JACC: CASE REPORTS VOL. 29, SUPPL S, 2024

ENHANCED PUBLICATION

Anticoagulation in Patients With Obesity

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The patient is a 52-year-old White man with history of morbid obesity, hypertension, hyperlipidemia, persistent atrial fibrillation, heart failure with reduced ejection fraction, obstructive sleep apnea, and peptic ulcer disease who presents to adult cardiac clinical electrophysiology clinic for evaluation of atrial arrhythmias, specifically candidacy for rhythm control strategies. The patient's most recent transthoracic echocardiogram demonstrates globally hypocontractile left ventricular function with an ejection fraction of 30%. On triage, the patient's weight is 174.1 kg (383.8 lb) with a body mass index (BMI) of 53.54 kg/m^2. Electrocardiogram demonstrates atrial fibrillation with a heart rate of 96 beats/min. The patient is currently on systemic oral anticoagulation with apixaban at a dose of 5 mg twice daily. Given the patient's history of morbid obesity and weight/BMI, is apixaban the most appropriate oral anticoagulant for reduction of stroke and systemic embolism?

This scenario referenced represents an increasing clinical dilemma for clinicians who manage patients with a history of venous thromboembolic (VTE) disease and/or atrial fibrillation. Obesity is a complex chronic disease process with rapidly increasing prevalence worldwide, particularly in Western societies (eg, United States, Europe).[1] Obesity is a risk factor for both atrial fibrillation and VTE disease, and is associated with enhanced platelet aggregation, impaired fibrinolysis, and chronic inflammation.[2] Given the exponentially increased risk of thrombotic complications in patients with obesity and comorbid atrial fibrillation or VTE disease, oral anticoagulation is a mainstay of treatment for the reduction of thromboembolic complications.

Unfortunately, randomized clinical trials on contemporary oral stroke reduction therapies (ie, direct oral anticoagulants [DOACs]) are underrepresented with respect to patients at the extremes of weight (low and high body weight), including patients with extremely high body weight (>120 kg, BMI >40 kg/m^2). Given the limited data on the safety and efficacy of DOACs in patients with high body weight, the International Society on Thrombosis and Haemostasis advised that treatment with DOACs in patients with VTE or atrial fibrillation and higher weight or BMI should be avoided due to limited published data.[3]

Several contemporary studies provide real-world insight into the use DOACs for the treatment of both venous thromboembolism and atrial fibrillation in patients with obesity. Barakat et al[4] evaluated the safety and efficacy DOACs vs warfarin across the spectrum of BMI in patients with atrial fibrillation. This single-center retrospective cohort study included 36,094 patients, of which ~50% were labeled as obese or morbidly obese (grade 1 and 2 obesity: BMI 30 to <40 kg/m^2 [n = 13,376; 37%]; grade 3 obesity: BMI ≥40 kg/m^2 [n = 3,924; 11%]). DOACs vs warfarin were associated with significantly lower risk of mortality, ischemic stroke, and hemorrhagic stroke

The following is the video related to this paper.

From the Duke University Medical Center, Durham, North Carolina, USA.
This paper was part of a supplement sponsored by Pfizer. The sponsor had no influence or involvement over the review or approval of any content. Geoffrey Barnes, MD, served as the Guest Editor-in-Chief for this content.
The author attests they are in compliance with human studies committees and animal welfare regulations of the author's institution and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2024.102685

across the spectrum of BMI, including grade 3 and 4 obesity.[4] Perino et al[5] used data from the Veterans Health Administration to analyze the safety and efficacy of DOACs vs warfarin across the spectrum of BMI in patients with venous thromboembolism. The analysis cohort included 51,871 patients prescribed either warfarin or DOACs within 30 days of index diagnosis of venous thromboembolism. For patients with a weight ≥120 kg (n = 6,934; 13.4% of the overall cohort), 38.4% were treated with DOACs. DOAC prescription was not associated with major bleeds, clinically relevant nonmajor bleeds, or recurrent venous thromboembolism for those in higher weight and BMI categories compared with those in average weight and BMI categories. Additionally, DOACs vs warfarin were not associated with increased recurrent venous thromboembolism in any weight or BMI category.

The emergence of newer data suggesting at least similar safety and efficacy DOACs vs warfarin in the management of venous thromboembolism and stroke reduction in patients with morbid obesity has led to changes in the guidelines for treatment of both atrial fibrillation and venous thromboembolism in patients who are obese. The 2023 American College of Cardiology/American Heart Association/American College of Clinical Pharmacy/Heart Rhythm Society Guideline for the Diagnosis and Management of Atrial Fibrillation[6] provides a Class IIa recommendation (benefit >> risk) for the use of DOACs over warfarin for stroke risk reduction in patients with AF and class III (BMI ≥40 kg/m^2) obesity. In 2021, the International Society on Thrombosis and Haemostasis[7] provided updated guidance for the use of DOACs for the treatment and prevention of venous thromboembolism in patients with BMI >35 kg/m^2 or body weight >120 kg. Based on phase 4 studies, rivaroxaban and apixaban have at least similar efficacy and safety (vs warfarin) in patients with obesity. In addition, studies pooling DOACs show similar rates of safety and efficacy outcomes compared with warfarin or across weight categories.[7]

Given initial concerns regarding DOAC use, specifically apixaban in the setting of a patient with morbid obesity, the decision was made to switch the patient from apixaban to a vitamin K antagonist oral anticoagulant (ie, warfarin) for the purposes of stroke reduction in atrial fibrillation. Unfortunately, the patient struggled to maintain therapeutic international normalized ratio values over the course of several years of treatment with warfarin. With the emergence of more contemporary data on the safety and efficacy of DOACs for stroke reduction in patients with atrial fibrillation and morbid obesity, the patient inquired on the risk vs benefit of switching back to DOAC therapy with apixaban. After a discussion with the patient, including a review of the contemporary data on the use of DOACs in patients with morbid obesity and shared decision-making to understand the patient's values and preferences, the decision was made to switch the patient back to stroke reduction therapy with apixaban.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Jackson serves as a consultant to Biosense Webster, Johnson and Johnson, Pfizer, and Sanofi and receives honoraria from PRIME Education.

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KEY WORDS atrial fibrillation, obesity, oral anticoagulation, venous thromboembolism