



Universitatea *Transilvania* din Braşov

HABILITATION THESIS

SUMMARY

**Title: MYOCARDIAL ISCHEMIA – FROM ATHEROSCLEROSIS
TO CLINICAL MANIFESTATIONS**

Domain: MEDICINE

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Summary

The professional, academic and scientific activity, in the period that followed the PhD thesis until present, belongs mainly to the field of cardiology and it was centered on two main directions: ischemic heart disease (from risk factors to treatment of clinical manifestations and prognosis) and atrial fibrillation with emphasis on the study of new interventional treatment techniques (ablation therapy).

The personal research in the field of acute myocardial infarction brought new elements regarding the study of risk factors and the prognosis estimation in such patients.

Even if currently, primary coronary angioplasty with stent implantation represents the first-line therapy in acute myocardial infarction, there are still many patients, particularly in Romania, which do not have access to this method of treatment. In this context, fibrinolytic therapy still plays an important role and, especially in this field, I conducted important research that brought new data concerning the assessment of the long-term prognosis in patients with acute myocardial infarction treated with thrombolytic therapy. These publications have appeared in the context of a relative abundance of data concerning the short-term estimation of the risk of death and unfavorable outcome, but studies regarding the long-term monitoring of the evolution of these patients have been extremely limited.

In direct correlation with the extension of myocardial infarction and its impact on prognosis, my research allowed the validation of a new and cost-efficient assessment method for the estimation of the area of necrotic myocardium. Previous research regarding the estimation of necrotic area was carried out using mainly the determination of the area under the curve of a certain enzymes of myocardial necrosis: creatin-kinase (CK), creatin-kinase-MB (CK-MB). We utilized and validated a much simpler method that only involved two measurements of plasma level of α -hidroxi-buthyrate-dehidrogenase (α -HBDH) determined at 36 and 72 hours after infarction.

The identification of some clinical and haemodynamic parameters that are easy to quantify at the patient's bedside, in conjunction with a biochemical method that allows the cheap and simple estimation of the amount of myocardial necrosis, led to development of an original algorithm useful to assess the risk of death at two years post myocardial infarction. All these aspects are important elements of originality in my research activity. This model for long term prognosis estimation was developed in a period of time when the factors influencing long-term death were relatively less investigated.

My interest to identify risk factors for myocardial infarction and to establish their impact on prognosis of such patients and the type of care they should receive, reached a higher level by the involvement in a large national project aimed to create a registry of acute myocardial infarction – the RO-STEMI registry. This registry has become one of the most comprehensive registries in Europe, collecting until now more than 50,000 patients. The data in the registry have provided an important amount of information about the demographic characteristics and about the treatment of patients with acute myocardial infarction in Romania. I was actively involved in both the recruitment of patients in the registry, as well as in the data analysis (especially data related to demographic and risk factors and their influence on the vital prognosis and mortality of patients with acute myocardial infarction). The publications authored by me on this subject represented the natural continuation of the research in the field of my PhD thesis.

After the PhD thesis, I have completed my professional training in the area of myocardial ischemia by performing a 6-month fellowship in Israel, with focus on interventional treatment of coronary artery disease. Expanding preoccupation in this area has been also materialized in publishing new articles that covered various aspects of the interventional treatment of acute myocardial infarction.

At the same time, the research area was widened, aiming also the characterization of the early stages of ischemic heart disease with a focus on early detection of vascular atherosclerosis with emphasis on the mechanisms underlying the progression of atherosclerosis and its complications. On this topic, it is noteworthy my collaboration with a group of researchers from the Nutrition Department, University of North Carolina in the United States. Together with the American researchers, we developed a research project aimed to position the role of therapy with α -linolenic acid in the evolution of the metabolic syndrome. The original aspects of the research consisted mainly in the characterization of the evolution of some parameters related to metabolic syndrome, chronic inflammatory syndrome and insulin resistance in patients treated with α -linolenic acid (ALA), but also in an attempt to characterize changes in the deoxyribonucleic acid (DNA) methylation profile and gene expression correlated with the level of DNA methylation, in human lymphocytes.

Winning a two-year European Fellowship with emphasis on electrophysiology and ablation therapy, allowed me to develop the knowledge and further research in a new area focused on the electrophysiological study of rhythm disorders and their interventional treatment.

Throughout the period of this fellowship, I was actively involved in research activities of Department of Cardiology of Debrecen University, Hungary, most of them dedicated to the study of the newest ablation therapies of atrial fibrillation. The collaboration with the Department of

Cardiology of Debrecen University continued after the conclusion of the two-year fellowship until present, I still participate in research projects developed in that center.

After the PhD thesis, I published 37 scientific papers, most of them in the field of cardiology. Fourteen papers have been published in journals indexed in ISI Thomson Reuters data base. Of all articles, 21 have been published as first author. My publications have accumulated a total of 66 citations and an H index of 5 in Google Scholar database and an H index of 4 in ISI Thomson Reuters database.

Since the time of the PhD thesis preparation until now, I was director of a scientific grant won through national competition, I was project responsible and scientific coordinator of an international research grant and I was a team member in another research project also obtained through a national competition. On top of these are the participations as principal investigator in four international and two national research studies, and as a team member in other five international studies.

My activities in the field of cardiology provide significant scientific and academic contribution through both original works and books published as a single author, co-author and editor. The involvement in the activity of the continuous training of doctors is noteworthy, leading to numerous post-graduate continuing education medical courses.

Future research are mainly centered on the cardiac ischemia, one research direction aiming the metabolic changes of the myocytes and endothelial cells during and after an ischemic episode and the protective mechanisms against ischemia such as the ischemic preconditioning.

The second research direction is done in a multinational consortium and aims to develop a new type of coronary endovascular prosthesis.

Concerning teaching activities, the internal medicine courses will be improved by the permanent addition of new information and internal medicine courses in English. The teaching activity will be complemented by collaboration with the Technical University and the creation of a new discipline within the Faculty of Materials Engineering, targeting implantable devices in cardiovascular pathology.

Given the involvement of teaching and academic activity, some of my further actions still regard the publication of new books in the field of cardiology and proposing new courses for master and doctoral school in order to ensure better training of medical students and young doctors.