Meta-analysis of Direct Oral Anticoagulants in Patients With Atrial Fibrillation and Bioprosthetic Valves

Valvular heart disease is frequently complicated by atrial fibrillation, which is associated with an increased risk of mortality. In the presence of a surgical or transcatheter bioprosthetic valve, patients with atrial fibrillation are at increased risks of systemic thromboembolism.[1] Although direct oral anticoagulants (DOACs) have been shown to be noninferior or superior to warfarin in preventing stroke or thromboembolism associated with nonvalvular atrial fibrillation, the utilization of DOACs in patients with previous bioprosthetic valves has been limited in randomized clinical trials (RCTs).[1] Therefore, we conducted a meta-analysis of all RCTs to assess the safety and efficacy of DOACs versus warfarin in this high-risk population.

A comprehensive electronic databases search for RCTs was performed (BK and RP). Two authors extracted and analyzed the data using RevMan v5.3 software. The primary outcome was stroke or systemic thromboembolism. Using a random-effects model, we calculated hazard ratios (HRs) and 95% confidence intervals (CIs) to account for differences in follow-up duration in the studies.

We identified 4 RCTs[2−5] which enrolled 1,379 patients with atrial fibrillation and previous bioprosthetic valve replacement (n = 723 [DOACs] vs n = 656 [warfarin]; 80.1% bioprosthetic mitral valve). The mean age was 62.4 ± 13.0 years, 54.7% female, 14.7% diabetic, 63.6% hypertensive, and mean HAS-BLED score (Hypertension, Abnormal renal or liver function, Stroke, Bleeding, Labile INRs Elderly [age >65 years], Drugs or alcohol) of 1.74 ± 0.94. There were no differences between groups in terms of stroke or systemic embolism (DOACs vs warfarin; HR = 0.79; 95% CI = 0.43−1.44; p = 0.44), all-cause mortality (HR = 1.09; 95% CI = 0.90−1.31; p = 0.37), any bleeding (HR = 0.85; 95% CI = 0.64−1.13; p = 0.27), or major bleeding (HR = 0.62; 95% CI = 0.34 −1.14; p = 0.13) (Figure 1).

This meta-analysis of RCTs demonstrated that DOAC use in patients with atrial fibrillation and preexisting bioprosthetic valve was associated with similar efficacy and safety outcomes as compared with warfarin.

Patients with moderate-to-severe valvular heart disease are at increased risks of systemic thromboembolism and mortality. In the RE-ALIGN (Randomized, Phase II Study to Evaluate the Safety and Pharmacokinetics of Oral Dabigatran Etexilate in Patients after Heart Valve Replacement) trial, the use of dabigatran in patients with mechanical heart valves was associated with increased rates of thromboembolic and bleeding complications compared with warfarin, and resulted in premature termination of the trial.[6] Therefore, current guidelines recommend against the use of DOACs in the presence of mechanical valve. The safety and efficacy of DOACs with bioprosthetic valves has been limited to subgroups and small sample sizes. In our study, we found similar efficacy or safety outcomes with DOACs in this population.[1]

Despite the limitations of our analysis due to low number of events, these data suggest that DOACs may be reasonable for the prevention of thromboembolism in patients with atrial fibrillation with previous bioprosthetic valves. These results are paramount to inform decision making in clinical care of patients, as DOACs do not require INR monitoring and are less prone to drug-drug and food-drug interactions compared with warfarin. We hope that the currently enrolling trials (Edoxaban Compared to Standard Care After Heart Valve Replacement Using a Catheter in Patients With Atrial Fibrillation [ENVISAGE-TAVI AF], NCT02943785; and Rivaroxaban or Aspirin for Biological Aortic Prosthesis, NCT02974920) provide further insight.

In conclusion, in patients with atrial fibrillation and bioprosthetic valves, DOAC use is noninferior to warfarin with respect to the incidence of stroke, systemic embolization, bleeding, and mortality.

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Author Agreement Form − American Journal of Cardiology

