INPLASY PROTOCOL

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None declared.

Growth differentiation factor 15 predicts adverse cardiovascular events in patients with chronic coronary syndromes: a meta-analysis

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Review question / Objective: **The objective of this meta-analysis is to evaluate whether growth differentiation factor 15 could predict adverse cardiovascular events in patients with chronic coronary syndromes.**
Eligibility criteria: **(1)studies comparing the risk of adverse cardiovascular events in patients with chronic coronary syndromes/stable coronary heart disease depending on the circulating levels of GDF-15.(2)thestudies provided original data such as the number of cardiovascular mortality,all-cause mortality ,heart failure,myocardial infarction or stroke different levels of GDF-15, the hazard ratio(HR),odds ratio (OR)or risk ratio (RR), 95% confidence intervals (CIs).(3)The follow-up time was more than 1 year.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 August 2022 and was last updated on 21 August 2022 (registration number INPLASY202280077).

INTRODUCTION

Review question / Objective: **The objective of this meta-analysis is to evaluate whether growth differentiation factor 15 could predict adverse cardiovascular events in patients with chronic coronary syndromes.**

Condition being studied: **Coronary artery disease (CAD), the leading cause of morbidity and mortality worldwide in recent years,is a pathological process characterized by atherosclerotic plaque accumulation in the epicardial arteries.According to the dynamic nature of**

the CAD process, it has been categorized as either acute coronary syndromes (ACS) or chronic coronary syndromes (CCS). Risk assessment and stratification is practical and critical for diagnosis and treatment in CAD.In addition to traditional cardiovascular (CV) risk factors, several potential novel biomarkers has been investigated to predict the clinical course and outcomes. Growth differentiation factor 15 (GDF-15) is currently one of the most attractive biomarkers that provides strong prognostic information. GDF-15 is a member of the transforming growth factor-βsuperfamily and was identified in a broad range of cells. Usually, it is expressed in most tissues except placenta only at very low levels in healthy conditions. However, it could be markedly increased in the case of cardiovascular injury, such as pressure overload, myocardial infarction,heart failure, and atherosclerosis.Several studies reported the correlation of high GDF-15 levels in baseline and mortality, myocardial infarction and heart failure in patients with ACS, and a meta-analysis demonstrated the prognosis value of GDF-15 in ACS cohort. However, whether GDF-15 levels could predict the adverse cardiovascular events and long-term prognosis in patients with CCS was uncertain because of the limited original studies and absence of meta-analysis. Hence, we intended to search the recent studies and pool the data to evaluate the prognosis value of GDF-15 in patients with CCS.

METHODS

Participant or population: Participants with chronic coronary syndromes/stable coronary heart disease.

Intervention: Follow up the participants with chronic coronary syndromes with higher levels of growth differentiation factor 15 in baseline.

Comparator: Follow up the participants with chronic coronary syndromes with normal/low levels of growth differentiation factor 15 in baseline.

Study designs to be included: observational studies.

Eligibility criteria: (1)studies comparing the risk of adverse cardiovascular events in patients with chronic coronary syndromes/ stable coronary heart disease depending on the circulating levels of GDF-15. (2)thestudies provided original data such as the number of cardiovascular mortality,all-cause mortality ,heart failure,myocardial infarction or stroke different levels of GDF-15, the hazard ratio(HR),odds ratio (OR)or risk ratio (RR), 95% confidence intervals (CIs).(3)The follow-up time was more than 1 year.

Information sources: We will review the Embase, Cochrane Library, Web of Science, and PubMed databases.

Main outcome(s): Correlation of GDF-15 values and cardiovascular mortality,all-cause mortality ,heart failure, myocardial infarction, stroke.

Quality assessment / Risk of bias analysis: The quality of the included studies was assessed by Newcastle-Ottawa Scale (NOS) criteria. The concrete content consists of the following items: patient selection, comparability, and ascertainment of outcome, with a score ranging from zero to nine.

Strategy of data synthesis: The data was analyzed using the STATA 14.0 statistics software.We calculate the total hazard ratio(HR) and its 95% CI.We assessed heterogeneity using I2 statistics.We pooled the study-specific estimate using a fixed-effect model in case of low statistical inconsistency (I2 ≤ 50%) or with a random-effect model in case of moderate or high statistical inconsistency (I2 >50%). Publication bias was evaluated using a funnel plot analysis and Begg's test if a sufficient number of trials (≥10 trials) was found.

Subgroup analysis: subgroup analyses by different GDF-15 cutoff point values, follow-up time, NOS points if a sufficient number of trials was found.

Sensitivity analysis: **Sensitivity analysis by omitting a trial at a time.**

Language restriction: **English.**

Country(ies) involved: **China.**

Keywords: **growth differentiation factor 15,chronic coronary syndromes, mortality, myocardial infarction, heart failure.**

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