UNIVERSITY OF MEDICINE AND PHARMACY OF TÎRGU MUREŞ

DOCTORAL SCHOOL

Abstract of the PhD thesis

Study of imaging-derived biomarkers associated with severity of pulmonary hypertension in scleroderma patients

Scientific coordinator: Prof. univ. dr. Theodora Benedek

PhD Student: Cucuruzac Roxana

The impact of pulmonary arterial hypertension (PAH) on left ventricular performance and its role in the development of ventricular adaptive response in patients with scleroderma is still unknown. This doctoral research aimed to investigate, using an advanced panel of imaging-derived biomarkers, the mechanisms associated with the development of ventricular adaptive response to pulmonary hypertension (PH) in two clinical scenarios associated with different etiological varieties of PH: PH caused by systemic sclerosis as a representative of systemic inflammatory diseases and PH caused by myocardial ischemia.

This original hypothesis was tested in two different sub-studies:

The first sub-study consisted in a prospective observational study on 82 patients. Based on the etiology of PAH, study population was divided into: group 1 – 48 patients diagnosed with scleroderma; and group 2 – 35 patients with coronary artery disease. Patients from each group were divided into two subgroups based on the diagnosis of PAH: subgroup 1A – subjects with scleroderma and associated PAH (n = 20); subgroup 1B – subjects with scleroderma without PAH (n = 28); subgroup 2A – ischemic patients with associated PAH (n = 16); and subgroup 2B – patients with ischemic disease without PAH (n = 19). A significant difference between LVEF values in patients with PAH versus those without PAH in the ischemic group ($p = 0.023$) was recorded. Compared to scleroderma subjects, ischemic patients presented significantly lower values of LVEF in both PAH and non-PAH subgroups ($p < 0.0001$ and $p < 0.0001$, respectively). Linear regression analysis between sPAP and LVEF revealed a significant negative correlation only for the ischemia group ($r = –0.52$, $p = 0.001$) and the scleroderma 2B subgroup ($r = –0.51$, $p = 0.04$). Tissue Doppler

analysis of left ventricular function revealed a significant impact of PAH on left ventricular diastolic performance in the ischemic group. This study concluded that compared to patients with coronary artery disease, those with scleroderma present a less pronounced deterioration of LVEF in response to pulmonary arterial hypertension.

*Study 2 c*onsisted in a propsective observational study on 52 patients with scleroderma, divided in 2 groups based on the presence of associated PH: group 1 – patients with scleroderma and PH (n=29); and group 2 – patients with scleroderma and no PH (n=23). Deceleration time on PW Doppler anvelope was 171.8 msec in group 1 vs. 213.5 msec in group 2, p=0.002, indicating that diastolic dysfunction is present in scleroderma patients in the early stages, before occurrence of PH, caused by a mechanisms independent from the presence of PH.

In conclusion, based on a complex assessment of a panel of imaging-derived biomarkers characterizing left and right, ventricular systolic, ventricular diastolic and atrial function, this research demonstrated that scleroderma patients present a distinctive pattern of adaptive response to tissue alterations occurring in sclerodermia, and installation of right ventricular failure occurs earlier in their evolution than PH, via an independent mechanism.