risks of stroke and bleeding remains to be determined.

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A network meta-analysis of new oral anticoagulants based antithrombotic regimens

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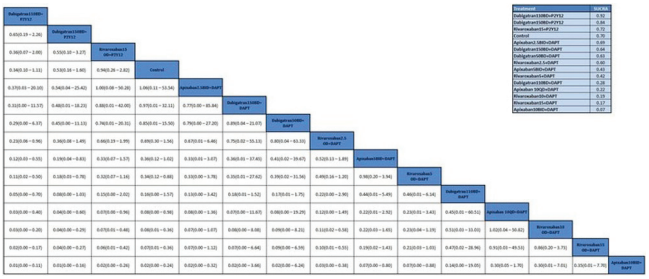
Background: The comparative effects of new oral anticoagulants (NOACs) with different dosages in addition to P2y12 inhibitor (I)or dual antiplatelet therapy (DAPT) remain unassessed.
Purpose: To assess relative risk of major bleeding and major adverse cardiovascular events (MACE: composite of myocardial infarction, stroke and all-cause mortality) across different dosages of NOACs with P2y12I or DAPT.
Methods: Eight randomized controlled trials (33, 947 patients) were selected using PubMed, EMBASE, and CENTRAL (Inception-November 2017). In Bayesian network meta-analysis, we calculated median estimate of odds ratio (OR) from the posterior distribution with 95% credible interval (CrI). Markov chain Monte Carlo (MCMC) modeling was used to estimate the relative ranking probability of each treatment group based on Surface under the Cumulative Ranking Curve (SUCRA).
Results: The risk of major bleeding was higher with higher NOACs dosages or when NOACs were added to DAPT versus P2y12 I (Figure 1). The MCMC ranked dabigatran (D) 110 mg BD+ P2y12 I as the safest therapy regarding the risk of major bleeding (SUCRA, 0.92), followed by D 150 mg BD+ P2y12 I (SUCRA, 0.84 and rivaroxaban (R) 15 mg OD + P2y12 I (SUCRA, 0.72). Whereas, apixaban (A) 10 mg BD +DAPT was ranked as the least safe treatment (SUCRA, 0.07) followed by R 5 mg OD+DAPT (SUCRA, 0.17), R 10 mg OD +DAPT (SUCRA, 0.19) and A 10 mg QD +DAPT (SUCRA, 0.22). In terms of MACE, R 10 mg OD +DAPT was ranked as the most effective treatment (SUCRA, 0.94) and caused 50% risk reduction compared to A 5 mg BD +DAPT [0.50 (0.27–0.89)], 64% compared to D 110 mg BD+P2Y12 I [0.36 (0.18–0.68)], and 48% compared to D 150 mg BD+P2Y12 I [0.52 (0.26–0.97)].



League table

Conclusion: Across all the antithrombotic regimens, R 10 mg OD+DAPT had the highest probability of reducing the MACE, while D 110 mg BD+P2Y12 I was ranked as the safest combination in terms of major bleeding complications.