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The HF-POL study: The first real-life multicenter study of Polish patients with heart failure and left ventricular ejection fraction >40%. Study rationale and design

Short title: The HF-POL study rationale and design

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INTRODUCTION

According to the new classification of heart failure (HF) presented in the 2021 guidelines of the European Society of Cardiology (ESC), HF with left ventricular ejection fraction (LVEF) higher than 40% covers 3 distinct phenotypes: HF with mildly reduced LVEF (41%–49%), HF with preserved LVEF (>50%), and HF with improved LVEF [1].

Data from the National Health Fund revealed that in 2018 there were more than 1.2 million patients with HF in Poland, about half of which had LVEF >40% [2]. Considering the statistics and the increasing healthcare costs, HF constitutes a significant clinical and economic burden in Poland. Hospitalizations are the key cost category in the HF setting. Despite advances in HF diagnosis and treatment, the rates of costly and at least partially preventable hospitalizations remain high in

Poland. According to the 2019 report of the Organization for Economic Co-operation and Development (OECD), Poland has the highest HF-related hospitalization rates in 2018 among OECD members, and these rates are more than twice as high as the OECD average [3]. Moreover, in 2018, the number of HF-related deaths accounted for 9.8% of all deaths in Poland, and for the first time, the rates for mortality were higher than those for morbidity [2].

In Poland, HF is the most common direct cause of death. Numerous international studies showed that HF with LVEF >40% is associated with a serious prognosis [4–6]. In contrast to HF with reduced LVEF, treatment aimed at improving prognosis in patients with LVEF >40% has a lower class of recommendation (up to IIa), based largely on weaker evidence and/or expert opinions — in 2021 ESC (class IIb) and in 2022 ACC/ACC/HFSA (class IIa) guidelines [1, 7, 8]. However, the results of the recently published trials (EMPEROR-Preserved and DELIVER) change the horizon for this HF population [9, 10].

The population of Polish patients with HF and LVEF >40% has not been well described so far. This is partly due to limitations in the International Classification of Disease coding, which does not reflect the classification of HF based on LVEF values. This is an important barrier to determining the actual percentage of HF patients with LVEF >40% in Poland. We still need reliable data on HF. Therefore, to assess this population in Poland, the Heart Failure Association of the Polish Cardiac Society designed a multicenter observational study as part of the society's Scientific Platform initiative. The aim of the study is to collect data on Polish patients with HF and LVEF >40% and to provide a better understanding of medical practice, based on observational data, including diagnosis, treatment, and prognosis over 1-year follow-up. The study will be a valuable source of clinical practice data and will provide useful information that will guide decisions and policies to improve the management and prognosis of patients with HF as well as prevent hospitalizations in Poland.

METHODS

The Heart Failure Poland (HF-POL) study is a multicenter observational study including patients with HF and LVEF >40%, conducted by the Heart Failure Association of Polish Cardiac Society in cooperation with the Committee for Clinical Initiatives of the Executive Board as part of the Scientific Platform initiative. The leading center of the study is the Military Medical Academy Memorial Teaching Hospital of the Medical University of Lodz, Poland, Primary Investigator,

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Patients have been recruited at each participating center since the center's activation on the eCRF.biz platform (a clinical data management system, https://rejestr.gbbsoft.pl/hf-pol). All consecutive patients meeting the inclusion criteria and not meeting the exclusion criteria are being enrolled. Patients are diagnosed and treated according to the current clinical practice guidelines and the standard of care at participating centers. Indications for diagnostic procedures and therapeutic interventions are assessed by the physicians at participating centers.

A phone interview with the patient or his or her family is scheduled at 1 year after enrollment to the study and the following data will be collected: general medical condition, HF-related or all-cause hospitalization, and death.

The study was approved by the Bioethics Committee at Medical University of Lodz (No. RNN/240/21/KE; October 21, 2021). The study execution is regulated by the Rules and Regulations of the Scientific Platform of Polish Cardiac Society and an agreement between Polish Cardiac Society, the participating centers, and the Primary Investigator, with attachments.

The study population includes patients with HF and LVEF >40%. In total a minimum of 1,000 patients from 14 Polish centers (Supplementary material, *Table S1*) will be enrolled. The study will include consecutive patients with the ICD codes 150 (150, I50.1, I50.9) and J81, who fulfill the following inclusion criteria: have recognized HF with documented LVEF >40% and are either treated for HF on ambulatory basis or hospitalized for HF (HF exacerbation or HF de novo) with the administration of intravenous therapy (diuretics and/or catecholamines). HF should be recognized according to 2021 ESC guidelines [1]. The study allows recruitment based on results documented in medical records, especially for outpatients with history of HF. However, not all patients had their results documented within 12 months prior to screening. In the case of HF de novo, the known from 2021 ESC guidelines criteria for this diagnosis should be applied as symptoms and/or signs, LVEF >40% and for HFpEF objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of left ventricle diastolic dysfunction/raised left ventricle filling pressure, including raised natriuretic peptides [1]. The exclusion criteria are age <18 years and dyspnea due to causes other than HF. The flowchart presents the study design (Figure 1).

