The Management and Outcome of Hospitalized and Ambulatory Israeli Heart Failure Patients Compared to European Heart Failure Patients: Results from the ESC Heart Failure Long-Term Registry

Avraham Shotan MD[1,6], Barak Zafrir MD[2,6], Tuvia Ben Gal MD[3,7], Alicia Vazan MD[1], Israel Gotsman MD[4] and Offer Amir MD[5,8]

[1]Heart Institute, Hillel Yaffe Medical Center, Hadera, Israel
[2]Department of Cardiology, Lin Medical Center, Haifa, Israel
[3]Heart Institute, Rabin Medical Center (Beilinson Campus), Petah Tikva, Israel
[4]Heart Institute, Hebrew University-Hadassah Medical Center, Jerusalem, Israel
[5]Department of Cardiology, Padeh Medical Center, Poriya, Tiberias
[6]Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel
[7]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[8]Faculty of Medicine in the Galilee, Bar Ilan University, Safed, Israel

ABSTRACT:
Background: The treatment of patients hospitalized with heart failure (HHF) and ambulatory chronic heart failure (CHF) differs in various countries.
Objectives: To evaluate the management and outcomes of patients with HFF and CHF in Israel compared to those in other European countries who were included in the ESC-HF Long-Term Registry.
Methods: From May 2011 to April 2013, heart failure patients – 467 Israelis and 11,973 from other countries – were evaluated. The Israeli patients comprised 178 with HHF and 289 with CHF. One year outcomes, including all-cause and cardiovascular mortality as well as HHF, were evaluated.
Results: The HHF Israeli patients were older than their CHF Israeli counterparts, had more co-morbidities, included more women, and were treated less frequently with medications suggested by European guidelines. The Israeli HHF patients had similar all-cause 1 year mortality rates compared to HHF patients from other participating countries, but their cardiovascular (CV) mortality was lower, while a significantly higher rate of all-cause and HHF was noted. The Israeli CHF patients were older, suffered from more co-morbidities and had prior cardio-electronic implantable devices. In addition, they had higher mortality rates, especially non-CV, and were more frequently hospitalized, compared to CHF patients from other countries.
Conclusions: The Israeli patients with heart failure differed in their baseline characteristics and the therapeutic approach. Despite high usage of treatments recommended by official guidelines, especially among CHF patients, mortality, particularly in HHF patients, remained high.

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KEY WORDS: heart failure (HF), angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, mortality, rehospitalization

The therapeutic approach to heart failure in various countries for patients hospitalized with heart failure (HHF) as well as for ambulatory patients with chronic heart failure (CHF) may differ [1]. A national survey of patients hospitalized with heart failure in Israel was first conducted in 2003 [2]. Although a relatively high usage of therapies based on guidelines was noted, long-term mortality was high [2]. During the past decade, despite improved medical care and advanced medical technology, long-term outcome of HHF remained poor while survival of patients with chronic heart failure gradually improved [3,4].

A previous European Society of Cardiology (ESC) HF survey reported the rate of guideline-recommended, evidence-based treatments [5]. The rate of use of beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), and aldosterone antagonists may be feasible. However, the number of patients who were given the recommended doses is still unsatisfactory. In addition, the rate of implantation of cardioverter defibrillators (ICDs) or cardiac resynchronization devices (CRTs), such as pacemakers (CRTP) or defibrillators (CRTD), is low [6]. The EUROMED Registry showed that the implantation rates of ICDs and CRTs increased significantly from 2004 to 2008, but under-utilization still existed, with major differences across countries [7].

The aims of our current study were to compare the outcome in the Israeli patients included in the ESC HF Long-Term Registry to that in registry patients from other participating countries, and to evaluate the differences in implementation of the recent guidelines regarding pharmacological and non-pharmacological treatments.

PATIENTS AND METHODS

The ESC-HF Long-Term Registry is a prospective, multicenter, observational study of patients presenting to 211 cardiology centers in 21 European and Mediterranean countries, which are members of the ESC [8]. The national cardiology societies of each country agreed to participate in the program and were asked to select hospitals with different levels of complexity from which patients would be recruited. The aim was to involve a broad spectrum of cardiology units and/or those treating patients with heart failure on an outpatient basis and those admitted with acute, pre-existing, or new-onset heart failure who would be representative of the situation in Europe.

