INPLASY PROTOCOL

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None declared.

The risk of postpolypectomy bleeding in patients receiving direct oral anticoagulants compared to warfarin or non-anticoagulants: a systematic review with meta-analysis of cohort studies

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Review question / Objective: **P (Population) : those who received endoscopic polypectomy (cold snare polypectomy or hot snare polypectomy) of esophagus, stomach, colon, or rectumPatients receiving direct oral anticoagulants. I (Intervention) : DOACs received before the endoscopic polypectomy. C (Comparison) : Patients receiving warfarin treatment or patients without any anticoagulants treatment. O (Outcome) : Post-polypectomy bleeding. S (Study design) : We identified only cohort studies.**

Condition being studied: **The aim of our systematic review and meta-analysis was to assess the risk of postpolypectomy bleeding (PPB) in patients exposed to direct oral anticoagulants (DOACs). Since there were contradictory results of whether DOACs could raise the risk of PPB, and which one lead to a higher risk of PPB among DOACs and warfarin, we performed this systematic review with meta-analysis.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 October 2022 and was last updated on 31 October 2022 (registration number INPLASY2022100124).

INTRODUCTION

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METHODS

Search strategy: The search terms used for all databases included the following: (nonvitamin K antagonist oral anticoagulants or NOAC or apixaban or dabigatran or rivaroxaban or edoxaban or DOAC or direct oral anticoagulants) and polypectomy. The search terms were slightly modified in different databases including Pubmed, EMBASE and Cochrane.

Participant or population: Patients who received endoscopic polypectomy (cold snare polypectomy or hot snare polypectomy) of esophagus, stomach, colon, or rectumreceiving direct oral anticoagulants (DOAC) treatment.

Intervention: DOACs received before the endoscopic polypectomyPolypectomy, including cold snare polypectomy and hot snare polypectomy.

Comparator: Patient receiving warfarin treatment or patients without any anticoagulants treatment.

Study designs to be included: Cohort Studies only.

Eligibility criteria: The data of patients who received ESD or EMR were excluded.

Information sources: Relevant studies were identified by searching PubMed (until December 2021), EMBASE (until December 2021), and the Cochrane Central Register of Controlled trials (Issue 12 of 12, until December 2021).

Main outcome(s): Pooled estimates revealed a higher risk of PPB among patients using DOACs than among those without anticoagulation (odds ratio [OR]: 6.170, 95% confidence interval [CI]: 3.079 to 12.363). The same result occurred when DOACs were stopped 24 hours before polypectomy (OR: 8.4, 95% CI: 5.53 to 12.759). No significant difference was noted between overall DOACs and warfarin (OR 0.826, 95% CI 0.583 to 1.172), while for subgroups, dabigatran showed a lower PPB rate than warfarin (OR: 0.536, 95% CI: 0.345 to 0.832). Publication bias was not determined. In conclusion, DOACs can significantly raise the risk of PPB, even with 24-hour withdrawal before polypectomy. In addition, a lower risk of PPB was detected for dabigatran than for warfarin.

Quality assessment / Risk of bias analysis: Two reviewers assessed the quality of each study independently using a 9-point Newcastle–Ottawa Scale (NOS). The scores were counted according to three aspects: selection of study subjects, comparability of groups, and assessment of outcome. Discrepancies between the reviewers were resolved by consulting a third reviewer for adjudication.

Strategy of data synthesis: Two independent investigators extracted the data using standardized data extraction forms. Any discrepancies were resolved by consensus. The data collected included the year of publication, study design, number of patients in each treatment arm, prevalence of postpolypectomy bleeding, and endoscopic procedures.

Subgroup analysis: In order to explore the different PPB risk between different DOAC regimens and warfarin, we conducted several subgroups. Since PPB risk in different endoscopic procedures may be distinct, we also performed subgroup analyses of DOAC and warfarin in hot /cold snare polypectomy groups. Regard of the difference of polyps' region, we simply classified them as upper and lower GI, and subgroup analyses were also performed in these groups. Since not only Japanese studies made a large part of our included studies, and also due to the different

dosage of warfarin suggested by Japanese guidelines, we deemed it necessary to conduct subgroup analyses of Japanese and non-Japanese studies to reduce bias. And regrettably, information of the size of polyps was not enough for us to perform a subgroup analysis about it.

Sensitivity analysis: To assess the stability of the results, a sensitivity analysis was also performed by excluding every single study. Publication bias was assessed by Egger's test and funnel plots.

Country(ies) involved: China.

Keywords: Direct oral anticoagulant; warfarin; post polypectomy bleeding; gastrointestinal hemorrhage.

Contributions of each author:

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