



BACKGROUND

- Obesity increases risk of cardiovascular disease (CVD), mortality and morbidity.¹
- Direct oral anticoagulants (DOACs) are becoming an increasingly popular treatment option in reduction of stroke risk in AFib, deep vein thrombosis, and pulmonary embolism (PE)
- More robust data is needed as DOAC validation studies contained a small subset of obese patients and available PK/PD evidence suggests decreased drug exposures, reduced peak concentrations and shorter half-lives occur with increasing weight²
- ISTH Guidelines: DOACs should not be used in morbidly obese patients because there are limited clinical data available for patients at the extreme of weights³

OBJECTIVES

- To characterize the therapeutic levels of apixaban as measured by an anti-factor Xa assay for patients with elevated BMI.
 - Determine the percent of patients with BMI ≥ 40 and/or a weight ≥ 120 kg who have therapeutic trough and peak apixaban anti-factor Xa levels
 - Evaluate whether any patient characteristics significantly impact apixaban anti-Xa levels

METHODS

- Study design: Observational (cross-sectional study)
- Inclusion:
 - All patients who are consistently taking apixaban and have a BMI ≥ 40 or a weight ≥ 120 kg
 - Received care at Samaritan Health Services
- Exclusion:
 - Unwilling or unable to consent to participate in the study
 - Recent significant changes in their BMI or weight, medications, or medical conditions.
- Patients were consented, anti-Xa levels and other pertinent study information (medical history etc.) were collected from the electronic medical record

RESULTS

- A total of 44 patients were included.
- Patient recruitment was cut short due to the COVID-19 pandemic
- Most patients met the recommended peak (86%) and trough (89%) ranges
- Proportion of participants with anti-xa levels within a therapeutic range did not significantly differ by BMI subgroup [fig 1 & 2] (peak p=0.33; trough p=0.99)
- An adjusted linear regression model exploring anti-Xa levels by weight (kg) showed that on average, for every 1 unit increase in weight (kg), peak anti-Xa levels are estimated to decrease by 1.5 ng/ml, and trough anti-Xa levels are estimated to decrease by 1.1ng/ml. This model adjusted for gender and creatinine clearance

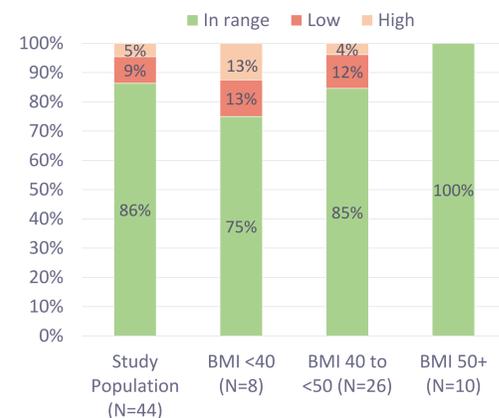


Figure 1. Percent of patients in the therapeutic range for peak anti-xa levels

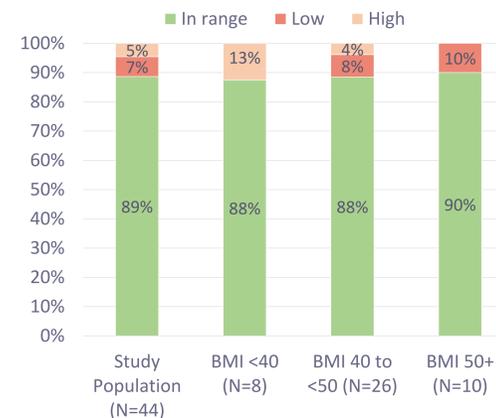
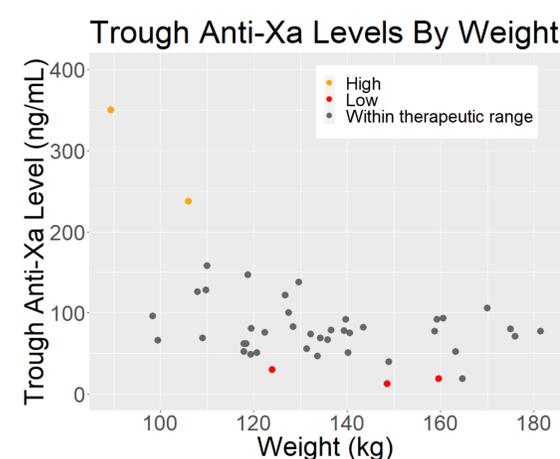
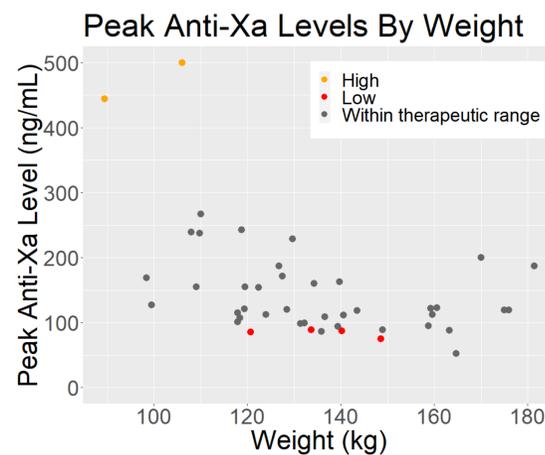


Figure 2. Percent of patients in the therapeutic range for trough anti-xa levels



CONCLUSIONS

- Our study shows that most obese patients utilizing apixaban for stroke prophylaxis attain recommended peak and trough ranges
- In addition to Apixaban being utilized with caution as recommended in obese patients, this study shows they can also be utilized effectively
- This study was limited by a smaller sample size
- If there is uncertainty with use of DOACs in a patient with a BMI of > 40 kg m² or a weight of > 120 kg, we recommend ordering a drug-specific anti-Factor Xa peak and trough level to determine course of therapy
- Larger studies are needed to determine if we can safely manage obese patients with DOACs without levels

FUTURE IMPLICATIONS

- Physician can expand DOAC use in patients with higher BMI's or weight
- Although monitoring is recommended in this patient population, physicians could be inclined to order less of peak and trough anti-Xa levels for obese patient as a standard of practice.
- Future studies can improve sample size by:
 - Doing a retrospective study after physicians have ordered labs as routine practice
 - Adjusting recruiting methods – including patients across a large geographical area or collaborating with other health systems

REFERENCES

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2. Upreti, V. et al Effect of extremes of body weight on the PK/PD of apixaban. *Br J Clin Pharmacol*, 2013; 76: 908-916.
3. Martin K et al. Use of the direct oral anticoagulants in obese patients: guidance from the SSC of the ISTH. *J Thromb Haemost* 2016 14:1308–1313