Similar to guidelines in European countries, we defined chronic kidney dysfunction as serum creatinine > 1.5 mg/dl and/or estimated glomerular filtration rate (GFR) < 60 ml/min, hepatic dysfunction as bilirubin > 1.5 mg/dl, and/or alanine aminotransferase (ALT), aspartate aminotransferase (AST) at least 3 times above upper normal limit, and/or alkaline phosphatase > 150 U/L, valvular disease as at least moderate regurgitation, or stenosis.

The Israeli centers that initially participated in the survey were the Hillel Yaffe Medical Center in Hadera and the Carmel Medical Center in Haifa. The two centers include a majority of HHF and CHF patients. Although only two Israeli centers were included, all consecutive patients at these centers were considered representative of the Israeli HF patient population.

To facilitate consecutive enrollment, patients were registered on a one day per week basis for 12 consecutive months at each participating facility. The EUR Observational Research Programme (EORP) department at the European Heart House coordinates the project, provides support to the committees and participating centers, controls the methodological concepts of the survey, collects the data input from each center in a database at European Heart House, and performs the statistical analysis.

PATIENT POPULATION

All outpatients with heart failure seen at the clinics, as well as those admitted for acute, pre-existing or new-onset heart failure, were included during the enrollment period. Therefore, during the course of the screening day, the following patients were entered in the survey:

- Outpatients with chronic heart failure diagnosed according to the clinical judgment of the responsible cardiologist at the participating centers

- Patients admitted to the hospital for acute heart failure for whom intravenous (IV) therapy (inotropes, vasodilators, or diuretics) was needed

There were no specific exclusion criteria, with the exception that all patients be over 18 years of age. The survey was approved by each local institutional review board according to the rules of each participating country. No data were collected before a signed informed consent was obtained.

STATISTICAL ANALYSIS

Continuous variables are reported as median and interquartile range (IQR). Categorical variables are reported as percentages and compared using the chi-square test. Continuous variables were compared by the t-test or the Mann-Whitney U-test. For 1 year outcomes χ^2 or the Fisher's exact test were used.

For qualitative variables with more than two possibilities, the Monte Carlo estimates of the exact P values were used. One year survival rates were calculated by Kaplan-Meier curves with differences evaluated by log-rank analysis. A P value < 0.05 was considered statistically significant. All tests were two-sided. Analyses were performed with SAS system software (SAS Institute, Inc., Cary, NC, USA).

RESULTS

From May 2011 to April 2013 a total of 12,440 patients were included in the ESC-HF Long-Term Registry: 5039 (40.5%) HHF patients and 7401 (59.5%) ambulatory patients with CHF. The HHF patients were older than the CHF patients, more often female, their HF was of ischemic etiology, and they suffered more frequently from co-morbidities. They had preserved left ventricular ejection fraction (LVEF ≥ 45%) and a lower rate of implanted devices. This large ESC-HF Long-Term Registry comprised 467 Israelis and 11,973 patients from other countries.

ISRAELI HEAT FAILURE PATIENTS

The Israeli patients with HHF were older than their Israeli CHF counterparts (median age 77 years, IQR 70–85 vs. 68 years, IQR 60–78, P < 0.0001), and the majority were 70 years or older (78% vs. 46%, respectively, P < 0.0001). The HHF compared to the CHF patients in the Israeli cohort included more women (44% vs. 25%, P < 0.0001) and more patients with hypertension treatment, chronic kidney disease (CKD), prior stroke or transient ischemic attack (TIA), peripheral vascular disease, and hepatic dysfunction [Table 1]. The most common primary etiology of heart failure was ischemic heart disease, which was somewhat less frequent among the Israeli HHF patients (55.6% vs. 59.2%, P < 0.0001). Dilated cardiomyopathy as a primary etiology was also less common among the Israeli HHF patients (4.5% vs. 19.4% respectively). Of the Israeli patients, 19% presented with prior cardiac electronic implantable device (CEID) implantation: pacemaker in 9%, CRT in 6.7%, and ICD in 3.4%.

