Differences in Mortality of New-Onset (De-Novo) Acute Heart Failure Versus Acute Decompensated Chronic Heart Failure

Anan Younis, MD[a],[*],[#], Wesam Mulla, MD, PhD[b],[#], Ronen Goldkorn, MD[a], Robert Klempfner, MD[a], Yael Peled, MD[a], Michael Arad, MD[a], Dov Freimark, MD[a], and Ilan Goldenberg, MD[c]

Minimal attention has been paid to understanding the implications of the chronicity of heart failure (HF) diagnosis on prognosis of hospitalized patients with acute HF (AHF). We aimed to assess the differences in outcomes between hospitalized patients with AHF that are new-onset (de-novo) AHF and acutely decompensated chronic HF (ADCHF). We analyzed data of 2,328 patients with AHF, who were enrolled in the HF survey in Israel. Patients were classified into de-novo AHF and ADCHF. A total of 721 (31%) patients were classified as de-novo AHF and 1,607 (69%) patients were classified as ADCHF. Patients with de-novo AHF were more likely to be younger, with fewer co-morbidities represented by lower Charlson index, and less likely to have past myocardial infarction as well as coronary revascularization. At 30 days mortality rates were similar in both groups (9% vs 8% in de-novo AHF and ADCHF, respectively). Survival analysis showed that at 1 and 10 years the all-cause mortality rates were significantly higher in patients with ADCHF (33% vs 22% and 90% vs 72%, 1 and 10 years, log-rank p < 0.001, respectively). Consistently, multivariable analysis showed that patients with ADCHF had an independently 58% and 48%, higher mortality risk at 1 and 10 years, respectively, (1-year hazard ratio = 1.58; 95% confidence interval 1.05 to 2.38, p = 0.03; 10-year hazard ratio = 1.48; 95% confidence interval = 1.23 to 2.77; p < 0.001). In conclusion, previous history of HF is an independent predictor of 1-year and 10-year mortality after hospitalization for AHF. Distinction between de-novo AHF and ADCHF may improve our understanding and risk stratification of patients with AHF. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;124:554−559)

Despite an ever growing body of literature centered on risk prediction in acute heart failure (AHF),[1−4] there are limited data regarding the clinical outcomes of hospitalized patients with AHF which are new-onset (de-novo) AHF compared with acutely decompensated chronic heart failure (ADCHF).[5] Actually, determining the clinical characteristics and outcomes of de-novo AHF as well as ADCHF may offer incremental insights into risk stratification, therapeutic management, and clinical trial design.[5,6] Therefore, the aim of the present study is: (1) To identify the clinical differences between hospitalized patients with ADCHF and de-novo AHF patients. (2) To assess the differences in early, intermediate, and long-term outcomes between hospitalized patients with ADCHF and de-novo AHF patients.

Methods

The present study population was comprised of 4,089 patients enrolled in the HF Survey in Israel, who were admitted to the hospital with a diagnosis of either acute de-novo without a previously known HF, acute decompensation of a previously known HF (ADCHF), or stable chronic HF. The prospective-cohort HF Survey in Israel was conducted in March and April 2003 in all 25 public hospitals in Israel. The study included 93 of the 98 internal medicine, and 24 of the 25 cardiology departments at that time; its design and methods have been previously published in detail.[7−9] The criteria used for diagnosing HF were symptoms of HF (at rest or during exercise) and objective evidence of cardiac dysfunction at rest. AHF was defined as a rapid onset or change in the signs or symptoms of HF, resulting in the need for urgent therapy and was determined including differentiation between its 2 groups (ADCHF and de-novo AHF) by the local survey team based on history, clinical presentation (symptoms and physical examination), response to HF therapy, chest radiography, echocardiography, radionuclide studies, cardiac catheterization findings, and in-hospital course. Detailed data regarding patient characteristics, in-hospital course, management during hospitalization, prehospital and discharge medications, and diagnoses were collected and recorded on prespecified structured forms. Of the total 4,089 patients, this study focused on 2,328 patients hospitalized with a diagnosis of either de-novo AHF or ADCHF. A total of 1,761 patients with chronic stable HF admitted for noncardiovascular causes were excluded from the analysis. The protocol was approved by the Ethics Committee at each of the participating hospitals. All data were recorded and analyzed in an

anonymous designed computer file. Also, validation of the enrolled patients was done by the primary investigators of the study.

