ORIGINAL ARTICLE

Clinical characteristics, treatment, and prognosis of patients with ischemic and nonischemic acute severe heart failure

Analysis of data from the COMMIT-AHF registry

Mateusz Ostręga[1], Marek J. Gierlotka[1], Grzegorz Słonka[1], Paweł Nadziakiewicz[2], Mariusz Gąsior[1]

1 3rd Department of Cardiology, School of Medicine with the Division of Dentistry in Zabrze, Medical University of Silesia in Katowice, Silesian Center for Heart Diseases in Zabrze, Zabrze, Poland
2 Department of Cardiac Anesthesia and Intensive Care, School of Medicine with the Division of Dentistry in Zabrze, Medical University of Silesia in Katowice, Silesian Center for Heart Diseases in Zabrze, Zabrze, Poland

KEY WORDS

12-month mortality, acute heart failure, ischemic heart injury, nonischemic heart injury, treatment modalities

ABSTRACT

INTRODUCTION There are limited data on the impact of ischemic etiology on the clinical status and long-term prognosis of patients with acute severe heart failure (HF) not associated with acute coronary syndrome (ACS).

OBJECTIVES The aim of this study was to assess the clinical characteristics, treatment, and 12-month mortality of patients with acute severe HF not associated with ACS, according to the etiology of HF.

PATIENTS AND METHODS Data from 112 patients with acute severe HF not associated with ACS were analyzed: 61 patients with ischemic HF and 51 patients with nonischemic HF. Acute severe HF was defined as acute HF on admission with at least one of the following characteristics: pulmonary congestion, cardiogenic shock, catecholamine or intraaortic balloon pump support, ultrafiltration, mechanical ventilation, prolonged use of intravenous diuretics, fluid in the body cavities requiring decompression, or multiorgan failure.

RESULTS Patients with ischemic HF were older (62 vs 54 years, $P = 0.001$), predominately male (84% vs 65%, $P = 0.02$), had more comorbidities, and had lower left ventricular ejection fraction (21% vs 27%, $P = 0.02$). There were no significant differences in treatment modalities (ie, mechanical ventilation, hemodiafiltration, intraaortic balloon pump, left ventricular assist device, heart transplantation), except for 14 percutaneous coronary interventions in the ischemic group. In-hospital adverse events were similar between the groups. Among 83 discharged patients with available follow-up, death was reported for 15 patients with ischemic and 11 patients with nonischemic HF (34% vs 28%, $P = 0.42$).

CONCLUSIONS Ischemic HF, accounting for approximately half of the cases of acute severe HF not related to ACS, was not associated with a significantly worse prognosis than nonischemic HF.

Correspondence to:
Mateusz Ostręga, MD, III Katedra i Oddział Kliniczny Kardiologii, Wydział Lekarski z Oddziałem Lekarsko-Dentystycznym w Zabrzu, Śląski Uniwersytet Medyczny w Katowicach, Śląskie Centrum Chorób Serca w Zabrzu, ul. M. Skłodowskiej-Curie 9, 41-800 Zabrze, Poland, phone: +48 32 373 38 60, e-mail: matost1@tlen.pl
Received: January 18, 2017.
Revision accepted: April 15, 2017.
Published online: April 18, 2017.
Conflict of interests: none declared.
Pol Arch Intern Med. 2017; 127 (5): 328-335
doi:10.20452/pamw.3996

INTRODUCTION Heart failure (HF) is an increasingly common health care problem.[1] The rising prevalence of HF is undoubtedly associated with extended survival of the general population and improved quality of treatment of cardiac and noncardiac conditions. According to the definition from the current guidelines of the European Society of Cardiology, HF is a combination of objective and subjective clinical symptoms caused by impaired structure or function of the heart, resulting in decreased cardiac output and/or increased pressures in cardiac cavities during rest or exercise.[2] Patients with HF have poor prognosis, with life expectancies shorter than in patients with breast, colon, or prostate cancers.[3] From a population point of view, 30-day, 1-year, and 5-year mortality rates associated with newly diagnosed HF are 10%, 20% to 30%, and 45%