The two Israeli study groups differed in their initial symptoms, physical examination findings and laboratory results. The HHF patients had higher systolic and diastolic blood pressure, heart rate, more preserved LVEF, and lower hemoglobin than CHF patients. The HHF patients presented mostly with acute decompensated heart failure (73%), while only 17% presented with pulmonary edema.

The HHF patients were treated less frequently with guidelines-recommended medications [ACE-I/ARBs, beta-blockers, mineralocorticoid antagonists (MRA), digoxin], and more with calcium-channel blockers, compared to the outpatients with CHF, reflecting the lower rates in HHF patients with reduced ejection fraction. The HHF patients had higher rates of treatment with beta-blockers (74% vs. 58%) and diuretics (92% vs. 75%) than the previous cohort of hospitalized HFSIS 2003 patients at discharge. Treatment rates with MRA (21% vs. 20%) and ACE-I/ARBs (65% vs. 68%) were similar.

ISRAELI vs. HHF PATIENTS OF OTHER COUNTRIES

When comparing the Israeli HHF patients (n=178) with those from other countries participating in the ESC-HF registry (n=4861), we noted substantial differences. In the Israeli study, HHF patients were older (77 vs. 71 years, $P < 0.0001$), more were ≥ 70 years old (78% vs. 52%, $P < 0.0001$), more were females (44% vs. 37%, $P < 0.05$), there were more co-morbidities such as diabetes (56% vs. 38%, $P < 0.001$) and CKD (64% vs. 25%, $P < 0.0001$), and more patients were treated for hypertension (92% vs. 63%, $P < 0.0001$) and prior stroke or TIA (23% vs. 13%, $P < 0.0001$) [Table 2]. The primary etiology was more frequently ischemic heart disease and less commonly dilated cardiomyopathy, valvular heart disease or hypertensive heart disease. The Israeli patients had higher systolic blood pressure, body mass index (BMI), median LVEF (45% vs. 38%, $P < 0.0001$), including higher rate of preserved LVEF (45% vs. 32% $P < 0.001$), and more frequent anemia. They presented to the hospital more frequently with acute decompensated heart failure and pulmonary edema but not with cardiogenic shock compared to the HHF patients from other countries. The Israeli HHF patients had more CEIDs implanted prior to the index hospitalization, including more pacemakers and CRTDs, but fewer CRTPs and ICDs. They were treated acutely with more IV diuretics, but substantially less often with IV nitrates and positive inotrops. At discharge they were treated more with ACE-I/ARB and diuretics, but less with MRAs and digitalis.

ISRAELI vs. CHF PATIENTS IN OTHER COUNTRIES

There were significant differences between the Israeli CHF patients (n=289) and those from other countries participating in the ESC-Long Term Registry (n=7112) [Table 2]. The Israeli CHF outpatients were older, were diagnosed more often with diabetes (52% vs. 31%, $P < 0.0001$), were treated for CKD (46% vs. 17%, $P < 0.0001$) and hypertension, but less frequently for

