Summary

It is of utmost importance to detect disease in an early phase, or even a predisease state, so that disease can be treated adequately or can even be prevented. Ancient Chinese literature already described prevention as the preferred strategy against medical diseases. In this thesis, we zoom in on different tools in medicine to discover individuals at risk for coronary events or detect coronary disease at an early stage.

Identification of high-risk patients using mass-screening. In chapter 2, we demonstrate that assessment of risk for developing a heart attack is useful and feasible in a large group of voluntary participants with simple, affordable, and largely digital screening tools. Personalized online coaching during 3 months after the first assessment, decreased this risk significantly.

Identification of high-risk patients using an established biomarker. In Chapter 3 and 4, a new generation of the widely used laboratory Troponin T blood test of was investigated. Troponin T is a protein that is almost exclusively present in the cardiomyocyte and can be measured in very low concentrations in the peripheral blood. In Chapter 3, we showed that even in mild coronary plaque burden, as determined by cardiac computed tomographic angiography (CCTA), a significantly higher concentration of Troponin T is present in the peripheral blood in comparison to individuals without any coronary plaques. Moreover, in Chapter 4 we show that troponin is an independent predictor of an acute coronary syndrome or (imminent) heart attack.

Identification of high-risk patients using 3 new biomarkers. A “biomarker” that can predict the risk of a coronary event or coronary disease in general, can be an affordable and easy to use clinical tool to determine the risk of an individual for a specific disease. With such a biomarker, a better categorization for patients with a high pretest likelihood of coronary disease can be obtained. The amount of CCTA’s of individuals without coronary disease could be limited, with associated reductions in radiation dose. In Chapter 5, we investigated the possible role of Annexin A5, Elastase and Myeloperoxidase. We conclude that these biomarkers, including myeloperoxidase that was previously reported to have potential, are not suitable as predictors of acute coronary syndrome or coronary disease.
Identification of high-risk patients for development of coronary calcifications using blood thinning medication. Chapter 6 shows that calcification of the coronary artery wall is accelerated significantly in the setting of Vitamin K-antagonist use. Murine studies show even development of vulnerable plaque characteristics in the setting of Vitamin K-antagonist use. These vulnerable plaques increase the risk of plaque rupture, local clot formation, and myocardial infarction.

Identification of high-risk patients using imaging biomarkers. Finally, in chapter 7, we discuss scientific advances in imaging biomarkers and molecular imaging. Ongoing cell death, in particular apoptosis or programmed cell death, is an important player in the transition stable to an unstable plaque that can rupture and cause infarction. With certain labeled proteins that specifically attach to cells in apoptosis, and specific scanners, it may for instance be possible to localize and quantify these processes. However, although very promising, to date there is no clinical molecular imaging tool that has been validated to predict unstable coronary artery disease.

This thesis provided additional understanding in the clinical use of the next generation (high sensitive) Troponin T.