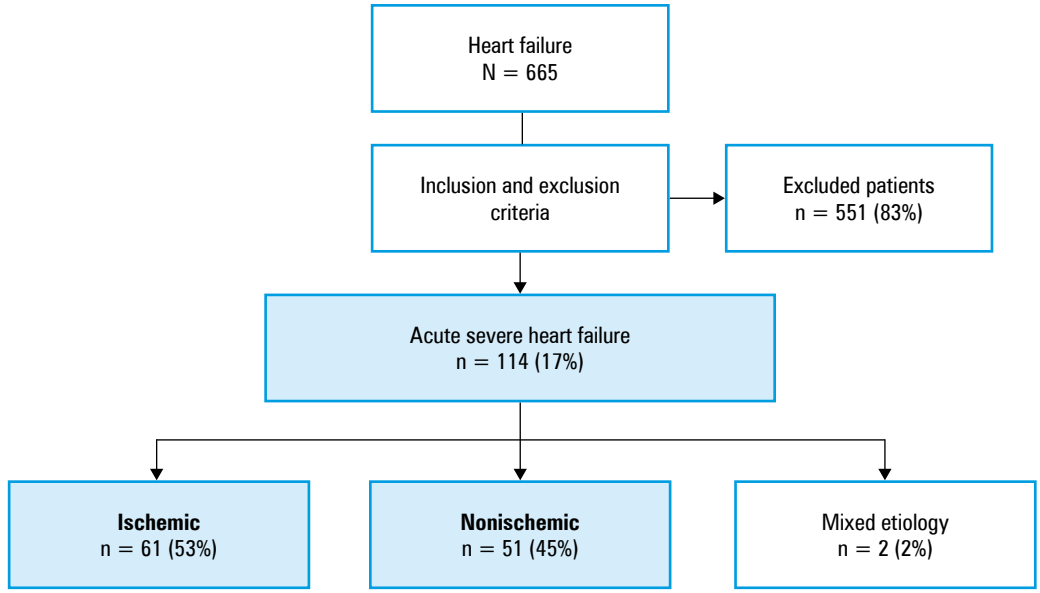

FIGURE 1 Flow chart of patients through the study

to 60%, respectively.[4] Over 1 million patients are admitted to hospitals in the United States and Europe annually with an initial diagnosis of HF. This accounts for approximately 1% to 2% of all hospitalizations. A high rate (as many as 50%) of patients with an incident of acute decompensation of HF requires rehospitalization within 6 months from the first episode, and each consecutive episode is associated with worse prognosis.[5] The prognosis is especially poor for elderly patients with numerous concomitant diseases, in cardiogenic shock, and with extremely impaired left ventricular systolic function.[6,7] These patients often require advanced diagnostic and therapeutic procedures performed by cardiologists, cardiac surgeons, and intensive care specialists.

Considering etiology, HF is a consequence of an ischemic, nonischemic, or complex heart injury. The most common cause of systolic HF is coronary artery disease, accounting for as many as 70% of cases.[8,9] The causes of nonischemic myocardial injury are mostly hypertension and cardiomyopathies, as well as valvular, metabolic, inflammatory, and systemic diseases. Studies conducted in the 1990s indicated better outcomes and lower mortality rates in patients with nonischemic HF compared with those with ischemic HF, but subsequent studies failed to confirm these results.[10-12] HF associated with acute coronary syndrome (ACS), particularly with myocardial infarction, has been well studied and has been repeatedly the focus of clinical trials, reported in numerous publications.[13,14] However, only a few studies compared patients with acute severe HF according to ischemic or nonischemic etiology.[15,16]

In our study, we compared the clinical characteristics, treatments, and outcomes of patients with ischemic and nonischemic etiology of acute severe HF not associated with ACS, hospitalized in a reference cardiac and cardiac surgery center with a full spectrum of diagnostic and therapeutic modalities.

PATIENTS AND METHODS

All patients with HF hospitalized in the 3rd Department of Cardiology of Silesian Center for Heart Diseases in Zabrze, Poland, between April 2011 and October 2014 were screened (FIGURE 1). Patients with the symptoms of acute HF (de novo or due to decompensation of chronic HF) meeting one of the following clinical criteria entered the COMMIT-AHF (The COnteMporary Modalities In Treatment of Acute Heart Failure) registry: 1) acute left ventricular decompensation with radiological features of increased congestion in the pulmonary circulation; 2) cardiogenic shock; 3) administration of catecholamines; 4) intraaortic balloon pump support; 5) hemodiafiltration; 6) mechanical ventilation; 7) intravenous administration of diuretics for at least 7 days; 8) signs of multiorgan failure (glomerular filtration rate of less than 60 ml/min/1.73 m^2 on admission or during hospitalization, aspartate aminotransferase or alanine transaminase levels more than double the upper limit of normal on admission, or an increase in these levels during hospitalization, and international normalized ratio of less than 2.0 without anticoagulation); and 9) the presence of fluid in the body cavities requiring surgical decompression.[17-19] The exclusion criterion for the COMMIT-AHF registry was ACS (unstable angina pectoris or myocardial infarction) as a reason for hospitalization. COMMIT-AHF shares the database with the recently published COMMIT-HF registry on patients with HF hospitalized in the same center.[20]

The etiology of acute severe HF was determined based on medical history and examinations.[15,21] The ischemic etiology was diagnosed on the basis of a history of myocardial infarction, prior percutaneous revascularization or coronary artery bypass grafting, and the presence of significant stenoses in epicardial coronary arteries. The nonischemic etiology was diagnosed if HF had developed secondary to conditions other than ischemic heart disease, or if

TABLE 1 Baseline characteristics of patients with ischemic and nonischemic acute severe heart failure

