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COMMENTARY

The skinny on treatment of venous thromboembolism in obesity

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See also Barba R, Marco J, Martín-Alvarez H, Rondon P, Fernández-Capitan C, Garcia-Bragado F, Monreal M for the RIETE Investigators. The influence of extreme body weight on clinical outcome of patients with venous thromboembolism: findings from a prospective registry (RIETE). This issue, pp 856–62.

The World Health Organization estimates that worldwide, more than 300 million persons are obese [1]. Obesity and malignancy are risk factors for development of venous thromboembolism (VTE) [2]. Patients with cancer may be cachexic. Therefore, any study of VTE treatment is likely to enrol patients who are at either end of the weight spectrum. Previously, little information was known regarding how such patients were treated. The most concrete clinical trial data we had was that from Merli *et al*. [3] who reported in a *post hoc* analysis that there was a 'non-significant' trend toward an increased rate of VTE recurrence with once vs. twice daily administration of enoxaparin in patients who were obese. Information on dosing low-molecular-weight heparin (LMWH) in patients who are obese is scarce [4,5]. In this issue of the Journal, Barba *et al*. [6] report the results of VTE treatment strategies and 15-day outcomes in more than 8000 patients from RIETE, an ongoing Spanish registry. In their report, anticoagulant treatment strategies, VTE recurrence, major and total bleeding were reported in two important sub groups of patients: those weighing < 50 kg ($n = 169$) and those weighing > 100 kg ($n = 294$). Outcomes were compared with each other and a group of patients weighing 50–100 kg. This study from the RIETE investigators was notable for the following findings.

1 Initial LMWH therapy was chosen for almost all patients (95% of patients weighing < 50 kg and 82% of patients weighing > 100 kg).
2 An unacceptable number of patients weighing < 50 kg (54%) received > 200 IU/kg day^{-1} of LMWH. (The usual dose is 150–200 IU kg^{-1} day^{-1}).
3 Only two patients weighing > 100 kg received > 200 IU kg^{-1} day^{-1}. However 74% received < 175 IU kg^{-1} day^{-1}. As the authors state, this may be secondary to an artificial dosing cap in place at individual institutions.
4 There was no difference in recurrent VTE and major bleeding between patient groups. Body weight was not associated with an increased risk for major bleeding.
5 Major bleeding was lower in patients initially treated with LMWH compared with unfractionated heparin (UFH).
6 In unadjusted analysis, the total bleeding rate was higher in patients weighing < 50 kg.

Limitations of this trial are summarized below.

1 Data was limited to 15-day outcomes.
2 There were no analyses of LMWH dose and outcomes.
3 Multivariate analysis was not performed on total bleeding outcome so other risk factors present in this group could play some role.
4 Patient weight rather than body mass index was analyzed and the more formal definitions of obesity are based upon body mass index.

Important messages from this trial are that clinicians may need to pay closer attention to patient weight when dosing anticoagulants. However, major bleeding was not influenced by body weight. LMWH have a lower rate of major bleeding and should be considered a first-line therapy (as recommended by the American College of Chest Physicians) [7] compared with UFH. LMWH did not increase bleeding in obese patients. Analyses that attempt to control for multiple factors that may influence outcome are the best approach to help discern the impact of body weight on clinical outcomes, as simple univariate analyses may be misleading.

The REITE investigators should be commended for their diligence in conducting such a large-scale registry that has the potential to help answer many more important questions for practitioners battling VTE.

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