Diagnosis, Clinical Course, and 1-Year Outcome in Patients Hospitalized for Heart Failure With Preserved Ejection Fraction (from the Polish Cohort of the European Society of Cardiology Heart Failure Long-Term Registry)

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Compared with heart failure (HF) with reduced ejection fraction (HF-REF), the diagnosis of HF with preserved EF (HF-PEF) is more challenging. The aim of the study was to assess the prevalence of HF-PEF among patients hospitalized for HF, to evaluate the pertinence of HF-PEF diagnosis and to compare HF-PEF and HF-REF patients with respect to outcomes. The analysis included 661 Polish patients hospitalized for HF, selected from the European Society of Cardiology (ESC)-HF Long-Term Registry. Patients with an EF of ≥50% were included in the HF-PEF group and patients with an EF of <50% - in the HF-REF group. The primary end point was all-cause death at 1 year. The secondary end point was a composite of all-cause death and rehospitalization for HF at 1 year. HF-PEF was present in 187 patients (28%). Of those 187 patients, mitral inflow pattern was echocardiographically assessed in 116 patients (62%) and classified as restrictive/pseudonormal in 37 patients (20%). Compared with HF-REF subjects, patients with HF-PEF were older, more often female, and had a higher prevalence of hypertension, atrial fibrillation and sleep apnea. Despite lower B-type natriuretic peptide concentrations and lower prevalence of moderate-to-severe mitral regurgitation in patients with HF-PEF, congestive symptoms at admission were as severe as in patients with HF-REF. There were no significant differences in in-hospital mortality between the HF groups. One-year mortality was high in both groups (17% in HF-PEF vs 21% in HF-REF, p = 0.22). There was a trend toward a lower frequency of the secondary end point in the HF-PEF group (32% vs 40%, p = 0.07). In conclusion, in clinical practice, even easily obtainable echocardiographic indexes of diastolic dysfunction are relatively rarely acquired. One-year survival rate of patients with HF-PEF is not significantly better than that of patients with HF-REF. **(Am J Cardiol 2016;118:535−542)**

The prevalence of heart failure (HF) with preserved ejection fraction (HF-PEF) has increased over the last years, with a further increase to be anticipated due to aging of the population and a growing incidence of arterial hypertension, obesity, and type 2 diabetes.[1−3] In clinical practice, adequate echocardiographic evaluation of diastolic function tends to be neglected, as it necessitates a comprehensive examination, incorporating all relevant 2-dimensional, pulsed-wave Doppler (PWD) and tissue Doppler imaging (TDI) data.[4,5] Thus, HF-PEF becomes a diagnosis by exclusion, potentially leading to HF misdiagnosis in patients in whom the actual cause of dyspnea or diminished exercise capacity fails to be identified. Another problem in HF-PEF is the choice of optimal pharmacotherapy, as - so far - no treatment has been shown to improve survival in HF-PEF.[3,6−8] The aim of the study was to estimate the prevalence of HF-PEF in patients hospitalized for HF decompensation, to validate the pertinence of HF-PEF diagnosis in these patients, and to assess their clinical profile and outcomes in comparison to patients with HF with reduced EF (HF-REF).

Methods

The European Society of Cardiology (ESC) HF Long-Term Registry is an on-going, prospective, international, observational survey, with 211 cardiology centers from 21 European countries participating.[9] The Registry includes both chronic HF patients presenting to ambulatory care clinics and patients admitted to hospital for new-onset or

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See page 541 for disclosure information.

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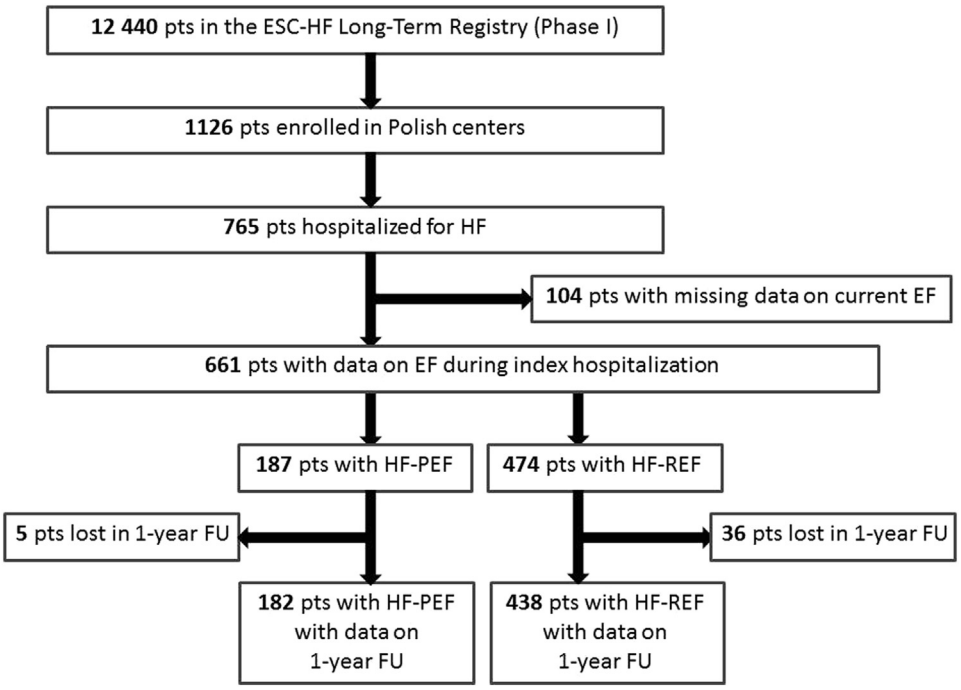