Variable	Acute severe HF		*P* value
	Ischemic (n = 61)	Nonischemic (n = 51)	
Age, y, mean (SD)	62.0 (9.8)	54.1 (14.9)	0.001
Female sex, n (%)	10 (16)	18 (35)	0.021
BMI, kg/m^2, mean (SD)	26.8 (4.8)	26.9 (5.9)	0.93
Prior myocardial infarction, n (%)	46 (75)	0 (0)	<0.0001
Prior PCI, n (%)	35 (57)	0 (0)	<0.0001
Prior CABG, n (%)	14 (23)	0 (0)	<0.0001
History of stroke, n (%)	7 (11)	1 (1)	0.069
Atrial fibrillation/flutter, n (%)	24 (39)	23 (45)	0.54
Diabetes mellitus, n (%)	33 (54)	14 (27)	0.004
Arterial hypertension, n (%)	35 (57)	23 (45)	0.20
History of renal failure, n (%)	34 (56)	15 (29)	0.005
Peripheral artery disease, n (%)	8 (13)	2 (4)	0.11
Tobacco smoking, n (%)	39 (64)	22 (43)	0.028
Hypercholesterolemia, n (%)	37 (61)	11 (22)	<0.0001
Chronic obstructive pulmonary disease, n (%)	4 (7)	4 (8)	1.0
Prior pacemaker implantation, n (%)	6 (10)	3 (6)	0.51
Prior ICD implantation, n (%)	13 (21)	5 (10)	0.099
Prior CRT-D implantation, n (%)	14 (23)	8 (16)	0.34

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; CRT-D, cardiac resynchronization therapy defibrillator; HF, heart failure; ICD, implantable cardioverter–defibrillator; PCI, percutaneous coronary intervention

the cause of HF had not been explained. Except for 4 young patients (<40 years) with a very low risk of coronary artery disease, coronary angiography was performed in all patients during the hospitalization prior to admission or during the index hospitalization.

The Acute Physiology and Chronic Health Evaluation – Heart Failure (APACHE-HF) scoring system was used to assess the objective level of severity of acute HF in patients with ischemic and nonischemic HF.[22] This score is based on 8 selected significant parameters obtained from the APACHE II score. One point is given for each of the following parameters: mean arterial pressure ≤90 mm Hg, heart rate ≤110 bpm, serum sodium concentration ≤137 mmol/l, serum potassium concentration ≥4.9 mmol/l, serum creatinine concentration ≥130.8 μmol/l, hematocrit ≤36.9%, age ≥72 years, and the Glasgow Coma Scale ≤13 points. Generally, on the basis of the multivariate Cox regression model and the Kaplan–Meier curves, the more points (from 0 to 8) the patient obtains, the higher the risk of HF events or death during the 90-day follow-up period.

Patients were diagnosed and treated in a 12-bed intensive cardiac care unit. They had constant, multispecialty medical care involving specialists in cardiology, anesthesia, intensive care, cardiac surgery, vascular surgery, transplantation, and diabetes care. Depending on clinical indications, the diagnostic and therapeutic process of acute severe HF also involved the use of various forms of mechanical heart support and heart transplantation. Data on patient mortality after discharge, along with a date of death, were obtained from the database of the National Health Fund for all patients, except for 2 foreign patients.

Continuous parameters were presented as the mean and SD, or as the median and interquartile range, and their statistical significance was determined with the *t* test or the Mann–Whitney test, depending on data distribution. Qualitative parameters were compared using the χ^2 test or the Fisher exact test. Long-term mortality was analyzed using the Kaplan–Meier method and log-rank tests. Independent factors associated with in-hospital and 12-month mortality were identified using the stepwise multiple logistic and Cox proportional hazard regression, respectively, and the results were presented as odds and hazard ratios with 95% CIs. The etiology of HF and clinical parameters on admission were included into multivariate models. Additionally, treatment-associated parameters were included into a model of 12-month mortality. *P* values of less than 0.05 (double-sided) were considered to be statistically significant. All calculations were done using the Statistica PL software, version 12 (Dell, StatSoft, Round Rock, Texas, United States).

RESULTS Based on inclusion and exclusion criteria, 114 of 665 patients (17%) hospitalized due to HF were entered into the COMMIT-AHF registry (FIGURE 1). Two patients (2%) met the criteria of both ischemic and nonischemic HF, presenting a complex etiology of myocardial injury. For that reason, they were excluded from further analyses. Finally, 61 patients were analyzed

TABLE 2 Clinical data on admission in patients with ischemic and nonischemic acute severe heart failure

Variable	Acute severe HF		*P* value
	Ischemic (n = 61)	Nonischemic (n = 51)	
Mean arterial pressure, mm Hg, mean (SD)	80 (13)	83 (13)	0.35
Systolic arterial blood pressure, mm Hg, mean (SD)	106 (19)	111 (21)	0.25
Diastolic arterial blood pressure, mm Hg, mean (SD)	68 (13)	70 (12)	0.37
Heart rate, bpm, mean (SD)	85 (22)	90 (25)	0.35
Cardiogenic shock on admission, n (%)	12 (20)	5 (10)	0.16
Cardiac arrest before admission, n (%)	6 (10)	1 (2)	0.12
Mechanical ventilation, n (%)	4 (7)	2 (4)	0.69
Infusion of catecholamines, n (%)	17 (28)	14 (27)	0.92
IABP, n (%)	9 (15)	4 (8)	0.26
APACHE-HF score, mean (SD)	3.8 (1.2)	3.4 (1.5)	0.095
Hemoglobin, mmol/l, mean (SD)	8.0 (1.2)	8.1 (1.2)	0.58
Creatinine, µmol/l, mean (SD)	140 (80.5)	111 (57.5)	0.037
Glucose, mmol/l, mean (SD)	6.7 (2.3)	6.4 (2.4)	0.47
CK-MB, ng/ml, mean (SD)	15 (40)	25 (63)	0.52
Troponin, ng/ml, mean (SD)	0.5 (1.5)	0.2 (0.5)	0.21
NT-proBNP, pg/ml, mean (SD)	11 456 (10 427)	9677 (9283)	0.42
LVEF, %, mean (SD)	21 (10)	27 (15)	0.019
Left ventricular end-diastolic diameter, mm, mean (SD)	65 (12)	65 (14)	0.75
Left ventricular end-systolic diameter, mm, mean (SD)	54 (14)	55 (16)	0.85
Severe mitral regurgitation, n (%)	34 (56)	19 (37)	0.051
Left atrial diameter, mm, mean (SD)	50 (7)	51 (11)	0.32

