

INPLASY PROTOCOL

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None declared.

Smoking and unstable plaque in acute coronary syndrome: the role of matrix metalloproteinases: A systematic review

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Review question / Objective: To identify the relationship between smoking and matrix metalloproteinase (MMPs) in patients with acute coronary syndrome (ACS)

Condition being studied: The prevalence of coronary artery disease (CAD) is increasing not only in developing countries, but also globally. The underlying pathology of CAD is atherosclerosis, which involves the accumulation of fats, inflammatory cells, smooth muscles and fibrous tissue at the intimal layer of the coronary artery wall. CAD usually presents with acute coronary syndrome (ACS), which includes ST elevation myocardial infarction (STEMI), non-STEMI and unstable angina (UA). One of the risk factors for CAD is smoking. Although the underlying pathogenesis of smoking-induced atherosclerosis is not completely recognized, it was proposed that modifications in the stability between production and degradation of extracellular matrix might be involved. Nicotine is an addictive component of cigarette smoke that induces the expression of MMP-2 and MMP-9, consequently contributing to unstable plaque formation.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 July 2022 and was last updated on 29 July 2022 (registration number INPLASY202270121).

INTRODUCTION

Review question / Objective: To identify the relationship between smoking and matrix metalloproteinase (MMPs) in patients with acute coronary syndrome (ACS).

Rationale: The most common cause of acute coronary syndrome (ACS) is

atherosclerotic plaque rupture which is usually associated with unstable plaque. Matrix metalloproteinases (MMPs) has been implicated to unstable plaque by disrupting the mechanical integrity of the plaque tissue. Smoking is one of the risk factors of ACS that could increase MMP levels, leading to plaque rupture. The current review aim to identify the

relationship between smoking and MMPs in patients with ACS.

Condition being studied: The prevalence of coronary artery disease (CAD) is increasing not only in developing countries, but also globally. The underlying pathology of CAD is atherosclerosis, which involves the accumulation of fats, inflammatory cells, smooth muscles and fibrous tissue at the intimal layer of the coronary artery wall. CAD usually presents with acute coronary syndrome (ACS), which includes ST elevation myocardial infarction (STEMI), non-STEMI and unstable angina (UA). One of the risk factors for CAD is smoking. Although the underlying pathogenesis of smoking-induced atherosclerosis is not completely recognized, it was proposed that modifications in the stability between production and degradation of extracellular matrix might be involved. Nicotine is an addictive component of cigarette smoke that induces the expression of MMP-2 and MMP-9, consequently contributing to unstable plaque formation.

METHODS

Search strategy: Literature search will be conducted through three online databases (PubMed, Ovid and Scopus). Studies that were published until March 2022 will be included. The keywords that will be used for the search strategy are: (coronary artery disease) OR (cardiovascular disease) OR (ischemic heart disease) OR (acute coronary syndrome) OR (coronary atherosclerosis) OR (myocardial infarction) AND (matrix metalloproteinase) AND (smoke). Reference list of the included studies will also be screened for potential eligible studies.

Participant or population: Subjects with acute coronary syndrome will be included.

Intervention: Smoking is the risk factor that will be studied.

Comparator: Subjects that were not smoking will be the comparator.

Study designs to be included: Clinical studies (case control study and cohort study) will be included.

Eligibility criteria: The inclusion criteria are; (1) original papers available in English language, (2) studies that reported statistical comparison involving MMPs and smoking status and (3) clinical studies involving adult human patients with CAD, both male and female regardless of ethnicity. Review articles, articles not in English, animal studies and studies without statistical analysis involving MMPs and smoking status among CAD patients will be excluded. The inclusion criteria are; (1) original papers available in English language, (2) studies that reported statistical comparison involving MMPs and smoking status and (3) clinical studies involving adult human patients with CAD, both male and female regardless of ethnicity. Review articles, articles not in English, animal studies and studies without statistical analysis involving MMPs and smoking status among CAD patients were excluded.

Information sources: Literature search will be conducted through three online databases (PubMed, Ovid and Scopus). Only published data will be included.

Main outcome(s): The main outcome is the correlation/comparison between MMPs and smokers. Comparison included the used of odds ratio (OR) and the mean differences.

Additional outcome(s): Additional outcomes will be the MMPs relevant gene.

Data management: The name of the studies' first author, study characteristic, age and sex of the participants, method of MMPs measurement, correlation/comparison between MMPs and smokers, and references of each study will be recorded into a table, independently by two researchers (AA and CS).

Quality assessment / Risk of bias analysis: Quality assessment for risk of bias will be

conducted by two reviewers (AA and CS) using the Newcastle-Ottawa Scale (NOS) for case-control and cohort study. The NOS tool for case-control study include assessment of three domains: (1) selection of study groups, (2) comparability between groups, and (4) ascertainment of exposure (Peterson et al., 2011). Meanwhile, the NOS tool for cohort study assesses the following domains: (1) selection of study groups, (2) comparability between groups, and (3) outcome assessment. The NOS tool consists of eight items within the three domains as described above. Each item will be allocated a maximum of one star with maximum of two stars in the comparability item where applicable. The maximum number of stars is nine with studies scoring from 9-7 are considered as high quality, 6-4 are considered as fair quality, and 3-1 are considered as low quality. Any disagreement between the reviewers will be settled by consensus or consultation with a third reviewer (NA). Quality assessment for risk of bias will be conducted by two reviewers (AA and CS) using the Newcastle-Ottawa Scale (NOS) for case-control and cohort study.

Strategy of data synthesis: Study characteristic and outcome data will be tabulated and describe narratively. A metaanalysis will be conducted if the data permit. Risk of bias will be presented narratively.

Subgroup analysis: Where possible, we plan to evaluate the association between MMPs gene and smoking status.

Sensitivity analysis: Sensitivity analysis will be conducted if metaanalysis was performed.

Language: English.

Country(ies) involved: Malaysia.

Keywords: Acute coronary syndrome; matrix metalloproteinase; smoking; atherosclerotic plaque rupture; cardiovascular disease.

Contributions of each author:

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