GEORGE EMIL PALADE UNIVERSITY OF MEDICINE, PHARMACY, SCIENCE AND TEHNOLOGY OF TARGU MURES

DOCTORAL SCHOOL

SUMMARY OF THE DOCTORAL THESIS

Atrial fibrillation: beyond the irregular rhythm – cognitive and psychosocial implications

PhD candidate: Tünde Pál

PhD Supervisor: Dan Dobreanu, University Professor, PhD, MD

TARGU MURES 2025

UNIVERSITATEA DE MEDICINĂ, FARMACIE, ȘTIINȚE ȘI TEHNOLOGIE „GEORGE EMIL PALADE" DIN TÂRGU MUREȘ

Background

There is a continuous increase in life expectancy, which brings several disadvantages, such as a growing number of patients who need sometimes permanent care and supervision, increased costs within the healthcare system, higher incidence and prevalence of diseases and were associated with high morbidity and mortality. Atrial fibrillation (AF) is the most common supraventricular arrhythmia after premature beats and its incidence also increases with age. Previous observations suggested a relationship between this arrhythmia and cognitive dysfunction (CD) and dementia. Although these conditions are present predominantly in older patients, not all elderly individuals with this arrhythmia develop CD or dementia. Identifying patients at risk of cognitive decline represents a complex research field that engages multidisciplinary preclinical and clinical studies in the attempt to identify individuals at risk, to prevent, and ideally to treat cognitive decline - but so far, there still lacks robust evidence and solutions. Although this topic has been extensively studied abroad, in our country, very little data is currently available.

The main objective of the doctoral thesis was to evaluate the prevalence of CD in patients with AF, to analyze the usefulness of cognitive tests in predicting AF - thus facilitating earlier diagnosis and preventing arrhythmia-related complications and to identify the risk factors associated with cognitive decline.

General Methodology

The present study employed an observational, cross-sectional design. Patients with cardiovascular diseases were enrolled between December 2016 and April 2023 from two cardiology departments: the Cardiovascular Rehabilitation Department of the County Emergency Clinical Hospital of Targu Mures and the 1st Department of Adult Cardiology of the Emergency Institute for Cardiovascular Diseases and Transplantation of Targu Mures. The main inclusion criterion was previous cognitive assessment, which was performed during hospitalization with the following tests: Montreal Cognitive Assessment (MoCA), Mini-Mental State Examination (MMSE), and General Practitioner Assessment of Cognition (GPCOG). The exclusion criteria consisted of refusal to participate in the study, the acute phase of any disease or hemodynamic instability, and severe renal dysfunction (stage V). In addition to cognitive performance testing, the following questionnaires were applied: the Beck Depression Inventory for assessing depression, the EQ-5D-5L questionnaire for evaluating quality of life, and the Psychosocial Questionnaire of the European Society of Cardiology. In the general database, we included demographic and clinical information such as anthropometric and hemodynamic parameters, cardiovascular risk factors, cardiac and vascular diseases, some extracardiac comorbidities, laboratory parameters, echocardiographic data, ankle-brachial index, 24-hour blood pressure and electrocardiogram monitoring. Cognitive test scores and results of the applied questionnaires were also integrated into the database. All patients provided written informed consent for study participation and personal data processing, as well as consent for participation in medical education activities. The research protocol was approved by the ethics committees of the participating institutions (19779/09.09.2016, 29866/04.02.2022, 1719/28.04.2022) and was conducted in accordance with the ethical principles for medical research involving human subjects, as outlined in the Declaration of Helsinki.

Study 1 aimed to evaluate the prevalence of CD in the most common cardiovascular diseases and to identify the associated risk factors. Among the 628 patients included in the study, mild cognitive impairment was more frequent than moderate or severe decline in cognitive performance. Both AF and ischemic stroke were associated with the severity of cognitive decline, although the association was weak. AF, ischemic stroke, and female sex increased the likelihood of advanced CD, but did not significantly influence the occurrence of mild cognitive impairment. The probability of both mild and advanced CD was higher among older individuals, those with a lower level of education, renal dysfunction, and non-smokers.

Study 2 investigated the relationship between CD and the presence of AF and ischemic stroke, to predict the risk of these conditions based on cognitive performance. The study included 469 patients, and our findings demonstrated that the scores of cognitive tests (MoCA, MMSE, and GPCOG) were to detect a history of AF, ischemic stroke, heart failure, and peripheral arterial disease. Scores below the thresholds of 23 for MoCA, 28 for MMSE, and 8 for GPCOG were associated with a history of ischemic stroke. The standard MoCA cut-off score of <26 points used for CD was also effective in detecting both AF and ischemic stroke history. Similarly, an MMSE score below 28 was identified as a risk factor for documented AF. A statistically significant association was also observed between MMSE scores below 28 and GPCOG scores below 8 with the presence of lower-limb peripheral arterial disease. This was a hypothesis-generating study, and further longitudinal research on larger cohorts is warranted to evaluate the predictive utility of cognitive tests in assessing AF risk.

Study 3 evaluated the prevalence of psychosocial risk factors and their association with CD in patients with AF, which are often neglected in clinical practice. A total of 798 patients were included, all of whom completed the psychosocial risk factors questionnaire recommended by the European Society of Cardiology. This questionnaire assesses nine psychosocial factors, and our findings revealed that such factors are highly prevalent among patients with AF, beyond the commonly examined aspects such as depression, anxiety, and stress. Among the nine investigated factors, six were present in more than half of the studied population. The prevalence of social isolation, depression, and hostility was notably higher in patients with AF. The coexistence of CD and AF was associated with a greater number of psychosocial risk factors, reflecting a complex interaction between psychological, cognitive, and cardiovascular dimensions. Furthermore, quality of life was significantly lower in patients with permanent AF compared to those with other AF patterns. Our findings underscore the potential value of psychosocial and cognitive assessments in patients with AF. Future longitudinal studies are warranted to confirm these observations and to evaluate the clinical impact of integrating such assessments into routine patient care.

General Conclusions

The findings of this doctoral thesis highlight the increased prevalence of CD among patients with cardiovascular diseases, indicating that mild forms of CD are more common, which typically affect minimally or at all independence. Conversely, a history of AF and ischemic stroke was associated with an increased risk of advanced cognitive decline. The study suggests that cognitive testing in cardiovascular diseases is feasible and relevant, with potential utility in the identification of patients with a history of AF or ischemic stroke. Moreover, a high prevalence of psychosocial risk factors was identified among patients with AF, and the coexistence of cognitive dysfunction and AF further emphasized the complex interplay between psychological, cognitive, and cardiovascular health. In conclusion, the integration of cognitive and psychosocial assessments into cardiac rehabilitation programs is essential to promote a holistic and multidisciplinary approach in the management of patients with cardiovascular disease.

Originality of the Thesis

This study contributes to the strengthening of existing scientific evidence regarding cognitive decline in cardiovascular disease, with a particular focus on AF, and provides novel insights in the specific context of the Romanian population, where available data remain limited. The present doctoral thesis demonstrates that, although CD has traditionally been considered a neurological issue, it is highly prevalent among patients with cardiovascular conditions. The thesis addresses under-investigated topics in the scientific literature on AF, such as psychosocial risk factors and their interaction with cognitive performance. Another innovative aspect of the thesis is the evaluation of the utility of cognitive tests in predicting a history of AF. Furthermore, the design and methodology of the studies included in this thesis were conceived to lay the basis for a longitudinal study with long-term follow-up, enabling future research on the progression and impact of cognitive decline in cardiovascular patients.