Impact of proton pump inhibitor on quality of anticoagulant control and outcomes in atrial fibrillation patients treated with an oral anticoagulant in the COOL-AF registry

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Introduction: Proton pump inhibitor (PPI) is commonly prescribed in patients treated with antithrombotic therapy, assuming it will reduce bleeding risk irrespective of the risk of bleeding. Although PPI may reduce the risk of gastrointestinal bleeding in those treated with an oral anticoagulant, PPI may increase INR by accelerating warfarin absorption, thereby increasing the risk of bleeding. We aimed to assess the impact of PPI use on outcomes and quality of anticoagulant control in AF patients treated with OAC.

Methods: The COOL-AF registry was a nationwide prospective observational study enrolling AF patients from 27 hospitals in Thailand between 2014 and 2017. The registry aimed to evaluate antithrombotic patterns, quality of OAC control, and clinical outcomes. Clinical information of patients was collected every six months and until three years. Patients treated with oral anticoagulants (either warfarin or non-vitamin K antagonist OAC (NOAC)) were included in the present analysis. Patients receiving any PPI type and dosage at the registry entry were counted as PPI users. Poor anticoagulant control was defined as time to therapeutic range (TTR) less than 65%. The association between PPI use and outcomes, including GI bleeding, overall bleeding, all-cause mortality, and ischemic stroke or systemic embolization, were assessed in the Cox model adjusted for age, prior GI bleeding, chronic alcohol use, chronic kidney disease, liver disease, smoking, and baseline anemia. Subgroup analyses were performed in patients at high bleeding risk (HAS-BLED score ≥ 3), and in patients concomitantly treated with antiplatelet.

Results: Of 3,402 patients in the registry, 2568 (75.5%) were treated with OAC at baseline. The prevalence of females was 43.4%, with a mean age of 68.4 years. The majority of patients (91.1%) received warfarin. The incidence of major bleeding was 2.11 (1.79–2.48) per 100 person-years. PPI was used at baseline in 707 patients (20.8%). Compared with their counterpart, PPI was more frequently used in high-bleeding risk patients (27.3% vs. 18.1%, p < 0.001) and in those with concomitant antiplatelet therapy (37.5% vs. 17.1%, p < 0.001).

The mean TTR was similar between PPI and non-PPI users (52.5% vs. 53.8%, p 0.37). PPI use was not associated with poor anticoagulant control (adjusted OR 1.12, 95%CI 0.89-1.40). The risk of GI bleeding in PPI users was similar to non-user (adjusted HR 1.01, 95%CI 0.59-1.75). The risk of all-cause mortality, ischemic stroke or systemic embolization, and overall bleeding was not different between PPI and non-PPI users.

Conclusion: PPI use has no impact on major outcomes, including bleeding in AF patients treated with OAC. The practice of concomitant prescribing of PPI in patients treated with OAC is needed to be re-examined, given the potentially high impact of health care costs.
PPI use and outcomes