UNIVERSITY OF MEDICINE AND PHARMACY OF TÎRGU MUREŞ

DOCTORAL SCHOOL

Abstract of the PhD thesis

Epicardial adipose tissue as a new imaging-derived biomarker in cardiovascular diseases

Scientific coordinator: Prof. univ. dr. Theodora Benedek

PhD Student: Raț Nora

Epicardial adipose tissue (EAT) is associated with increased cardiovascular risk, being directly linked with an overexpressed inflammation. Epicardial fat serves as a reliable source of pro-inflammatory cytokines which are released in the systemic circulation and exert pro-inflammatory effects, on systemic and local level as well. However, the impact of EAT on various clinical settings such as pulmonary arterial hypertension (PAH) or in the presence of unstable coronary lesions is still under investigation. Furthermore, the impact of local accumulation of EAT around an atheromatous plaque, on plaque phenotype is not elucidated.

This research aimed to study the role of EAT, measured by coronary CT angiography (CCTA) (volumetric assessment) or by transthoracic echocardiography (based on diameter measuring) as a new imaging-derived marker associated with cardiovascular diseases in 3 clinical settings: PAH, vulnerable coronary plaques and patients at high-risk for an acute coronary event based on plaque phenotype modification.

The first study addressed the effect of EAT on the right and left ventricular function in subjects with various etiological types of PAH: caused by congenital heart defects (atrial septum defects with left-to- right shunt), systemic sclerosis, and secondary to heart failure caused by myocardial ischemia. The study included 50 patients with documented PAH, out of which 25 pts with atrial septum defect (12 receiving septal defect correction by implanting Amplatzer occluding devices), 12 pts with PAH induced by systemic sclerosis and 13 pts with PAH caused by advanced myocardial ischemia. The largest EAT was found in patients with PAH caused by myocardial ischemia (11.08 ± 2.39 mm), followed by scleroderma patients (9.14 ± 2.03 mm), and patients with atrial septum defects (8.16 ± 1.57 mm) ($p = 0.0003$). In the 12 patients who received implantation of an Amplazer occluding devices, serial measurements did not indicate any progression of epicardial fat thickness in time.

The second study investigated the association between periplaque epicardial adipose tissue (PPAT) and CT markers of plaque vulnerability. Eighty-two symptomatic patients with unstable angina and at least one feature of vulnerability in the culprit lesion were classified as low-PPAT (n=41) and high-PPAT (n=41) according to the median of 0.58 mm^3. Culprit lesions surrounded by a large PPAT presented a significantly higher remodeling index (p=0.04) and larger plaque volume (208.9 vs 158.9 mm^3, p=0.02), and exhibited the main vulnerability markers in a significantly higher extent as compared to those surrounded by smaller PPAT (p= 0.03 for napkin-ring sign, p=0.03 for low-attenuation plaque and p=0.01 for positive remodeling). By linear regression analysis, PPAT correlated well with plaque volume (r=0.42, p<0.0001), NCP (r=0.43, p<0.0001) and fibro-fatty volume (r=0.43, p<0.0001).

The aim of the third study was to investigate the association between PPAT and plaque phenotype in high-risk patients with angina. We prospectively enrolled 77 patients who presented minimum one lesion with >50% stenosis. CCTA analysis included measurements of: total EAT and PPAT volumes, coronary plaque characteristics, markers for plaque vulnerability: positive remodeling (PR), low attenuation plaque (LAP), spotty calcifications (SC,) napkin ring sign (NRS). Study subjects were divided into two categories: Group 1 – 1 marker of plaque vulnerability (n = 36, 46.75%) and Group 2 – ≥1 marker of vulnerability (n = 41, 53.25%). Group 2 presented significantly longer plaques (16.26 ± 4.605 mm vs. 19.09 ± 5.227 mm, p = 0.02), remodeling index (0.96 ± 0.20 vs. 1.18 ± 0.33, p = 0.0009), and more voluminous plaques (147.5 ± 71.74 mm3 vs. 207.7 ± 108.9 mm3, p = 0.006) compared to Group 1. Group 2 also presented larger volumes of PPAT (512.2 ± 289.9 mm3 vs. 710.9 ± 361.9 mm3, p = 0.01) and of thoracic fat volume (1,616 ± 614.8 mm3 vs. 2,000 ± 850.9 mm3, p = 0.02). Patients with 3 or 4 vulnerability markers (VM) presented significantly larges PPF volumes compared to those with 1 or 2 VM, respectively (p = 0.008). The total EAT volume was significantly correlated only with the volume of lipid-rich plaques (p = 0.02). The study demonstrated that an increased PPAT assessed by CCTA is associated with a more vulnerable plaque phenotype in patients with high-risk coronary artery disease

In conclusion, this study shows that: (1) pulmonary arterial hypertension caused by myocardial ischemia is associated with a larger volume of epicardial fat as compared to PAH associated with congenital heart diseases or sclerodermia; (2) in high-risk patients with vulnerable coronary plaques, a large PPAT is associated with a more vulnerable type of atheromatous plaque in the culprit lesions, suggesting the PPAT could serve as a new CT marker of plaque-associated risk; and (3) in patients with stable angina, periplaque fat volume induces transformation of the adjacent plaque phenotype into o more vulnerable type, inducing plaque progression and vulnerabilization.