The primary end point of the present study was all-cause mortality at 1 and 10 years of follow-up. Mortality, at 1 and 10 years after index hospitalization, was assessed in 99% of patients by matching their identification numbers with the Israeli National Population Registry. A total of 99% of patients were not lost to follow up during the first as well as 10 years of follow-up. The secondary end point was 30 days mortality.

Continuous variables are expressed as means ± standard deviation (SD), and categorical data are summarized as percentages. The clinical characteristics of the patients at baseline by the different categories of AHF were compared with the use of the t test for continuous variables and by the chi-square test for categorical variables. Kaplan-Meier survival analysis was used to graphically present survival estimates according to the different categories of AHF and the subsequent 1 and 10 years survival probability. Cumulative event rates were compared using the log-rank test. Multivariate Cox proportional hazard regression modeling was used to assess the independent effect of AHF type on the primary end point of all-cause mortality. The following covariates were introduced using the best subset method, following a univariate analysis of all relevant variables: age, gender, renal failure (estimated glomerular filtration rate < 60 ml/min/1.73 m^2), diabetes mellitus, severe HF (NYHA > 2), history of hypertension, history of ischemic heart disease, past cerebrovascular accident/transient ischemic attack, chronic obstructive lung disease, Left ventricular ejection fraction (LVEF) < 40%, body mass index, history of atrial fibrillation/flutter, admission heart rate, admission systolic blood pressure, prescription of diuretics, digoxin, and spironolactone at discharge. Proportionality of hazard assumption was verified using Schoenfeld residuals and the log minus log method. Statistical significance was accepted for a 2-sided p < 0.05. The statistical analysis was performed with IBM SPSS version 20.0 (Chicago, Illinois) and SAS version 9.2 (SAS institute Inc.).

Results

The cohort of the study included 2,328 patients who were hospitalized with a diagnosis of either ADCHF or de-novo AHF. Based on our classification of the different AHF groups, 1,607 (69%) patients were classified as ADCHF and 721 (31%) patients as de-novo AHF. Baseline characteristics of the 2 AHF groups are presented in Table 1.

ADCHF patients were older, had higher rates of past history of myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, and higher rates of global co-morbidities represented by higher Charlson co-morbidity index compared with those with de-novo AHF. Moreover, patients classified as ADCHF had higher rates of systolic dysfunction (LVEF < 40%), severe HF (NYHA > 2), atrial fibrillation or flutter and infection as precipitating factors of acute de-compensation compared with patients classified as de-novo AHF. Notably, patients classified as ADCHF had lower rates of acute coronary syndrome (ACS) as a precipitating factor of decompensation, were less likely to be treated with thrombolysis and less

likely to have primary percutaneous intervention compared with patients classified as de-novo AHF. Importantly, patients with ADCHF were more likely to be hospitalized in the internal medicine department compared with those with de-novo AHF. In regard the laboratory values, ADCHF patients had lower hemoglobin and estimated glomerular filtration levels, higher creatinine levels, and no difference in sodium levels compared with de-novo AHF patients. At admission patients with ADCHF were significantly more likely to be treated with antiplatelets (aspirin/clopidogrel), β blockers, angiotensin converting enzyme inhibitors (ACEI), or angiotensin II receptor blockers (ARBS), loop diuretics, potassium sparing diuretics as well as digoxin. Interestingly at discharge there were no significant differences in the rates of use of β blockers as well as ACE I/ARBS between those with ADCHF compared with those with de-novo AHF and the rates of prescription of those medications was almost identical between both groups. However, patients with ADCHF were still more likely to be discharged with digoxin, loop diuretics as well as potassium sparing diuretics unlike aspirin/clopidogrel that were prescribed more for patients with de-novo AHF at discharge (Table 2).

At 30 days mortality rates were similar in both groups (9% vs 8% in de-novo AHF and ADCHF, respectively). Survival analysis showed that at 1 and 10 years the rates of all-cause mortality were significantly higher in patients with ADCHF (33% vs 22% and 90% vs 72%, 1 and 10 years; p < 0.001). Consistently multivariable analysis showed that patients with ADCHF had an independently 58% and 48%, higher mortality risk at 1 and 10 years of follow-up, respectively, (1-year hazard ratio = 1.58; 95% confidence interval 1.05 to 2.38, p = 0.03; 10-year hazard ratio = 1.48; 95% confidence interval = 1.23 to 2.77; p < 0.001) (Figures 1 and 2).

