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

El Mahdiui, M.

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.

REFERENCES

1. Global health estimates 2019: Life expectancy, 2000–2019. Geneva: World Health Organization; 2018 (https://www.who.int/docs/default-source/gho-documents/global-health-estimates/ghe2019_cod_global_2000_20194e572f53-509f-4578-b01e-6370c65d9fc5.xlsx?sfvrsn=eaf8ca5_7, accessed 18 July 2021).
2. World Health Organization. The top 10 causes of death. Geneva: World Health Organization; 2012 (https://www.who.int/cardiovascular_diseases/en/cvd_atlas_25_future.pdf?ua=1, accessed 18 July 2021).
3. Man JJ, Beckman JA, Jaffe IZ. Sex as a Biological Variable in Atherosclerosis. Circ Res 2020;126:1297-1319.
4. Heseltine TD, Murray SW, Ruzsics B, Fisher M. Latest Advances in Cardiac CT. Eur Cardiol 2020;15:1-7.
5. de Graaf MA, Broersen A, Kitslaar PH, Roos CJ, Dijkstra J, Lelieveldt BP, et al. Automatic quantification and characterization of coronary atherosclerosis with computed tomography coronary angiography: cross-correlation with intravascular ultrasound virtual histology. Int J Cardiovasc Imaging 2013;29:1177-1190.
6. Stocker TJ, Deseive S, Leipsic J, Hadamitzky M, Chen MY, Rubinshtein R, et al. Reduction in radiation exposure in cardiovascular computed tomography imaging: results from the PROspective multicenter registry on radiaTion dose Estimates of cardiac CT angIOgraphy iN daily practice in 2017 (PROTECTION VI). Eur Heart J 2018;39:3715-3723.
7. Chang SM, Nabi F, Xu J, Peterson LE, Achari A, Pratt CM, et al. The coronary artery calcium score and stress myocardial perfusion imaging provide independent and complementary prediction of cardiac risk. J Am Coll Cardiol 2009;54:1872-1882.
8. Engbers EM, Timmer JR, Ottervanger JP, Mouden M, Knollema S, Jager PL. Prognostic Value of Coronary Artery Calcium Scoring in Addition to Single-Photon Emission Computed Tomographic Myocardial Perfusion Imaging in Symptomatic Patients. Circ Cardiovasc Imaging 2016;9.
9. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2018;39:119-177.
10. Kim RJ, Wu E, Rafael A, Chen E-L, Parker MA, Simonetti O, et al. The Use of Contrast-Enhanced Magnetic Resonance Imaging to Identify Reversible Myocardial Dysfunction N Engl J Med 2000;343:1445-1453.
11. Russell K, Eriksen M, Aaberge L, Wilhelmsen N, Skulstad H, Remme EW, et al. A novel clinical method for quantification of regional left ventricular pressure-strain loop area: a non-invasive index of myocardial work. Eur Heart J 2012;33:724-733.
12. Russell K, Eriksen M, Aaberge L, Wilhelmsen N, Skulstad H, Gjesdal O, et al. Assessment of wasted myocardial work: a novel method to quantify energy loss due to uncoordinated left ventricular contractions. Am J Physiol Heart Circ Physiol 2013;305:H996-1003.
13. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Europace 2016;18:1609-1678.

14. Sultan A, Luker J, Andresen D, Kuck KH, Hoffmann E, Brachmann J, et al. Predictors of Atrial Fibrillation Recurrence after Catheter Ablation: Data from the German Ablation Registry. Sci Rep 2017;7:16678.

15. Thanassoulis G, Massaro JM, O'Donnell CJ, Hoffmann U, Levy D, Ellinor PT, et al. Pericardial fat is associated with prevalent atrial fibrillation: the Framingham Heart Study. Circ Arrhythm Electrophysiol 2010;3:345-350.

16. Sacks HS, Fain JN. Human epicardial adipose tissue: a review. Am Heart J 2007;153:907-917.