Atrial fibrillation (AF) is the most common arrhythmia amongst adult population. It has been reported that 5.0–10.0% of the patients undergoing percutaneous coronary intervention (PCI) have concomitant AF [1–3]. Furthermore, AF is associated with a prothrombotic or hypercoagulable state [4]. It has been proven that the patients with AF had had far higher amounts of the platelet microparticles and the soluble P-selectin than the healthy controls in sinus rhythm. The abnormalities of the coagulant factors, including tissue factor, von Willebrand factor, factor IX and X, thrombin and fibrinogen were detected [5]. Patients with a history of AF who undergo PCI represent a group of patients where balancing between risks of thromboembolism and bleeding complications is accentuated. The combination of anticoagulant and antiplatelet therapy, particularly triple oral antithrombotic therapy (vitamin K antagonist/VKA + aspirin + clopidogrel), significantly increases the risk of bleeding complications [6,7]. Only sparse data are currently available on the combination of VKA with newer P2Y12 inhibitors, which impacts the efficacy of P2Y12 receptor antagonists in the group of patients with atrial fibrillation. The aim of presented study was to verify whether the presence of AF impacts the efficacy of P2Y12 receptor antagonists in the group of patients after stent-PCI, and to investigate whether there is a correlation between CHA2DS2-VASc score and the efficacy of P2Y12 receptor antagonists in this group of patients.

The prospective LAPCOR (Laboratory AntiPlatelet efficacy and Clinical Outcome Registry; ClinicalTrials.gov Identifier: NCT02264912) registry was analyzed. The consecutive patients who underwent stent-PCI were included. The registry protocol was approved by the Ethics Committee of the University Hospital Kralovske Vinohrady in Prague (Czech Republic). Patients were included after signing an informed consent for participation. No exclusion criteria were applied. The population of presented analysis consisted of 896 patients who underwent stent-PCI between June 2009 and June 2014.

The platelet reactivity was measured by phosphorylation of the protein VASP (vasodilator stimulated phosphoprotein) 24 ± 4 h after loading a dose of one of P2Y12 receptor antagonists (clopidogrel 600 mg, prasugrel 60 mg, ticagrelor 180 mg) and it was expressed by Platelet Reactivity Index (PRI). The high on treatment platelet reactivity (HTPR) was defined by PRI ≥ 50. CHA2DS2-VASc score was assessed in all patients.

Continuous data are presented as arithmetic means and standard deviations (SD). Two-sample t-test and Mann–Whitney test were used to examine differences between the groups. Categorical data were described using absolute and relative frequencies. Differences in proportions between the groups were analyzed using Fisher’s exact test. Logistic regression model was used to compare study subgroups and to identify independent predictors of the HTPR. Variables included in the model were age, sex, body mass index, diabetes mellitus, hypertension and renal insufficiency. All statistical tests were evaluated as two-sided at a significance level of 0.05. Statistical analysis was performed by software Stata, release 9.2 (Stata Corp LP, College Station, TX).

Characteristics of the study population are presented in Table 1. Clopidogrel group consists 639 patients (16.28% with AF, 65.4% acute PCI), prasugrel group of 136 (5.15% with AF) and ticagrelor group of 121 patients (14.05% with AF).

We came to a conclusion that prasugrel and ticagrelor are significantly more effective than clopidogrel regardless of the presence of AF. Within the clopidogrel group, the median PRI was 44.9% (IQR 36.1) vs the prasugrel/ticagrelor group 12.6% (IQR 17.2) (p < 0.001). HTPR was detected in 42.8% of the patients with clopidogrel, while in the prasugrel/ticagrelor group, the proportion of the patients with HTPR was 7.5% (p < 0.001).

No difference in the efficacy of clopidogrel in patients with AF was observed, regardless of whether PCI was performed in a setting of ACS or electively. In patients who underwent elective PCI, the median PRI
was 35.7% (IQR 42.3) in those with AF vs 42.8% (IQR 32.1) in those without AF (p = 0.643). HTPR was discovered in 42.2% of clopidogrel patients with AF and elective PCI and in 34.1% patients without AF (p = 0.384). Within the subpopulation of patients with ACS, the median PRI was 41.6% (IQR 38.5) in the group with AF vs 46.0% (IQR 36.1) without AF (p = 0.429). HTPR was assessed in 39.9% of the clopidogrel patients with ACS and AF, and in 43.4% patients without AF (p = 0.572).

We did not demonstrate the impact of AF on the efficacy of prasugrel or ticagrelor. In this subpopulation, the median PRI was 11.6% (IQR 10.5) in the patients with AF vs 12.7% (IQR 18.0) in the patients without AF (p = 0.195). HTPR was revealed in 4.4% of prasugrel/ticagrelor patients with AF and in 7.9% without AF (p = 1.000).

The other finding was that periprocedural administration of glycoprotein IIb/IIIa inhibitors was associated with significantly higher efficacy of P2Y12 receptor antagonists. In patients treated with GP IIb/IIIa inhibitors, the median PRI was 23.3% (IQR 35.3) in contrast to patients not treated with GP IIb/IIIa inhibitors, the median PRI was 35.3% (IQR 42.6) (p = 0.008).

The univariate and multivariate logistic regressions were used to test the correlation between CHA2DS2VASc score and the efficacy of P2Y12 receptor antagonists. Using the univariate analysis, CHA2DS2VASc score was recognized as a significant predictor of the HTPR in the clopidogrel group of patients who underwent stent-PCI in setting of ACS (p = 0.015), primarily if CHA2DS2VASc score was ≥5 (odds ratio 1.72 [95% CI 1.13 to 2.63, p = 0.011]). This result became also significant after adjusting for confounding variables in the multivariate analysis (adjusted odds ratio 1.74 [95% CI 1.02 to 2.98, p = 0.041]). In clopidogrel group of patients undergoing elective PCI, CHA2DS2VASc score was not revealed as a predictor of the HTPR (p = 0.641). There was also no significant correlation between the efficacy of prasugrel and ticagrelor and CHA2DS2VASc score (p = 0.879) (Fig. 1).

The main finding of the presented study is that the presence of AF does not impact the efficacy of prasugrel or ticagrelor. For the replacement of clopidogrel one of prasugrel or ticagrelor should be considered in patients with AF who undergo stent-PCI in a setting of ACS and who are in a high risk of thrombotic events and low bleeding risk. Periprocedural administration of GP IIb/IIIa inhibitors in this high risk population increases the efficacy of clopidogrel.

**Conflict of interest statement**

The authors have no conflicts of interest to declare.


References


