Metabolic syndrome as a risk factor for peripheral artery disease: a systematic review and meta-analysis

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Background: Metabolic syndrome is a well-known risk factor for cardiovascular disease; however, it has not been determined if it is associated with peripheral arterial disease (PAD). Hence, the systematic review aimed to evaluate metabolic syndrome as a risk factor for the development of PAD.

Methods: We conducted a systematic review searching in four databases: 1) PubMed, 2) Web of Science, 3) Scopus, and 4) Embase until March 2021. We included cohort studies that evaluated the risk of PAD in patients with and without metabolic syndrome. Study selection, data extraction, and risk of bias analysis were performed independently by two authors. We used a random-effects model to conduct a meta-analysis of effect measures (RR, HR, odds ratio, OR). To date, no systematic reviews have been performed according to the diagnostic criterion used for metabolic syndrome.

Results: We included 7 studies with a total of 43,824 participants. Most of the studies were performed in the general adult population. The metabolic syndrome and PAD diagnostic criteria were heterogeneous. Almost all studies using RR found an association between metabolic syndrome and the development of PAD. RR: 1.31; 95% CI: 1.03 - 1.59, I2: 15.6% (11,13). On the other hand, almost all the studies that used HR found no association between the two variables. All studies had a low risk of bias.

Conclusions: The association between metabolic syndrome and the risk of developing PAD is inconsistent. However, patients with metabolic syndrome should undergo testing to rule out PAD due to the high prevalence of risk factors in the population.

Introduction

Metabolic syndrome is a complex syndrome that involves high levels of glucose and lipids in the blood, as well as high blood pressure and central obesity (1). Although it is a global problem, it has been estimated that over a billion people live with metabolic syndrome (2). Peripheral artery disease (PAD) is a chronic disease that affects 15% of the population and is the second most common cardiovascular disease after coronary artery disease affecting 200 million people worldwide (3). Although PAD has a double risk of mortality and myocardial infarction (4), most people are not aware of the condition (5). Although the diagnosis and treatment of PAD are important, the risk of developing PAD in people with metabolic syndrome is not well known (6). Therefore, the objective of the present study was to evaluate metabolic syndrome as a risk factor for PAD.

Methods

We conducted a systematic review according to the indications of the guidelines of the 2020 Preferred Reporting Items for Systematic and Meta-Analysis (PRISMA)(9). The study protocol is registered in the PROSPERO platform (CRD42021234165). We included cohort studies that reported the following measures of effect: relative risk (RR), odds ratio (OR), hazard ratio (HR), or that reported data that allowed estimation of the RR, OR, or HR of the association of interest. The study selection, data extraction, and risk of bias analysis were performed independently by two authors. We used a random-effects model to conduct a meta-analysis of effect measures (RR, HR, odds ratio, OR). To date, no systematic reviews have been performed according to the diagnostic criterion used for metabolic syndrome.

Results: We included 7 studies with a total of 43,824 participants. Most of the studies were performed in the general adult population. The metabolic syndrome and PAD diagnostic criteria were heterogeneous. Almost all studies using RR found an association between metabolic syndrome and the development of PAD. RR: 1.31; 95% CI: 1.03 - 1.59, I2: 15.6% (11,13). On the other hand, almost all the studies that used HR found no association between both variables in the studies that used HR (12,15,16), with the exception of one study(11).

Discussion

This systematic review and meta-analysis of cohort studies, included 7 studies and found inconsistent results regarding the association between metabolic syndrome and the development of PAD. Four of the five included studies that used RR found an association between both variables (2,11,13,16). While the studies that used HR or OR found no association (12,14,16), except for one study(11).

The most important difference we observed was that none of the studies in which they found a significant association adjusted for the diabetes variable (2,11,13,16). On the other hand, all the studies that used HR or OR found no association (12,14,16). These results suggest that diabetes could be the true risk factor and not the metabolic syndrome itself.

We found some limitations of the included studies. Although all the studies used a validated criterion to define metabolic syndrome and PAD, these were heterogeneous among themselves. In addition, the measures of effect among the studies were not equal, because some used HR, others RR or OR, which could make the estimation vary and do not allow us to compare the studies directly. However, in general, most of the studies had a low risk of bias.

We recommend that future studies use the ATP III, NHDL, or JSH definitions of the metabolic syndrome, because they are more applicable in clinical practice and have similar criteria when defining metabolic syndrome, unlike other definitions ( IDF, WHO, among others). For the definition of PAD, we recommend following the American Heart Association or European Society of Cardiology criteria that include: clinical history, physical examination suggestive of PAD, or an ABI at rest ≥ 0.90 (3,17).

Although we did not find clear evidence that metabolic syndrome is a risk factor for PAD, periodic control examinations should be performed in this population given that 7% of patients with metabolic syndrome have asymptomatic PAD(18). In addition, efforts should be made to reduce the risk factors identified in these patients to avoid the progression of atherosclerosis and insulin resistance, since this population has a 5 to 10 times increased risk of developing diabetes. It turns the risk of developing cardiovascular disease in 5 years (8,19).

References

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