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Comparative safety of anticoagulant, antiplatelet and combine both for acute coronary syndrome: a systematic review and network meta-analysis

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 April 2024 and was last updated on 29 April 2024.

INTRODUCTION

Review question / Objective Antithrombotic therapy plays an important role in acute coronary syndrome (ACS). The combination of anticoagulant and antiplatelet therapy resulted in fewer complications and stronger potency compared to traditional monotherapy. Our net-meta aimed to compare and rank the safety of different treatments used in patients with acute coronary syndrome.Our net-meta aimed to compare and rank the safety of different treatments used in patients with acute coronary syndrome.

Condition being studied Acute coronary syndrome arises from the rupture or erosion of unstable atherosclerotic plaques within the coronary arteries, leading to thrombus formation and subsequently causing an acute myocardial ischemic syndrome. Of course, approximately 14% of overall patients with acute coronary syndrome failed to survive. It is notable that elderly have the highest incidence of cardiovascular disease and frequently present with acute coronary syndrome. However, recent studies showed that increasing incidence and presence was observed in younger individuals with ACS. This emerging phenomenon significantly contributes to the substantial economic burden that acute coronary syndrome imposes on society . Long-term antiplatelet and anticoagulant therapies play a key role in preventing complications associated with acute coronary syndrome. Oral antiplatelet therapy (aspirin or P2Y12 inhibitors) and anticoagulants (unfractionated heparin, low molecular weight heparin, direct thrombin inhibitors, or Xa factor inhibitors) are recommended therapeutic approaches in the initial management of acute coronary syndrome, regardless of whether the treatment is invasive or non-invasive.

METHODS

Search strategy (apixaban OR edoxaban OR darexaban OR rivaroxaban OR otamixaban OR direct oral anticoagulants) AND (myocardial ischemia OR acute coronary syndrome OR PCI OR

coronary disease OR MI) AND (aspirin OR P2Y12 receptor antagonists OR antiplatelet).

Participant or population Patients were administered direct oral warfarin, anticoagulants, aspirin or P2Y12 receptor antagonists after coronary heart disease.

Intervention Eight types of interventions were included: VKA, NOAC, DAPT, SAPT, VKA+DAPT, VKA+SAPT, NOAC+DAPT, NOAC+SAPT.

Comparator Eight types of comparetors were included: VKA, NOAC, DAPT, SAPT, VKA+DAPT, VKA+SAPT, NOAC+DAPT, NOAC+SAPT.

Study designs to be included (1) randomized controlled trials and observational studies that compared anticoagulant, antiplatelet or combination therapy, (intervention group or control group) in patients with coronary heart disease; (2) patients were administered direct oral warfarin, anticoagulants, aspirin or P2Y12 receptor antagonists after coronary heart disease; (3) efficacy and safety endpoints.

Eligibility criteria (1) Letters to the editor, reviews, and animal studies; (2) there was a combination of heparin or other non-antithrombotic interventions; and (3) the studies were duplicates.

Information sources Our research take place in three major databases including PubMed/MEADLINE, Cochrane/CENTRAL, and Scopus.

Main outcome(s) Bleeding, death, myocardial infarct, stroke, and stent embolism were the main outcomes in this net meta-analysis.

Quality assessment / Risk of bias analysis The identified studies were imported into Endnote X9. Initially, we eliminated redundant studies. Two autonomous researchers conducted data extraction and assessed the quality of references, followed by a cross-validation process. A third researcher was included to conduct the discussion and reach a consensus if there was any disagreement. Basic information, inclusion and exclusion criteria, type of research, sample size, type and dosage of intervention treatment, control group, follow-up and outcome indicators were recorded. A method recommended in the Cochrane Handbook 5.1.0 was used to evaluate the quality (Nasser, 2020). The following aspects were examined: (i) allocation concealment, (ii) sequence generation, (iii) blinding of outcome assessment, (iv) blinding of participants and personnel, (v) selective reporting, (vi) incomplete outcome data, and (vii) other bias.

Strategy of data synthesis Stata software version 17 (Stata corporate, USA) used for the data net meta-analysis (NMA). STATA packages used include mvmeta, network, st0411, and sencode package. Assessment of heterogeneity was done using RevMan 5.3. The rates of events with each antiplatelet, anticoagulant or combination treatment were entered as an individual study arm, and data were pooled in a multiple treatment NMA that allows integration of direct and indirect comparisons. Heterogeneity was also quantified using chi-square tests and the inconsistency statistic (I2). Heterogeneity was considered significant for values of P 50%. When a moderate or high heterogeneity (I2 > 50% and p-value < 0.1) was observed, a random-effect model was employed; otherwise, a fixed-effect model was applied (Higgins, Thompson, Deeks, & Altman, 2003). Risk ratio (OR) with confidence interval (CI) of 95% was adopted as a representative measure of dichotomous outcomes. The level of statistical significance was set as $p < 0.05$. The area under the cumulative ranking (SUCRA) showed the possibility of each intervention being the best.

Subgroup analysis This is a network meta-analysis with low heterogeneity, so we did not conduct subgroup analysis.

Sensitivity analysis Two autonomous researchers conducted data extraction and assessed the quality of references, followed by a cross-validation process. A third researcher was included to conduct the discussion and reach a consensus if there was any disagreement. Basic information, inclusion and exclusion criteria, type of research, sample size, type and dosage of intervention treatment, control group, follow-up and outcome indicators were recorded.

Country(ies) involved China.

Keywords Acute coronary syndrome, anticoagulant, antiplatelet, safety, network meta.

Contributions of each author

Author 1 - Qingsheng Niu performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.
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