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**IMAGE-DERIVED BIOMARKERS AT THE LEVEL OF COMMON ILIAC  
ARTERIES AS PREDICTORS OF ATHEROSCLEROSIS SEVERITY IN CRITICAL  
LIMB ISCHAEMIA**

**PhD Thesis  
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**Introduction:** Peripheral artery disease (PAD) represents a particular manifestation of systemic atherosclerosis, in which atheromatous plaques are located at the level of the peripheral arteries. The incidence of PAD is increasing with age and affects more than 200 million people worldwide. In most of the cases PAD is associated with concomitant coronary artery disease (CAD), presenting a high mortality rate. Early diagnosis and initiation of proper treatment are required to reduce the rate of mortality and to optimize the quality of life of patients with critical limb ischaemia. Multiple studies have investigated the association between the severity of peripheral artery disease and the severity of coronary artery disease. This doctoral study investigated the association between these two conditions, using a Multislice Angio Computer Tomography examination for evaluation of TASC class and calculation of coronary Calcium Score and Syntax Score. This research presents a computer-aided image postprocessing technique for the calculation of the amount of periiliac adipose tissue (PIAT) and investigates its relationship with the severity of PAD.

**Aim of the study:** The aim of the first study was to demonstrate the correlation between the severity of PAD, characterized by TASC class, and severity of CAD characterized by coronary Calcium Score and Syntax Score, and to investigate the prevalence of significant coronary artery lesions at patients with peripheral artery disease.

It is known that adipose tissue is a reservoir of different inflammatory mediators, and has an important role in the inflammatory process, which contributes to the progression of the peripheral artery disease. However, there is no study so far to investigate the potential role of the perivascular adipose tissue, located at the level of iliac arteries, in the complex pathophysiology of peripheral arterial disease. The aim of the second study was to compare the volume of the periiliac, subcutaneous and visceral adipose tissue with the severity of PAD characterized by TASC class.

**Material and method:** The first study included 24 patients with peripheral arterial disease, 10 of them with critical limb ischaemia. In all cases, cardiovascular risk factors, left ventricular dysfunction and left ventricular ejection fraction were analyzed. Peripheral Multislice Angio CT examination was used to determine the TASC class and to assess the lesions of the peripheral arteries. The calculation of Coronary Calcium Score and Syntax Score were performed on the basis of coronary angio CT images. Statistical analyses were used to determine the correlation between the severity of peripheral artery disease and coronary artery disease.



The second study used a semi-automated, computer-aided imaging technique to quantify the amount and distribution of perivascular fat at the level of the common iliac arteries. This technique was developed within this doctoral research and validated in 34 patients known with PAD, and to investigate the association between the volume of the periiliac adipose tissue and the severity of peripheral artery disease characterized by TASC class.

**Results:** The first study shows that the majority of patients with PAD (88 %) present hypertension, 53 % high values of total cholesterol and 54.3 % diabetes. A significant correlation was demonstrated between TASC class and Syntax Score, patients in advanced TASC class presenting higher values of Syntax Score ( $p=0.0005$ ). Significant left main stenosis (LM) was present in 59 % of patients, severe triconary lesions in 35 % of patients, bicorony lesions in 23 % of patients and one significant coronary lesion with indication for angioplasty in 28 % of patients. Significant LM stenosis, severe triconary and bicorony lesions were present especially in patients with critical limb ischaemia, and in class TASC C. The presence of significant LM stenosis presented a positive correlation with TASC class ( $p=0.03$ ). A good correlation was demonstrated between coronary Calcium Score and Syntax Score ( $p=0.03$ ). The presence of segmental left ventricular (LV) hypokinesia presented a positive correlation with the TASC class, which means that the severity of peripheral artery disease is directly related to the deterioration of the LV function produced by ischaemic coronary artery disease ( $p=0.04$ ).

The second study shows a significant correlation between the right and left PIAT volume, the fat distribution between left and right iliac axis revealing a quasi-uniform distribution of perivascular adipose tissue ( $p=0.005$ ). Mean PIAT volume presented a good correlation with TASC class ( $p<0.0001$ ), patients with increased volume of PIAT having more complex arterial lesions. Linear regression analyses indicated a positive correlation between serum cholesterol levels and PIAT volume ( $p=0.02$ ,  $r=0.39$ ). The mean PIAT volume was significantly associated with the amount of visceral fat at this level ( $p=0.02$ ,  $r=0.38$ ) but not with the subcutaneous fat measured at the level of common iliac arteries.

**Conclusion:** Patients with PAD present concomitant coronary artery disease, which is proven by the positive correlation found between TASC class and Syntax Score. There is a significant correlation between the severity of PAD and the presence of LM stenosis. The LV wall motion alteration is correlated with PAD severity expressed by the TASC class.

PIAT represents a novel biomedical imaging derived biomarker which characterizes the distribution of adipose tissue in the pelvic area and may serve as an indicator of the severity and complexity of lower limb ischaemia.