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Preventing Bleeding with Direct-acting Oral Anticoagulants

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Brief Title: DOACs and preventing bleeding

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Tweet: Prevent bleeding with DOACs: don't combine with aspirin, NSAIDs, SSRIs and SSNRI or supplements with bleeding risks and consider DOAC levels in patients of older age, with diabetes, decreased renal function, history of bleeding, anemia.

#CardioTwitter, #ACCEP, #InstaCardio

We appreciated the meta-analysis from Gomez-Outes, *et al.* describing the high risk of death in patients receiving direct oral anticoagulant (DOAC) reversal agents. (1) The accompanying editorial advocates use of DOACs and states “the best way to deal with bleeding is to prevent it” by avoiding/stopping antiplatelet therapy and using proton pump inhibitors in patients with prior gastrointestinal bleeding. (2)

We agree prevention is the best strategy and want to call attention to non-cardiovascular agents that increase bleeding risk: non-steroidal anti-inflammatory agents and selective-serotonin and serotonin-norepinephrine reuptake inhibitor antidepressants. Alcohol, fish oils, and supplements [St. John’s wort, ginger, ginko biloba, horsechestnut, turmeric, and plants used in Traditional Chinese Medicine] are also variably reported to increase bleeding risks.

It may also be time to consider another factor associated with increased risks for bleeding: DOAC concentrations. A well-established relationship exists between increasing DOAC concentrations and increased bleeding, experimentally and in randomized trials. Relationships between strokes and DOAC concentrations are less steep or flat (3) suggesting that above a therapeutic level further increases in concentrations increase bleeding risk without additional benefit. A small patient series reported higher DOAC concentrations in patients with intracranial hemorrhage.(4) Although simplified dosing is an advantage of DOACs over warfarin, that is not to say that DOAC prescribing cannot be optimized to reduce bleeding complications. It is time to evaluate the plausible hypothesis that excessive DOAC concentrations are an important and modifiable risk factor for bleeding during DOAC therapy.

Clinicians should address use of concomitant medications, alcohol, and supplements to reduce bleeding with DOACs. Clinicians may also want to consider assessing DOAC

measurements in patients at higher risks of bleeding (older age, prior hemorrhage, stroke or TIA, diabetes, lower creatinine clearance, or decreased hematocrit).(5)

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Sincerely,

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