Targeting the vessel wall in cardiovascular prevention

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Myeloperoxidase
Testing an upcoming biomarker

Part 2 explores the possible usefulness of myeloperoxidase (MPO) as biomarker for (future) cardiovascular disease in different populations. Myeloperoxidase is an enzyme of the innate immune system, which activity is helpful in the elimination of microorganisms. However, at the same time MPO activity can damage the vessel wall. Our research suggests that the use of MPO as a biomarker in risk assessment in primary prevention and in a non-acute setting is limited.
INTRODUCTION

Predicting who is and who is not likely to suffer from cardiovascular disease (CVD), is difficult. Age, gender, smoking habit, family history, diabetes, blood pressure, cholesterol and CRP levels all contribute to the estimation of risk. However, the vast majority of cardiovascular events occur in people with normal cholesterol levels and/or low risk estimates (1). Therefore, finding better biomarkers for prediction of CVD risk is warranted.

Myeloperoxidase (MPO) has been put forward as a promising biomarker (2). Moreover, it may be one of the most excruciating enzymes affecting the protective mechanisms of the vessel wall. Therefore, it may not only be a risk marker, but also risk factor. Myeloperoxidase is a leukocyte-derived enzyme and part of the first line defense of the immune system. It is present in the circulation as well as within the vessel wall (3). There it catalyzes the formation of a number of reactive oxidant species and causes nitrosylation of proteins. Unfortunately, this not only kills microorganisms, but also has several pro-atherogenic effects. The radicals could also potentially damage the endothelial glyocalyx, as they fragment its components hyaluronan and chondroitin sulphate (4). Interestingly, uptake and transcytosis of MPO by the endothelium depends on heparin/heparan glycosaminoglycans (3).

Previous studies showed that MPO levels are higher in patients with coronary artery disease (CAD) and can predict future cardiovascular events in these patients and patients with chest pain (5-7). In line, individuals with total or subtotal MPO deficiency appear less likely to develop CVD (7). Therefore, MPO and its downstream inflammatory pathways may represent attractive targets for both prognostication and therapeutic intervention in the prevention of CVD.

HYPOTHESIS

We hypothesized that high MPO levels are already associated with a higher risk of CAD in individuals without overt CAD and/or acute chest pain and therefore might be a clinically useful marker in a primary prevention as well as in patients with cardiac complaints in a non-acute setting.

OUTLINE

In chapter 8, we present the results of a large case control study nested in a prospective population study. This study assesses the association between MPO levels and risk of CAD.
in a normal, apparently healthy population. Next, we investigate the association between MPO levels and indicators of cardiovascular risk, i.e. carotid intima-media thickness (IMT) and myocardial perfusion scintigraphy, in patients at higher risk of CAD (chapter 9 to 12). These patient groups consisted of patients with familial hypercholesterolemia (FH), diabetic patients and patients with anginal complaints.

REFERENCES