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Summary and Conclusions
SUMMARY AND CONCLUSIONS

The general introduction of the thesis outlines the value of non-invasive imaging modalities (including coronary artery calcium scoring and multi-slice computed tomography [MSCT] coronary angiography, conventional echocardiography, myocardial deformation imaging, real-time three-dimensional echocardiography [RT3DE] and contrast-echocardiography) in the diagnostic process. The main applications are described in patients with suspected coronary artery disease and in patients with acute myocardial infarction (AMI).

Part I
The first part of the thesis discusses the clinical utility of non-invasive imaging modalities for diagnosis and risk stratification of patients with suspected coronary artery disease. In Chapter 2, an overview of the literature regarding the prognostic value of CACS assessment is provided; in addition, potential other applications of CACS assessment as well as the limitations of the technique are discussed. In Chapter 3, the prevalence of coronary artery disease across the Framingham Risk Score categories using CACS and MSCT coronary angiography was evaluated; a strong positive relationship was observed between Framingham Risk Score and the prevalence and extent of atherosclerosis. Especially in intermediate Framingham Risk Score patients, CACS and MSCT coronary angiography provided useful information on the presence of subclinical atherosclerosis. In these patients, who represent a substantial part of the population, clinical management is frequently uncertain and refinement of risk using atherosclerosis imaging may allow more appropriate targeting of preventive measures.

CACS and MSCT coronary angiography, despite providing meaningful information about the presence and extent of coronary atherosclerosis, do not provide information about the functional relevance of the observed coronary lesions. In Chapter 4, a better understanding of the
complementary information provided by these non-invasive methods (imaging of coronary atherosclerosis versus evidence of inducible ischemia), especially in relation to traditional risk assessment, is provided and a flow chart describing the proposed integration of non-invasive imaging of coronary arteries and stress testing into the traditional risk assessment of coronary artery disease events is presented.

In Chapters 5 and 6 the prevalence of coronary artery disease, by means of MSCT, and of abnormal stress testing were evaluated among patients with paroxysmal or persistent atrial fibrillation and compared with patients without a history of AF. Interestingly, a higher prevalence of obstructive coronary artery disease was observed among patients with AF, while the prevalence of functionally-relevant coronary lesions was similar to non-AF patients. The higher burden of subclinical coronary atherosclerosis observed in patients with AF may explain the previously observed higher long-term risk of coronary artery disease event in this group; accordingly, more aggressive medical therapy and risk factor modification may be justified in AF patients.

The presence of cardiac and aortic calcium shares many risk factors and a similar cause with both systemic and coronary atherosclerosis; as shown in Chapter 7, a simple echocardiography-derived calcium score, obtained through the comprehensive assessment of the burden of cardiac and ascending aorta calcium, is able to predict CACS and the presence of obstructive coronary artery disease, assessed using MSCT coronary angiography. Accordingly, recognition of cardiac and ascending aorta calcium using transthoracic echocardiography, a simple, low-cost, radiation-free and widely available technique, may be used to optimize the identification of patients with obstructive coronary artery disease in clinical practice.

As previously observed by the Multiethnic Study of Atherosclerosis (MESA) study, a progressive impairment of myocardial contraction (despite normal left ventricular ejection fraction) is associated with an increasing severity of coronary atherosclerosis (detected by MSCT or
EBCT) in patients without known coronary artery disease. In Chapter 8, the relation between obstructive coronary artery disease (assessed by MSCT coronary angiography), left ventricular diastolic dysfunction, and subclinical left ventricular systolic dysfunction (assessed by speckle-tracking echocardiography) and the potential incremental value of left ventricular diastolic dysfunction and subclinical left ventricular systolic dysfunction over the initial estimate of pretest likelihood of obstructive coronary artery disease were investigated. Of note, both left ventricular diastolic dysfunction and subclinical left ventricular systolic dysfunction were independently related to obstructive coronary artery disease and the presence of subclinical left ventricular systolic dysfunction provided significant incremental value over the Duke Clinical Score for the identification of patients having obstructive coronary artery disease. Especially among the patients with low or intermediate Duke Clinical Score, the presence of subclinical left ventricular systolic dysfunction significantly increased the likelihood of having obstructive coronary artery disease. Accordingly, routine screening for subclinical left ventricular systolic dysfunction among patients without known coronary artery disease may possibly refine the traditional clinical assessment and may be useful for selection of further diagnostic tests.

Part II
In this part of the thesis the clinical value of novel echocardiographic techniques is evaluated in patients with AMI. At present, transthoracic echocardiography is a frequently used imaging modality in the management of patients with AMI. Echocardiography is a low-cost and safe modality, which can be easily applied at the bedside and is valuable for patient follow-up. The accuracy of RT3DE acquisitions with and without contrast early after AMI was investigated in Chapter 9; of note, the administration of contrast agents in these patients was of incremental value, improving endocardial border visualization and reproducibility of left ventricular function assessment. As shown in Chapter 10, the use of
echocardiographic contrast agents permits also the assessment of left ventricular fluid dynamics, which are related to the remodelling and deformation properties of the left ventricle. The assessment of vortex formation with contrast echocardiography represents indeed a novel measurement of left ventricular diastology; vortex formation time and morphology were indeed good correlated with infarct size and with left ventricular untwisting rate. This technique also allows for the evaluation of myocardial perfusion and therefore of myocardial infarction extension, which is an important parameter to take into account in the evaluation of cardiac mechanics at short- and long-term follow-up after AMI. In fact, left ventricular function immediately after AMI was demonstrated to be independently associated with infarct size and left ventricular twist (Chapter 11). Of note, the impairment of left ventricular twist early after AMI was significantly and independently related to the occurrence of left ventricular remodelling at 6 months follow-up, representing a sensitive global parameter of left ventricular systolic performance after infarction.

Advances in echocardiographic techniques (i.e., tissue Doppler echocardiography, speckle-tracking echocardiography, and RT3DE) have demonstrated an impaired left ventricular synchronicity in patients with AMI; in Chapters 12 and 13, the relation between this decrease in left ventricular synchronicity and left ventricular systolic function at baseline and at 6 months follow-up was investigated. Early after AMI, the severity of impairment of left ventricular synchronicity had an additional detrimental impact on left ventricular performance, beyond the infarct size itself. The impairment in left ventricular synchronicity observed early after AMI is not however a permanent phenomenon in all patients; in patients having restoration of left ventricular synchronicity at 6 months follow-up, left ventricular functional recovery was also observed. Conversely, progressive worsening of left ventricular dyssynchrony during the follow-up appeared to be an ominous mechanism, which independently contributed to progression of left ventricular dysfunction.
Accordingly, beside the essential role of timely and effective revascularization of the culprit vessel, therapeutic strategies to restore a more synchronous left ventricular contraction could potentially be useful in this group of patients.

CONCLUSIONS

Non-invasive cardiac imaging modalities play a crucial role in the diagnostic process and clinical management of patients without known coronary artery disease and patients with AMI. Non-invasive coronary angiography with MSCT has witnessed an enormous development in the last decade allowing accurate detection of significant coronary stenosis; its implementation in clinical practice helps to refine traditional patients’ risk stratification. Conventional two-dimensional echocardiography, the use of echo-contrast agents, myocardial deformation imaging, and RT3DE have been demonstrated to be useful techniques for the identification of patients with obstructive coronary artery disease and for the risk stratification of patients with recent AMI.