Discussion

In this study we have found that in clinical practice, patients with ADCHF display significant differences in baseline clinical characteristics compared with de-novo AHF patients. Notably, patients with ADCHF represent a more severe condition. They were older, had higher rates of past myocardial infarction as well as revascularization, in addition they tend to be with higher rates of systolic dysfunction as well as advanced HF (NYHA > 2). Moreover, and most importantly patients with ADCHF independently had higher mortality rates at both 1 and 10 years of follow-up.

Our findings are in line with other recent reports showing a strong association of the chronicity of HF with long-term mortality.[5,10−12] In the present study, the strong association of the chronicity of HF with mortality is so long as 10 years showing higher mortality rates for ADCHF patients compared with de-novo AHF patients and was significant upon adjustment for co-morbidities and established risk factors in HF. This implies that other features inherent to this group of patients underlie their increased mortality compared with de novo AHF patients and highlights the importance of systematically defining and categorizing patients with AHF.

In fact, the decompensation and need for hospitalization in patients with ADCHF could partly be regarded as a treatment

Table 1
Baseline characteristics of patients with acute de-novo heart failure versus acute decompensated chronic heart failure

Variable	Acute de-novo heart failure n = 721	Acute decompensated chronic heart failure n = 1607	p Value
Demographics			
Age (years)*	71 ± 14	75 ± 11	<0.001
Men	387 (54%)	900 (56%)	0.30
Body mass index (kg/m^2) ≥ 30	103 (23%)	224 (25%)	0.47
Hospitalization in cardiology department	263 (37%)	198 (12%)	<0.001
Hospitalization in internal medicine department	458 (63%0	1409 (88%)	<0.001
Past medical history			
Hypertension	486 (67%)	1147 (70%)	0.05
Diabetes mellitus	292 (41%)	713 (44%)	0.081
Chronic obstructive pulmonary disease	100 (14%)	350 (22%)	<0.001
Ischemic heart disease	546 (77%)	1231 (78%)	0.44
Past myocardial infarction	171 (24%)	695 (43%)	<0.001
Past cerebrovascular accident/transient ischemic attack	61 (9%)	210 (13%)	0.001
Charlson comorbidity index	4.73 ± 1.73	5.72 ± 1.61	<0.001
Past percutaneous coronary intervention	74 (10%)	264 (16%)	<0.001
Past coronary artery bypass grafting	52 (7%)	311 (19%)	<0.001
Treatment with thrombolysis	35 (5%)	8 (0.5%)	<0.001
Primary percutaneous intervention	87 (12%)	42 (3%)	<0.001
Atrial fibrillation	170 (24%)	588 (37%)	<0.001
Current or past smoker	231(32%)	461 (29%)	0.10
Heart failure features			
Heart failure with reduced ejection fraction	391 (71%)	821 (70%)	0.65
Left ventricular ejection fraction <40%	248 (45%)	623 (53%)	0.002
New york heart association functional classification >2	153 (22%)	875 (55%)	<0.001
Main heart failure presentation			
Dyspnea	389 (54%)	1098 (68%)	<0.001
Fatigue	60 (8%)	149 (9%)	0.46
Fluid retention	35 (5%)	254 (16%)	<0.001
Pulmonary edema	215 (29%)	309 (19%)	<0.001
Cardiogenic shock	21 (3%)	15 (1%)	<0.001
Rhythm disorder	20 (2.8%)	35 (2.2%)	0.38
Killip 1	220 (31%)	296 (18%)	<0.001
Killip 2	238 (33%)	818 (51%)	<0.001
Killip 3	202 (28%)	401 (25%)	0.12
Killip 4	57 (8%)	89 (6%)	0.03
Heart failure etiology			
Coronary artery disease	519 (72%)	1127 (70%)	0.36
Diabetes mellitus	169 (23%)	369 (23%)	0.80
Hypertensive heart disease	287 (40%)	707 (44%)	0.06
Any cardiomyopathy	81 (11%)	282 (14%)	0.04
Any valvular heart disease	152 (21%)	478 (30%)	<0.001
Precipitating factors			
Acute coronary syndrome	389 (54%)	416 (26%)	<0.001
Atrial fibrillation/flutter	176 (24%)	598 (37%)	<0.001
Valvular disease	66 (9%)	153 (10%)	0.779
Infection	98 (14%)	307 (19%)	0.001
Clinical presentation			
Heart rate (b/min)	89 ± 23	85 ± 20	<0.001
Systolic blood pressure (mm Hg)	145 ± 35	144 ± 32	0.404
Left ventricular ejection fraction (%)	40.4 ± 12.2	36.9 ± 15.1	<0.001
Laboratory values			
Hemoglobin(g/l)	12.5 ± 2.1	12.1 ± 1.9	<0.001
Creatinine (mg/dl)	1.3 ± 0.86	1.6 ± 1.03	<0.001
Estimated glomerular filtration rate (ml/min/1.73m^2)	66.2 ± 34.12	54.1 ± 29.2	<0.001
Sodium (meq/L)	139.8 ± 46.1	138.1 ± 8.1	0.16
C-reactive protein (mg/dl)	44.9 ± 67.2	34.1 ± 54.9	0.23
All-cause mortality			
30 days	66 (9%)	135 (8%)	0.54
1 year	159 (22%)	520 (33%)	<0.001
10 years	518 (72%)	1450 (90%)	<0.001