Table 1. Heart failure long-term analyses for Israel: baseline characteristics

	HHF (n=178)	CHF (n=289)	P value
Demographics			
Age, median (IQR)	77.0 (70.0–85.0)	68.0 (60.0–78.0)	‹ 0.0001
Age ≥ 70 years	139/178 (78.1%)	132/289 (45.7%)	‹ 0.0001
Female	79/178 (44.4%)	72/289 (24.9%)	‹ 0.0001
BMI (kg/m²), median (IQR)	28.7 (25.6–31.9)	28.4 (25.3–32.5)	0.9359
BMI ≥ 30 kg/m²	72/178 (40.4%)	115/289 (39.8%)	0.8881
Smokers (current/former)	96/178 (53.9%)	145/289 (50.2%)	0.4298
Initial symptoms and evaluation			
NYHA classIII/IV	125/178 (70.2%)	136/289 (47.1%)	‹ 0.0001
SBP (mmHg), median (IQR)	139.0 (121.0–160.0)	124.0 (111.0–136.0)	‹ 0.0001
HR (bpm) median (IQR)	82.5 (72.0–97.0)	71.0 (64.0–80.0)	‹ 0.0001
EF (%) median (IQR)	45.0 (30.0–60.0)	30.0 (25.0–44.0)	‹ 0.0001
EF › 45%	71/157 (45.2%)	56/288 (19.4%)	‹ 0.0001
Atrial fibrillation	86/178 (48.3%)	119/289 (41.2%)	0.1311
Hemoglobin (g/dl) median (IQR)	11.8 (10.4–12.8)	12.7 (11.5–13.9)	‹ 0.0001
Hemoglobin ≤ 12 g/dl	95/178 (53.4%)	104/285 (36.5%)	0.0004
Medical history			
Prior HF without previous hospitalization	105/178 (59.0%)	195/289 (67.5%)	0.0632
MI/Angina	107/178 (60.1%)	175/289 (60.6%)	0.9246
Diabetes	99/178 (55.6%)	150/289 (51.9%)	0.4345
Hypertension treatment	163/178 (91.6%)	206/289 (71.3%)	‹ 0.0001
Chronic kidney dysfunction	114/178 (64.0%)	134/289 (46.4%)	0.0002
COPD	41/178 (23.0%)	23/289 (8.0%)	‹ 0.0001
Prior stroke/TIA	41/178 (23.0%)	32/289 (11.1%)	0.0005
Peripheral vascular disease	33/178 (18.5%)	18/289 (6.2%)	‹ 0.0001
Hepatic dysfunction	26/178 (14.6%)	17/289 (5.9%)	0.0015
Primary etiology			
Ischemic heart disease	99/178 (55.6%)	171/289 (59.2%)	‹ 0.0001
Dilated cardiomyopathy	8/178 (4.5%)	56/289 (19.4%)	
Valve disease	17/178 (9.6%)	15/289 (5.2%)	
Hypertension	6/178 (3.4%)	4/289 (1.4%)	
Other	48/178 (27.0%)	43/289 (14.9%)	
Medications			
ACE-I/ARBs	116/178 (65.2%)	248/289 (85.8%)	‹ 0.0001
Beta-blockers	132/178 (74.2%)	271/289 (93.8%)	‹ 0.0001
MRAs	37/178 (20.8%)	124/289 (42.9%)	‹ 0.0001
Diuretics	163/178 (91.6%)	277/289 (95.8%)	‹ 0.0001
Statins	120/178 (67.4%)	238/289 (82.4%)	0.0002
Antiplatelets	125/178 (70.2%)	213/289 (73.7%)	0.4143
Nitrates	43/178 (24.2%)	61/289 (21.1%)	0.4417
CCBs	162/178 (34.8%)	66/289 (22.8%)	0.0048

ACE-I = angiotensin-converting enzyme inhibitor, ARB= angiotensin receptor blocker, BMI = body mass index, bpm = beats per minute, CCB = calcium-channel blocker, CHF = chronic heart failure, COPD = chronic obstructive pulmonary disease, EF = ejection fraction, HR = heart rate, HHF = hospitalized heart failure, IQR = interquartile range, MI = myocardial infarction, MRA = mineralocorticoid receptor antagonists, SBP = systolic blood pressure, TIA = transient ischemic attack

chronic obstructive pulmonary disease (COPD) and peripheral vascular disease (PVD). They had lower LVEF (30% vs. 35%, $P < 0.01$), more frequently ischemic heart disease etiology, and less frequently dilated cardiomyopathy. The Israeli CHF patients had more prior CEIDs implanted. They were treated more frequently with beta-blockers, diuretics, digitalis, calcium-channel blockers, antiplatelets and statins, and less often with MRAs and ivabradine.

