Response to Letters Regarding Article, “Periprocedural Bleeding and Thromboembolic Events With Dabigatran Compared With Warfarin: Results From the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Randomized Trial”

RE-LY is the largest randomized experience reporting outcomes after interruption of anticoagulant therapy.¹ There was no excess of bleeding in patients taking dabigatran, including those having major or urgent surgery.¹ David and colleagues correctly state that the majority of procedures performed during the RE-LY trial were minor. Nonetheless, our analysis included 1482 major procedures that had a 6% to 8% rate of major bleeding,¹ which was numerically lower among dabigatran-treated patients.¹ Hjemdahl et al. opine that the high rate of major bleeding in RE-LY patients assigned to dabigatran 150 mg twice daily who had interruption for >72 hours before surgery suggests accumulation of dabigatran in patients with renal impairment. However, data from RE-LY do not support this interpretation, because the same pattern of bleeding based on the timing of study drug interruption was seen in the subgroup of patients with an estimated creatinine clearance of <60 mL/min. Instead, we believe that the results reflect the selection of longer interruption for >72 hours before surgery suggests accumulation of dabigatran in patients with renal impairment. Nonetheless, our analysis included 1482 major procedures that had a 6% to 8% rate of major bleeding,¹ which was numerically lower among dabigatran-treated patients.¹

David et al. suggest that the rate of bleeding among warfarin-treated patients requiring emergency surgery in RE-LY is higher than observed in Europe; however, the Mayo Clinic study they cite reported a 1% to 3% bleeding rate in patients undergoing elective surgery;¹ similar to the rate for comparable RE-LY patients.¹ David et al. also refer to increased bleeding among patients undergoing catheter ablation for atrial fibrillation who were treated with dabigatran.² However, this was an observational study in which dabigatran was held on the morning of the procedure, whereas warfarin was continued; thus, the relative hazards of interrupted compared with maintained anticoagulation could explain these findings.³ The assertion by David et al that there is a “clear advantage” to vitamin K antagonists in the setting of emergency surgery is not supported by data and is clearly refuted by the evidence from the RE-LY trial.

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