Abbreviations: APACHE-HF, Acute Physiology and Chronic Health Evaluation – Heart Failure; CK-MB, creatine kinase--MB; IABP, intraaortic balloon pump; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; others, see **TABLE 1**

in the ischemic group and 51 in the nonischemic group. Among them, 34 patients (30%) presented symptoms of de novo acute HF, and 78 patients (70%)—symptoms of acute HF due to decompensation of chronic HF. In the group of patients with nonischemic HF, myocardial injury was due to a valvular cause in 43% of the cases, due to arterial hypertension in 18%, due to infective endocarditis in 6%, due to a postinflammatory cause in 4%, due to hypertrophic cardiomyopathy in 4%, due to idiopathic pulmonary hypertension in 4%, and due to amyloidosis in 2%; in the remaining 19% of the cases, the cause was insufficiently documented or unknown (mainly dilated cardiomyopathy, but not genetically confirmed).

The baseline characteristics of the patients are presented in **TABLE 1**. Patients with ischemic HF were significantly older (8 years) compared to those with nonischemic HF. Male patients dominated in both groups, and the male-to-female ratio was higher in the ischemic group. Patients with ischemic HF more often had a history of diabetes mellitus, chronic renal disease, hypercholesterolemia, and smoking, and presented a trend for more frequent history of stroke and peripheral artery disease.

Basic hemodynamic parameters on admission, including mean arterial pressure and heart rate, were not significantly different between the groups (**TABLE 2**). However, the percentage of patients admitted in cardiogenic shock was 2-fold higher in patients with ischemic etiology compared with those with nonischemic etiology. Patients with ischemic HF were more often admitted after cardiac arrest and with intraaortic balloon pump support. In total, 25% of the patients received an intravenous infusion of catecholamines. Higher creatinine concentrations were measured on admission in patients with ischemic HF. Of note, the mean baseline N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentration was over 9000 pg/ml in both groups. The mean APACHE-HF score on admission was 3.8 points in patients with ischemic HF and 3.4 in those with nonischemic HF (P = 0.095). For the selected echocardiographic parameters presented in **TABLE 2**, a lower left ventricular ejection fraction (LVEF; 21%) was noted in patients with ischemic etiology compared with those with nonischemic etiology (27%).

Patients in both groups often presented signs of cardiogenic shock or low cardiac output syndrome, and for that reason, they often required inotropes and vasopressors (in many cases, 2 or more inotropes/vasopressors during hospitalization). Data on treatment and procedures are presented in **TABLE 3**. Considering the clinical characteristics of the patients, an intensive nonpharmacological therapy was used in both groups, including intraaortic balloon pump, hemodiafiltration,

TABLE 3 Treatment and procedures performed during hospitalization in patients with ischemic and nonischemic acute severe heart failure

Type of treatment/procedure	Acute severe HF		*P* value
	Ischemic (n = 61)	Nonischemic (n = 51)	
Dopamine	28 (46)	28 (56)	0.29
Dobutamine	23 (38)	26 (51)	0.16
Norepinephrine	17 (28)	18 (35)	0.36
Epinephrine	14 (23)	14 (27)	0.54
Milrinon	4 (7)	0 (0)	0.12
Infusion of 1 catecholamine	14 (23)	5 (10)	0.065
Infusion of 2 catecholamines	11 (18)	14 (27)	0.23
Infusion of 3 catecholamines	9 (15)	4 (8)	0.26
Infusion of 4 catecholamines	4 (7)	10 (20)	0.038
Hemodiafiltration	13 (21)	9 (18)	0.63
Mechanical ventilation	19 (31)	15 (29)	0.84
Parenteral nutrition	6 (10)	2 (4)	0.23
Blood transfusion	20 (33)	19 (37)	0.62
Pleurocentesis	7 (11)	7 (14)	0.72
Right heart catheterization	18 (30)	15 (29)	0.74
Coronary angiography	32 (52)	20 (39)	0.16
Coronary angioplasty	14 (23)	0 (0)	0.0001
Pacemaker implantation	2 (3)	0 (0)	0.50
ICD implantation	5 (8)	6 (12)	0.53
CRT-D implantation	3 (5)	3 (6)	1.0
IABP	19 (31)	10 (20)	0.17
Mechanical support of the heart	2 (3)	3 (6)	0.66
Heart valve surgery	0 (0)	9 (18)	0.002
Heart transplantation	2 (3)	0 (0)	0.50

Data are presented as number (percentage) of patients.