Table 2. Comparison between Israel and other countries participating in the ESC-HF Long-Term Registry

HHF	Israel (n=178)	Other countries (n=4861)	P value
Demographics			
Age, median (IQR)	77.0 (70.0–85.0)	71.0 (61.0–79.0)	‹ 0.0001
SBP, median (IQR)	139.0 (121.0–160.0)	130.0 (110.0–150.0)	‹ 0.0001
BMI, median (IQR)	28.7 (25.6–31.9)	27.7 (25.0–31.2)	0.0321
Females	79/178 (44.4%)	1798/4861 (37.0%)	0.0451
EF (%), median (IQR)	45.0 (30.0–60.0)	38.0 (30.0–50.0)	0.0001
EF › 45%	71/157 (45.2%)	973/3023 (32.2%)	0.0007
Atrial fibrillation	86/178 (48.3%)	2133/4861 (43.9%)	0.2418
Diabetes	99/178 (55.6%)	1861/4861 (38.3%)	‹ 0.0001
Hypertension treatment	163/178 (91.6%)	3083/4854 (63.5%)	‹ 0.0001
Chronic kidney dysfunction	114/178 (64.0%)	1213/4858 (25.0%)	‹ 0.0001
Prior stroke/TIA	41/178 (23.0%)	32/289 (11.1%)	0.0005
Smokers (current/former)	96/178 (53.9%)	2471/4798 (51.5%)	0.5238
Ischemic heart disease	99/178 (55.6%)	2598/4817 (53.9%)	‹ 0.0001
Hemoglobin ≤ 12 g/dl	95/178 (53.4%)	104/285 (36.5%)	0.0004
Hospital presentation			
Pulmonary edema	30/178 (16.9%)	566/4565 (12.4%)	0.0001
Cardiogenic shock		120/4565 (2.6%)	
Decompensated HF	130/178 (73.0%)	2865/4565 (62.8%)	
Hypertensive HF	5/178 (2.8%)	238/4565 (5.2%)	
In-hospital mortality devices	9/178 (5.1%)	240/4860 (4.9%)	0.9432
PM	16/178 (9.0%)	295/4834 (6.1%)	
CRT-P		31/4834 (0.6%)	
CRT-D	12/178 (6.7%)	143/4834 (3.0%)	0.026
ICD	6/178 (3.4%)	234/4834 (4.8%)	
Acute treatment			
IV diuretics	159/178 (89.3%)	3691/4547 (81.2%)	0.0060
IV nitrates	4/178 (2.2%)	958/4540 (21.1%)	‹ 0.0001
Inotropic support	4/178 (2.2%)	579/4842 (12.0%)	‹ 0.0001

CHF	Israel (n=178)	Other countries (n=4861)	P value
Demographics dff			
Age, median (IQR)	68.0 (60.0–78.0)	66.0 (57.0–75.0)	‹ 0.0001
SBP, median (IQR)	124.0 (111.0–136.0)	120.0 (110.0–137.0)	0.1545
BMI, median (IQR)	28.4 (25.3–32.5)	27.5 (24.6–30.8)	0.0002
Females	72/289 (24.9%)	2057/7112 (28.9%)	0.1399
EF (%), median (IQR)	30.0 (25.0–44.0)	35.0 (28.0–45.0)	0.0079
EF › 45%	56/288 (19.4%)	1458/6254 (23.3%)	0.1280
Atrial fibrillation	119/289 (41.2%)	2662/7111 (37.4%)	0.1980
Diabetes	150/289 (51.9%)	2203/7112 (31.0%)	‹ 0.0001
Hypertension treatment	206/289 (71.3%)	4095/7099 (57.7%)	‹ 0.0001
Chronic kidney dysfunction	134/289 (46.4%)	1215/7110 (17.1%)	‹ 0.0001
Smokers (current/former)	145/289 (50.2%)	3737/7062 (52.9%)	0.3597
COPD	23/289 (8.0%)	1000/7100 (14.1%)	0.0031
Peripheral vascular disease	18/289 (6.2%)	855/6818 (12.5%)	0.0014
Ischemic heart disease	171/289 (59.2%)	2985/7056 (42.3%)	‹ 0.0001
Previous devices			
PM	22/289 (7.6%)	406/7092 (5.7%)	
CRT-P	6/289 (2.1%)	165/7092 (2.3%)	
CRT-D	55/289 (19.0%)	757/7092 (10.7%)	‹ 0.0001
ICD	59/289 (20.4%)	1117/7092 (15.8%)	
Medications at outpatient visit			
ACE/ARBs	248/289 (85.8%)	6347/7108 (89.3%)	0.0621
Beta-blockers	271/289 (93.8%)	6308/7109 (88.7%)	0.0074
MRAs	124/289 (42.9%)	4264/7110 (60.0%)	‹ 0.0001
Diuretics	277/289 (95.8%)	5868/7109 (82.5%)	‹ 0.0001
Digitalis	85/289 (29.4%)	1613/7108 (22.7%)	0.0078
Statins	238/289 (82.4%)	4264/7109 (60.0%)	‹ 0.0001
Antiplatelets	213/289 (73.7%)	3386/7109 (47.6%)	‹ 0.0001
Nitrates	61/289 (21.1%)	1321/6832 (19.3%)	0.4557
CCBs	66/289 (22.8%)	737/6832 (10.8%)	‹ 0.0001
Anticoagulants	121/289 (41.9%)	3012/7109 (42.4%)	0.8660
Amiodarone	44/289 (15.2%)	944/6889 (13.7%)	0.4619
Ivabradine	602/6833 (8.8%)	–	‹ 0.0001
Anticoagulants	121/289 (41.9%)	3012/7109 (42.4%)	0.8660

