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WNIOSEK PROJEKTU DOKTORSKIEGO

Szkoła Doktorska Nauk Medycznych i Nauk o Zdrowiu

IMIĘ I NAZWISKO AUTORA PROJEKTU	Jacek Kubica
AFILIACJA AUTORA PROJEKTU (jednostka organizacyjna, telefon, e-mail)	Katedra Kardiologii i Chorób Wewnętrznych CM UMK
DYSCYPLINA NAUKOWA	☐ Nauki farmaceutyczne X Nauki medyczne ☐ Nauki o zdrowiu

CZĘŚĆ A: OPIS PROJEKTU

1. TEMAT PROJEKTU
Impact of an Artificial Intelligence–Based Virtual Physician Assistant on Therapeutic Decision-Making and Guideline-Directed Medical Therapy Optimization in Patients with Heart Failure
2. STRESZCZENIE PROJEKTU (max. 1000 znaków)
The ASSIST-HF SIRIO trial was the first randomized study to evaluate a Generative Artificial Intelligence (AI)-powered Virtual Physician Assistant for optimization of Guideline-Directed Medical Therapy (GDMT) in patients with heart failure with reduced ejection fraction (HFrEF). The pilot study demonstrated improved GDMT optimization, lower NT-proBNP levels, fewer heart failure-related hospitalizations, and high patient satisfaction without safety concerns. The proposed study is a randomized controlled continuation of the ASSIST-HF program designed to validate these findings in patients hospitalized for acute decompensation of chronic HFrEF (NYHA III–IV). A total of 400 patients will be randomized 1:1 to AI-supported management using a Virtual Physician Assistant or standard care. The primary endpoints will include length of hospital stay, time to first rehospitalization, and all-cause mortality. Based on preliminary unpublished ASSIST-HF data, 298 patients are required to achieve adequate statistical power; therefore, the sample size has been increased to 400 to account for an anticipated dropout rate of 20–25%. The study will provide robust evidence regarding the clinical utility of AI-assisted decision-making in heart failure care.
3. CEL NAUKOWY PROJEKTU I ZNACZENIE PODJĘTEGO PROBLEMU BADAWCZEGO (max. 3000 znaków)
Heart failure with reduced ejection fraction (HFrEF) remains a major cause of hospitalization, rehospitalization, and premature mortality worldwide. Despite the availability of effective guideline-directed medical therapy (GDMT), treatment optimization remains suboptimal, particularly in patients hospitalized with acute decompensation of chronic heart failure. Therapeutic decision-making in this population is complex and frequently results in delayed initiation or inadequate optimization of evidence-based therapies. Recent advances in artificial intelligence (AI), particularly large language models and AI-powered clinical decision support systems, have created new opportunities to improve therapeutic decision-making. The ASSIST-HF SIRIO trial was the first

randomized study to evaluate a Generative AI-based Virtual Physician Assistant supporting GDMT optimization in patients with HFrEF. Importantly, although the study was conceived and scientifically designed at the Department of Cardiology and Internal Medicine, Collegium Medicum, Nicolaus Copernicus University in Bydgoszcz, it was intentionally conducted in an independent clinical center in London, United Kingdom, to ensure objective evaluation by investigators independent of the developers of the AI-supported care model. The pilot study demonstrated superior optimization of heart failure pharmacotherapy, lower NT-proBNP concentrations, fewer heart failure-related hospitalizations, high patient satisfaction, and no safety concerns compared with standard care. However, owing to its pilot nature and limited sample size, the study was not powered to assess major clinical outcomes.

The primary scientific objective of the proposed project is to determine whether AI-supported therapeutic decision-making improves clinically relevant outcomes in patients hospitalized for acute decompensation of chronic HFrEF (NYHA class III–IV). Specifically, the study will assess the impact of a Virtual Physician Assistant on length of hospital stay, time to first rehospitalization, and all-cause mortality. In addition, the project will evaluate whether AI-assisted optimization of GDMT during hospitalization translates into sustained benefits after discharge.

The proposed study represents the next stage of the ASSIST-HF research program and the first adequately powered randomized controlled trial designed to assess the effect of AI-assisted clinical decision support on hard clinical endpoints in heart failure. By investigating whether artificial intelligence can facilitate implementation of evidence-based therapy in routine practice, the project addresses an important unmet clinical need. Positive findings would support the integration of AI-powered decision support systems into everyday heart failure care and contribute to the development of scalable, cost-effective, and personalized models of chronic cardiovascular disease management.

4. KONCEPCJA I PLAN BADAŃ Z UWZGLĘDNIENIEM METODYKI (max. 4000 znaków)

The study is designed as a multicenter, prospective, randomized, open-label, controlled clinical trial evaluating the impact of an Artificial Intelligence (AI)-based Virtual Physician Assistant on the management of patients hospitalized due to acute decompensation of chronic heart failure with reduced ejection fraction (HFrEF).

