Congestive Heart Failure in the Department of Medicine: Demographic and Clinical Characteristics

Avishay Elis MD[1,4], Ella Giladi MD[3], Ahmad Raiyan MD[1], and Alaa Atamna MD[2,4]

[1]Department of Internal Medicine C and [2]Infectious Diseases Unit, Rabin Medical Center (Beilinson Campus), Petah Tikva, Israel
[3]Department of Cardiology, Meir Medical Center, Kfar Saba, Israel
[4]Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

ABSTRACT **Background:** Congestive heart failure (CHF) with reduced ejection fraction (HFrEF) or with preserved ejection fraction (HFpEF) is a common diagnosis in patients hospitalized in the department of internal medicine. Recently, the therapeutic regimens were updated, as the sodium-glucose cotransporter-2 (SGLT2) inhibitors became an integral part of the therapeutic regimen for either HFrEF or HFpEF.

Objectives: To define the demographic and clinical characteristics of CHF patients hospitalized in the department of medicine.

Methods: We conducted a retrospective cohort study that included all patients hospitalized in the departments of medicine at the Rabin Medical Center, Israel, between 2016 and 2019. Demographic and clinical background, in-hospital procedures, discharge regimens, and outcome parameters were evaluated according to HFrEF/HFpEF.

Results: The cohort included 4458 patients. The majority (97%) presented with a preexisting diagnosis, whereas HF was an active condition in only half of them. The rates of HFrEF/HFpEF were equal. In most cases, the trigger of the exacerbation could not be determined; however, infection was the most common cause. There were basic differences in the demography, clinical aspects, and therapeutic regimens at discharge between HFrEF and HFpEF. Both conditions were associated with high in hospital mortality (8%) and re-admissions rates (30 days [20%], 90 days [35%]) without any difference between them.

Conclusions: HFrEF/HFpEF patients differed by demographics and co-morbidities. They were equally represented among patients admitted to medical wards and had similar prognosis. For both diagnoses, hospitalization should be considered for updating therapeutic regimens, especially with SGLT2 inhibitors.

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KEY WORDS: congestive heart failure (CHF), heart failure with preserved ejection fraction (HFpEF), heart failure with reduced ejection fraction (HFrEF), sodium-glucose cotransporter-2 (SGLT2) inhibitors

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Congestive heart failure (CHF) is a pathophysiological state in which an abnormality in cardiac function and structure results in the failure of the heart to pump blood under normal cardiac pressures at a rate that meets the requirements of metabolizing tissues. It is divided into HF with reduced ejection fraction (HFrEF), defined as ≤ 40%, and with preserved ejection fraction (HFpEF), defined as left ventricular ejection fraction (LVEF) ≥ 50%. Patients with a LVEF between 41% and 49% have mildly reduced LV systolic function (HFmrEF). Both HF phenotypes are accompanied by substantial morbidity and mortality risks as well as impaired quality of life and functional capacity [1,2].

CHF is one of the most prevalent diagnoses among patients hospitalized in the department of medicine. It may be acute or a non-active co-morbidity, it could be the first presentation or an already preexisting diagnosis. Hospitalization, although a short episode in a patient's life, might have a major impact by treating the acute illness, but also by updating the therapeutic regimens of chronic illnesses, including for CHF.

Recently, guidelines for the treatment of heart failure, mainly HFrEF, were updated, as the sodium-glucose cotransporter-2 (SGLT2) inhibitors became part of the therapeutic regimens for CHF, first for HFrEF and later for HFpEF, with significant impact on cardiovascular outcomes (CVO) [3-7].

The aim of the study was to define the demographic and clinical characteristics of CHF patients hospitalized in the department of medicine.

PATIENTS AND METHODS

A retrospective cohort study was conducted, which included all patients hospitalized in the departments of medicine at both campuses of the Rabin Medical Center between 2016 and 2019.

The inclusion criteria included computerized data diagnosis of CHF, either acute or chronic, as well as main or background diagnoses. Patients with missing data were excluded from the cohort. Only the first admission during these years was included.

