Comparative efficacy and safety of new oral anticoagulants in patients with atrial fibrillation and percutaneous coronary intervention: a network meta-analysis with multicriteria decision analysis

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OBJECTIVES

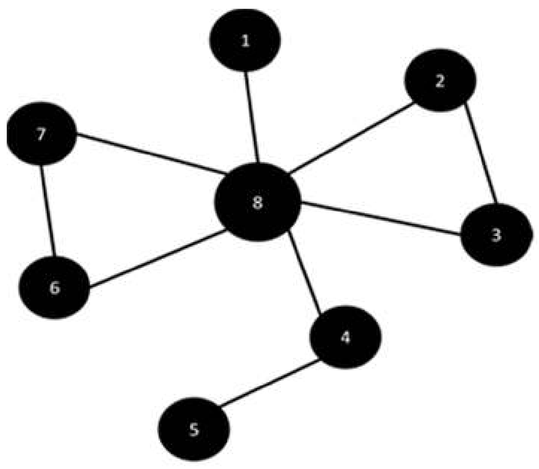
To evaluate further evidence on the clinical profile of new oral anticoagulants (NOACs) for patients with atrial fibrillation (AF) and percutaneous coronary intervention (PCI).

METHODS

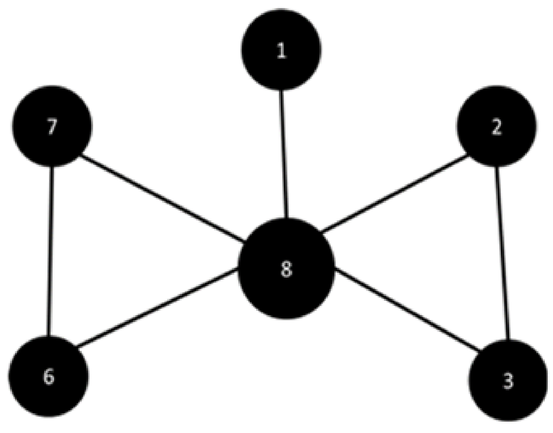
A systematic review with network meta-analysis (NMA) was performed (CRD42019146813). Searches were conducted in PubMed and Scopus. Randomized controlled trials (RCT) evaluating anticoagulant regimens compared head-to-head or against placebo were included. Networks were built for each outcome of interest (i.e. major or clinically relevant non-major (ISTH), major bleeding (TIMI), major or minor bleeding (TIMI), stent thrombosis, stroke, myocardial infarction, death). Results were reported as odds ratio with 95% credibility intervals. Surface under the cumulative ranking curve analyses (SUCRA) were calculated. A multicriteria decision analysis (stochastic multicriteria acceptability analysis - SMAA) was used to quantitatively estimate the benefit-risk of the therapies. Different scenarios were built considering the combination of one or more benefit (efficacy) or risk (safety) criteria.

RESULTS

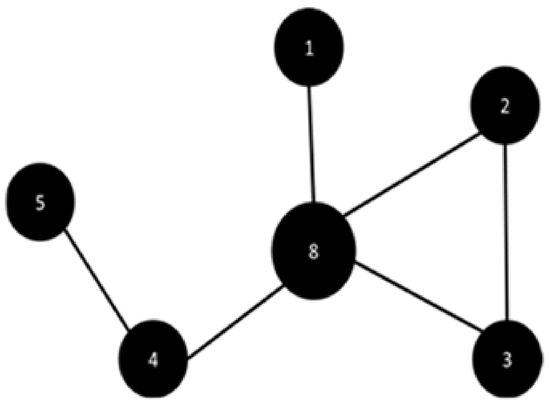
Five RCTs were included (n=11532; WOEST, PIONEER AF-PCI, RE-DUAL PCI, AUGUSTUS and ENTRUST AF-PCI) (see Figure 1). No significant statistical differences were observed among the therapeutic alternatives (vitamin K antagonist + P2Y12 inhibitor, vitamin K antagonist + P2Y12 inhibitor + aspirin, apixaban 5mg + P2Y12 inhibitor, dabigatran 110mg + P2Y12 inhibitor, dabigatran 150mg + P2Y12 inhibitor, rivaroxaban 2.5mg + P2Y12 inhibitor + aspirin, rivaroxaban 15mg + P2Y12 inhibitor, edoxaban 60mg + P2Y12 inhibitor) for all outcomes, including bleeding, stroke and death.



a) Network for the outcomes: major bleeding (TIMI), major or minor bleeding (TIMI), myocardial infarction, stent thrombosis, stroke



b) Network for the outcome: major or clinically relevant non-major bleeding (ISTH)



c) Network for the outcome: death from cardiovascular causes

Figure 1. Network diagrams
1 = Edoxaban + P2Y12; 2 = Rivaroxaban 2.5mg + DAPT; 3 = Rivaroxaban 15mg + P2Y12; 4 = VKA + P2Y12; 5 = Apixaban + P2Y12; 6 = Dabigatran 150mg + P2Y12; 7 = Dabigatran 110mg + P2Y12; 8 = VKA + DAPT

SUCRA and SMAA demonstrated that the association edoxaban 60mg + P2Y12 inhibitor was the worst option (28% chances), leading to more major bleeding, while apixaban 5mg + P2Y12 inhibitor seemed to be the safest alternative (63%) (see Figures 2 and 3).

