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**RISK FACTORS STUDIES - FROM ENDOTHELIAL  
DYSFUNCTION TO CARDIOVASCULAR DISEASE**

**ABSTRACT**

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## **ABSTRACT OF THE HABILITATION THESIS** **RISK FACTORS STUDIES - FROM ENDOTHELIAL DYSFUNCTION TO** **CARDIOVASCULAR DISEASE**

**SEF LUCRARI DR. MINODORA ANDOR**

This Habilitation Thesis is a result of my academic and research activities for the last 15 years, carried out mainly in the field of cardiovascular risk factors and prevention of the cardiovascular diseases. The thesis is divided into four sections, according to the recommendations: scientific achievements, academic accomplishments, professional activity and the future academic and scientific perspectives.

**Scientific achievements.** After the PhD thesis, which referred to the risk factors which aggravates the evolution after acute myocardial infarction, the research focused on the *early diagnosis of the endothelial dysfunction*, which is a first step in the development of the cardiovascular injuries.

Synthetically, the scientific activity materialized through 50 in extenso articles, 20 of them in ISI indexed journals (13 of them as first or principal author), which received a total of 169 citations. Thus, a Hirsch Index of 6 in Web of Science was attained, the cumulated

impact factor of the published papers in which the candidate is the principal author being 32.3. It is important to be mentioned that the majority of the research work was done in the multidisciplinary teams.

The post-doctoral research and professional work represents, in general, a continuation of the researches from the doctoral period, comprising also a widening of the research area by some collaborations, but still keeping the focus on the assessment of the cardiovascular risk factors which can generate and/or aggravate the evolution of the cardiovascular diseases. Thus, we tried to get a deeper insight by assessing the endothelial dysfunction and evaluating the factors which can either improve or aggravate that. Later on, we revealed the importance of the early diagnosis of the cardiovascular impairment in psychiatric patients.

The main research activity was aligned to two main directions related to the assessing the patient at risk to develop cardiovascular impairment: ***the endothelial dysfunction, diagnosis, testing new markers easy to use to diagnose this early change in the patient's homeostasis and medical treatment*** which can improve or delay the atherosclerotic process. The second direction addressed ***chronic psychiatric patients, which develop cardiovascular diseases earlier than the non-psychiatric population***. The research was focused on the identification and evaluation of the changes which are more frequent and to find if these changes are due to the disease per se or are due to a life-time treatment.

The main scientific achievements are enumerated here by briefly presenting the results of the most important studies in which I have participated.

In 2016 a study was developed regarding the ***role of pentraxin 3 (PTX3) in endothelial dysfunction***. The PTX3 values were measured in a group of hypertensive patients compared with a control group and was concluded that PTX3 could be a better inflammatory biomarker than other usually used, and Perindopril decreases more powerful PTX3 than other antihypertensive drugs.

Following these results, the next study, published in 2017, is an experimental one, in collaboration with the Faculty of Pharmacy from University of Medicine and Pharmacy "Victor Babes" Timisoara, being a comparative study between the solid-state stability of Perindopril active substance vs pharmaceutical formulation.

In 2017 we followed the idea that the inhibition of renin-angiotensin-aldosterone system could be beneficial for endothelial dysfunction, and we studied ***the effect of candesartan on PTX3 plasma levels as marker of endothelial dysfunction in hypertensive patients***. We concluded that candesartan induces greater reduction in plasma PTX3 than other classes of antihypertensive drugs, these findings suggested that candesartan may be more potent in reversing endothelial dysfunction and may offer a higher degree of vascular protection.

According with these results, we continued our collaboration with Faculty of Pharmacy initiating an extensive study on the ***stability and kinetics of degradation of candesartan***, paper published in 2020.

Afterwards, our group decided ***to find another specific marker of endothelial dysfunction*** and study if renin-angiotensin-aldosterone system inhibition improve also these markers. Going further with this idea, we conducted a study with ***thrombospondin-1 (TSP-1) in hypertensive patients***, materialized in two published papers (2017, 2019). According to our results, we may say that patients under chronic treatment with perindopril have a more decreased level of endothelial inflammation, reflected through both TSP-1 and PTX3 plasma levels.