* Continuous variables are reported as mean ± standard deviation if normally distributed; otherwise, as median with twenty-fifth to seventy-fifth range. Categorical variables are reported as numbers (%).

Table 2

Admission and discharge medications in patients with acute de-novo heart failure versus acute decompensated chronic heart failure

Variable	Admission medications			Discharge medications		
	Acute de-novo heart failure	Acute decompensated chronic heart failure	p Value	Acute de-novo heart failure	Acute decompensated chronic heart failure	p Value
Aspirin/clopidogrel	344 (48%)	999 (62%)	<0.001	532 (79%)	1007 (66%)	<0.001
Angiotensin converting enzyme inhibitor/angiotensin II receptor blockers	398 (45%)	996 (62%)	<0.001	482 (72%)	1054 (70%)	0.299
Loop diuretics	242 (34%)	1225 (76%)	<0.001	439 (65%)	1321 (87%)	<0.001
Beta blockers	246 (34%)	853 (53%)	<0.001	429 (63%)	911 (60%)	0.144
Potassium sparing diuretics	20 (3%)	290 (18%)	<0.001	67 (10%)	419 (28%)	<0.001
Digoxin	37 (5%)	263 (16%)	<0.001	67 (10%)	275 (18%)	<0.001

Table 3

Independent predictors of 1- and 10-year all-cause mortality outcomes

Variable	1 year		10 years	
	HR; (95%CI)	p Value	HR; (95%CI)	p Value
Acute decompensated chronic heart failure vs. acute de-novo heart failure	1.505; (1.122-2.020)	0.006	1.444; (1.225-1.661)	<0.001
Age*	1.032; (1.020-1.044)	<0.001	1.045; (1.039-1.052)	<0.001
Male gender	0.96; (0.763-1.208)	0.76	1.146; (1.013-1.297)	0.030
Hypertension	0.89; (0.697-1.124)	0.32	0.913; (0.797-1.045)	0.185
Diabetes mellitus	1.015; (0.811-1.271)	0.089	1.382; (1.226-1.557)	<0.001
Past cerebrovascular accident	1.351; (0.998-1.828)	0.05	1.154; (0.975-1.366)	0.097
Chronic obstructive pulmonary disease	1.173; (0.908-1.514)	0.22	1.219; (1.061-1.400)	0.005
Past myocardial infarction	0.911; (0.729-1.140)	0.42	0.919; (0.815-1.037)	0.169
Atrial fibrillation/flutter	1.13; (0.89-1.44)	0.31	1.01; (0.88-1.15)	0.89
Left ventricular ejection fraction < 40%	1.061; (0.835-1.350)	0.63	1.015; (0.895-1.151)	0.817
Estimated glomerular filtration rate < 60 ml/min/1.73m^2	1.465; (1.153-1.861)	0.002	1.376; (1.220-1.552)	<0.001
New york heart association > 2	1.482; (1.182-1.857)	0.001	1.395; (1.238-1.571)	<0.001
Digoxin at discharge	1.340; (1.016-1.767)	0.04	1.157; (0.981-1.364)	0.083
Admission systolic blood pressure (per 1 mm Hg increase)*	0.992; (0.998-0.995)	<0.001	0.998; (0.996-0.999)	0.011
Admission heart rate (per beat/min increase)*	1.001; (0.996-1.006)	0.69	1.003; (1.001-1.006)	0.02