Because of the coronavirus disease 2019 (COVID-19) pandemic, patients have been recruited retrospectively over the period of 3 months before the activation of the center on the eCRF.biz platform and prospectively over 4 months. The total duration of recruitment will be 7 months. The study was started in January 2022.

Statistical analysis

Normally distributed continuous variables were reported as mean (SD) values. Not normally distributed continuous variables and ordinal variables were presented as median values and interquartile ranges (IQR). Categorical data were reported as the number and percentage of patients. The statistics were calculated with STATISTICA 13 software (TIBCO Software, Palo Alto, CA, US).

PRELIMINARY RESULTS AND DISCUSSION

Until May 26, 2022, a total of 790 patients have been recruited to the study (mean age, 72.9 [11.2] years; range 31–106 years; 51% male). More than half of patients have ischemic etiology of HF (57%). The following cardiovascular risk factors and comorbidities were reported: hypertension (87%), diabetes (73%), hyperlipidemia (67%), atrial fibrillation (58%), chronic obstructive pulmonary disease (12%), and cancer (11%). COVID-19 was reported in 18% of the studied population.

In most patients, a history of hospitalization in the previous 12 months was reported (80%), while 53% of patients were enrolled to the study during HF hospitalization. Most patients were in New York Heart Association functional class II and III (332 and 311 patients, respectively). The mean blood pressure was reported at 132/77 (19.85/12.56) mmHg; body mass index, 29.6 (6.2) kg/m^2; LVEF of 52.7 (7.5) %, median N-terminal pro-B-type natriuretic peptide level of 1,177 (430-12,798) pg/ml; estimated glomerular filtration rate, 62 (24.79) ml/min/1.73 m^2; and six-minute walk distance, 287.5 (105-310) m. At baseline 72% of the studied patients were on ACEi/ARB, 67% had loop diuretics, 79% beta-blockers, 61% MRA, 71% statins, and 12% flozins.

Our preliminary results are consistent with the literature and other registries apart from the higher concentration of NTproBNP, the higher frequency of HF hospitalization subpopulation, diabetes, MRA therapy and male gender.

Limitations

The presented study has limitations typical of such projects. These are limited information on clinical characteristics, treatment and adverse events. The participating centers are selected and the majority of them represents university centers, with invloved teams of experienced cardiologists that may not reflect the clinical practice of regional and lower reference centers. For technical and budgetary reasons, the opportunities of verifying the entered data, monitoring and detailed follow-up are also restricted. On the other hand cardiovascular registries play an integral role in providing real-world data. Additional limitation is the retrospective-prospective design of the study what resulted of the pandemic time. And not all outpatients had their laboratory and echocardiographic results what also resulted of pandemic.

SUMMARY

The HF-POL study is the first real-life national multicenter observational study including patients with HF and LVEF >40%, conducted by the Heart Failure Association of Polish Cardiac Society. The population of patients with HF and LVEF >40% has been growing and constitutes an increasing health burden. Considering the statistical, economic, and epidemiological data for Poland from real life, it is necessary to identify prognostic factors that could help improve the management of these patients by reducing the risk of hospitalizations and death.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

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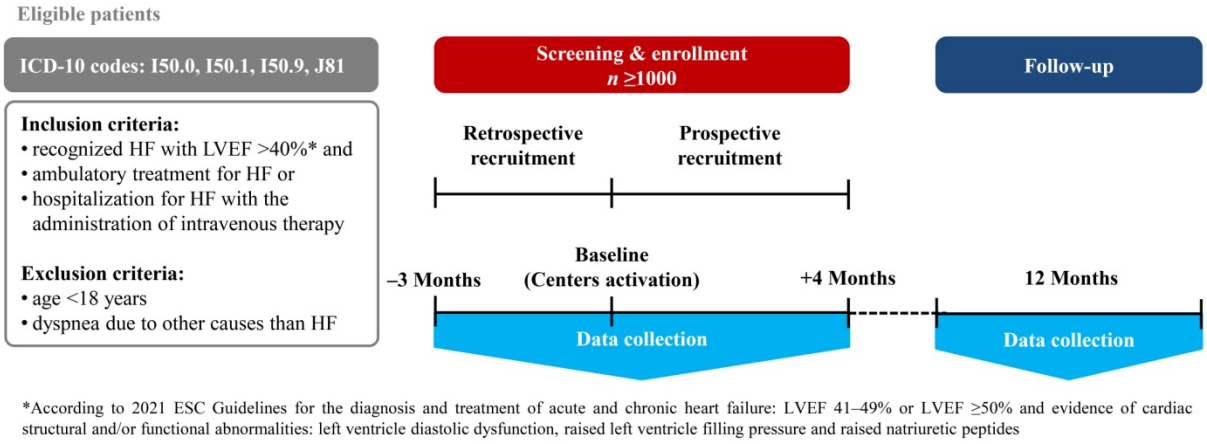

Figure 1. Study flowchart

Abbreviations: ESC, European Society of Cardiology; HF, heart failure; LVEF, left ventricle ejection fraction