Abbreviations: see TABLES 1 and 2

TABLE 4 Adverse events during hospitalization in patients with ischemic and nonischemic acute severe heart failure

Adverse event	Acute severe HF		*P* value
	Ischemic (n = 61)	Nonischemic (n = 51)	
Cardiac arrest	8 (13)	7 (14)	0.92
Stroke	0 (0)	1 (2)	0.46
Myocardial infarction	1 (2)	0 (0)	1.0
Bleeding requiring transfusion	7 (11)	5 (10)	0.76
Pulmonary edema	7 (11)	3 (6)	0.34
Death	15 (25)	11 (22)	0.71

Data are presented as number (percentage) of patients.

Abbreviations: see TABLE 1

mechanical ventilation, and implantation of pacemakers or decompression of the pleural cavity, with no significant differences in the frequency of those procedures between the groups. As a direct consequence of the study design, patients with ischemic etiology were more often subject to coronary angiography, after which nearly half of them underwent percutaneous coronary intervention. Among patients with nonischemic HF with severe valvular heart disease, 40% (9 of 22 patients) underwent mitral, aortic, or tricuspid valve surgery. None of the patients had coronary artery bypass grafting. Of all 112 patients, 27 were referred for heart transplantation and 2 of them (ischemic group) required urgent procedure. The remaining 25 patients were referred for elective heart transplantation.

No significant differences in adverse events were found between patients with ischemic and nonischemic HF (TABLE 4). The in-hospital mortality rate was similar in both groups: 25% in the ischemic group and 22% in the nonischemic group. The median hospitalization time was similar in both groups and was less than a month (26 days). In both groups, discharged patients presented signs of HF in functional New York Heart Association (NYHA) classes I through IV. However, patients in the functional NYHA class III predominated, constituting 54% and 46% of the cases in the ischemic and nonischemic groups, respectively (TABLE 5).

The Kaplan–Meier analysis (FIGURE 2) showed that patients with HF of ischemic etiology died earlier after discharge compared with those with nonischemic etiology. However, the 12-month mortality rate was similar in both groups, reaching 51% and 44% counting from the admission date, and 34% and 28% counting from the discharge date, in patients with ischemic and nonischemic HF, respectively.

In multivariate models, only higher concentrations of NT-proBNP and lower sodium concentrations on admission were independent factors associated with a higher in-hospital mortality rate. For the 12-month mortality rate, independent predictors were higher NT-proBNP concentrations, history of renal failure, and concomitant chronic obstructive pulmonary disease on admission (TABLE 6).

DISCUSSION The prognosis of patients with HF is poor, particularly of those with severe and advanced HF and with acute clinical symptoms.[3,4] Our analysis of 112 patients from the COMMIT-AHF registry demonstrated that, independently of the cause of myocardial injury and despite the use of a broad spectrum of invasive and noninvasive treatments, the mortality of patients with acute severe HF remains high, and 1 in 4 patients dies during hospitalization. In our 12-month follow-up (starting from the admission date), death was reported for nearly half of the patients with ischemic HF (51%) and nonischemic HF (44%). Undoubtedly, high in-hospital and long-term mortality rates are associated with the clinical profile of the patients. According to established criteria, only patients with highly advanced HF symptoms, with multiorgan failure, and usually in the decompensation phase of HF, were included in the registry. It is a unique population in that there have been no such analyses

TABLE 5 Functional New York Heart Association class and pharmacological treatment at discharge in patients with ischemic and nonischemic acute severe heart failure

Variable		Acute severe HF		*P* value
		Ischemic (n = 46)	Nonischemic (n = 40)	
NYHA class	I	1 (2)	2 (5)	0.60
	II	16 (35)	17 (42)	0.46
	III	25 (54)	18 (45)	0.39
	IV	4 (9)	3 (8)	1.0
β-blocker		44 (96)	35 (88)	0.24
ACEI		28 (61)	21 (53)	0.43
ARB		3 (7)	1 (3)	0.62
MRA		40 (87)	31 (78)	0.25
Digoxin		23 (50)	23 (58)	0.49
Ivabradine		0 (0)	4 (10)	0.04
Oral diuretics		39 (85)	32 (80)	0.56
Sildenafil		3 (7)	4 (10)	0.70

Data are presented as number (percentage) of patients.

Abbreviations: ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; others, see **TABLE 1**

in Poland to date. Among the very few comparable reports, the CONSENSUS trial revealed that the 1-year mortality rate was 50% among the 253 patients with congestive HF in the functional NYHA class IV.[16] In the COMMIT-AHF registry, the ischemic etiology was linked with approximately half of the cases of acute severe HF hospitalized in the reference cardiac and cardiac surgery center and had no significant effect on outcome, both in-hospital and during 1 year after discharge. Interestingly, patients from the ischemic group died earlier after discharge compared with those from the nonischemic group, as revealed in the Kaplan–Meier survival curves.