A total of 400 adult patients with HFrEF (NYHA class III–IV) will be enrolled and randomized 1:1 to:

1. AI-supported management using a Generative AI-based Virtual Physician Assistant;
2. Standard care according to current clinical practice and guideline recommendations.

In the AI-supported arm, pharmacotherapy will be evaluated at two predefined time points: hospital admission and hospital discharge. Based on clinical, laboratory, echocardiographic, and therapeutic data, the system will generate recommendations regarding optimization of guideline-directed medical therapy (GDMT), including initiation, continuation, modification, or up-titration of treatment. Final therapeutic decisions will remain entirely under the responsibility of the treating physician.

The Virtual Physician Assistant platform has already been developed and successfully tested in the ASSIST-HF SIRIO pilot trial. Consequently, the proposed project focuses on clinical validation of the system rather than software development.
The study is an independent investigator-initiated research project. Essential technological and organizational support has been provided by the Centre for Modern Medical Technologies Ltd. (Centrum Nowoczesnych Technologii Medycznych Sp. z o.o.), which supports the digital infrastructure of the project but will not participate in patient recruitment, data analysis, interpretation of results, or publication decisions, thereby ensuring scientific independence.
The study will be conducted in three participating centers:

- University Hospital No. 1 Dr. Antoni Jurasz, Bydgoszcz,
- Stanisław Staszic Specialist Hospital, Piła,
- Polish Baptism Memorial Hospital, Gniezno.

All participating institutions have formally agreed to participate, and approval from the relevant Bioethics Committee has already been obtained.
At enrollment, demographic, clinical, laboratory, echocardiographic, and pharmacological data will be collected. During hospitalization, therapeutic interventions, medication changes, achievement of GDMT targets, adverse events, and discharge treatment will be recorded using standardized electronic case report forms.
Primary endpoints will include:

- length of hospital stay,
- time to first rehospitalization,
- all-cause mortality.

Secondary endpoints will include GDMT optimization, achievement of target medication doses, treatment modifications during hospitalization, and healthcare resource utilization.
Long-term follow-up will be performed using the national Individual Patient Account (IKP) platform after obtaining informed consent from each participant. This approach will enable reliable assessment of rehospitalizations, mortality, and healthcare utilization while minimizing loss to follow-up.
Patient recruitment is planned over 12 months. Each participant will be followed for 12 months after randomization. Completion of follow-up is therefore expected approximately 24 months after study initiation. Data analysis and manuscript preparation will begin immediately thereafter, with the first scientific publications anticipated approximately 30 months after study initiation.
Based on preliminary unpublished ASSIST-HF SIRIO data, the estimated sample size required to achieve adequate statistical power is 298 patients. To compensate for an anticipated dropout rate of 20–25%, the planned study population has been increased to 400 participants (200 per study arm).
The combination of a multicenter randomized design, a validated AI platform, established digital infrastructure, prior ethical approval, and comprehensive long-term follow-up provides a robust framework for evaluating the clinical effectiveness of AI-assisted therapeutic decision-making in advanced heart failure.

5. SPODZIEWANE ZNACZENIE WYNIKÓW BADAŃ (max. 1500 znaków)

The proposed project has the potential to make a significant contribution to both cardiovascular medicine and the rapidly evolving field of artificial intelligence applications in healthcare. The ASSIST-HF SIRIO pilot trial, which preceded the present study, was the first randomized investigation worldwide to demonstrate the feasibility, safety, and clinical utility of a Generative AI-based Virtual Physician Assistant supporting therapeutic decision-making in patients with heart failure. As such, it represents a landmark achievement and the first documented evidence that generative artificial intelligence can effectively support optimization of evidence-based pharmacotherapy in routine heart failure care.

The scientific importance of these findings is reflected by their publication in the *Journal of the American College of Cardiology* (Impact Factor 22.3), one of the world's leading cardiovascular journals. The proposed study will provide the first adequately powered evaluation of the impact of AI-supported decision-making on major clinical outcomes, including rehospitalization and mortality. Positive findings could support the integration of AI-based clinical decision support systems into routine heart failure management and contribute to the development of a new paradigm of AI-assisted cardiovascular care.

Beyond its scientific value, the project has important strategic significance. Continuation of the ASSIST-HF research program will strengthen and maintain the leading international position of the Department of Cardiology and Internal Medicine, Collegium Medicum, Nicolaus Copernicus University, in the emerging field of AI-assisted therapeutic decision-making. Given the innovative character of the project and the anticipated clinical relevance of its findings, we expect that the results of the planned main trial will be suitable for publication in an even higher-impact international medical journal. The project may therefore not only advance scientific knowledge but also further establish our research group among the global leaders shaping the future of artificial intelligence in cardiovascular medicine.

6. PLANOWANA FORMA ROZPRAWY DOKTORSKIEJ

☐ MANUSKRYPT

X CYKL PUBLIKACJI

☐ TRYB HYBRYDOWY