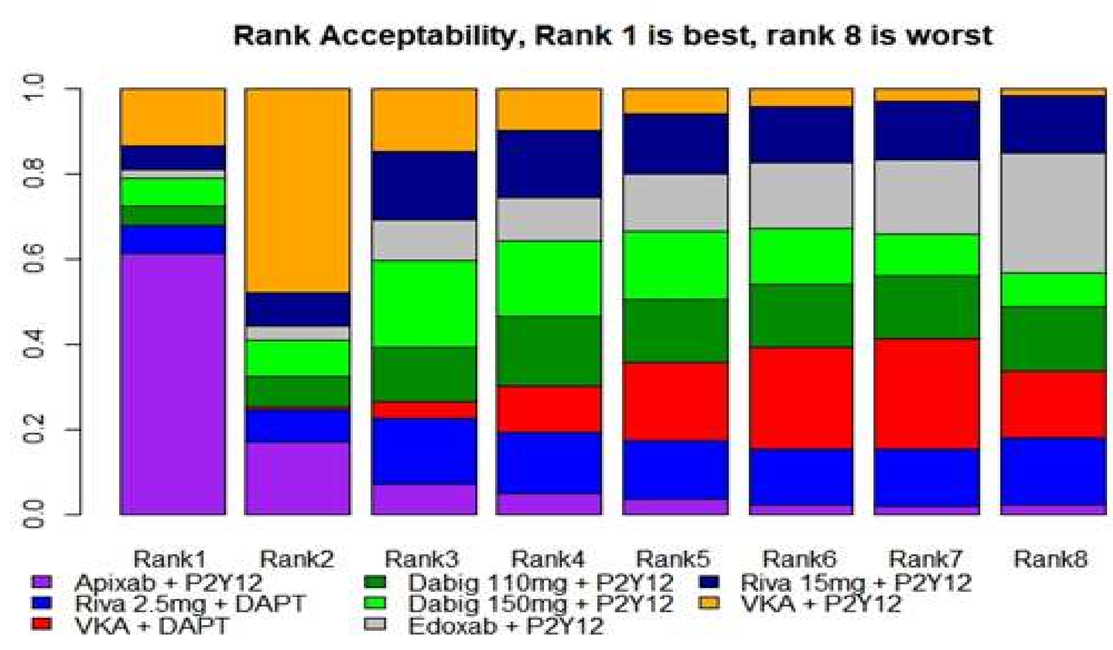


Figure 2. Rank acceptability from SMAA
Each drug has a probability of being the best treatment (rank 1) or the worst treatment (rank 8) considering overall its benefits and risks.

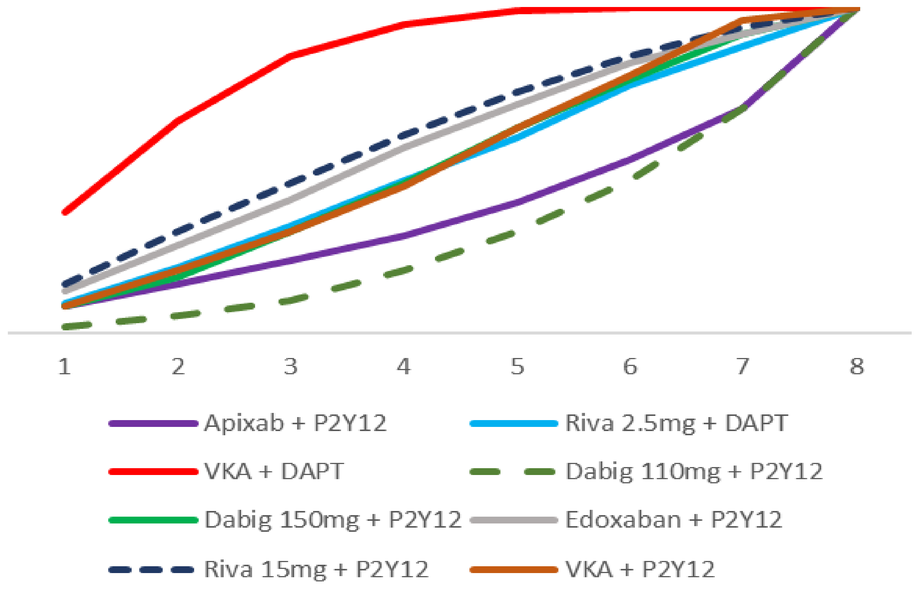


Figure 3. Surface under the cumulative ranking curve (SUCRA) for the outcome of Major bleeding (TIMI)
SUCRA is the inverse ratio of the cumulative frequency of probability ranking, where the larger the area below the curve the greater the probability of the evaluated therapy generating a certain outcome. Apixab + P2Y12 = apixaban + inhibitor P2Y12; Riva 2.5mg + DAPT = rivaroxaban 2.5mg + aspirin + inhibitor P2Y12; VKA + DAPT = vitamin K antagonist + aspirin + inhibitor P2Y12; Dabig 110mg + P2Y12 = dabigatran 110mg + inhibitor P2Y12; Dabig 150mg + P2Y12 = dabigatran 150mg + inhibitor P2Y12; Edoxaban + P2Y12 = Edoxaban + inhibitor P2Y12; Riva 15mg + P2Y12 = Rivaroxaban 15mg + inhibitor P2Y12; VKA + P2Y12 = vitamin K antagonist + inhibitor P2Y12.

CONCLUSIONS

Apixaban + P2Y12 showed a slightly better clinical profile for the treatment of patients with AF undergoing PCI. Edoxaban + P2Y12 is probably the less safe alternative. Cost-minimization analyses should be performed to strengthen the evidence. Meanwhile, the therapeutic choice of antithrombotic regimen should consider, among others, the risks of thromboembolism, bleeding and stroke, patient preferences (e.g. treatment convenience, adherence), access and treatment costs.

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