

University of Medicine and Pharmacy Tîrgu Mureş

Doctoral School

PhD Thesis Summary

**RESEARCH OF CT, IVUS, AND OCT MARKERS OF ATHEROMATOUS PLAQUE
VULNERABILITY IN ACUTE CORONARY SYNDROMES**

PhD Student: Nyulas Tiberiu

PhD Scientific coordinator: Prof. Univ. Dr. Benedek Imre Sandor

Introduction. Coronary artery disease represents the main cause of global morbidity and mortality and accounts for over half of all cardiovascular events in men and women in Europe and other continents. Atherosclerosis is a chronic condition characterized by the formation of plaques within the arteries as a result of the complex interaction between lipoproteins, endothelium and inflammatory cells. The development and progression of atherosclerosis is determined by modifiable and non-modifiable risk factors as well as by other unidentified risk factors and the susceptibility of the host. In most men and women with coronary atherosclerosis, the initial presentation is acute myocardial infarction or sudden cardiac death, and two thirds of acute coronary syndromes are due to atherosclerotic plaque disruption. The characteristics of the disrupted plaques on histopathology include large volumes of large necrotic plaques and cores that are coated with a thin fibrous cap and typically infiltrated with monocytes and macrophages.

Studies on culprit plaques with invasive intravascular imaging, such as intravascular ultrasound, have identified the imaging characteristics of plaque vulnerability. These features include positive remodeling, high lipid core and calcification of plaques. Intravascular techniques are, however, limited by the high cost and invasive nature of the test. Therefore, it is desirable to have a non-invasive imaging technique that can evaluate the plaque burden and detect the vulnerable plaques. Computed CT scan angiography (CCTA) has been established as a noninvasive method with high sensitivity and high negative predictive value for the detection of coronary artery stenosis.

Aim. Through this PhD thesis, we want to identify, evaluate and characterize imaging markers of atheromatous plaque vulnerability in acute coronary syndromes by CT, IVUS and OCT imaging techniques, in order to identify the most effective invasive or non-invasive technique to characterize the atheromatous plaque in patients with acute coronary syndrome.

Material and Methods. In this research, the total sample comprised 164 patients admitted at Cardio Med Medical Center Tirgu Mures. The collection of patients data was done through three different studies:

Study I: 50 patients - Investigation of different correlations between vulnerable atherosclerotic marker markers and non-vulnerable plate markers that could cause plate progression to unstable, based on multislice computerized tomography 64.

Study II: 89 patients - Evaluation of the role of epicardial adipose tissue as a marker of vulnerability in establishing clinical cardiovascular prognosis in a group of patients diagnosed with stable angina and myocardial infarction.

Study III: 25 patients - Identification of neoaterosclerotic tissue characteristics of restenosis in the stent compared to native coronary atherosclerotic lesions.

The data collected in the study included information on demographic data, anamnesis, risk factors of vulnerability, cardiovascular risk factors, clinical status, smoking status, anthropometric indices, laboratory tests (hemogram, glycemia, urea, creatinine, triglycerides, total cholesterol, uric acid, transaminases), paraclinical explorations (electrocardiogram - ECG, echocardiography, OCT, VH-IVUS, Angio CT).

Results. Regarding the frequency of cardiovascular risk factors, following the medical history and interviewing the patients evaluated in this paper, the following conditions were highlighted: 32% of the patients declared being active smokers, over half of them 63% (n=102) had type 2 diabetes, a significant proportion of 69% (n=112) were diagnosed with hypertension and a proportion of 43% of patients had dyslipidemia.

In first study we observed that the vulnerable atherosclerotic plaques cause a larger lesion (6.80 +/- 3.86 mm) than the non-vulnerable plaques (5.51 +/- 4.09 mm), the difference being statistically insignificant (p=0.16), the minimum thickness of the vulnerable plaque having 0.77 +/- 0.59 mm, compared to the minimum thickness of the non-vulnerable plaque 0.29 +/- 0.34, the difference between these two media indicating an extreme association statistically significant, p=0.0005, resulting in the vulnerable plaque has a minimum thickness greater than the stable plaque, plaque burden was higher (85.23 +/- 8.39%) in the case of unstable plaques compared to the stable plaques (78.86 +/- 9.85%), the difference being statistically significant, p=0.01.

In the second study we found that patients with stable angina were not associated with the increased frequency of dyslipidemia, the presence of this risk factor was observed only in 13.95% of patients with stable angina and 31.91% of patients with myocardial infarction, p=0.077, OR=2.891, 95%CI:1.003-8.332, the absence of dyslipidemia representing a protective factor, and comparing the mean thickness of epicardial adipose tissue values of patients with myocardial infarction (MI) to patients with stable angina (SA), results in a statistically significant difference p <0.0001, the mean EAT of patients with IM being higher than the mean EAT of SA patients 2 (9.12 +/- 2.28 vs. 6.30

+/- 2.03), so we can state that epicardial adipose tissue is a marker of vulnerability for establishing cardiovascular clinical prognosis.

In the third study we observed that de novo lesions have a thickness >100, 87.17% compared to 48% of the ISR lesions, 52% of ISR lesions having a thickness <100, statistically significant difference, $p=0.001$, $OR=7.36$, $CI:2.16-25.05$. Based on the statistical analysis of lesion density, the following results were found: the frequency of low density plaques was higher (74.35%) in de novo injuries compared to a much lower value for ISR (32%) plaques, and a share of 68% ISR lesions showed low density versus 25.64% of de novo lesions, $p=0.002$, $OR=6.16$, $CI:2.039-18.63$.

Conclusions. Through this doctoral thesis, it was desired to identify, evaluate and characterize the imaging markers of atheromatous plaque vulnerability in acute coronary syndromes by CT, IVUS and OCT imaging techniques, in order to identify the most effective invasive or non-invasive technique to characterize the atheroma plate at patients with acute coronary syndrome. In this regard the following conclusions were observed and elaborated:

The analysis of our research on morphology and composition of the culprit and non-culprit plaques using CCTA as well as quantification of the plate showed that the presence of a larger plate volume and a larger volume of fibrous and fibro-adipose tissue in unstable lesions of ACS patients, these being vulnerable markers that correlated well with other derived vulnerability features through CCTA, especially with the necrotic core of the plaque.

There is a relationship between epicardial adipose thickness and coronary atherosclerotic burden in CAD patients. The increased thickness of epicardial adipose tissue was associated with other biomarkers of disease severity, such as the left ventricular ejection fraction with DTSVS, and total cholesterol. Therefore, the epicardial fat volume could represent a new biomarker derived from imaging useful to characterize the severity of coronary artery disease. Information provided by epicardial adipose tissue can be used as predictors of major cardiovascular events in patients with acute coronary syndromes, both in the short and long term. Our results indicate that epicardial adipose tissue is significantly higher in patients with acute coronary syndrome, so we can state that epicardial adipose tissue plays a role of marker of vulnerability in establishing cardiovascular clinical prognosis.

In ISR patients with acute coronary syndrome, neoaterosclerosis in coronary implanted stents is associated with signs of plaque vulnerability to a significantly greater extent than atheromatous plaques in native coronary arteries. Therefore, neoaterosclerosis may be considered a different process from classical neointimal hyperplasia, which increases the risk of acute cardiac events in coronary stent patients. Early detection of neoaterosclerosis is possible through imaging techniques such as Angio CT, IVUS and OCT, which can identify markers of instability in this restenotic tissue, triggering appropriate therapeutic measures.