Hazard ratios are further adjusted to: age, gender, advanced renal failure (eGFR< 60 ml/min/1.73m^2), diagnosis of diabetes mellitus (DM), severe HF (NYHA > 2), history of hypertension (HTN) history of ischemic heart disease (IHD), past cerebrovascular accident/ Transient ischemic attack (TIA/ CVA), chronic obstructive lung disease (COPD). Left ventricular ejection fraction (EF) < 40%, body mass index (BMI) history of atrial fibrillation/flutter, admission heart rate, admission systolic blood pressure, prescription of diuretics, digoxin and spironolactone at discharge.

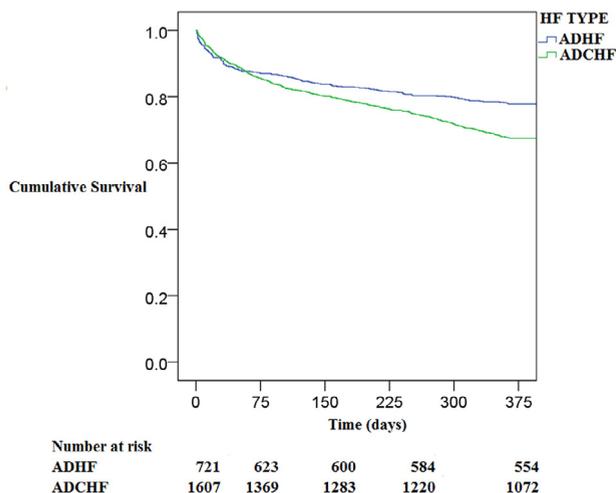* denote for variable introduced as continuous into the multivariable cox model.

Figure 1. Kaplan Meier 1-year survival estimates based on acute de-novo HF versus acute decompensated chronic HF (log-rank p <0.001).
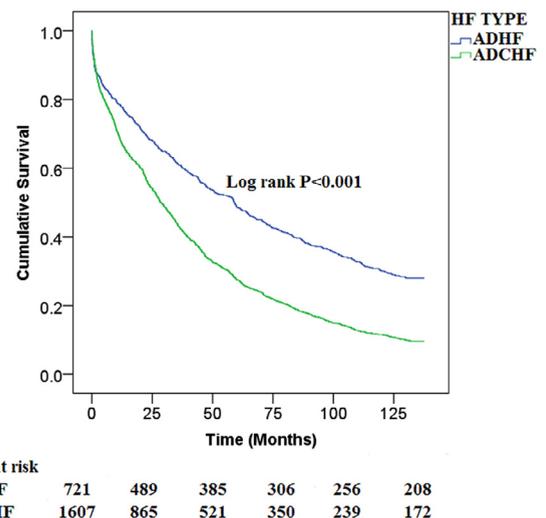

Figure 2. Kaplan Meier 10-years survival estimates based on acute de-novo HF versus acute decompensated chronic HF (log-rank p <0.001).

failure. Patients with ADCHF tend to present with signs and symptoms of congestion and fluid retention rather than with pulmonary edema or cardiogenic shock that characterize acute left ventricular systolic dysfunction. This is the result of the long-term, often dysregulated, neuro-humoral compensatory mechanisms which act to maintain a hemodynamic status quo despite worsening left ventricular function. Decompensation occurs when the balance tips toward fluid overload as the compensatory mechanisms prove inadequate or indeed fail all-together.[13] This seems to emphasize that de-novo AHF and ADCHF are in themselves 2 different conditions. The finding that de-novo AHF patients more often had ACS as precipitating factor could imply that cardiac dysfunction in some forms of de-novo AHF is transient in nature and might thus be curable along with the precipitating factor.[14] In the case of ACS, management is focused not only on hemodynamic compromise but also on reperfusion with the aim of restoring myocardial contractile function. This might explain, at least partly, the better survival of de-novo AHF patients at 1 and 10 years but not at 30 days follow-up. The secondary analysis of the ASCEND-HF trial which showed better survival of de-novo AHF patients at 30 days follow-up did not include patients with ACS.[5]

