Universiteit
Leiden
The Netherlands

Multi-modality imaging in ischemic heart disease, arrhythmia and cardiac-mechanics

El Mahdiui, M.

Citation
El Mahdiui, M. (2022, May 10). *Multi-modality imaging in ischemic heart disease, arrhythmia and cardiac-mechanics*. Retrieved from https://hdl.handle.net/1887/3303502

Version:	Publisher's Version
License:	Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden
Downloaded from:	https://hdl.handle.net/1887/3303502

Note: To cite this publication please use the final published version (if applicable).

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General introduction and outline of the thesis

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in adults worldwide.[1] The worldwide incidence of CVD deaths has increased from 18.1 million in 2010 to 20.5 million in 2020 and is expected to increase to 24.2 million in 2030.[2] Adequate diagnosis, risk stratification and treatment to decrease mortality, morbidity and the burden on health care systems is therefore crucial. Multimodality imaging has emerged as an important tool for the management of patients with cardiovascular disease.

Ischemic heart disease

Ischemic heart disease is the largest contributor to CVD and the single largest cause for worldwide mortality.[1] The development of coronary artery disease (CAD) is a complex process of accumulation of atherosclerotic plaque in the span of several years before the development of symptoms.[3] Although sex-related differences in CAD have been reported, the role of sex on plaque progression and composition has not been studied in a low-to-intermediate risk population in stable clinical conditions over a long follow-up period. While assessment of coronary plaque composition was previously reserved solely for invasive imaging modalities or histology, increased spatial resolution has allowed cardiac computed tomography (CT) to quantitatively asses plaque composition.[4,5] Indeed, cardiac CT has demonstrated a dramatic change in the last decade with increasingly lower radiation exposure and better imaging quality.[4,6]

The clinical manifestation of CAD is divers, and includes stable angina and myocardial infarction with possible adverse effects on left ventricular (LV) function leading to heart failure and sudden cardiac death. In patients presenting with symptoms of stable angina, risk stratification is indicated. Both coronary artery calcium (CAC) score, an anatomical marker of CAD, and nuclear imaging, a functional marker of CAD, have demonstrated independent and complementary prognostic value in patients with stable CAD, with also intermodality correlation.[7,8] The relationship between CAC score and CT myocardial perfusion, also a functional marker of CAD, which could be performed directly after CAC score, has however not been studied before.

In post-myocardial infarction patients, following treatment, imaging is performed to assess possible treatment options; for that purpose, assessment of ischemia, the extent of damage and myocardial viability is important.[9] Late gadolinium

contrast enhanced cardiac magnetic resonance (LGE CMR) has a high diagnostic accuracy for assessment of the extent of transmural scar. [10] Although, LGE CMR has several important advantages, it is not without limitations, for instance the need for intravenous contrast, the limited clinical availability and the relative high cost. Non-invasive myocardial work is a novel echocardiographic based parameter for assessment of LV function which overcomes these limitations. [11,12]

Arrhythmias

Heart failure is an important complication following myocardial infarction. Heart failure patients have an increased risk for developing ventricular arrythmias and therefore implantable cardioverter defibrillator (ICD) therapy might be appropriate. Evaluation of patients with heart failure, both ischemic and non-ischemic, who might benefit from ICD therapy continues to be a clinical challenge. Currently, LV ejection fraction <35% is used as a cut-off value to recommend ICD therapy. However, a substantial portion of patients with an ICD never develop ventricular arrythmias. Anatomical and functional characterization of the arrhythmogenic substrate using multimodality imaging may permit superior risk stratification for the occurrence of ventricular arrythmias (and accordingly, the need for ICD implantation).

Atrial fibrillation (AF) is the most prevalent arrhythmic disease worldwide with considerable impact on morbidity and mortality. AF catheter ablation is a safe and established treatment option for AF and is more effective in maintaining sinus rhythm compared to medical therapy.[13] However, AF recurrence rates remain high following AF catheter ablation.[13,14] Adequate patient selection prior to ablation might prevent unnecessary interventions and complications. Epicardial adipose tissue (EAT) in close proximity of the LA, is the adipose tissue which actively secretes hormones and cytokines and may play a role in the development of AF.[15,16] The quantity and attenuation of EAT can be derived from cardiac CT scans, and may provide a marker of inflammation. It is however, unknown whether volumetric assessment of quantity and attenuation of EAT (located posterior to the LA) predicts AF recurrence following catheter ablation.

Objectives and outline of the thesis

The main objective of this thesis is to investigate the role of multi-modality imaging in ischemic heart disease. Specifically various chapters have been dedicated to how and when cardiac mechanics (a new, echocardiographically derived parameter of LV function) and other novel imaging parameters can be used for risk stratification and treatment guidance in ischemic heart disease.

In Part 1 of this thesis, different imaging modalities are utilized to evaluate the extent and severity of CAD in different patient populations. In Chapter 2, the progression of CAD is evaluated with focus on the role of sex (with longer term follow-up) in a low-to-intermediate risk population. In Chapter 3, the relationship between an anatomical marker of CAD (CAC score derived from CT) and a functional marker of CAD (CT perfusion imaging), is assessed. A novel imaging parameter for evaluating LV function based on non-invasive pressure-strain loops, is introduced in Chapter 4 and reference values of global LV myocardial efficiency are presented in distinct patient populations. In Chapter 5, this novel imaging parameter is then further related to infarct transmurality, which is characterized on LGE CMR in patients with previous ST-segment elevation myocardial infarction.

In Part 2 of this thesis the role of multimodality imaging in arrythmias is assessed. Several imaging parameters are evaluated for risk stratification of ventricular arrhythmias in heart failure patients in Chapter 6, while in Chapter 7, imaging parameters are tested for prediction of AF recurrence following catheter ablation.

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