Studies completed over several decades have not elucidated whether the etiology of HF affects prognosis. The majority of those studies involved patients with HF in different clinical conditions (functional NYHA classes II–IV), which hinders a comparative analysis with a group of patients with acute severe HF.[10-12,23] Bradley et al[18] demonstrated that in 3787 patients with a LVEF of 40% or lower and confirmed as having ischemic or nonischemic HF by coronary angiography (25% and 57% of the patients were in the NYHA classes III and IV, respectively), ischemic etiology of HF was an independent, unfavorable prognostic factor of 5-year mortality ($P < 0.0001$). Laurenco et al[15] demonstrated a higher in-hospital mortality of patients in the ischemic group compared with those in the nonischemic group (11.0% vs 4.0%, $P = 0.02$), although no significant differences in long-term survival were noted (70.0% vs 76.8%, $P = 0.258$).[15] On the other hand, the SOLVD trial,[24] involving over 6000 patients with symptomatic HF and a LVEF of 35% or lower, failed to demonstrate that the etiology of HF (ischemic vs nonischemic) affected total mortality, and the mortality was 18% in the 1-year follow-up.[24]

Of note, in our registry, patients with ischemic etiology of acute severe HF were on average 8 years older and were admitted in a more severe condition than patients with a nonischemic etiology. Not surprisingly, risk factors for coronary artery disease were more common in the ischemic group. Lourenco et al[15] analyzed a cohort of 286 patients with advanced HF in 2 groups: with ischemic acute HF (n = 109) and with nonischemic acute HF (n = 177). The clinical characteristics observed in this study in terms of the distribution of age and sex were similar to those in our analysis. In both groups, approximately 60% of patients showed multiorgan failure on admission and during hospitalization. Together with high NT-proBNP levels, this indicates a highly elevated risk of unfavorable clinical outcome, which was confirmed in the current and previous studies.[25-27]

Treatment methods used in patients with ischemic and nonischemic HF were different in terms of the intensity of pharmacological treatment and use of various invasive therapeutic procedures. Percutaneous coronary interventions were performed in some patients in the ischemic group. Patients in the nonischemic group were more intensely treated with intravenous inotropes and/or vasopressors. Considering the various hemodynamic profiles of patients (ie, dominating signs of fluid retention, low cardiac output or even cardiogenic shock), an appropriate strategy of intensive pharmacotherapy based on diuretics, vasodilators, inotropes, vasoconstrictors, and intraaortic balloon pump was used. Of note, 5 patients had left ventricular assist device implants and 2 others were referred for heart transplantation. The low prescription rate of angiotensin-converting-enzyme inhibitors and angiotensin receptor blockers at discharge resulted mainly from hypotension, hyperkalemia, renal failure or intolerance to this type of drugs.

Among the numerous analyzed parameters, the multivariate analysis demonstrated that higher NT-proBNP and lower sodium concentrations on admission were independent factors associated with in-hospital mortality. From a pathophysiological point of view, increased levels of natriuretic peptides reflect acute or chronic high pressures in cardiac chambers and abnormal sodium concentrations indicate cardiorenal syndrome. The significance of hyponatremia as an independent predictor of death was confirmed in numerous studies.[15,17,28,29] On the other hand, higher NT-proBNP concentrations on admission, chronic renal failure, and chronic obstructive pulmonary disease were independent risk factors of death during a 12-month follow-up, which was confirmed by other analyses.[30-32]

Our study has several limitations. Our population of the most severely ill patients with HF was treated in a single center with a full range of diagnostic and therapeutic facilities; therefore, the results of the therapy in a similar group in other