IQR = interquartile range, SBP = systolic blood pressure, BMI = body mass index,
EF = ejection fraction, COPD = chronic obstructive pulmonary disease, TIA = transient
ischemic attack, ACS = acute coronary syndrome, HF = heart failure, PM = pacemaker,
CRT = cardiac resynchronization therapy, D = defibrillator, ICD = implantable
cardioverter defibrillator, ACEI = angiotensin-converting enzyme inhibitor,
ARB = angiotensin receptor blocker, MRA = mineralocorticoid receptor antagonists

HHF OUTCOME

The Israeli HHF patients had the same all-cause 1 year mortality as the HHF patients from other countries (27.8% vs. 27.9%, respectively). However, cardiovascular mortality was lower among the Israeli HHF patients (30.6% vs. 52.5% of all-cause mortality, $P < 0.0001$) [Table 3]. The Israeli HHF patients had a significantly higher rate of 1 year all-cause hospitalizations (74.7% vs. 43.5%, $P < 0.001$) including HF hospitalizations (35.2% vs. 25.8%, $P = 0.0079$) than the HHF patients from other countries.

CHF OUTCOME

The Israeli CHF patients had a higher all-cause 1 year mortality than did their counterparts from other countries (15.5% vs. 8.3%, $P < 0.0001$), especially non-CV 1 year mortality (62.8% vs. 20.2% of all-cause mortality), while their CV 1 year mortality (23.3% vs. 51.8%) and unknown 1 year mortality (14.0% vs. 27.9%) were significantly lower [Table 3]. The Israeli patients with CHF were hospitalized more frequently during the 1 year of follow-up: all-cause hospitalizations (49.3% vs. 26.4%, $P < 0.0001$) and heart failure hospitalizations (21.6% vs. 11.6%, $P < 0.0001$). The combined end-point of all-cause 1 year mortality and/or HHF was therefore higher among the Israeli CHF patients (31.9% vs. 18.2%, $P < 0.0001$).

Figure 1 shows all-cause mortality and heart failure hospitalization rates during follow-up, which were significantly higher among the HHF in comparison to the CHF patients in Israel.

DISCUSSION

The current study compares the 467 Israeli patients with the 11,973 patients from other countries included in the ESC-HF Long-Term Registry. Overall, the Israeli heart failure patients were older, and more were female. The Israeli participants suffered from more co-morbidities, such as diabetes, hyperten-

sion, prior stroke/TIA and CKD. The primary etiology was more frequently ischemic heart disease. These differences may be due, at least partially, to their advanced age.