Other important point worth mentioning is the fact that patients with ADCHF were more likely to be under treatment with ACEI/ARBS, β blockers, potassium sparing diuretics, and loop diuretics compared with those with de-novo AHF. This is in line with other studies showing an increased rate of these drugs prescription as there is an increase in the duration of HF chronicity.[5,10]

At discharge there were similar rates of prescription of β blockers and ACEI/ARBS between those with ADCHF as compared with those with de-novo AHF. Nevertheless, patients with ADCHF still were more likely to be discharged with recommendation to use loop diuretics as well as potassium sparing diuretics and digoxin. Although patients with de-novo AHF were more likely to be prescribed antiplatelets at discharge. These interesting findings extend similar findings reported by Al-Habib et al and Lassus et al, respectively.[6,10]

Despite decades of randomized clinical trials, the treatment of AHF is largely unchanged from the 1970s and there remain no class I, level of evidence A guideline recommendations for patients hospitalized with AHF.[15] Moreover, the burden of acute worsening of chronic HF continues to increase, and its poor outcomes remain a challenge globally. The use of real-world data allows for the in-depth prospective examination of AHF type effect on mortality of these everyday patients. In this study, other than describing the main groups of drugs prescribed at both admission and discharge, we did not evaluate specific drug regimens and drug dosages, and this aspect of preadmission, in-hospital, and postdischarge therapeutic clinical management should be further investigated, particularly by AHF type stratification, for their effect on survival in AHF.

Several limitations of our study are worth mentioning. Although the components of AHF were predefined in the registry protocol, the adjudication is subjective; study results can be influenced by differences in disease assessment and documentation patterns at participating institutions. Thus; exclusion of 1,761 patients who were regarded

as having chronic stable HF a small number of whom could have been in fact with AHF may affect the current analysis. However, we still believe that the number of these clinically borderline patients with overlapping symptoms is marginal. Echocardiography was performed in two−thirds of the patients. We had no data on brain natriuretic peptide levels and no data on causes of death. Nevertheless, our study includes a large cohort of patients hospitalized due to AHF in all public hospitals in a country and describes a "real−world" picture of AHF outcome.

In conclusion, in patients hospitalized due to AHF, patients with ADCHF demonstrate a graver prognosis. Distinction between ADCHF and de-novo AHF may improve our understanding and risk stratification of patients with AHF. Our findings suggest that more focus on follow-up and optimization of medical therapy should be provided in chronic HF patients who are hospitalized with an acute event and support the notion that ADCHF is an end point that should be formalized and systematically reported in both real life data and in clinical trials.

Disclosures

The authors have no conflicts of interest to disclose.

