INPLASY PROTOCOL

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None declared.

Aspirin versus low molecular weight heparin for the avoidance of venous thromboembolism in major orthopedic operation: a systematic review and meta-analysis

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Review question / Objective: **We performed a systematic review and meta-analysis of the existing evidence of aspirin in preventing thromboembolism in major orthopedic operation.**
Condition being studied: **Recently, numerous significant improvements have been found in anticoagulation treatment. However, thromboembolism risk is still a main trouble, and aspirin has functioned as an underlying beneficial focus to diminish thromboembolism risk.Venous thromboembolism (VTE), including deep venous thrombosis (DVT) and pulmonary embolism (PE), is a severe and deadly obstacle after major orthopedic surgery. Emerging evidence suggests that about 2.4% to 6.5% of orthopedic patients develop VTE, and the occurrence of VTE is as high as 50% in fracture patients who have not received thrombus prevention measures. In addition, VTE patients without inducement have a higher risk of recurrence after stopping anticoagulation. Therefore, preventing VTE after surgery and preventing recurrence after VTE anticoagulant withdrawal is very important.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 May 2023 and was last updated on 22 May 2023 (registration number INPLASY202350081).

INTRODUCTION

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METHODS

Participant or population: Patients who underwent lower limb joint surgery, including THA, TKA, etc., who had no inducement of VTE in the past, or other patients who needed to prevent VTE; 3) the interventions were: aspirin group was given oral aspirin with total dose, while the control group was treated with LMWH (including enoxaparin, nadroparin, dalteparin, etc.), or without any drug prophylaxis/placebo, and the dose of preventive drugs was unlimited.

Intervention: The interventions were: aspirin group was given oral aspirin with total dose, while the control group was treated with LMWH (including enoxaparin, nadroparin, dalteparin, etc.), or without any drug prophylaxis/placebo, and the dose of preventive drugs was unlimited.

Comparator: The control group was treated with LMWH (including enoxaparin, nadroparin, dalteparin, etc.), or without any drug prophylaxis/placebo, and the dose of preventive drugs was unlimited.

Study designs to be included: The main outcome event was the occurrence of VTE, and the secondary outcome was major hemorrhage or all-cause death. At least one predetermined outcome event was reported in the study. Studies were excluded when they were: 1) review, meta-analysis, or guidelines; 2) experimental groups did not meet the requirements; 3) no relevant outcome indicators or incomplete; 4) patients have a history of hemorrhagic disease or bleeding tendency in preoperative blood coagulation test, and the use of drugs that might affect the results; 5) repeatedly published articles. The data were extracted independent

Eligibility criteria: Articles were included when they were: 1) randomized controlled trial (RCT) and cohort study; 2) patients who underwent lower limb joint surgery, including THA, TKA, etc., who had no inducement of VTE in the past, or other patients who needed to prevent VTE; 3) the interventions were: aspirin group was given oral aspirin with total dose, while the control group was treated with LMWH (including enoxaparin, nadroparin, dalteparin, etc.), or without any drug prophylaxis/placebo, and the dose of preventive drugs was unlimited; 4) the main outcome event was the occurrence of VTE, and the secondary outcome was major hemorrhage or all-cause death. At least one predetermined outcome event was reported in the study. Studies were excluded when they were: 1) review, meta-analysis, or guidelines; 2) experimental groups did not meet the requirements; 3) no relevant outcome indicators or incomplete; 4) patients have a history of hemorrhagic disease or bleeding tendency in preoperative blood coagulation test, and the use of drugs that might affect the results; 5) repeatedly published articles.

Information sources: We systematically explored PubMed, EMBASE, Cochrane Library, and Scopus databases until November 30, 2022. This systematic search used the MeSH terms and free keywords for “aspirin," "VTE," " venous thromboembolism," " deep venous thrombosis," "DVT," "pulmonary embolism," "PE," "major bleeding," "enoxaparin," “nadroparin," “dalteparin," " low molecular weight heparin," "LMWH," “placebo," and subject words, derivative words, etc.

Main outcome(s): The main outcome event was the occurrence of VTE, and the secondary outcome was major hemorrhage or all-cause death.

Quality assessment / Risk of bias analysis: Publication bias was initially assessed by visual observation of the degree of funnel plot asymmetry. Then, we used Egger's bias test and Begg-Mazumdar Kendall's to objectively confirm the visual perception from the funnel plot. A p-value < 0.1 was considered as evidence of publication bias. Funnel plots and Egger's plots are available. When there was evidence of publication bias, we adjusted the effect sizes using the trim-and-fill method.

Strategy of data synthesis: All computations and visualizations were carried out using R version 4.0.4 (R Core Team [2020]. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria), and STATA 16 (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC) for metaregression and Egger's plots. We used following packages: "meta" (version 4.17–0), "metafor" (version 2.4–0), "dmetar" (version 0.0–9), and "tidyverse" (version 1.3.0). All forest plots and the drapery plot were designed using R. A p-value of <0.05 was considered statistically significant.

Subgroup analysis: To reduce the heterogeneity among individual studies, we conducted a subgroup analysis based on the type of intervention used in each study.

Sensitivity analysis: We conducted a sensitivity analysis to identify influential cases for meta-analyses with significant heterogeneity and including ten or more studies. Each time we omitted one study and recalculated the effect size (Leave-One-Out Analyses). To reduce the heterogeneity among individual studies, we conducted a subgroup analysis based on the type of intervention used in each study.

Country(ies) involved: China.

Keywords: aspirin; major orthopedic surgery; venous thromboembolism; low molecular weight heparin; meta-analysis.

Contributions of each author:
Author 1 - Lin Wang.
Author 2 - Xiang wen Yao.
Author 3 - Hongxue Qu.