INPLASY PROTOCOL

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None declared.

The Effect of Ticagrelor on Coronary Microcirculation Function post-PCI in patients with CAD Compared to Clopidogrel, Prasugrel, and Cangrelor: A Systematic Review and Meta-Analysis

Qiu, XH[1].

Review question / Objective: **Ticagrelor, as a type of oral P2Y12 inhibitors, is widely prescribed in CAD patients and can improve the prognosis. However, the efficiency of ticagrelor on coronary microcirculation is still ambiguous. The objective of this meta-analysis is to determine the efficacy of ticagrelor on coronary microcirculation function post-PCI in patients of coronary artery disease (CAD). The meta-analysis of RCTs, based on the most comprehensive and systematic search, was performed to summarize the effects of ticagrelor on coronary microcirculation function.**
Information sources: **A comprehensive study was conducted on databases including PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov websites. A historical search was performed for a reference list of the selected studies published in English until May 2022.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 November 2022 and was last updated on 12 November 2022 (registration number INPLASY2022110064).

INTRODUCTION

Review question / Objective: **Ticagrelor, as a type of oral P2Y12 inhibitors, is widely prescribed in CAD patients and can improve the prognosis. However, the efficiency of ticagrelor on coronary microcirculation is still ambiguous. The objective of this meta-analysis is to determine the efficacy of ticagrelor on coronary microcirculation function post-PCI in patients of coronary artery disease (CAD). The meta-analysis of RCTs, based on the most comprehensive and systematic**

search, was performed to summarize the effects of ticagrelor on coronary microcirculation function.

Condition being studied: Microcirculation dysfunction is a systemic pathological change involving the coronary arteries and pathophysiological processes of various disease states, including heart failure, hypertension, and diabetes. Recent clinical studies have shown that ticagrelor has a better effect than clopidogrel in improving the short-term prognosis of CAD patients after PCI. As a new anti-platelet drug, ticagrelor has rapid and stable effect. Furthermore, ticagrelor can inhibit adenosine reuptake and increase the effects of adenosine on blood vessels, both endogenous and exogenous. Several clinical trials investigated the effect of ticagrelor on coronary microcirculation function. However, these studies showed conflicting results about whether ticagrelor improved coronary microcirculation. Several studies suggested that ticagrelor ameliorated coronary microcirculation. In contrast, other studies demonstrated that ticagrelor exhibited no additional beneficial effect on coronary microcirculation function. Therefore, the experimental data can be obtained, the operation can be realized, the personnel funds are sufficient, and the research purpose is meaningful.

METHODS

Participant or population: The patients with coronary artery disease (CAD) (i.e., stable CAD, unstable angina (UA), non-ST elevation myocardial infarctions, ST-segment elevation myocardial infarction ,with stent implantation).

Intervention: The treatment of ticagrelor.

Comparator: The treatment of clopidogrel, prasugrel, and cangrelor.

Study designs to be included: The randomized controlled trials (RCTs) were included.

Eligibility criteria: Eligibility CriteriaWe searched all the randomized, controlled, parallel, or cross-over trials that analyzed the effects of ticagrelor on coronary microcirculation. Control groups receiving the treatment of clopidogrel, prasugrel or cangrelor. Other studies, such as review articles, animal experiments, case reports, trials without a control group, trials without ticagrelor intervened, and studies from which we could not extract data, were excluded.

Information sources: A comprehensive study was conducted on databases including PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov websites. A historical search was performed for a reference list of the selected studies published in English until May 2022.

Main outcome(s): The index of microvascular resistance (IMR); Coronary flow reserve (CFR); Fractional flow reserve (FFR); Thrombolysis in myocardial infarction flow grade (TIMI); Corrected TIMI frame count (cTFC).

Quality assessment / Risk of bias analysis: Two reviewers independently assessed the methodological quality of the included studies using the Cochrane Risk of Bias Tool.

Strategy of data synthesis: Changes in IMR, CFR, FFR, TIMI, and cTFC were used to assess the effect of ticagrelor on these outcomes determining the difference between the intervention and control groups with mean and SD. Continuous variables were used to analyze the mean difference (MD) with the 95% CI effect size. Dichotomous outcomes were used to analyze the relative risk (RR) with a confidence interval (CI) of 95%. Statistical heterogeneity was assessed using the chi-squared test ($p < 0.10$ was considered statistically significant for heterogeneity) and was quantified using the I2 statistic. I2 > 50% was considered high heterogeneity [20]. We used the fixed-effect model or the random-effect model in the meta-analysis according to the chi-squared values. Review Manager 5.3 (Cochrane

Collaboration, Oxford, UK) were used for data analyses.

Subgroup analysis: Subgroup analysis was not performed.

Sensitivity analysis: Heterogeneity analysis was performed by Stata software, and the sensitivity of the article was reflected by the change of effect size after the deletion of one of the articles.

Country(ies) involved: China.

Keywords: Ticagrelor AND Coronary Microcirculation Function AND coronary artery disease (CAD).

Contributions of each author:
Author 1 - Qiu Xiaohan.