## INPLASY PROTOCOL

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**Review Stage at time of this submission:** Piloting of the study selection process.

Conflicts of interest: None. Postoperative bleeding of therapeutic endoscopy in patients using direct oral anticoagulant or warfarin: A systematic review and meta-analysis

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**Review question / Objective:** To compare the postoperative bleeding after therapeutic endoscopy between direct oral anticoagulant (DOAC) and warfarin. Patients: patients who underwent therapeutic endoscopy for gastric or colorectal lesions; Intervention: patients prescribed DOAC before endoscopic procedure; Comparator: patients prescribed warfarin or no anticoagulant therapy before endoscopic procedure; Outcome: postoperative bleeding after endoscopic procedures.

Condition being studied: There is an increasing number of patients undergoing therapeutic endoscopic procedures with prescriptions for direct oral anticoagulant (DOAC) or warfarin. And DOAC has not only been shown to significanlty reduced the thrombotic cerebrovascular accidents, but also has higher rates of satisfaction among patients due to its concenience. So DOAC is more and more widely used in clinic. But DOACs have been associated with a higher risk of postoperative bleeding compared with warfarin according to several previous retrospective studies. There is often inconsistent designation of a periprocedural anticoagulation decision maker. Therefore, it is necessary to conduct a systematic review and meta-analysis to compare the postoperative bleeding between DOAC and warfarin.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 April 2020 and was last updated on 25 April 2020 (registration number INPLASY202040172).

## INTRODUCTION

**Review question / Objective:** To compare the postoperative bleeding after therapeutic endoscopy between direct oral anticoagulant (DOAC) and warfarin. Patients: patients who underwent therapeutic endoscopy for gastric or colorectal lesions; Intervention: patients prescribed DOAC before endoscopic procedure; Comparator: patients prescribed warfarin or no anticoagulant therapy before endoscopic procedure; Outcome: postoperative bleeding after endoscopic procedures.

**Rationale:** The review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. A protocol specifying the eligibility criteria and analysis methods for the studies included in this systematic review and meta-analysis was established and documented prior to the start of this review.

Condition being studied: There is an increasing number of patients undergoing therapeutic endoscopic procedures with prescriptions for direct oral anticoagulant (DOAC) or warfarin. And DOAC has not only been shown to significanly reduced the thrombotic cerebrovascular accidents, but also has higher rates of satisfaction among patients due to its concenience. So DOAC is more and more widely used in clinic. But DOACs have been associated with a higher risk of postoperative bleeding compared with warfarin according to several previous retrospective studies. There is often inconsistent designation of a periprocedural anticoagulation decision maker. Therefore, it is necessary to conduct a systematic review and metaanalysis to compare the postoperative bleeding between DOAC and warfarin.

## **METHODS**

Search strategy: PubMed, Web of Science, Embase were searched for relevant articles. The date range of literature searching is from the inception of the database. The studies were limited to publish in English. Synonyms for " anticoagulants " such as warfarin, anticoagulant agent, anticoagulation, antithrombotic were combined using the Boolean operator "OR". A similar search strategy was used for "endoscopy" which combined with endoscopic submucosal dissection, endoscopic mucosal resection, polypectomy by using the Boolean operator "OR". Both search results were combined using the Boolean operator "AND". The MeSH terms such as "Warfarin", "Anticoagulants", "Factor Xa Inhibitors", "Endoscopy, Digestive System", "Endoscopy, Gastrointestinal", "Endoscopic Mucosal Resection", "Warfarin", "Anticoagulants", "Factor Xa Inhibitors" were also used when possible.

Participant or population: Patients who underwent therapeutic endoscopy for gastric or colorectal lesions.

Intervention: Patients prescribed direct oral anticoagulant before endoscopic procedures.

**Comparator:** Patients prescribed warfarin or no anticoagulant therapy before endoscopic procedures.

Study designs to be included: Prospective studies or retrospective studies.

Eligibility criteria: Studies meeting each of the following criteria were eligible: (a) patients: patients who underwent therapeutic endoscopy for gastric or colorectal lesions; (b) intervention: patients prescribed direct oral anticoagulant before endoscopic procedure; (c) comparator: patients prescribed warfarin or no anticoagulant therapy before endoscopic procedure; (4) outcome: postoperative bleeding after endoscopic procedures.

**Information sources:** Electronic databases: Pubmed, Web of Science, and Embase.

Main outcome(s): To compare the postoperative bleeding after endoscopic procedures between direct oral anticoagulant and warfarin.

Quality assessment / Risk of bias analysis: The quality of each study was evaluated based on Newcastle-Ottawa Scale (NOS) which assessed each study in three areas including (1) the selection of the study subjects, (2) the comparability of the groups, and (3) the assessment of the outcome of interest. Strategy of data synthesis: Data analysis was performed using Review Manager 5.3 software. Odds ratio (OR) was chosen to assess the risk of bleeding. All statistical tests were two-sided. Pooled estimates with 95% confidence intervals (CI) were calculated using the weighted variance technique.

Subgroup analysis: Subgroup analyses were based on different types of therapeutic endoscopic procedures such as ESD or not ESD and different strategies of anticoagulants such as whether switch to heparin bridge before procedures.

Sensibility analysis: To determine whether any particular study skewed the results of this meta-analysis, we conducted a sensitivity analysis by excluding studies one by one.

Language: English.

Country(ies) involved: China.

Keywords: Anticoagulant agent; Therapeutic endoscopy; Postoperative bleeding.