

Anticoagulation in Surgery

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Abstract

We reviewed available data in the current trends in the anticoagulants use in patients undergoing surgery in addition to hypercoagulability management in patients with malignancy. There is a comparison between oral anticoagulants vs conventional methods of thrombosis prevention as warfarin vs. other methods like anti-platelet drugs like aspirin and clopidogrel. We found that current data suggests that oral anticoagulants provide superior outcomes compared to other options.

Introduction

Perioperative frequency of hemorrhage and thromboembolism complications differs for different interventions. While ophthalmologic surgery and orthopedic interventions were found to have lower risk of complications, thoracic surgery was found to be associated with higher number of such events. Patients with atrial fibrillation (A.fib) were found to be especially prone to experience thromboembolic events [1]. The current guidelines for patient on chronic anticoagulant treatment undergoing surgery or interventional procedure depend on the risk associated with the procedure [2]. The Centre for Disease Control (CDC) estimates that 2.7 million people suffer from Non-valvular atrial fibrillation (NVAF) in the US and at least 250,000 of them require evaluation for a procedure or surgery annually [3,4].

Conventionally, anticoagulation was maintained by heparin parenterally or warfarin orally. However, since warfarin requires laboratory monitoring, there has since been development of various newer anticoagulants.

Anticoagulant Class

Anticoagulants can be classified as A) Vitamin K antagonists as warfarin, B) Heparins as enoxaparin and unfractionated heparin, C) Factor Xa inhibitors as fondaparinux and rivaroxaban, D) Direct thrombin inhibitors as dabigatran and bivaluridin, E) Fibrinolytics as alteplase and reteplase [5], F) Direct oral anticoagulant as dabigatran, endoxaban and rivaroxaban [6] and G) Antiplatelets that include salicylate as Aspirin, which causes inhibition of platelet aggregation by irreversibly inactivating cyclooxygenase-1 dependent production of thromboxane thus preventing thrombus formation, and clopidogrel that prevents platelet aggregation by inhibiting the platelets P2Y₁₂ receptors [7,8].

Oral Anticoagulants Vs Aspirin

Anticoagulation is an important modality to prevent thromboembolic events especially in patients suffering from atrial fibrillation.

Nazha *et al.* [9] recently conducted a meta-analysis of all available phase III randomized clinical trials (RCTs) comparing peri-procedural outcomes of Direct Oral Anticoagulants (DOACs) with Warfarin in patients with NVAF. They included 19353 patients and they found A) Similar risk of stroke/systemic embolism (SSE) between the 2 groups (RR=0.70, 95%CI=0.41-1.18), B) Comparable major bleeding (MB) and death risk were found in DOAC and warfarin treated patients (RR=1.05, 95% CI=0.85-1.30 and RR=1.24, 95%CI=0.76-2.04). While MB rate was similar in interrupted strategy (RR=1.05, 95%CI=0.85-1.3), it was 38% lower in DOAC vs warfarin treated patients in an uninterrupted strategy (RR = 0.62, 95%CI=0.47-0.82). Figure 1. Their study suggested that A) continuing a DOAC peri-procedurally or interrupting it without assays relates to a low rate of periprocedural adverse event when compared to a similar strategy with warfarin, B) DOAC offer a potential advantage over warfarin owing to a shorter half-life (7-14 hours) compared to warfarin (60 hours) and a more predictable pharmacokinetics and pharmacodynamics of the anticoagulant effect of DOACs [9].

