INTRODUCTION

Review question / Objective: P: Patients who were diagnosed with gastrointestinal malignancies with cancer-associated thrombosis; I: Direct oral anti-coagulants; C: Low molecular weight heparins; O: Bleeding events.

Condition being studied: The association between gastrointestinal (GI) cancer and a high incidence of venous thromboembolism (VTE) is well known. Previous randomized controlled studies demonstrated that direct oral anticoagulants (DOACs) effectively treat cancer-associated VTE (CAT). However, some DOACs appeared to increase the risk of bleeding, particularly in patients with GI malignancies. So, we plan to conduct a systematic review and meta-analysis to evaluate the safety and efficacy of DOACs in GI cancer-associated thrombosis.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 August 2021 and was last updated on 30 August 2021 (registration number INPLASY202180113).
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METHODS

Search strategy: Two investigators separately examined the included articles from the search terms ‘DOACs’, ‘anticoagulants’, and ‘GI cancer’ from two databases (EMBASE and MEDLINE).

Participant or population: Adults with gastrointestinal malignancies with cancer-associated thrombosis.

Intervention: Direct oral anti-coagulants.

Comparator: Low molecular weight heparins.

Study designs to be included: Both randomized controlled trial and cohort study (retrospective or prospective).

Eligibility criteria: 1) the type of study must have been a randomized controlled trial (RCT) or a cohort studies (either retrospective or prospective); 2) the study must have compared the efficacy between at least one DOAC and at least one LWMH in GI cancer-associated venous thromboembolism; 3) the study must have included the primary outcome of the study; and, 4) the study must have defined the definition of major bleeding according to the criteria of the International Society on Thrombosis and Haemostasis (ISTH).

Information sources: Electronic databases including MEDLINE and EMBASE.

Main outcome(s): The primary outcome was either recurrent VTE or major bleeding after anticoagulant therapy according to the ISTH criteria.

Quality assessment / Risk of bias analysis: The Jadad Quality Assessment Scale and the Newcastle-Ottawa Scale were used to evaluate the quality of the included randomized controlled trials and the non-randomized studies, respectively.

Strategy of data synthesis: Review Manager 5.3 software from the Cochrane Collaboration (London, UK) was used to analyze all data. Two investigators extracted all data from the selected studies using a standardized data extraction form. The effect was estimated and combined with 95% confidence intervals (CIs) using the Mantel-Haenszel method. Cochran’s Q test was calculated, and the statistical heterogeneity among the studies was estimated using the I² statistic. A p-value less than 0.05 was considered statistically significant.

Subgroup analysis: The subgroup analysis in this study including major, clinically relevant non-major bleeding, and recurrent thrombosis according to the type of DOACs and type of GI cancers (luminal vs non-luminal).

Sensitivity analysis: No sensitivity analysis is planned to perform in this systematic review and meta-analysis.

Language: English.

Country(ies) involved: Thailand.

Keywords: Acute treatment, venous thromboembolism, Direct oral anticoagulants, Gastrointestinal cancer, Low-molecular-weight heparin, Patients.

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