INPLASY PROTOCOL

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None declared.

Effect of sodium-glucose cotransporter 2 inhibitor on outcomes in patients with atrial fibrillation: a systematic review and meta-analysis

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Review question / Objective: **To evaluate the effect of SGLT2 inhibitors on the long-term prognosis of patients with atrial fibrillation (AF).**
Rationale: **Through searching PubMed, Embase, Web of Science,and Google Scholar to collect outcomes in patients with atrial fibrillation treated with SGLT2(sodium-glucose cotransporter 2) inhibitors. The hazard ratio (HR) and 95% confidence interval (CI) in each study were used for the meta-analysis. The primary outcomes were cardiovascular death, all-cause death, hospitalization for heart failure(HHF), Ischemic stroke or thromboembolic events, Myocardial Infarction(MI) or acute coronary syndrome(ACS).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 March 2023 and was last updated on 03 March 2023 (registration number INPLASY202330008).

INTRODUCTION

Review question / Objective: **rognosis of patients with atrial fibrillation (AF).**

Rationale: **Through searching PubMed, Embase, Web of Science,and Google Scholar to collect outcomes in patients with atrial fibrillation treated with SGLT2(sodium-glucose cotransporter 2) inhibitors. The hazard ratio (HR) and 95% confidence interval (CI) in each study were used for the meta-analysis. The primary outcomes were cardiovascular death, all-cause death, hospitalization for heart failure(HHF), Ischemic stroke or**

thromboembolic events, Myocardial Infarction(MI) or acute coronary syndrome(ACS).

Condition being studied: Atrial fibrillation is the most common persistent arrhythmia.As of 2019, there were about 59.7 million patients with atrial fibrillation (including atrial flutter) worldwide.In people of European ancestry older than 55 years, 1 in 3 people has AF.The prevalence and incidence of atrial fibrillation are still increasing year by year.It is estimated that 6 – 120 million people in the US will have AF by 2050 and 17.9 million in Europe by 2060.AF can significantly increase the prevalence of many diseases,for example,increase the risk of ischemic stroke by 4 to 5 times, increase the risk of myocardial infarction by 2-fold,increase all-cause mortality by 1.5 times in men and all-cause mortality in women,and can lead to a 2 times increase in the incidence of heart failure.The annual hospitalization rate of AF patients is twice that of non-AF patients, and about 30% of the AF patients are hospitalized at least once a year.Not only that, more than 60% of AF patients have significantly decreased quality of life/ exercise tolerance, and 17% have disabling symptoms. AF has become a major cardiovascular disease that seriously endangers human health.
Sodium-glucose co-transporter 2 inhibitor is a novel glucose-lowering drug that reduces blood glucose by inhibiting proximal tubular reabsorption and promoting urinary glucose excretion,has been recommended by the American Diabetes Society for glucose lowering treatment of type 2 diabetes.A large phase 3 randomized controlled trial (RCT) showed that SGLT2 inhibitor reduced the risk of cardiovascular death and heart failure hospitalization, even in the absence of diabetes.A systematic review and meta-analysis of 16 randomized controlled trials proved that SGLT2 inhibitor can reduce the incidence of atrial fibrillation.The study by Arjun K. Pandey et al. suggested that SGLT2 inhibitors may reduce AF events and may reduce hospitalization for heart failure or cardiovascular death in both AF and non-AF patients,but Michael Böhm et al. consider that patients with AF have no indication for SGLT2 inhibitors.Therefore, it is currently controversial whether SGLT2 inhibitors can be used in patients with AF and can improve their cardiovascular outcomes.This paper provides further research on whether SGLT2 inhibitor is applicable for patients with AF and improves their long-term outcomes.Atrial fibrillation is the most common persistent arrhythmia.

METHODS

Search strategy: We searched four databases (Pubmed, EMBASE, Web of Science, and Google Scholar) from inception to November 2022. The search strategy was constructed around PICOS tool :(P) population: patients with atrial fibrillation ; (I) SGLT2 (sodium-glucose cotransporter 2 inhibitor) inhibitor; (C) control group: placebo or no-SGLT2 inhibitor; (O) Outcomes: cardiovascular death, all-cause death, hospitalization for heart failure(HHF), Ischemic stroke or thromboembolic events, Myocardial Infarction(MI) or acute coronary syndrome(ACS). (S) Study type: randomized controlled trial or cohort study.

Participant or population: Patients with Atrial Fibrillation.

Intervention: Sodium-glucose cotransporter 2 (SGLT2) inhibitors.

Comparator: Patients with atrial fibrillation who did not use SGLT2 inhibitor or use placebo.

Study designs to be included: Randomized controlled trial or cohort study.

Eligibility criteria: None.

Information sources: PubMed, Embase, Web of Science,and Google Scholar.

Main outcome(s): Cardiovascular death, all-cause death, hospitalization for heart failure(HHF), Ischemic stroke or thromboembolic events, Myocardial

Infarction(MI) or acute coronary syndrome(ACS).

Data management: The literature was screened and excluded using the literature management software EndNote 20. RevMan 5.4.1 software was used for Meta-analysis.

Quality assessment / Risk of bias analysis: RCTS were evaluated according to the RCT ROB assessment tool of the Cochrane Handbook version 5.1.0. We considered the following seven aspects :(1) Random sequence generation(selection bias) (2) Allocation concealment(selection bias), (3)Blinding of participants and personnel (performance bias), (4) Blinding of outcome assessment (detection bias), (5) Incomplete outcome data(attrition bias),(6) selective reporting(reporting bias), and (7) other sources of bias.Trials were categorized into three levels of ROB by the number of components for which high ROB potentially existed: high risk (five or more), moderate risk (three or four) and low risk (two or less) [26]. Cohort studies were evaluated according to the Newcastle-Ottawa Scale (NOS). It evaluates cohort studies with three modules and eight items in total. It includes: (1) selection of study population, (2) comparability, and (3) exposure/ outcome evaluation. NOS used the semi-quantitative principle of star system to evaluate the quality of literature. Except for comparability, the other items could be rated up to 1 star, and the full score was 9 stars.Higher scores suggest higher study quality.

Strategy of data synthesis: RevMan 5.4.1 software was used for Meta-analysis. Assess the extent to which the outcomes of the included studies are consistent.If I2 is 50%, the heterogeneity is considered to be high. If high heterogeneity between studies was found, we used the random-effects (RE) model. Otherwise, the fixed-effects (FE) model was used. We further investigated heterogeneity across studies by performing sensitivity analyses. P-value<0.05 was considered to be associated with the occurrence of the outcome.

Subgroup analysis: None.

Sensitivity analysis: RevMan 5.4.1 software was used for sensitivity analysis. The results show that the included studies were stable.

Language restriction: No.

Country(ies) involved: China.

Keywords: Sodium-glucose cotransporter 2 inhibitors,Atrial fbrillation,systerm review and Meta-analysis.

Dissemination plans: The article will be published in the journal as soon as it is completed.

Contributions of each author:

Author 1 - Xiaojing Shi - Draft and complete the writing of the manuscript.
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Author 2 - Hongmei Gao - The author provided statistical expertise , guided the writing of the article and supported the scientific research funding.
Author 3 - Ruirui Song - The author contributed to the development of the selection criteria, and the risk of bias assessment strategyLiterature search and screening.
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