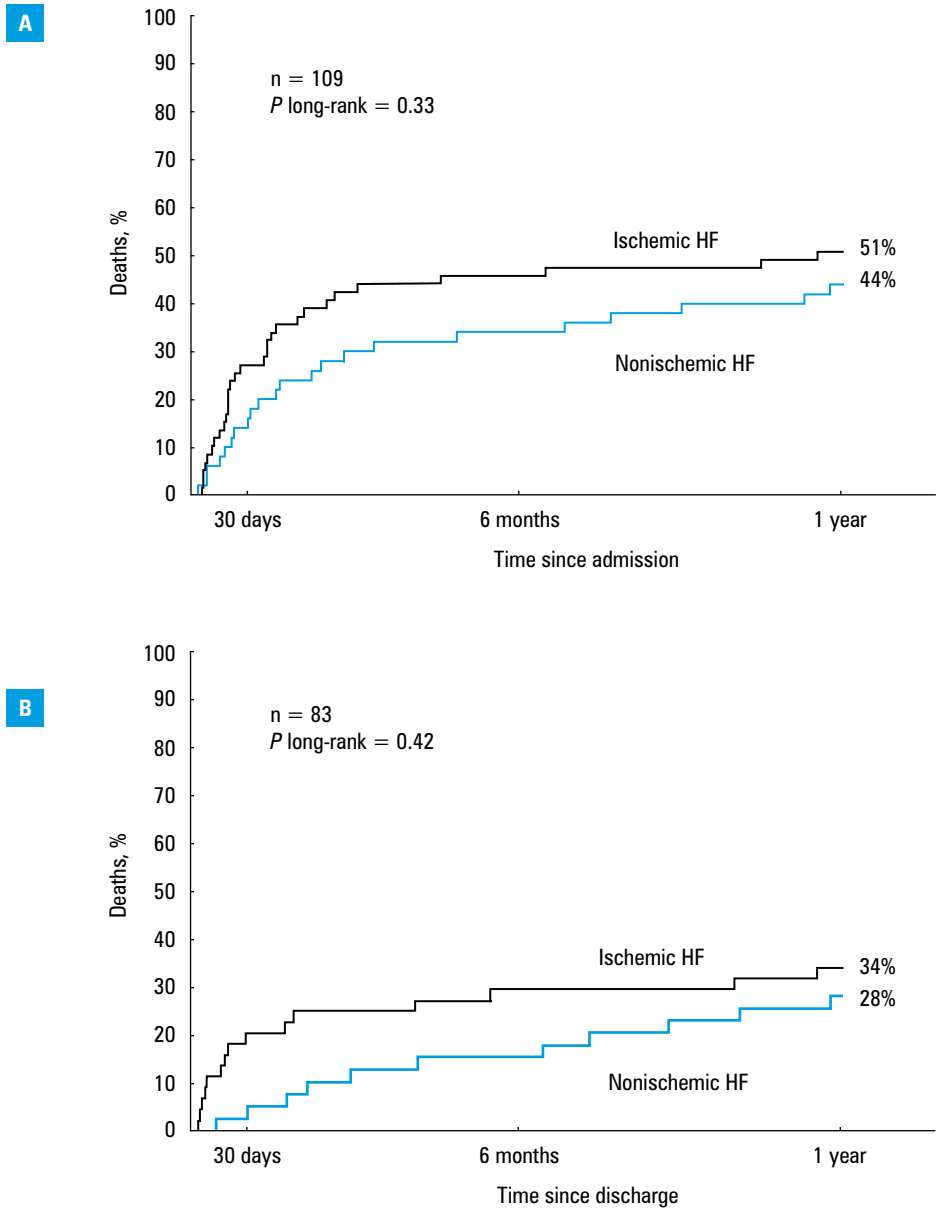

FIGURE 2 Total 12-month mortality (**A**) and 12-month mortality after discharge for patients who survived hospitalization (**B**)

TABLE 6 Independent predictors of death during hospitalization and 1-year mortality after discharge

Mortality during hospitalization	Wald's χ^2	Odds ratio (95% CI)	*P* value
NT-proBNP level on admission (per 5000-pg/ml increment)	4.89	1.31 (1.03–1.67)	0.027
Sodium level on admission (per 5-mmol/l increment)	4.15	0.68 (0.46–0.98)	0.042
12-month mortality after discharge	**Wald's statistics**	**Hazard ratio (95% CI)**	***P* value**
NT-proBNP on admission (per 5000 pg/ml increment)	12.5	1.42 (1.17–1.73)	0.0004
History of renal failure	8.6	3.58 (1.52–8.41)	0.0034
Chronic obstructive pulmonary disease	5.0	4.32 (1.20–15.5)	0.025

Abbreviations: see TABLE 2

centers may be different. Moreover, our study sample was quite small. That is why, we cannot draw a definitive conclusion as to whether acute severe HF of ischemic and nonischemic etiologies have similar outcomes.

Conclusions HF remains a challenge for modern healthcare systems and requires a comprehensive and multidisciplinary approach. Increasingly effective diagnostic and therapeutic methods undoubtedly result in extended life expectancies

but at the same time increase the number of patients with advanced severe HF. Complex medical care and modern therapeutic methods may efficiently delay progression of HF, although the development of a severe, terminal form of the disease seems inevitable. The analysis of data from the COMMIT-AHF registry indicates that the ischemic etiology, responsible for acute severe HF not related to ACS in approximately half of the patients hospitalized in the reference cardiac and cardiac surgery center, was not associated with a significantly worse prognosis compared with the nonischemic etiology of acute severe HF. However, after 1 year since admission for acute severe HF, only half of the patients are alive.

Contribution statement MO and MG conceived the idea for the study. MO and MJG contributed to the design of the research. MO and GS were involved in data collection. MO analyzed the data and edited the manuscript. All authors critically reviewed and approved the final version of the manuscript.

REFERENCES

1 Gąsior M, Pres D, Wojakowski W, et al. Causes of hospitalization and prognosis in patients with cardiovascular diseases. Secular trends in the years 2006–2014 according to the SILesian CARDiovascular (SILCARD) database. Pol Arch Med Wewn. 2016; 126: 754-762.

2 Ponikowski P, Voors A, Anker S, et al; Authors/Task Force Members. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016; 37: 2129-2200.

3 Ponikowski P, Anker SD, AlHabib KF, et al. Heart failure: preventing disease and death worldwide. ESC Heart Fail. 2014; 1: 4-25.

4 Lloyd-Jones DM, Larson MG, Leip EP, et al. Lifetime risk for developing congestive heart failure: the Framingham Heart Study. Circulation. 2002; 106: 3068-3072.

5 Zannad F, Mabazza A, Julliere Y, et al. Clinical profile, contemporary management and 1 year mortality in patients with severe acute heart failure syndrome. The EFICA study. Eur J Heart Fail. 2006; 8: 697-705.

6 Davison BA, Metra M, Senger S, et al. Patient journey after admission for acute heart failure: length of stay, 30-day readmission and 90-day mortality. Eur J Heart Fail. 2016; 18: 1041-1050.

