

The mechanism of atherosclerosis and atheromatous process in peripheral arterial disease: a clinico-morphopatological study

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Currently arteriosclerosis is a major problem worldwide with high prevalence, affecting 10-15% of the general population and 70-75% of the elderly, being present in 90% of men and 67% in women over 70 years. According to WHO data in civilized countries over 50% of mortality is caused by diseases associated with atherosclerosis.

As a research topic, the present study falls within the boundary between endovascular surgery / angiology and the pathology of peripheral vascular atherosclerosis, “hot” and very active research areas, which have been declared particularly important for the future by several international organizations. Peripheral arterial disease (PAD), morphologically characterized by chronic atherosclerosis / chronic obliterative atherothrombosis, is considered the third leading cause of death in Europe and the US, and in Romania, according to WHO statistics, is in the first place both in terms of morbidity and of mortality.

In the present paper we proposed a complex clinical-morphological characterization of PAD in four distinct chapters, respectively four studies. Starting from the epidemiological data and the pathophysiology of atherosclerosis, we looked for answers to the following questions: The evolution and incidence of complications (amputation) after revascularization is it dependent on age, sex, body mass index, smoking and patients' comorbidities? Do the number of neutrophils, lymphocytes or platelets have a prognostic value in estimating the occurrence of revascularization complications in patients with diabetes? Redefining the calcified plate according to the extent and architectural appearance of mineral salt deposits combined with the calculation of the pathological calcification score by morphometric methods can reliably characterize the evolution of the disease? What are the various causes?

The mentioned objectives were fulfilled using a complex methodology from clinical and paraclinical to histological and digitized morphometry. The results were statistically processed and critically interpreted compared to the literature data.

The first study followed the clinical, epidemiological and paraclinical features of PAD. Patients diagnosed with PAD and carotid artery atherosclerosis in the SCJUM Vascular Surgery Clinic during the period 2017-2018 were included in the study based on their medical history (intermittent claudication), physical examination (examination of arterial pulse by measuring segmental pressures, muscle atrophy, hair loss, ingros), ankle-arm index ≤ 0.9 and ≥ 1.3 , respectively with neurological symptoms caused by cerebral ischemia. In the case of PAD, the determination of the degree of ischemia was based on the Fontaine classification, respectively the Rutherford classification.

During the above-mentioned period, 138 patients with PAD were diagnosed, of which 101 met the criteria for creating the examined cohort (the rest of the patients were with incomplete data).

In the second study based on the pathophysiology of atherosclerosis, in which chronic inflammation plays a key role in the evolution of the disease, we aimed to investigate the prognostic value of NLR in the evolution of PAD, interpreting the degree of ischemia in the mirror of leukocytes and circulating platelets by calculating neutrophil / lymphocytes ratio (NLR), platelets / lymphocytes ratio (PLR) and lymphocytes / monocytes ratio (LMR) respectively.

This retrospective study enrolled consecutive patients with PAD and DM admitted to the Târgu Mureș County Emergency Clinical Hospital for revascularization surgery between January 2019 and December 2020. 100 consecutive patients hospitalized for a revascularization intervention were divided into two groups : group A- which requires any type of amputation after the revascularization operation (n = 33) and group B-which not (n = 67).

In this study, an association between NLR, MLR, PLR and postprocedural amputation rate was observed in patients with PAD and DM who underwent revascularization.

In the third topic included in this doctoral thesis, we performed a retrospective study, obtaining data from the medical records of the Vascular Surgery Department of the Mureș County Emergency Clinical Hospital. The inclusion criteria in the study were the presence of TASC C and D lesions, in which endarterectomy with ring dissector was performed between January 2016 and February 2019, 134 patients with chronic lower limb ischemia between January 2016 and February 2019 were reviewed retrospectively.

Detailed cross-sectional morphological comparative characterization of intra-plaque calcification of advanced atherosclerotic lesions based on morphometric methods involving the most important segments of the deep femoral artery and carotid artery were the subject of interest of the study 4. In this prospective comparative study, tissue fragments collected by conventional transluminal angioplasty from patients diagnosed with peripheral asymptomatic arterial disease (PAD) and carotid artery atherosclerosis were included. The material was collected from different patients between January 2017 and December 2018, from the Vascular Surgery Clinic, within the Mureș County Emergency Clinical Hospital (Romania). A total of 101 cases were selected for the clinical pathological study, based on strict criteria: patients with complete clinical documentation and written consent to enroll in the study and an appropriate quantitative and structural specimen for histological examination.

The conclusions of this doctoral topic cover a wide range of information and are as follows. The distribution of patients by decades of age and gender shows a peak grew comprising decade 7th in men, female sex has a large gap (a "delay") in the development of severe PAD that equals only in decade 9th with male sex.

The anatomical location of atherosclerotic lesions shows the development of lesions with high histological grade (AHA VI-VIII) predominantly in the distal segment of the superficial femoral artery, compared to the carotid artery which is approximately equally interested in different histological forms of plaques.

Evolution and incidence of complications (amputation) after revascularization does not depend on age, sex, body mass index, smoking, or assessed comorbidities (all $p > 0.05$). The calculation of the neutrophil / lymphocyte (NLR), platelet / lymphocyte (PLR) and lymphocyte / monocyte (LMR) ratio has a prognostic value in estimating the occurrence of revascularization complications in patients with DM. A higher NLR

associated with low MLR was observed in patients who underwent post-procedural amputation compared to the group without post-intervention complications ($p < 0.01$).

Endarterectomy with ring dissector in the case of femoral-popliteal lesions TASC C and D can be considered a highly successful therapeutic option. It combines both the advantages of minimally invasive surgery and endovascular techniques, which makes it useful for patients with prominent comorbidities due to the shorter duration of surgery and shortening the duration of anesthesia, a faster healing time due to smaller incisions, which also leads to decreased hospitalization costs.

Histopathological study of the types of calcification of the carotid artery and femoral artery, that despite being exposed to similar risk factors, peripheral arteries develop different lesions. The femoral and carotid lesions show varied morphology and calcification tendencies. In our paper we demonstrated that in a population with similar demographic and biological data, larger areas of calcification develop at the level of smaller caliber arteries (femoral-popliteal artery / popliteal) than at the level of larger caliber arteries (femoral / carotid). These results suggest that the mechanism is site-specific and wall-dependent.