The following parameters were extracted from the electronic medical records and were evaluated: demographic parameters (age, sex), body mass index (BMI), co-morbidities (ischemic

heart disease [IHD], cerebrovascular disease, atrial fibrillation, diabetes mellitus [DM], hypertension, hyperlipidemia, chronic kidney disease, chronic obstructive lung disease, hyperthyroidism, active malignancy [solid/hematologic]), smoking status, CHF parameters (new onset/preexisting, active condition, HFrEF/HFpEF), triggers for CHF exacerbation (extracted from the electronic records by searching key wards at the free texts, only for patients with active CHF, infection, myocardial ischemia, tachyarrhythmia, valvular disease, anemia), laboratory results during hospitalization (mean hemoglobin, leucocytes, platelets, creatinine, troponin, and proBNP levels), mechanical ventilation, intravenous inotropes, intravenous diuretics, cardiac isotope scan, coronary angiography, revascularization procedures (CABG/PCI), valve replacement procedures, pacemaker insertion, therapeutic regimens at discharge (beta-blocker, vasodilation [ACE inhibitors, angiotensin II receptor blockers, hydralazine], diuretics [frusemide, aldospirone], nitrates, calcium channel blockers, digoxin, aspirin, SGLT2 inhibitors), length of hospitalization, in hospital mortality, and 30- and 90-day re-admissions at Rabin Medical Center only. Emergency department visits were not included.

The diagnosis of the HF subtypes was based on echocardiography conducted during hospitalization or the most recent one. HFrEF was defined as LVEF ≤ 40% and HFpEF as LVEF ≥ 50%. Patients with LVEF between 41% and 49% were defined as HFmrEF and were considered as part of the HFrEF group.

The parameters were evaluated for the entire cohort and according to the diagnosis of HFrEF/HFpEF.

The study was approved by the Rabin Medical Center internal review board.

STATISTICAL ANALYSIS

Statistical analyses were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC, USA). Continuous data was expressed as mean ± standard deviation or as median and interquartile range (25–75 percentile) as appropriate and was compared using *t*-test. Chi-square test was used for comparing dichotomous variables.

RESULTS

During the study period, 2016–2019, 43,222 patients were admitted at least once to the internal medicine wards of Rabin Medical Center; 4458 (10.3%) had a diagnosis of CHF and represented the study cohort.

The median age of the entire cohort was 77 years, slightly more males (54%) were included. Only 143 (3%) were hospitalized with a new onset of HF. In half of the patients, HF was an active condition. The rates of CHF subtypes were equal between: HFpEF (48%) and HFrEF (41%). The main co-morbidities were hypertension (62%), DM (40%), atrial fibrillation (31%), and IHD (29%). The trigger for the acute exacerbation could not be determined in most of the patients (62%), while infection was the main contributor in 20%. The overall median length of hospitalization was 4 days (range 2–7 days). The in-hospital mortality was 8% with high re-admission rates (20% in 1 month and 35% in 3 months).

The demographic and clinical characteristics, the in-hospital and discharge management regimens, as well as the outcomes measures of the subjects according to the type of HF (HFrEF/HFpEF) are provided in Table 1. The HFpEF patients were older (81 vs. 77 years, $P < 0.0001$). Most were females and more obese (BMI 28.3 vs. 26.6 kg/m^2, $P < 0.0001$).

There were differences in the baseline co-morbidities between the HF types. Higher rates of DM and IHD were found among the HFrEF patients, whereas higher rates of hypertension and atrial fibrillation were found among the HFpEF patients. There were no clinically significant differences concerning clinical presentation (only 3% had new onset HF), CHF triggers, or laboratory results, except higher proBNP levels among HFrEF (8357 vs. 3307 pg/ml, $P < 0.0001$).

During hospitalization, more HFrEF patients underwent coronary angiography and revascularization procedures, while similar rates of intravenous diuretics or inotropes treatments were noted.

The medications at discharge were according to the HF types and co-morbidities. Among the HFrEF, higher rates of beta blockers, vasodilators (ACE inhibitors, hydralazine, and nitrates), and digoxin were found, while calcium channel blockers were more frequently used among the HFpEF. Treatment with diuretics was equal between the HF types, aldospirone was more common among the HFrEF patients. Angiotensin receptor/neprilysin inhibitor (ARNI) was not prescribed at all and only a few patients (1.7/0.65%) were treated with SGLT2 inhibitors.