In 2019 we studied also ***soluble endoglin (sEng) as a biomarker of endothelial damage***. We found a decreased sEng plasma levels in hypertensive patients with endothelial dysfunction under chronic treatment with perindopril.

In 2018 ***we started a new direction of research***, linked with the endothelial dysfunction in collaboration with the Department of Psychiatry from our university. These studies started from the observation that patients with different types of psychosis have a lower life expectancy than the general population, most deaths being attributed to cardiovascular complications.

The results were published still in 2018, concluding that ***metabolic syndrome appears to be induced by both the disorder and the antipsychotic treatment***, regardless of the molecules involved in treatment, and hypertension may be a consequence of disorder in the absence of a continuous antipsychotic treatment.

After these studies, in 2019 we published the outcome of ***a novel approach to cardiovascular disturbances in patients with schizophrenia***. We investigated the

patients biologically, ECG, routine echocardiography and speckle tracking. According to our results, a delay in initiating the treatment is statistically relevant risk factor for cardiovascular impairment, detected echocardiographically in early stages, using 2D strain method.

In 2020 we published a state-of-art paper regarding the ***co-morbidity between schizophrenia and cardiovascular changes***, which are multifactorial, but in majority of cases is secondary to the metabolic syndrome induced by psychotropic medication and also by the psychosis itself.

Besides the basic clinical research activities, detailed in this Thesis, I also had some external collaborations in multidisciplinary teams: with Dentistry School, UMF Carol Davila (member in a research project) and with Discipline of Medical Informatics (the “clinician” of the team studying the sonic representation of medical data – ECG, HR etc.)

**Academic accomplishments.** Didactic activity brings both challenges and satisfaction. A permanent work to improve the teaching was materialized by producing several didactic materials – *handbooks for students and residents, ppt presentations* and a collection of clinical cases. Last but not least, I tried to harmonize the informative side of education with the formative aspects and involve students also in research teams.

**Professional activity.** As an integrant part of daily life, closely related to both academic and scientific activities, I paid great attention to the permanent raising of my professional training to ensure a high quality of clinical activity and patient care. Acting as an ***expert for project evaluation for the European Commission in Brussels, under the Horizon 2020 frame*** had an important impact on my activity and career. And, as a responsible citizen, I have also considered to be active in the College of Physicians.

**Candidate`s future perspectives.** ***On the scientific plan:*** the results obtained up to now, the provocative topics still waiting deeper studies as well as the nice and lucrative atmosphere within the research teams I have collaborated – all give me solid reasons to *continue the research fields already started, regarding the medical intervention on the endothelial dysfunction* and the early diagnosis of the endothelial dysfunction using the new techniques which can diagnose molecular changes and even genetically changes in the patients more predisposed to develop an early disease or they have more severe evolution after the cardiovascular diagnosis. Also for *early cardiovascular changes in*

*psychiatric patients* is very important to find a method to diagnose in the early stages the cardiac impairment or endothelial dysfunction with an easy to use method, to find potential cardiovascular unfriendly psychiatric medication and to start as soon as possible a medical intervention to delay the development of the diseases.

***On the academic and professional plan:*** new educational tools and methods can be developed: a database with clinical cases, including images and signals or computer-aided interactive clinical stage classes.

All of the proposed future research activities imply a tight collaboration with researchers from other disciplines or departments of the University of Medicine and Pharmacy. In order to widen the studied population, but also to improve the chance for funding, it is important to maintain and extend the existing collaborations with researchers from other universities or research centers, both nationally but especially internationally. In the proposed areas of research, future PhD students will be pro-actively involved in applied and theoretical state-of-the-art medical research.

Finally, I hope that my activity will bring a contribution to the fulfillment of the future plans of development of the University of Medicine and Pharmacy “Victor Babes” Timisoara.