Real-world comparison of standard versus reduced dose apixaban in stroke prevention and bleeding risk in atrial fibrillation patients with chronic kidney disease: A retrospective analysis of TriNetX data.

Introduction

Atrial fibrillation (AF) is the most prevalent heart arrythmia affecting over 2% of the population worldwide. Chronic kidney disease (CKD) is an independent risk factor for AF; both conditions lead to a prothrombotic state, and both independently increase the risk of stroke. ARISTOTLE trial has demonstrated the superiority of apixaban over warfarin in thromboembolic risk mitigation and reduced bleeding risk. Apixaban dose reduction criteria were implemented to account for the variability in the drug's renal metabolism. However, efficacy of standard versus reduced dose of apixaban was never compared in a randomized controlled trial. Real world adherence to the dose reduction criteria is uncertain and presumably incomplete especially in the high-risk groups of elderly and CKD patients. Our research aims to assess apixaban efficacy in stroke prevention and effect on bleeding in high-risk populations in the real-world clinical practice.

Methods

This is a retrospective cohort study utilizing the TriNetX database to assess the risk, risk difference and risk ratio (RR) of developing ischemic stroke and bleeding in atrial fibrillation patients with CKD after apixaban initiation. Two cohorts were selected based on the use of apixaban 2.5 mg twice a day(bid) and 5.0 mg bid dose. Propensity score matching (PSM) was performed by age, BMI and confounding comorbidities. Further analysis was performed after stratification by CKD staging.

Results

After matching, the cohort included 84,032 patients in 2.5 mg bid and 5.0 mg bid groups.

The risk of stroke was not significantly different between the groups. The risk of stroke was 6.62 % in the 2.5 mg bid group and 6.83% in the 5.0 mg bid group with a risk difference of -0.215% (95% CI= -0.475%, 0.044%) p= 0.104. The risk of bleeding was significantly higher in the 5.0 mg bid group. The risk of bleeding in the 2.5 mg bid group was 18.84% and 20.411% in the 5.0 mg bid group. The risk difference is -1.57 % (95% CI =-2.023%, -1.119%) P< 0.0001. Risk ratio between groups is 0.923 (95% CI = 0.902,0.945). Further subgroup stratification by CKD staging have found increased bleeding risk for apixaban 5 mg bid for stages III, IV and V with risk differences of -1.682 % (95% CI = -2.206%,-1.05%) P<0.001, -4.193% (95%CI = -5.239%, -3.147%) P<0.001, -2.481% (-4.465%,-0.498%) P=0.0143. There was no significant difference in the risk of stroke except for stage IV where the risk of stroke was lower in the 2.5 mg bid group than the 5 mg bid group -0.653% (95% CI= -1.238%, -0.68%) P= 0.0286.

Conclusion

Our results suggest that apixaban 2.5 mg bid dose is safer and equally effective when used in AF patients with concomitant CKD regardless of other demographic factors and comorbid conditions. There is a significant decrease in the risk of major bleeding with preserved effect on stroke prevention in comparison to the 5 mg bid dose. This dose effect is particularly evident in patients with CKD stage III and above. Based on this data, we propose that apixaban 2.5 mg bid dose should be used preferentially in all patients with moderate to severe CKD including patient with end stage renal disease.