There were no differences in the outcomes, although the length of hospitalization tended to be somewhat longer for the HFpEF patients (4 vs. 3 days).

DISCUSSION

Our study results provide important insights concerning CHF in patients hospitalized at the department internal of medicine. First, CHF is very common among these patients (10%), and in the majority (97%) it is a preexisting diagnosis, while in only half it was an active problem during the hospitalization. Second, the rates of HFrEF and HFpEF are equal. Third, in most of the cases, the trigger of the exacerbation could not be determined, while infection is the most common etiology. Last, although there are basic differences in the demography, clinical aspects, and therapeutic regimens at discharge between HFrEF and HFpEF, both are associated with unfavorable prognosis, either high in hospital mortality (8%) or high rate of short- and long-term re-admissions (30 days [20%], 90 days [35%]), without any difference between them.

Table 1. Demographics and clinical characteristics of hospitalized patients with HFrEF and HFpEF

Parameters	HFrEF (n=1839)	HFpEF (n=2140)	*P*-value
Age (years), median (IQR)	77 (67–84)	81 (72–87)	< 0.0001
Male sex, n (%)	1273 (69%)	879 (41%)	< 0.0001
BMI (kg/m^2), mean (IQR)	26.6 (23.3–30.2)	28.3 (24.7–33)	< 0.0001
Co-morbidities			
Hypertension, n (%)	1107 (60%)	1417 (66%)	< 0.001
Diabetes mellitus, n (%)	795 (43%)	813 (38%)	< 0.001
Ischemic heart disease, n (%)	702 (38%)	483 (23%)	< 0.001
Atrial fibrillation, n (%)	494 (27%)	782 (37%)	< 0.001
Chronic kidney disease, n (%)	276 (15%)	283 (13%)	NS
Cerebrovascular accident, n (%)	213 (12%)	237 (11%)	NS
Chronic obstructive pulmonary disease, n (%)	159 (9%)	232 (11%)	NS
Active smoking, n (%)	171 (9%)	123 (6%)	< 0.001
Hyperlipidemia, n (%)	104 (6%)	110 (5%)	NS
New onset CHF, n (%)	56 (3%)	66 (3%)	NS
Hyperthyroidism, n (%)	13 (0.7%)	26 (1.2%)	NS
Clinical presentation			
Active problem, n (%)	767 (42%)	950 (44%)	NS
Pre-existing CHF, n (%)	1783 (97%)	2074 (97%)	NS
CHF triggers (active problem)			
Not mentioned, n (%)	483 (63%)	570 (60%)	< 0.001
Infection, n (%)	138 (18%)	190 (20%)	< 0.001
Myocardial Ischemia, n (%)	46 (6%)	29 (3%)	< 0.001
Tachyarrhythmia, n (%)	47 (6%)	67 (7%)	NS
Anemia, n (%)	38 (5%)	56 (6%)	NS
Valvular disease, n (%)	15 (2%)	38 (4%)	< 0.001
Laboratory results			
Hemoglobin (g/dl) mean (IQR)	11.6 (10.2–13.1)	11.5 (10.1–12.9)	0.04
Leucocytes (× 10^3/mm^3), mean (IQR)	8.4 (6.5–11.1)	8.59 (6.57–11.36)	NS
Platelets (× 10^3/mm^3), mean (IQR)	210 (165–272)	216 (164–279)	NS
Creatinine (mg/dl) mean (IQR)	1.39 (1.01–2.05)	1.22 (0.91–1.73)	< 0.0001
Troponin (ng/ml), mean (IQR)	56 (32–125)	43 (27–78)	< 0.0001
proBNP (pg/ml), mean (IQR)	8357 (3129–21,915)	3307 (1457–7726)	< 0.0001
Interventions during hospitalization			
Mechanical ventilation	94 (5%)	107 (5%)	NS
Intravenous furosemide during hospitalization, n (%)	797 (43%)	950 (44%)	NS
Intravenous inotropes during hospitalization, n (%)	54 (3%)	54 (2.5%)	NS
Cardiac isotope scan, n (%)	137 (7%)	95 (4%)	NS
Cardiac catheterization, n (%)	133 (7%)	90 (4%)	< 0.001
Revascularization, n (%)	64 (3.5%)	35 (1.6%)	< 0.001
Pacemaker, n (%)	13 (0.7%)	34 (1.6%)	NS
Valve procedures, n (%)	17 (0.9%)	27 (1.3%)	NS
Medications at discharge			
Aspirin, n (%)	1400 (76%)	1498 (70%)	< 0.001
Furosemide, n (%)	1391 (76%)	1613 (75%)	NS
Beta-blocker, n (%)	1268 (69%)	1409 (66%)	NS
ACE Inh, n (%)	659 (36%)	543 (25%)	< 0.001
Aldospirone, n (%)	496 (27%)	479 (22%)	0.002
Nitrates, n (%)	405 (22%)	238 (11%)	< 0.001
CCB, n (%)	356 (19%)	649 (30%)	< 0.001
ARB, n (%)	202 (11%)	222 (10%)	NS