7 Asanoa R, Kajimotob K, Okaa T. On behalf of the investigators of the Acute Decompensated Heart Failure Syndromes (ATTEND) registry. Association functional class IV symptoms at admission and clinical features with outcomes in patients hospitalized for acute heart failure syndromes. Int J Cardiol. 2016; 230: 585-591.

8 Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008. Eur Heart J. 2008: 29; 2388-2442.

9 Jessup M, Abraham WT, Casey DE, et al. 2009 Focused Update Incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults: A Report of the American College of Cardiology Foundation/American Heart Association. J Am Coll Cardiol. 2009; 53: e1-e90.

10 Nony P, Boissel JP, Girard P, et al. Relative efficacy of angiotensin converting enzyme inhibitors on mortality of patients with congestive heart failure: implications of randomized trials and role of the aetiology (ischaemic or nonischaemic) of heart failure. Eur Heart J. 1992; 13: 1101-1108.

11 CIBIS Investigators and Committees. A randomized trial of beta-blockade in heart failure. The Cardiac Insufficiency Bisoprolol Study (CIBIS). CIBIS Investigators and Committees. Circulation. 1994; 90: 1765-1773.

12 Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. JAMA. 1995; 273: 1450-1456.

13 Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK Investigators. Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock. N Engl J Med. 1999; 341: 625-634.

14 Juillièrea Y, Camboub JP, Bataillec V, et al. Heart failure in acute myocardial Infarction: a comparison between patients with or without heart failure criteria from the FAST-MI registry. Rev Esp Cardiol. 2012; 65: 326-333.

15 Lourenco C, Saraiva F, Martins H. Ischemic versus non-ischemic cardiomyopathy – are there differences in prognosis? Experience of an advanced heart failure center. Rev Port Cardiol. 2010; 30: 181-197.

16 CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). N Engl J Med. 1987; 316: 1429-1435.

17 Gheorghiade M, Rossi JS, Cotts W, et al. Characterization and prognostic value of persistent hyponatremia in patients with severe heart failure in the ESCAPE Trial. Arch Intern Med. 2007; 167: 1998-2005.

18 Køber L, Torp-Pedersen C. Increased mortality after dronedarone therapy for severe heart failure. N Engl J Med. 2008; 358: 2678-2687.

19 The Criteria Committee of the New York Heart Association. Diseases of the Heart and Blood Vessels: Nomenclature and Criteria for Diagnosis 6-th ed. Boston, Little Brown; 1964.

20 Gąsior M, Pyka Ł, Gorol J, et al. COnteMporary Modalities In Treatment of Heart Failure: a report from the COMMIT-HF registry. Kardiol Pol. 2016; 74: 523-538.

21 Bart BA, Shaw LK, McCants CB. Clinical determinants of mortality in patients with angiographically diagnosed ischemic or nonischemic cardiomyopathy. J Am Coll Cardiol. 1997; 30: 1002-1008.

22 Okazaki H, Shirakabe A, Hata N, et al. New scoring system (APACHE-HF) for predicting adverse outcomes in patients with acute heart failure: evaluation of the APACHE II and Modified APACHE II scoring systems. J Cardiol. 2014; 64: 441-449.

23 Franciosa JA, Wilen M, Ziesche S, Cohn JN. Survival in men with severe chronic left ventricular failure due to either coronary heart disease or idiopathic dilated cardiomyopathy. Am J Cardiol. 1983; 51: 831-836.

24 SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. N Engl J Med. 1991; 325: 293-302.

25 Fonarow GC, Peacock WF, Phillips CO, et al. Admission B-type natriuretic peptide levels and in-hospital mortality in acute decompensated heart failure. J Am Coll Cardiol. 2007; 49: 1943-1950.

26 Januzzi JL Jr, Rehman S, Mueller T, et al. Importance of biomarkers for long-term mortality prediction in acutely dyspneic patients. Clin Chem. 2010; 56: 1814-1821.

27 Harrison A, Morrison LK, Krishnaswamy P, et al. B-type natriuretic peptide predicts future cardiac events in patients presenting to the emergency department with dyspnea. Ann Emerg Med. 2002; 39: 131-138.

28 Bettari L, Fiuzat M, Shaw LK. Hyponatremia and long-term outcomes in chronic heart failure – an observational study from the Duke Databank for Cardiovascular Diseases. J Card Fail. 2012; 18: 74-81.

29 Kapłon-Cieślicka A, Ozierański K, Balsam P, et al. Clinical characteristics and 1-year outcome of hyponatremic patients hospitalized for heart failure. Pol Arch Med Wewn. 2015; 125: 120-131.

30 Hawkins NM, Petrie MC, Pardeep S, et al. Heart failure and chronic obstructive pulmonary disease: diagnostic pitfalls and epidemiology. Eur J Heart Fail. 2009; 11: 130-139.

31 Sean AV, Khosla A, Levin A. Chronic kidney disease, heart failure and anemia. Can J Cardiol. 2008; 24 (Suppl B): 22B-24B.

32 Ozierański K, Balsam P, Tymińska A, et al. Heart failure in elderly patients: differences in clinical characteristics and predictors of 1-year outcome in the Polish ESC-HF Long-Term Registry. Pol Arch Med Wewn. 2016; 126: 502-513.