The Israeli HHF patients had higher rates of preserved LVEF and presumably diastolic heart failure. They presented more frequently with acute decompensated heart failure. The Israeli CHF patients had more systolic dysfunction with lower LVEF. There were some differences in the acute parenteral treatment of HHF, mainly more IV diuretics and fewer inotropes and nitrates. The Israeli heart failure patients, both HHF and CHF, were treated more frequently with ACE-I/ARBs and diuretics, but less often with MRAs and ivabradine. In addition, the Israeli CHF patients were treated more often with beta-blockers, antiplatelets and statins, most likely due to the higher rate of ischemic heart disease etiology, including acute coronary events and coronary interventions. The lower use of MRAs was probably due to the higher rate of CKD. Ivabradine, which was given to 9% of the CHF patients from other European countries, was not prescribed to any of the Israeli patients with heart failure, most probably due to administrative reasons and high cost. Overall, the Israeli patients with heart failure had more CEID implants.

The current ESC Long-Term HF Registry shows that despite a relatively high rate of adherence to guidelines-recommended therapies, the outcome, especially 1 year mortality, is still high. If we compare the 1 year mortality of the Israeli HHF (27.8%) to that of HFSIS (27.2%), which was conducted in 2003, nothing seems to have changed [2]. However, this is not completely true, since in the HFSIS registry heart failure stages B-D were included, while the current HHF registry included only patients with symptomatic stages C-D who are sicker and presumably have a higher mortality. Therefore, when we compare the current ESC Long-Term Heart Failure Registry [5] to the previous ESC Long-Term Heart Failure [6] registries and to the Israeli HFSIS 2003 registry [2], some improvement is evident. However, the outcome is still grave and unsatisfactory.

Non-cardiac mortality was significantly higher in the Israeli patients. This may be the result of more prevalent co-morbidities such as diabetes, hypertension, chronic kidney disease, as well as older age in the Israeli cohort.

Despite the high usage of guidelines-recommended therapies, not all the patients received the full range of treatments. We are aware that the Israeli cohort, especially the patients with CHF, were treated in two centers that specialize in heart failure and therefore do not fully reflect the management of the whole patient population in Israel. However, the patients who chose to be followed in these two centers may be a more morbid population who need closer and specialized care.
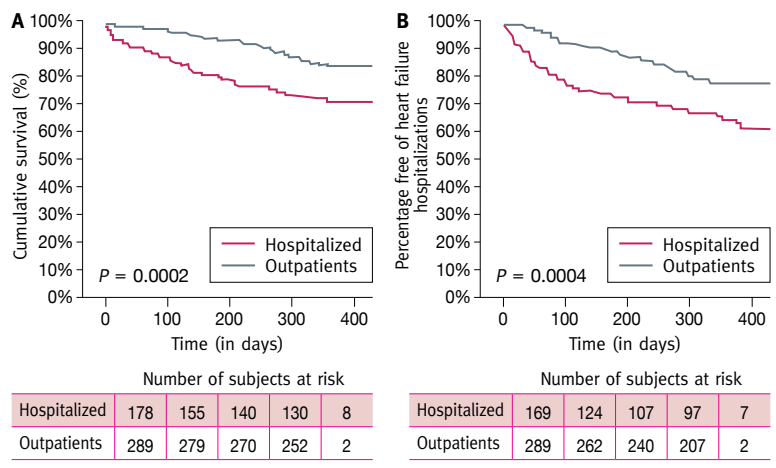
There is still a large variability in the implementation of the guidelines-recommended treatments among the European countries that participate in the ESC Long-Term HF Registry, especially CEID implantation rates and usage of other relatively expensive medications [1]. Since the publication of

Table 3. One year outcomes for Israeli patients compared to other European patients

