The Efficacy and Safety of Novel Anticoagulants for Preventing Thromboembolic Events in Patients with Chronic Kidney Disease and Arial Fibrillation: A Systematic Review and Meta-Analysis

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Background

Chronic kidney disease (CKD) and atrial fibrillation (AF) are common medical conditions that often occur together, creating complex challenges for patient management. Traditional anticoagulants like warfarin require close monitoring and have numerous interactions. Direct oral anticoagulants (DOACs) have emerged as alternatives, but their use in CKD patients is debated. Understanding the potential benefits and risks of novel anticoagulation therapies in CKD patients with AF is essential for optimizing their management and reducing the burden of stroke and thromboembolic events in this vulnerable population. The coexistence of CKD and AF requires a careful evaluation of anticoagulation strategies.There are many conflicting results based on cohort analysis and prospective registries. Consequently, the choice of a specific anticoagulant should be based on solid evidence obtained from randomized clinical trials, which shows the relevance of this research.

Aim

This study provides a Systematic Review of the currently available RCTS on the use of anti-coagulants for Atrial Fibrillation in patients with CKD to address the gaps in knowledge regarding the efficacy and safety of novel anticoagulation therapies, ultimately improving the care and outcomes of patients with these two prevalent conditions.

Method

We conducted electronic searches to identify relevant studiesin PubMed, Embase, and the Cochrane Library for this systematic review. Out of 386 studies, 9 Randomized controlled trials published up to September 2023, which met the inclusion criteria of AF+CKD, were included. Review Manager (Revman) 5.4, a variance-weighted random effects model, was used to estimate event rates and odds ratio. A composite of thromboembolic stroke and systemic embolism defined our primary efficacy. All cause of mortality defined our secondary efficacy, and our primary safety was defined by a composite of major or clinically relevant non-major bleeds.

Research Gap

Research on the safety and efficacy of Novel Oral Anticoagulants (NOACs) in individuals with severe chronic renal disease is limited. This review highlights the lack of clinical data regarding the use of NOACs in patients with advanced Chronic Kidney Disease (CKD) and Atrial Fibrillation (AF). Conflicting outcomes from various studies underscore the uncertainty surrounding the suitability of NOACs in this patient population. Therefore, the selection of an appropriate anticoagulant regimen requires evidence from randomized clinical trials. This research emphasizes the need for robust clinical investigations to determine the optimal management strategy for patients with severe CKD and AF.

Result

Pooled analysis of 9 RCTs showed that the primary endpoint for efficacy occurred in 1606 out of 50430 patients. 797 events out of 27713 patients occurred in the DOAC group, and 809 out of 22717 patients occurred in the warfarin group (OR=0.80;95%CI 0.72,0.89; P<0.0001) (Fig 1). The primary safety endpoint (major and clinically relevant non-major bleeding) happened more frequently than stroke and systemic embolism. Total major and clinically relevant non-major events occurred in 2671 out of 46214 patients. 1227 out of 25633 in the DOAC group and 1444 out of 20581 in the warfarin group (OR=0.63;95%CI 0.49,0.82; P=0.0006) (Fig 2). The pooled estimate event for all-cause mortality was 2711 out of 25810. 1493 out of 15230 occurred in the DOAC group vs 1218 out of 10508 in the warfarin group (OR=0.91;95%CI 0.84, 0.99; P=0.02) (Fig 3). Comparing DOAC with warfarin showed a decreased risk of stroke or systemic embolism and a significantly reduced risk of bleeding and death.

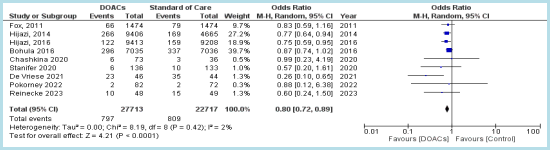

Figure 1 Primary Efficacy Endpoints (Composite of Stroke and Systemic Embolism)

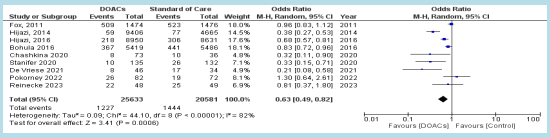

Figure 2 Primary safety endpoint (Major and Non-Major Clinically relevant Bleeding)

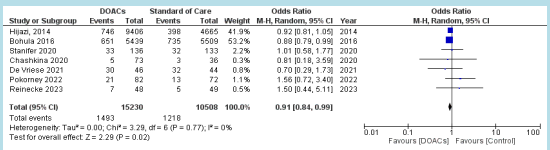

Figure 3Secondary efficacy Outcome (All Cause of Mortality)

Conclusion

From the pooled analysis of the RCTs, we can conclude that DOACs shows better efficacy and safety of novel anticoagulants for preventing thromboembolic events in patients with chronic kidney disease and Atrial fibrillation. The Beneficial effect of DOAC over warfarin is consistent with all stages of CKD.