Background: The European Society of Cardiology recommends addition of a second antithrombotic drug (a P2Y12 inhibitor or rivaroxaban 2.5 mg twice daily) on top of aspirin in selected patients with chronic coronary syndrome (CCS) at high residual risk of ischemic events. However, this treatment increases bleeding risk, and identifying subsets of patients with the most favorable trade-off between ischemic and bleeding risk thus is essential. We hypothesized that patients undergoing percutaneous coronary intervention (PCI) who tolerate subsequent dual antiplatelet therapy (aspirin plus a P2Y12 inhibitor) without any bleeding complications selected themselves as candidates for prolonged dual antithrombotic therapy.

Methods and results: We included 30,531 patients with CCS treated with dual antiplatelet therapy after first-time PCI with a drug-eluting stent in Western Denmark (3.5 million inhabitants) from 1999 to 2018. Of these, 1,220 (4%) were hospitalized for bleeding within one year after PCI (bleeders) and 29,311 (96%) were not (non-bleeders). Patients were followed for maximum nine years (median follow-up 5.4 years). Bleeders had an increased nine-year risk of death (adjusted hazard ratio [aHR] 1.54, 95% CI 1.37–1.73) and hospitalization for bleeding (aHR 2.53, 95% CI 2.20–2.90). These associations were particularly strong for women. Looking at types of bleeding, the strongest predictors of death were gastrointestinal bleeding, cerebral bleeding, and anemia due to bleeding. Risks of myocardial infarction and ischemic stroke did not differ between bleeders and non-bleeders (Table). We then stratified non-bleeders according to their thromboembolic risk using the CHADS-P2A2RC score—a validated clinical risk prediction model developed to estimate thromboembolic risk in patients without atrial fibrillation. Non-bleeders with a high estimated thromboembolic risk (CHADS-P2A2RC score ≥4) had higher nine-year risks of myocardial infarction (hazard ratio [HR] 1.88, 95% CI 1.78–2.07), ischemic stroke (HR 3.02, 95% CI 2.66–3.43), hospitalization for bleeding (HR 1.98, 95% CI 1.81–2.16) and, in particular, death (HR 4.48, 95% CI 4.21–4.77) than non-bleeders with a low-to-moderate predicted risk (CHADS-P2A2RC score <4).

Conclusions: Patients with CCS experiencing a bleeding event during the first year after first-time PCI had a substantially higher long-term risk of death and recurrent bleeding, but not a higher risk of ischemic events. Therefore, bleeding events during the first year after PCI may guide the preclusion of selected patients from long-term dual antithrombotic therapy. Among non-bleeders, the risk of ischemic events rose proportionately more than the risk of bleeding when comparing high-risk with low-risk patients. This is an important finding for clinicians, for whom accurate identification of patients at highest risk of ischemic events is an essential step in treatment allocation.

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