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New Imaging-derived Biomarkers Based on Tridimensional CTA/MRI Hybrid Models for Complex Assessment of Myocardial Viability after Myocardial Infarction

PhD Thesis

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Introduction: Multimodality assessment of coronary artery lesions has demonstrated superior effectiveness compared to the conventional approach, for assessing both anatomical and functional significance of a coronary stenosis. Multiple imaging modalities can be integrated into a fusion imaging tool to better assess myocardial ischemia. The concept of hybrid imaging combines more than one imaging method and offers precious information regarding anatomy and functionality in a spatial view.² Multimodality imaging for assessment of coronary artery disease, especially myocardial infarction, became necessary in the complex assessment of these patients.³ Hence, Coronary Computed Tomography Angiography (CCTA) is a trustworthy method for the assessment of the coronary anatomy, this non-invasive tool becoming more available in many cardiac centers. CCTA allows to perform 3D cardiac reconstruction, to evaluate coronary plaques and also a detailed view on the cardiac geometry with high specificity.⁴⁻⁹ On the other hand, Cardiac Magnetic Resonance (CMR) is a non-harmful diagnostic tool, non-invasive, that gives information also on functionality, especially kinetics, perfusion, mass and volume.¹⁰⁻¹³ Integration of information from two different imagistic tools allows us to combine the provided parameters and obtain a superior analysis of cardiac function and anatomy but also to have a better view on patient outcome and his risk stratification. One of the applicability of hybrid imaging is the assessment of myocardial viability, which is mandatory in order to evaluate the ability of ischemic tissue to recover after revascularization therapy. Moreover, hybrid imaging improve the ability to distinguish the hibernating myocardium from stunning one. It is well known the huge implication of the inflammation on the pathogenesis of the myocardial ischemia provoked by the vulnerable coronary plaques. Thus, for the better assessment of the cardiovascular patient outcome, should be considered to analyze the level of the inflammatory biomarkers.

Aim of the study: The aim of the study is to develop new imaging markers for the complex assessment of myocardial viability based on hybrid imaging tools CCTA\MRI models and to validate these models in the correlation of coronary plaques vulnerability with the infarcted myocardial mass and on the other hand, in the correlation of inflammatory status and the myocardial viability. This study is the first study according to our knowledge which assess viability using hybrid imaging CCTA\MRI. This thesis is based on three studies. The first study is the development of the hybrid CCTA\MRI prototype, and the second study investigated the correlation between myocardial viability and coronary plaques vulnerability based on the hybrid models and the third study aimed to investigate the correlation between inflammation evaluated by the level of different inflammatory biomarkers and myocardial vulnerability.

Materials and methods: We included in the study 45 patients with recent history of myocardial infarction and associated coronary lesions nearby the ischemic myocardial territory, and in the same time had the inflammatory biomarkers quantitative analysis during the acute event. For all the patients was performed CCTA and MRI and was calculated different cardiac scores such as Duke Jeopardy Score, Syntax Score, Calcium Score. All the acquired images were processed using a dedicated imaging platform with specials postprocessing software, in order to develop the hybrid prototype CCTA\MRI and to assess the myocardial viability, coronary plaques vulnerability. The first study from the present thesis consisted on the development of the hybrid prototype applied on 10 patients from the 45 patients cohort. The study lot of the second study was divided into 3 groups based on the coronary plaques vulnerability degree, thus the first group consisted of 7 patients, the second one 28 patients and the third group of patients was formed of



12 patients. The third study divided the 45 patients into 2 groups based on the myocardial transmural index, thereby the group 1 included 23 patients and the group 2 included 22 patients. Statistical analysis was performed using Graph Pad InStat 3.10 software, firstly all data being checked for normality test.

Results:

The principal characteristics of the study population are that 77.70% from the patients are male with an average age of 60 years. 93.3% patients from the study population were diagnosed with hypertension and 40% of them were active smokers. Regarding the cardiovascular risk scores, 60% of the patients presented a Syntax Score higher than 22 points and 57.7% had a Duke Jeopardy Score higher than 8 points. As respects the myocardial ischemic transmural index, 53.5% from the patients had subendocardic coronary lesions. The first study included 10 patients from the total of 45 patients for whom was performed the hybrid imaging CCTA\MRI using the dedicated software, being the first prototype developed in this way. The CCTA images were fused with MRI images late gadolinium enhancement sequences (LGE) and the quantitative infarcted myocardial mass was calculated using a semiautomatic analysis. The second study showed that the leucocyte cell value was higher in patients with high vulnerability degree coronary plaques and also the in this group dyslipidemia was diagnosed in 50% of the patients. There were significant differences between the groups of vulnerability regarding the infarcted myocardial mass ($p=0.0001$), also regarding the level of HsCRP and the level of MMP9, which were higher in the third group, ($p=0.02$). Duke Jeopardy score was correlated with the vulnerability degree of coronary plaques, ($p=0.01$). Although the other cardiovascular risk score Syntax Score and Calcium Scoring did not show statistically significant differences between the 3 groups of subjects. The third study shows a significant correlation between the coronary lesion transmural index and the level of inflammatory biomarkers such as HsCRP, IL6 ($p=0.042$) and ($p=0.0005$). The level of MMP9 was higher in the second group of patients but didn't reached the level of significance, ($p=0.2$). As well the mean level of adhesion molecules VCAM was higher in the second group of patients (1086 U/L vs 904 U/L) but was not correlated with the myocardial transmural index.

Concluzii:

This study showed that the hybrid imaging can be helpful in the assessment of myocardial viability a concept that is suitable to be investigated in patients with stable coronary artery disease before revascularization. Hybrid images CCTA\MRI can be a feasible method to assess the impact of the coronary artery atherosclerotic plaques on the subtended myocardium. Moreover, the infarcted myocardial mass can be increased in patients who suffered an acute myocardial infarction and have associated coronary artery plaques assessed with high vulnerability degree.