Figure 1. Flow chart of patient selection for the current analysis. FU = follow-up; pts = patients.

worsening HF. All patients with a diagnosis of HF who are aged ≥18 years are eligible for enrollment. The survey was approved by local ethical review boards according to the regulations of each participating country. A signed, informed consent was obtained from each patient after providing him/her with detailed information on the Registry.

During phase I of the Registry, lasting from May 2011 to April 2013, patients were enrolled on 1 specific day of the week for 12 consecutive months in each of the participating centers. In phase II/III of the Registry (currently on-going), patients are enrolled during 5 consecutive days per trimester. Data on clinical characteristics, diagnostic tests performed, and implemented treatment are collected in the Registry. Electronic case report forms (eCRFs) enable to describe echocardiographically evaluated left ventricular (LV) diastolic function by (1) denominating whether LV filling pattern, assessed by PWD, is restrictive/pseudonormal or not (yes vs no); (2) entering the value of the early (E) to late (A) LV filling velocity ratio (E/A ratio); and (3) entering the value of wave E deceleration time. Information on the presence of LV hypertrophy (LVH) is given dichotomically (yes vs no). It is also possible to enter left atrial (LA) dimension (measured in parasternal long-axis view) and LA volume in the Registry's eCRF. All patients are followed for 12 months.

The current analysis included Polish patients hospitalized for HF, enrolled during phase I of the Registry. To discriminate between patients with HF-PEF and patients with HF-REF, the analysis included only those patients who had an echocardiographic examination (with EF assessment) performed during index hospitalization. Patients with an EF of ≥50% were included in the HF-PEF group, and patients with an EF of <50% were included in the HF-REF group.

To verify the pertinence of HF diagnosis in patients with EF ≥50%, we assessed whether they met the echocardiographic criteria for HF-PEF according to the 2012 ESC HF guidelines, that is, the presence of LVH and/or LA enlargement (defined as LA dimension of >40 mm and/or LA volume of >34 ml/m^2) and/or LV diastolic dysfunction (defined, for the sake of the current analysis, as restrictive/pseudonormal LV filling pattern and/or as E/A ratio of ≥2).[6] We also evaluated serum concentrations of B-type natriuretic peptide (BNP) and of N-terminal pro-BNP (NT-proBNP) in these patients, and, after 2012 ESC guidelines, adopted a threshold of ≥100 pg/ml for BNP levels and of ≥300 pg/ml for NT-proBNP as justifying HF suspicion in patients hospitalized for exacerbation of symptoms suggestive of HF.[6] We applied ESC guidelines, as the Registry was conducted in the European population.

The HF-PEF and HF-REF groups were compared with regard to clinical profile, initial presentation, diagnostic tests results, clinical course and management during index hospitalization, as well as in-hospital and 1-year outcomes.

The primary end point was all-cause death at 1 year. The secondary end point was a composite of all-cause death and hospital readmission for HF worsening at 1 year. We assessed the frequency of the primary and the secondary end points in both HF groups. In addition, we sought to determine predictors of the primary and the secondary end points separately for the HF-PEF and for the HF-REF group.

All statistical analyses were conducted using the SAS software, version 9.2 (SAS Institute Inc., Cary, NC). Normally distributed continuous variables were presented as mean (±SD), whereas ordinal variables and nonnormally distributed continuous variables were presented as median (interquartile range). The HF-PEF and HF-REF groups were compared using the Fisher's exact test for categorical variables and the Mann−Whitney test for continuous and ordinal variables. Kaplan−Meier curves were plotted for the