	Total (n=12,440)	Israel (n=467)	Other countries (n=11,973)	P value
Hospitalized patients	5039	178	4861	
All-cause death	1310/4698 (27.9%)	49/176 (27.8%)	1261/4522 (27.9%)	0.9896
CV death	677/1310 (51.7%)	15/49 (30.6%)	662/1261 (52.5%)	‹ 0.0001
Non-CV death	179/1310 (13.7%)	23/49 (46.9%)	156/1261 (12.4%)	
Unknown	454/1310 (34.7%)	11/49 (22.4%)	443/1261 (35.1%)	
All-cause hospitalization	1687/3766 (44.8%)	121/162 (74.7%)	1566/3604 (43.5%)	‹ 0.0001
HHF	987/3766 (26.2%)	57/162 (35.2%)	930/3604 (25.8%)	0.0079
All-cause death and/or HFF	2019/4278 (47.2%)	88/174 (50.6%)	1931/4104 (47.1%)	0.3619
Outpatients	7401	289	7112	
All-cause death	612/7173 (8.5%)	43/286 (15.0%)	569/6887 (8.3%)	‹ 0.0001
CV death	305/612 (49.8%)	10/43 (23.3%)	295/569 (51.8%)	‹ 0.0001
Non-CV death	142/612 (23.2%)	27/43 (62.8%)	115/569 (20.2%)	
Unknown	165/612 (27.0%)	6/43 (14.0%)	159/569 (27.9%)	
All-cause hospitalization	1789/6528 (27.4%)	139/282 (49.3%)	1650/6246 (26.4%)	‹ 0.0001
HHF	783/6528 (12.0%)	61/282 (21.6%)	722/6246 (11.6%)	‹ 0.0001
All-cause death and/or HHF	1251/6673 (18.7%)	91/285 (31.9%)	1160/6388 (18.2%)	‹ 0.0001

CV = cardiovascular, HHF = hospitalized with heart failure

Figure 1. Kaplan-Meier curves for **[A]** all-cause mortality and **[B]** hospitalized with heart failure (Israel)

Number of subjects at risk					
Hospitalized	178	155	140	130	8
Outpatients	289	279	270	252	2

Number of subjects at risk					
Hospitalized	169	124	107	97	7
Outpatients	289	262	240	207	2

HF = heart failure

HFSIS 2003, there has been a substantial improvement in the treatment of patients with heart failure in Israel. New clinics specializing in the treatment of heart failure have been added to public hospitals. More important, most of the public care providers in Israel have established ambulatory centers and services to treat heart failure, including online and home monitoring. There is still room for improvement in the rates of medications prescribed at discharge of HHF

patients. However, almost half the HHF patients (similar to the previous HFSIS survey) had heart failure with preserved ejection fraction, for which no therapies have been proven to reduce mortality. We are probably on the right track, but the results of the current survey in Europe and in Israel show that we still have a long way to go.

We believe there is no simple answer that will dramatically change the situation. The therapeutic approach toward acute and chronic patients with heart failure consists of many steps. In addition to better adherence to medications, recommended dosages and dosage adjustment when clinically indicated, CEID implantation, cardiac surgery including revascularization, valve repair or replacement and assist device implantation, are all viable therapeutic possibilities for advanced heart failure. Moreover, better management of co-morbidities, like CKD, diabetes, anemia, obesity, cachexia and sleep apnea, is needed. Patients with heart failure should perform regular physical activity, return early to work and/or to leisure activities, and receive social as well as psychological support when needed. Additional novel therapies should be explored to achieve the therapeutic goals. Moreover, national and international heart failure registries, including additional Israeli centers joining the ongoing ESC Long-Term HF Registry, will allow us to better understand the gaps and unmet needs in the management of heart failure.

STUDY LIMITATIONS

This survey did not include an intervention cohort. The therapeutic approach was at the discretion of the treatment team. There were only a few participating centers from each country, and not all the European countries are part of the registry, although the majority have joined; therefore, the overall data may not fully reflect a participating country, nor the entire European HF patient population. Moreover, the two participating Israeli medical centers differ in their patient characteristics and treatment. The data analysis was centrally performed by the EUR Observational Research Program (EORP) department at European Heart House, and therefore we did not have any access to the data for additional statistical analysis. This may have limited our ability to perform subgroup analysis.

CONCLUSIONS

There has been progress in the utilization of and adherence to guidelines-recommended heart failure therapies [1,2], but the 1 year mortality and recurrent hospitalization rates are still high. A more comprehensive Israeli national approach, as well as European and international efforts, are needed to reduce the current morbidity and exceptionally high mortality among patients with heart failure.

Correspondence

Dr. O. Amir
Dept. of Cardiology, Padeh Medical Center, Tiberius, 15208 Israel
Phone: (972-4) 665-2655
Fax: (972-9) 956-0390
email: oamir@poria.health.gov.il

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