Parameters	HFrEF (n=1839)	HFpEF (n=2140)	*P*-value
Digoxin, n (%)	136 (7%)	68 (3%)	< 0.001
Hydralazine, n (%)	88 (5%)	55 (0.2%)	< 0.001
SGLT2 Inh, n (%)	31 (1.7%)	14 (0.65%)	0.002
Outcomes			
Length of hospital stay, days, median (IQR)	3 (2–7)	4 (2–7)	NS
In-hospital mortality	129 (7%)	174 (8%)	NS
Re-admission within 1 month	361 (20%)	426 (20%)	NS
Re-admission within 3 months	642 (35%)	768 (36%)	NS

ACE Inh = angiotensin-converting-enzyme inhibitors, ARBs = angiotensin II receptor blockers, BMI = body mass index, CCB = calcium channel blocker, CHF = congestive heart failure, HFpEF = heart failure with preserved ejection fraction, HFrEF = heart failure with reduced ejection fraction, IQR = interquartile range, NS = not significant, SGLT2 Inh = sodium-glucose cotransporter 2 inhibitors

Retrospective analyses from randomized controlled trials of both HFrEF and HFpEF that have included patients with ejection fractions in the 40–50% range have shown that these patients benefit from similar therapies to those with LVEF ≤ 40%. For methodological reasons, this group was regarded as HFrEF in our study.

We provided data on the demographic and clinical differences between HFrEF and HFpEF patients. Individuals with HFpEF tend to be older, female, have a history of hypertension, and concomitant atrial fibrillation. Male sex, left ventricular hypertrophy, bundle branch block, previous myocardial infarction, and smoking are more strongly associated with HFrEF [8-10]. Our findings, like those of others, revealed equal rates of HFrEF and HFpEF [11,12], while it was suggested that 30–75% of the CHF population have HFpEF [13].

Serum creatinine, troponin, and proBNP levels were higher among the HFrEF patients, reflecting the ischemic and under perfusion nature of HFrEF. It is also reflected by the fact that more patients underwent revascularization procedures. Nevertheless, the acute treatment modalities (intravenous loop diuretics or inotropes and mechanical ventilation) did not differ.

The natural history of CHF carries frequent re-admissions. They are characterized by a series of decompensations, after which the patient's prior baseline can no longer be achieved and requires more intense care [14]. Our data revealed 30- and 90-day re-admission rates of 20% and 35%, respectively, without any difference between HFrEF or HFpEF. Consistent with previous reports, we noted a 25% re-admission rate within 30 days and almost 50% within 6 months [15-17], and a 1-year hospitalization rate of 31.9% [18]. The fact that the complicated prognosis of HFrEF/ HFpEF is challenging highlights the need to treat both and the importance of revising the therapeutic regimens to include all modalities concerning CVO [3].