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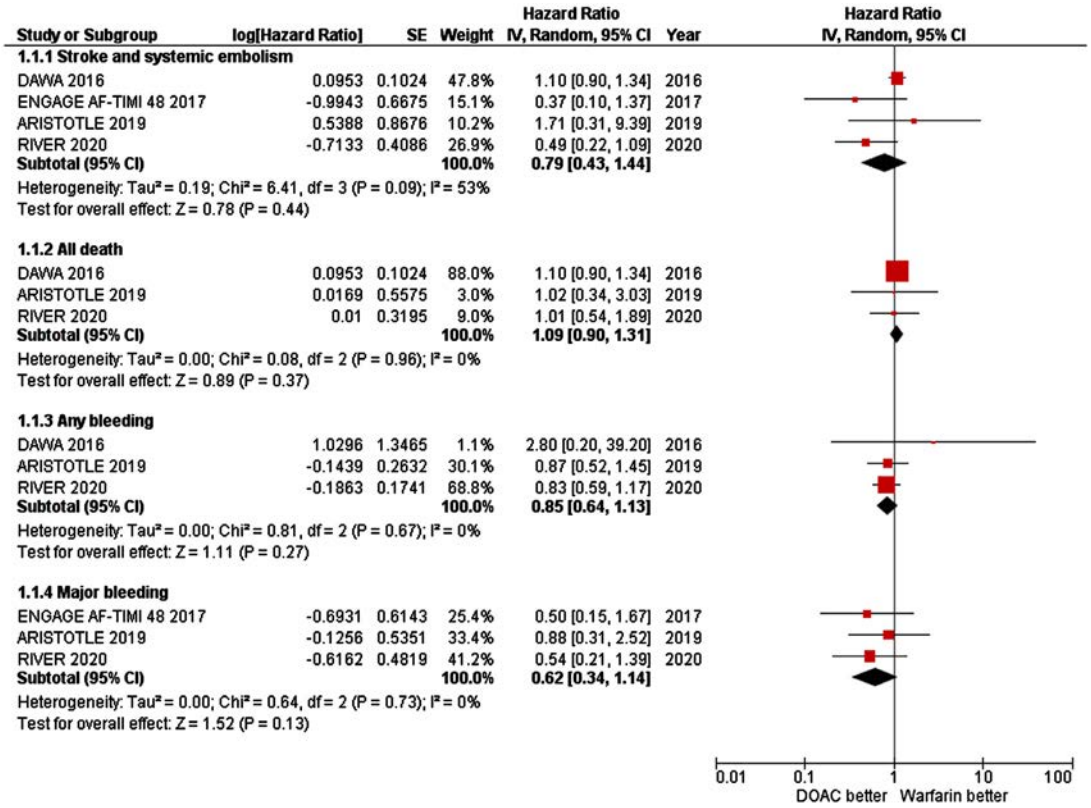

Figure 1. Forest plots of clinical outcomes. Abbreviations: ARISTOTLE: apixaban for reduction in stroke and other thromboembolic events in atrial fibrillations; DAWA: dabigatran versus warfarin after bioprosthesis valve replacement for the management of atrial fibrillation postoperatively; DOAC: direct oral anticoagulants; ENGAGE AF-TIMI 48: effective anticoagulation with factor Xa next generation in atrial fibrillationthrombolysis in myocardial infarction 48; RIVER: rivaroxaban for valvular heart disease and atrial fibrillations.

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Change in Hospitalization Rates After Percutaneous Coronary Intervention for Chronic Total Occlusion (from a Nationwide Cohort Sample)

Successful percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) has been associated with improvement of disabling anginal symptoms in patients with maximal medical therapy, improvement of left ventricular function, and reduces risk of ventricular arrhythmias.[1] Despite these benefits, patients continue to suffer from high hospitalization rates post-CTO PCI with chest pain being the most common cause.[2] In order to better understand the influence of CTO PCI on hospitalization rates, we aimed to explore the change in hospitalization rates pre- and post-CTO PCI by using the Nationwide Readmission Database (NRD).

NRD is a deidentified publicly available all-payers discharge database accounting for 58.2% of US hospitalizations.[3] By utilizing ICD-9/10 codes, we identified hospitalized patients with a diagnosis of CTO and underwent a single-vessel PCI during the same index admission from 2010 to 2017. We excluded patients with a diagnosis of acute coronary syndrome (ST-elevation or non-ST-elevation myocardial infraction (MI), and unstable angina). This approach was designed before to identify patients undergoing CTO PCI using administrative database.[4] We excluded patients who died during index admission and were admitted January-March or October-December in each year to capture 90-day follow-up before and after index admission since NRD data do not cross the calendar year.[5] The primary outcome was the change in 90-day all-cause hospitalization rate pre- and post-CTO PCI. The secondary outcomes included: (1) Change in 90-day hospitalization rates for heart failure, acute MI, chest pain without MI, and ventricular tachycardia-related hospitalizations; (2) a 30-day time frame analysis for the 90-day all-cause hospitalization rates pre- and post-CTO PCI; (3) change in all-cause 90-day hospitalization rates among key subgroups (Figure 1A). McNemar test was used to compare the hospitalization rates pre- and post-CTO PCI. A p value <0.05 was considered statistically significant. This study was exempted by the institutional review board due to the deidentified nature of the database.