

# Non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation and valvular heart disease: systematic review and meta-analysis

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## **Abstract**

The non-vitamin K antagonist oral anticoagulants (NOACs) were approved for non-valvular atrial fibrillation (AF) but this term may be misnomer. Thus, the term non-mechanical and rheumatic mitral valvular (non-MARM) AF was proposed to exclude patients with valvular heart disease (VHD) without contraindications for NOACs. We aimed to review the efficacy and safety of NOACs in patients with AF and VHD compared to Vitamin K Antagonists (VKA). We performed a systematic review with meta-analysis (PROSPERO CRD42015024837) including data from randomized controlled trials (RCTs) retrieved in November 2016. The efficacy and safety data were pooled using random-effects meta-analyses using the hazard ratio (HR) with the 95% confidence interval (95%CI). Trial sequential analysis (TSA) was performed in statistical significant results to evaluate whether cumulative sample size was powered for the obtained effect. In 5 RCTs (with 12 653 VHD AF patients), NOACs significantly reduced the risk of stroke and systemic embolism (HR 0.73, 95%CI:0.60–0.90; TSA showed estimate was robust — O'Brien-Fleming  $\alpha$ -spending boundary crossed before reaching the estimated information size) and intracranial hemorrhage (HR 0.45, 95%CI:0.24–0.87) compared with VKA. Major bleeding risk was not significantly different. In patients with bioprosthesis (3 trials-280 patients) the risks of thromboembolism (HR 0.65, 95%CI:0.20–2.08) and major bleeding (HR 0.94, 95%CI:0.28–3.18) with NOACs were similar to VKA. NOACs are efficacious and safe in patients with non-MARM VHD AF, showing significant reduction in the risk of stroke and systemic embolism and intracranial hemorrhage compared with VKA.

## **Keywords:**

Apixaban, Dabigatran, Edoxaban, Rivaroxaban, Valve, Bioprosthesis