

# APIXABAN IS SAFE AND EFFECTIVE IN MORBIDLY OBESE PATIENTS: A RETROSPECTIVE ANALYSIS OF 341 PATIENTS WITH BMI ≥40

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## BACKGROUND

In patients with venous thromboembolism (VTE), warfarin had been considered standard of care until the new direct oral anticoagulants (DOACs) were developed. Studies in patients with acute VTE and non-valvular atrial fibrillation (AF) have shown comparable efficacy and a similar, or lower, bleeding risk for DOACs compared to warfarin. However, low representation of morbidly obese patients in these studies and the unknown effect of obesity on pharmacokinetics and pharmacodynamics of these drugs have raised questions about efficacy, adequacy of fixed dosing, and safety of DOACs in patients with BMI ≥40 kg/m<sup>2</sup>. We investigated clinical outcomes of VTE recurrence, stroke and bleeding in morbidly obese patients on apixaban.

## METHODS

**Study population.** All adult (age ≥18 years) patients with BMI ≥40 who were initiated on anticoagulation with apixaban or warfarin, between March 1, 2013 and March 1, 2017, at Montefiore Medical Center (MMC) were identified from Clinical Looking Glass (CLG), a patented database application developed at MMC. A subset with BMI ≥50 was also investigated. All patients on apixaban were included. Patients on warfarin were selected using a random number generator to match the sample size of the apixaban cohort. Patients with indications for anticoagulation other than AF or prior VTE were excluded.

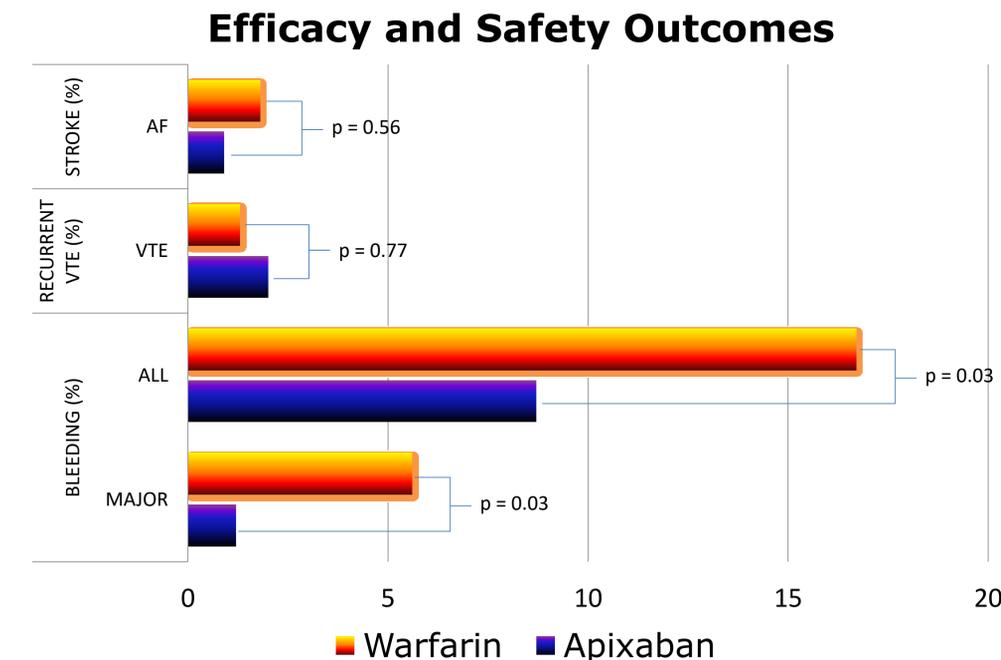
**Data Collection.** Charts were reviewed to document demographic information and recurrent thrombotic and bleeding events while on anticoagulation during the follow-up period (at least 30 days). Initiation date of anticoagulation was based on the first prescription of warfarin or apixaban. VTE and CVA episodes were confirmed by imaging (compression sonography, ventilation/perfusions scans, CT scans, and MRIs). Bleeding events were classified according to criteria from Control of Anticoagulation Subcommittee of the International Society on Thrombosis and Haemostasis.

**Statistical analysis.** Data were analyzed according to anticoagulation indication. Summary statistics and chi-square tests were used to assess statistical significance of the differences in the VTE, CVA and bleeding rates between apixaban and warfarin groups.

## RESULTS

**Table 1: Characteristics of Study Population**

		Apixaban n = 161	Warfarin n = 180
Mean Age on Prescription Date (yrs)		61.9	60.8
BMI	Mean	45.82	47.20
	≥ 50, n (%)	31 (19.3)	45 (25.0)
Male, n (%)		63 (39.1)	63 (35.0)
Race	White, n (%)	41 (25.5)	43 (23.9)
	Black, n (%)	65 (40.4)	77 (42.8)
	Other, n (%)	55 (34.2)	60 (33.3)
AC Indication	AF, n (%)	111 (68.9)	111 (61.7)
	VTE, n (%)	51 (31.7)	76 (42.2)
Follow-up Time, total person-days		54,753	76,306
Mean follow-up time (days)		340	424



- ❖ There was no statistical difference between CVA rates in patients with AF and BMI ≥40 (0.9% with apixaban; 1.8% with warfarin, p = 0.56)
- ❖ There were similar rates of recurrent VTE in patients with prior VTE (2% with apixaban, 1.3% with warfarin, p = 0.77)
- ❖ There was significantly less bleeding, including major bleeding, with apixaban compared to warfarin
- ❖ One patient on apixaban and 7 patients on warfarin had both AF and prior VTE. One patient on warfarin for AF had VTE. One patient on apixaban and 3 patients on warfarin had more than one bleeding event.
- ❖ Mean INR at the time of bleeding events on warfarin was 4.4; it was 6 with major bleeding events. Mean INR at the time of recurrent VTE or stroke was 2.
- ❖ Among the subset of 31 patients with BMI ≥50 on apixaban:
  - One of 21 patients with AF had CVA (4.8%)
  - None of 11 patients with prior VTE had a recurrent VTE
- ❖ Among the subset of 45 patients with BMI ≥50 on warfarin:
  - None of 31 patients with AF had CVA
  - None of 18 patients with prior VTE had a recurrent VTE

## CONCLUSIONS

**Our study provides further evidence of comparable efficacy and safety of apixaban and warfarin in patients with AF and VTE. Although not powered to detect statistical differences between thrombotic events, the overall low recurrence rate in morbidly obese patients is reassuring. Our study also suggests that there may be a decreased risk of bleeding with apixaban, even in the morbidly obese population.**