The pharmacologic management differs between HFrEF and HFpEF. Modulation of the renin-angiotensin-aldosterone and sympathetic nervous system with ACE inhibitors or ARNI, beta blockers, and mineralocorticoid receptor antagonists (MRA) have been shown to improve survival, reduce the risk of CHF hospitalizations, and reduce symptoms in patients with HFrEF [3]. Beta blockers were given to only 76% of our patents, half were given ACE inhibitors or ARBs, and only one-third were treated by MRA. ARNI was not prescribed at all.

Recently, the SGLT2 inhibitors have been shown to lower the risk of worsening heart failure or death from cardiovascular causes (dapagliflozin) and to reduce the risk and total number of inpatient and outpatient worsening heart failure events with benefits seen early after initiation of treatment (empagliflozin), regardless of the presence or absence of diabetes [4,5]. These agents were part of the guidelines in 2021 that were approved for treating HFrEF [3]. As our study included patient who were hospitalized between 2016 and 2019, the use of these agents is expected to increase with further discussions about the timing for prescribing as well as contraindications and unfavorable factors for use such as severely reduced renal function, type 1 DM, and history of ketoacidosis.

To date, no treatment has been shown to convincingly reduce mortality and morbidity in patients with HFpEF. Treatment was aimed at alleviating symptoms of congestion with diuretics and to treat underlying risk factors and co-morbidities. In accordance, most of our patients (75%) were treated by diuretics and beta blockers (70%). One-third were given calcium channel blockers. In 2021–2022, the SGLT2 inhibitors, empagliflozin and dapagliflozin, were shown to reduce the combined risk of cardiovascular death or hospitalization for heart failure in patients with HFpEF, regardless of the presence or absence of diabetes [6,7]. Their use is expected to increase after implementation of the guidelines.

Although only half of our patients experienced decompensated heart failure during hospitalization, we believe that admission to a medical ward is an opportunity to attend to all medical aspects, whether active and non-active, as well as to re-evaluate the therapeutic regimens and to adopt current guideline [3].

STRENGTHS AND LIMITATIONS

The strengths of the study include the various data concerning demographic, clinical, and therapeutic regimens for both HFrEF

and HFpEF patients, and the ability to use the data to further enhance treatment, as provided by the guidelines and shown in recent studies. The study limitations include its single center origin, its retrospective nature, and rates of patients who were treated with renal replacement therapy. Patients with an implantable cardioverter defibrillator or those who were diagnosed with dementia were not extracted from the electronic medical data. Furthermore, the recorded diagnoses were not validated. Nevertheless, we believe it reflects the real-world reality.

CONCLUSIONS

Although HFrEF and HFpEF patients differed by demographics and co morbidities, they were equally represented among patients admitted to medical wards, and they had similar outcomes. For both HF phenotypes, hospitalization was an opportunity for subsequent improvement of the therapeutic regimens, especially concerning the use of the SGLT2 inhibitors.

Correspondence

Dr. A. Elis
Dept. of Medicine C, Rabin Medical Center (Beilinson Campus), Petah Tikva 4941492, Israel
Phone: (972-3) 937-6301
Fax: (972-3) 937-6311
Email: avishayel@clalit.org.il

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Capsule

Immune sensing of food allergens promotes avoidance behavior

In addition to its canonical function of protection from pathogens, the immune system can also alter behavior. The scope and mechanisms of behavioral modifications by the immune system are not yet well understood. Using mouse models of food allergy, **Florsheim** and co-authors showed that allergic sensitization drives antigen-specific avoidance behavior. Allergen ingestion activates brain areas involved in the response to aversive stimuli, including the nucleus of tractus solitarius, parabrachial nucleus, and central amygdala. Allergen avoidance requires immunoglobulin E (IgE) antibodies and mast cells but precedes the development of gut allergic inflammation. The ability of allergen-specific IgE and mast cells to promote avoidance requires cysteinyl leukotrienes and growth and differentiation factor 15. A comparison of C57BL/6 and BALB/c mouse strains revealed a strong effect of the genetic background on the avoidance behavior. These findings thus point to antigen-specific behavioral modifications that probably evolved to promote niche selection to avoid unfavorable environments.

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Eitan Israeli