Acknowledgment

1. Solomon SD, Dobson J, Pocock S, Skali H, McMurray JJ, Granger CB, Yusuf S, Swedberg K, Young JB, Michelson EL, Pfeffer MA, Candesartan in Heart failure: Assessment of Reduction in M, morbidity I. Influence of nonfatal hospitalization for heart failure on subsequent mortality in patients with chronic heart failure. *Circulation* 2007;116:1482–1487.
2. O'Connor CM, Miller AB, Blair JE, Konstam MA, Wedge P, Bahit MC, Carson P, Haass M, Hauptman PJ, Metra M, Oren RM, Patten R, Pina I, Roth S, Sackner-Bernstein JD, Traver B, Cook T, Gheorghiade M, Efficacy of Vasopressin Antagonism in heart Failure Outcome Study with Tolvaptan i. Causes of death and rehospitalization in patients hospitalized with worsening heart failure and reduced left ventricular ejection fraction: results from Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study with Tolvaptan (EVEREST) program. *Am Heart J* 2010;159:841–849. e841.
3. Gheorghiade M, Abraham WT, Albert NM, Greenberg BH, O'Connor CM, She L, Stough WG, Yancy CW, Young JB, Fonarow GC, Investigators O-H, Coordinators. Systolic blood pressure at admission, clinical characteristics, and outcomes in patients hospitalized with acute heart failure. *JAMA* 2006;296:2217–2226.
4. Greene SJ, Fonarow GC, Vaduganathan M, Khan SS, Butler J, Gheorghiade M. The vulnerable phase after hospitalization for heart failure. *Nat Rev Cardiol* 2015;12:220–229.
5. Greene SJ, Hernandez AF, Dunning A, Ambrosy AP, Armstrong PW, Butler J, Cerbin LP, Coles A, Ezekowitz JA, Metra M, Starling RC, Teerlink JR, Voors AA, O'Connor CM, Mentz RJ. Hospitalization for recently diagnosed versus worsening chronic heart failure: from the ASCEND-HF Trial. *J Am Coll Cardiol* 2017;69:3029–3039.
6. Lassus JP, Siirila-Waris K, Nieminen MS, Tolonen J, Tarvasmaki T, Peuhkurinen K, Melin J, Pulkki K, Harjola VP, group F-As. Long-term survival after hospitalization for acute heart failure−differences in prognosis of acutely decompensated chronic and new-onset acute heart failure. *Int J Cardiol* 2013;168:458–462.
7. Barsheshet A, Shotan A, Cohen E, Garty M, Goldenberg I, Sandach A, Behar S, Zimlichman E, Lewis BS, Gottlieb S, Committee H.S., Investigators. Predictors of long-term (4-year) mortality in elderly and

young patients with acute heart failure. *Eur J Heart Fail* 2010;12: 833–840.

8. Garty M, Shotan A, Gottlieb S, Mittelman M, Porath A, Lewis BS, Grossman E, Behar S, Leor J, Green MS, Zimlichman R, Caspi A, Committee H.S., Investigators. The management, early and one year outcome in hospitalized patients with heart failure: a national Heart Failure Survey in Israel—HFSIS 2003. *Israel Med Assoc J* 2007;9:227–233.

9. Lewis BS, Shotan A, Gottlieb S, Behar S, Halon DA, Boyko V, Leor J, Grossman E, Zimlichman R, Porath A, Mittelman M, Caspi A, Garty M, Investigators H. Late mortality and determinants in patients with heart failure and preserved systolic left ventricular function: the Israel Nationwide Heart Failure Survey. *Israel Med Assoc J* 2007;9:234–238.

10. AlHabib KF, Kashour T, Elasfar AA, Alfaleh H, Hersi A, Alshamiri M, Alshaer F, Mimish L, Almasood A, AlHabeeb W, AlGhamdi S, Ghabashi A, Asfina K, Altaradi H, Alnobani O, Alkamel N, Thalib L. Long-term mortality rates in acute de novo versus acute-on-chronic heart failure: from the heart function assessment registry trial in Saudi Arabia. *Angiology* 2015;66:837–844.

11. Harjola VP, Follath F, Nieminen MS, Brutsaert D, Dickstein K, Drexler H, Hochadel M, Komajda M, Lopez-Sendon JL, Ponikowski P, Tavazzi L. Characteristics, outcomes, and predictors of mortality at 3 months and 1 year in patients hospitalized for acute heart failure. *Eur J Heart Fail* 2010;12:239–248.

12. Degoricija V, Trbusic M, Potocnjak I, Radulovic B, Teresak SD, Pregartner G, Berghold A, Tiran B, Frank S. Acute heart failure developed as worsening of chronic heart failure is associated with increased mortality compared to de novo cases. *Sci Rep* 2018;8:9587.

13. O'Connor CM, Stough WG, Gallup DS, Hasselblad V, Gheorghiade M. Demographics, clinical characteristics, and outcomes of patients hospitalized for decompensated heart failure: observations from the IMPACT-HF registry. *J Cardiac Fail* 2005;11:200–205.

14. Kurmani S, Squire I. Acute heart failure: definition, classification and epidemiology. *Curr Heart Fail Rep* 2017;14:385–392.

15. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr., Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR, Kasper EK, Levy WC, Masoudi FA, McBride PE, McMurray JJ, Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Tang WH, Tsai EJ, Wilkoff BL. American College of Cardiology F. American Heart Association Task Force on Practice G. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013;62:e147–e239.