Practical considerations on non-vitamin K oral anticoagulants in patients with high body weight

To the Editor,

I have read with keen interest the systematic review by Güler et al. (1) entitled "A review of the fixed dose use of new oral anticoagulants in obese patients: Is it really enough?" published in Anatol J Cardiol 2015:1020-9. This review is of importance in everyday practice where patients with high body weights are encountered much more commonly than in clinical trials. The authors summarized the current clinical data based on the efficacy and safety of non-vitamin K oral anticoagulants (NOAC) used in patients with atrial fibrillation (AF) and in the prevention and therapy of venous thromboembolism (VTE) with the emphasis on obesity, which is also a rapidly rising epidemic among subjects requiring long-term anticoagulation. The manufacturers of dabigatran, rivaroxaban, and apixaban currently suggest that no dose adjustments are necessary for patients with high body weights even if the present evidence to support such a recommendation is rather weak (2). Although clinical trials on NOAC showed no weight-associated differences in the outcomes of NOAC in AF or VTE, several reports indicate that clinical outcomes of anticoagulant therapy with NOAC could be unsatisfactory in extremely obese patients in part because of the increased clearance of anticoagulants and distribution volume with largely unaltered drug absorption (2). The authors of the current review (1) highlighted the intriguing concept that compared with factor Xa inhibitors, dabigatran, whose renal elimination is the largest (80%), is more prone to provide insufficient anticoagulation intensity in individuals with high body weights. Although no comprehensive subgroup analysis for rivaroxaban or apixaban administered in obese patients has been published to date, the influence of body weight on the anticoagulant effects of these agents appear small. In our cohort of patients with VTE, subjects with a body mass index (BMI) of >35 kg/m^2 represent approximately 10% patients, whereas those with BMI below 18 kg/m^2 represent 5%, with the predominance of young women (A. Undas, unpublished data). From our experience, low BMI is associated with a higher risk of bleeding, which is a more consistent feature than similar rate of VTE recurrences in patients with BMI of >35 kg/m^2 versus those with BMI of <35 kg/m^2. The choice of appropriate regimens of an NOAC in subjects with high body weights is difficult, particularly if the bleeding risk is increased for example in a form of heavy menstrual bleedings. Therefore, monitoring the anticoagulant effects of NOAC is important in this subset of anticoagulated patients; the need for anticoagulation at high body weights is considered one of the well-established indications to determine the blood concentrations of NOAC (3, 4). However, the association between the blood levels of NOAC measured using coagulation assays and thrombotic or bleeding complication is uncertain because of a large variability of the results (5).

Taken together, each patient on NOAC who weighs below 50 kg or above 100–120 kg requires regular visits to the outpatient clinic, particularly within the first weeks of the therapy. The appropriate supervision aims to minimize the risk of bleeding or thromboembolic events in particular individuals who at baseline are at a high risk of these complications. As suggested in the current review (1), more common control visits may increase the safety and efficacy of long-term anticoagulation at high body weights regardless of age and sex. In our opinion, laboratory monitoring of trough anticoagulant effects as well as creatinine clearance should be considered in selected patients. Further clinical studies, particularly registries, are needed to determine whether a fixed dose of NOAC is truly efficacious in patients with morbid obesity.

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