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Risk of major adverse cardiovascular events in patients with metabolic syndrome after revascularization: A meta-analysis of eighteen cohorts with 18457 patients

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ABSTRACT

Objective. To provide a comprehensive evaluation of the association between metabolic syndrome (MetS) and major adverse cardiovascular events (MACE) and to clarify the effect of revascularization methods among them in patients with coronary artery disease (CAD) undergoing successful revascularization.

Methods. PubMed and Embase databases were searched. Cohort studies evaluating the association between MetS and risk of MACE and providing the hazard ratio (HR) with 95% confidence interval (CI) or sufficient data to calculate HR and its 95%CI among patients after revascularization were included. The pooled estimates were performed by using a random-effects model despite heterogeneity. Subgroup and sensitivity analyses were also conducted adherence to guidelines.

Results. Eighteen trials with 18457 patients were included. Overall, MetS was associated with significant increased risks of MACE (HR 1.47, 95%CI 1.26–1.72, I^2 = 46.4%, P_H = 0.016, P < 0.001) and all-cause mortality (HR 1.58, 95%CI 1.29–1.92, I^2 = 45.6%, P_H = 0.075, P < 0.001) in CAD patients received revascularization. The results remained stable and robust in our subgroup analysis. However, no significant increased risk of MACE or all-cause mortality was found in patients undergoing coronary artery bypass graft (CABG) or drug-eluting stent (DES) in the sensitivity analysis.

Conclusion. MetS was associated with increased risks of MACE and all-cause mortality in patients after revascularization, but not in patients receiving CABG or DES. Therefore, prevention and treatment of MetS are extremely necessary in patients undergoing revascularization. Moreover, CABG and DES should be recommended for CAD patients with MetS and future researches are still warranted.

Abbreviations: MetS, Metabolic syndrome; MACE, Major adverse cardiovascular events; CAD, Coronary heart disease; HR, Hazard ratio; CI, Confidence interval; CABG, Coronary artery bypass graft; DES, Drug-eluting stent; SES, Sirolimus-eluting stent; BMS, Bare-metal stent; NCEP/ATPIII, National Cholesterol Education Program/Adult Treatment Panel III; AHA/NHLBI, American Heart Association and the National Heart Lung, and Blood Institute; IDF, International Diabetes Federation; PCI, Percutaneous coronary intervention; MOOSE, Meta-analysis of observational studies in epidemiology; BMI, Body mass index; DM, Diabetes mellitus; CKD, Chronic kidney disease.

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1. Introduction

Coronary artery disease (CAD) is one of the leading causes of morbidity and death globally [1]. With advances in both coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI), the mortality of CAD has been significantly decreased [2]. However, these two therapeutic options are expensive and remain unsatisfactory. Moreover, the poor prognosis and high cost of medical care of CAD have imposed a considerable burden on both the personal family and society, necessitating exploring risk factors that affect the prognosis of patients subjected to revascularization.

Metabolic syndrome (MetS), a cluster of cardiovascular risk factors including hypertension, hyperglycemia, hypertriglyceridemia, decreased high-density lipoprotein-cholesterol, and central obesity, is increasingly prevalent worldwide [1,3,4]. MetS was reported to be associated with increased risks of type 2 diabetes mellitus (DM), cardiovascular and cerebrovascular events, and chronic kidney disease (CKD) [5–8]. Several studies [9–20] have reported that MetS is an independent risk factor of major adverse cardiovascular events (MACE) in patients with CAD undergoing revascularization, nevertheless, some others indicate that no impact [21–28] and even protective effect [29] of MetS exists in these patients.

Given the existing controversy, we, therefore, summarized the current evidence in the meta-analysis of cohort studies, to provide a comprehensive evaluation of the association between MetS and MACE and clarify the effect of revascularization methods among them in patients undergoing successful revascularization. Our hypothesis is that patients with MetS will be more likely to suffer from MACE.

2. Materials and Methods

We conducted and reported the study following the guideline of meta-analysis of observational studies in epidemiology (MOOSE) [30].

2.1. Search Strategy and Study Selection

We conducted a systematical literature search in PubMed and Embase (from the inception to May 2015). The searches were performed via the combination of free-text terms and subject terms related to myocardial revascularization and MetS without additional restrictions. The detailed search strategy is shown in Appendix 1. Reference lists of the included studies and relevant reviews were also hand-searched by full-text screening. The study selection was achieved through two steps, firstly screening the titles/abstracts and then reading the full texts according to the eligibility criteria. The search strategy and study selection were performed by two investigators independently, and the discrepancies were solved through consent.

2.2. Eligibility and Outcome Measure

Studies meeting the following inclusion criteria were adapted to our meta-analysis: (1) Population: patients who received successful revascularization; (2) Exposure (intervention): MetS; (3) Control: non-MetS; (4) Outcome: the incidence of MACE; (5) Study design: cohort studies with follow-up ≥1 years. Studies evaluating the effect of MetS vs. non-MetS on the incidence of MACE and providing the hazard ratio (HR) with 95% confidence interval (CI) or sufficient data to calculate HR and related 95%CI were included. When there were multiple publications from the same population, only one of them was included in each meta-analysis to avoid overlapping information.

We took the risk of MACE as the inclusion criteria and the primary outcome. Additionally, all-cause mortality, as the secondary outcome, was also assessed.

2.3. Data Extraction and Quality Assessment

Data extraction was performed by two investigators independently using a standard extraction form. The following information was extracted from each study: authors, publication year, country, period of enrollment, patients' characteristics (sample size, age, gender, body mass index (BMI), and DM), revascularization method, study design, definition of MetS, duration of follow-up, comparison, definition of MACE, outcomes (risks of MACE and all-cause mortality), adjusted factors. If the HR of MACE from different follow-ups were reported within a single study, the longest one would be used. HRs and 95%CIs from studies presenting results as Kaplan–Meier curves were estimated using the software Digitizer according to the instruction [31]. When several adjustment models were used, results from the most fully adjusted one were used. The corresponding authors would be contacted if the essential data were unavailable. All extracted information was entered into an Excel file and rechecked by the third investigator.

Risk of bias in each cohort was evaluated using the Newcastle–Ottawa quality scale [32] — a validated scale for assessing the quality of non-randomized studies. The scale consists of three domains (selection of participants, comparability of study groups, and the outcomes) with a maximum of nine stars. The more stars mean better quality. We treated studies as low (0–3 stars), moderate (5–6 stars), and high quality (7–9 stars), respectively. The disagreements in data extraction and quality assessment were settled by discussion.

2.4. Data Analysis

HRs and 95%CIs were used to calculate the pooled effect by using the random-effects model with DerSimonian and Laird weights in all meta-analyses. Studies assessing the effect of MetS on MACE in several subgroups of patients were treated as separate trials. Average or median was used to reflect the age of participants and duration of follow-up. Heterogeneity among the results of individual studies was assessed by I^2 statistic [33], which represented the percentage of total variation attributed to heterogeneity instead of sampling error. The heterogeneity was considered to be low if I^2 statistic between 25% and 50%, moderate if I^2 statistic between 50% and 75%, and high if I^2 statistic more than 75%. Subgroup analyses, based on study design, follow-up, data extraction