Bleeding Risk in Surgical Patients Receiving Sugammadex: Definitive Conclusions Are Not Yet Possible

To the Editor:
I read with great interest the article by Rahe-Meyer et al., evaluating the effect of sugammadex on postsurgical bleeding and coagulation tests in patients receiving thromboprophylaxis after major hip or knee surgery. It provides important evidence in support of the safety of sugammadex in reversing rocuronium (or vecuronium)-induced neuromuscular blockade. However, there is one aspect of this study that deserves comment.

The authors estimated the relative risk (RR) and 95% CI of bleeding events to be 0.70 (0.38 to 1.29) for sugammadex versus usual care. Four groups were considered for stratified analysis. The two largest were a group of 990 patients (84% of cases) treated with low-molecular-weight heparin and a group of 144 patients (12% of cases) treated with antiplatelet plus anticoagulant drugs. Davidson et al. recently demonstrated that by inhibiting platelet aggregation, aspirin and other nonsteroidal antiinflammatory drugs increase the risk of bleeding in patients receiving anticoagulant therapy to prevent recurrent venous thromboembolism. In their study, the hazard ratios, adjusted for sex, age, and creatinine clearance, were 1.59 (95% CI, 1.17 to 2.17) for clinically relevant bleeding and 1.50 (95% CI, 0.74 to 3.05) for major bleeding during concomitant aspirin–anticoagulant treatment and 1.65 (95% CI, 1.26 to 2.17) for clinically relevant bleeding and 2.28 (95% CI, 1.28 to 4.04) for major bleeding during concomitant nonsteroidal antiinflammatory drug–anticoagulant treatment.

Although sugammadex was not associated with an increased risk of bleeding in the study by Rahe-Meyer et al., no data are presented regarding the potential difference in RR (95% CI) of bleeding events for the anticoagulant therapy (such as with low-molecular-weight heparin, unfractionated heparin, or vitamin K antagonists) versus antiplatelet–anticoagulant treatment groups. Considering the results of the study by Davidson et al., it is possible that the RR (95% CI) for sugammadex versus usual care may be higher in patients receiving antiplatelet–anticoagulant therapy than in those receiving anticoagulant therapy. As the results of the previous reports by Rahe-Meyer et al. confirmed in surgical patients that sugammadex produces minor and transient (<1 h) prolongation of the activated partial thromboplastin time and prothrombin time (international normalized ratio), the question arises whether sugammadex has the potential to increase the risk of early postoperative bleeding in a larger group of patients receiving concomitant antiplatelet–anticoagulant treatment. Considering the results of Rahe-Meyer et al. and previous studies, it appears unlikely that sugammadex administered at the end of a surgical procedure will cause clinically significant bleeding. Additional data, however, are necessary to definitively conclude that sugammadex does not produce clinically important postoperative bleeding, even in patients receiving concomitant antiplatelet–anticoagulant therapy.

Competing Interests
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References
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In Reply:
Dr. Carron raises the question that patients receiving thromboprophylaxis with low molecular weight heparins (LMWH) and antiplatelet drugs acetylsalicylic acid (ASA) might have an increased bleeding risk if exposed to sugammadex. He referred to the study by Davidson et al. that showed an increased bleeding risk for the combination of antithrombotic and antiplatelet drugs. In contrast to the