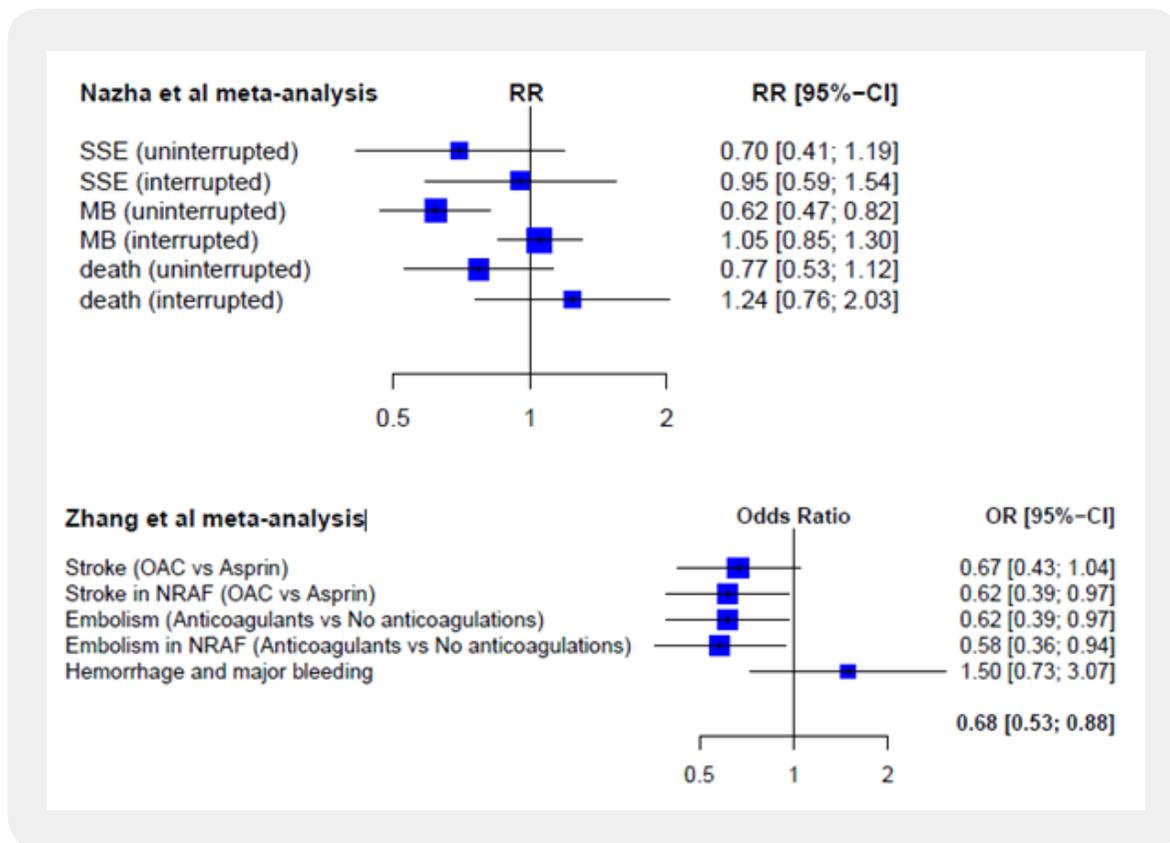


Figure 1. Summary outcomes of the included Nazha and Zhang studies

In a prior meta-analysis by Zhang *et al.* [10], oral anticoagulants were compared to aspirin in patients suffering from atrial fibrillation. They reported 8 (RCTs) with 4363 patients, where 2169 patients received oral anticoagulation while 2194 patients received aspirin. They did not find any statistically significant difference in stroke rate between the two groups (Odds Ratio (OR)=0.667, 95%CI=0.426-1.045, p=0.8). However, in patients with non-rheumatic atrial fibrillation (NRAF), they found anticoagulants to have a lower risk of stroke (OR=0.557, 95% CI 0.411-0.753, P<0.001). Anticoagulants were found to be associated with lower risk of embolism (OR=0.616, 95%CI=0.392-0.966, p=0.04) as well as in the NRAF group (OR=0.581, 95%CI=0.359-0.941, p=0.03). Hemorrhage and major bleeding remained comparable between the two modalities (OR=1.497, 95%CI=0.730-3.070). Thus they concluded that oral anticoagulants to be more effective in preventing embolism than aspirin in patients with AF [10].

In another meta-analysis, Columbo *et al.* [11] sought to determine the effect of perioperative bleeding risk associated with aspirin vs aspirin + clopidogrel (dual anti-platelet therapy [DAPT]) in adults undergoing cardiac surgery. This meta-analysis included >30,000 patients and compared single and DAPT vs placebo or no therapy in adults undergoing on cardiac surgery. They reported that relative risk (RR) of transfusion in Aspirin was 1.14 (95% CI= 1.03-1.26, p=0.009) and in clopidogrel was 1.33 (95% CI=1.15-1.55, p=0.001) while the RR of bleeding in aspirin was 0.96 (95%CI=0.76-1.22, P = 0.76), clopidogrel was 1.84

(95%CI=0.87-3.87, P = 0.11) and DAPT was 1.51 (95%CI=0.92–2.49, P=0.10) and they concluded that at the time of noncardiac surgery, antiplatelet therapy confers minimal bleeding risk with no difference in thrombotic complications.

Conclusion

Conventionally, heparin or warfarin have been used to provide long term anticoagulation in patients with atrial fibrillation to decrease thromboembolic risk. Recently newer anticoagulants as clopidogrel and aspirin are being used. Oral anticoagulants are found to be more efficient in preventing embolism compared to other anticoagulants. They were also associated with lower rate of periprocedural adverse events. On the other hand, aspirin was found to have higher rates of bleeding in patients undergoing surgeries.

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