INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Role of matrix metalloproteinase-2 in the development of atherosclerosis among patients with coronary artery disease: A systematic review

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Review question / Objective: **The aim of the study is to determine the role of MMP-2 in atherosclerosis progression among patients with CAD. P: Patients diagnosed with CAD. I: MMP-2 involvement in atherosclerosis and expression in CAD patients. C: Compared with healthy group. O: MMP-2 are associated with atherosclerosis progression among CAD and its expression level is higher in CAD. S: Human study.**
Condition being studied: **Studies that measure MMP-2 levels among CAD and involving adult human patients with CAD, both male, and female regardless of ethnicity were included.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 April 2023 and was last updated on 02 May 2023 (registration number INPLASY202340058).

INTRODUCTION

Review question / Objective: **The aim of the study is to determine the role of MMP-2 in atherosclerosis progression among patients with CAD. P: Patients diagnosed with CAD. I: MMP-2 involvement in atherosclerosis and expression in CAD patients. C: Compared with healthy group. O: MMP-2 are associated with atherosclerosis progression among CAD and its expression level is higher in CAD. S: Human study.**

Rationale: **1) The prevalence of coronary artery disease (CAD) is increased. 2) MMP-2 was found to be involved in all stages of atherosclerosis process, the main pathogenesis of CAD through invitro and invivo studies. 3) There is a lack of studies**

on MMP-2 role in atherosclerosis among CAD that use human samples. 4) There is a lack of studies reported or reviewed on the latest published papers (5 years of publications) related to the topic.

Condition being studied: Studies that measure MMP-2 levels among CAD and involving adult human patients with CAD, both male, and female regardless of ethnicity were included.

METHODS

Search strategy: The literature search was conducted through four online databases (ovid, scopus, pubmed, and google scholar) and only studies that were published from 2018 until February 2023 were included. The keywords that were used for the search were: (cardiovascular disease)) OR (coronary artery disease)) OR (ischemic heart disease)) OR acute coronary syndrome)) OR (coronary atherosclerosis)) OR (myocardial infarction)) AND (matrix metalloproteinase).

Participant or population: Patients diagnosed with coronary artery disease (CAD), including patients with myocardial infarction (MI), acute MI, acute (unstable) coronary syndrome, stable coronary syndrome, and coronary atherosclerosis. Normal healthy people also will be included.

Intervention: MMP-2 level measured in group of patients diagnosed with CAD.

Comparator: MMP-2 level measured in group of patients diagnosed with CAD compared to normal healthy individuals.

Study designs to be included: Human study (case-control, cross sectional and cohort)

Eligibility criteria: Inclusion criteria: Original papers to be review are available in English language. While, exclusion criteria are studies that are review articles, in vitro and animal studies.

Information sources: The articles were searched from online databases through UKM Library Website. Then, using Mendeley, the articles were exported and downloaded.

Main outcome(s): A total of 10 622 articles were identified and only eight studies were included. Based on the results, atherosclerosis-related inhibiting drugs were found to significantly reduce the activity of MMP-2. MMP-2 was also found higher in unstable CAD than in stable CAD and healthy controls. There are associations between MMP-2 and MMP-14, a pro-MMP-2 activator that is highly associated with CVD. In addition, two MMP-2 genes (rs243865 and 243866) were found higher in allele and genomic frequency of atherosclerosis patients compared to healthy, with haplotype CA, CG, and TA associated with atherosclerosis.

Data management: Not applicable.

Quality assessment / Risk of bias analysis: Quality assessment for risk of bias was conducted by two reviewers (NS and AA) using the Newcastle-Ottawa Scale (NOS) for case-control and cohort study. For both case-control and cohort studies, there are three domains that NOS assessed. Case-control study, NOS assessed the selection of study groups (including cases and controls), comparability between groups, and ascertainment of exposure for both cases and control groups. While, cohort study, NOS assessed on the selection of study groups (exposed and non-exposed), comparability between groups, and outcome assessment. In each three domains, there are eight items to be scored with star. Each item was allocated for a minimum of one star or a maximum of two stars. Studies score 9 to 7 stars are considered high-quality papers, 6 to 4 as fair quality, and 3 to 1 as low quality.

Strategy of data synthesis: After searching papers using online databases, article selection and data extraction were conducted. Article selection was conducted in three stages by two independent researchers (Nazirah Samah and Amilia Aminuddin). Initially, papers

were omitted primarily on the title. Then, papers that were irrelevant to MMPs and atherosclerosis were omitted by evaluating the abstracts. Lastly, papers that were not following the inclusion criteria were omitted by evaluating the full paper completely. For data extraction, the name of the studies' first author, study design, subject characteristics, age and sex of the participants, methods of MMP-2 levels measurement, and involvement of MMP-2 in atherosclerosis progression among CAD of each study were recorded in a table, independently by two researchers (Nazirah Samah and Amilia Aminuddin).

Subgroup analysis: Not applicable.

Sensitivity analysis: Not applicable.

Language restriction: English.

Country(ies) involved: Malaysia.

Other relevant information: Not applicable.

Keywords: Cardiovascular disease; coronary artery disease; ischemic heart disease; acute coronary syndrome; coronary atherosclerosis; myocardial infarction; matrix metalloproteinase.

Contributions of each author:

Author 1 - Nazirah Samah - Author 1 conduct the conceptualization, methodology (literature search, article selection, and data extraction), writing the original draft and editing.
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