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ORIGINAL PAPER

Characteristics, management modalities and outcome in chronic systolic heart failure patients treated in tertiary care centers: results from the EVIdence based TreAtment in Heart Failure (EVITA-HF) registry

W. von Scheidt · C. Zugck · M. Pauschinger · R. Hambrecht · O. Bruder · A. Hartmann · M. Rauchhaus · R. Zahn · J. Brachmann · U. Tebbe · T. Neumann · R. H. Strasser · M. Böhm · S. Störk · M. Hochadel · P. Heidemann · J. Senges

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Abstract
Background Limited data exist regarding baseline characteristics and management of heart failure with reduced ejection fraction (EF) in tertiary care facilities.
Methods EVITA-HF comprises web-based case report data on demography, comorbidities, diagnostic and therapy measures, quality of life, adverse events and 1-year follow-up of patients hospitalized for chronic heart failure and an ejection fraction of less than 40 %.
Results Between February 2009 and June 2011, a total of 1,853 consecutive, hospitalized patients (pts) were included in 16 centers in Germany. Mean age was 70 years, 76 % were male. Median EF was 30 %, and 63 % were in NYHA III/IV. Ischemic cardiomyopathy was present in 56 %, history of hypertension in 76 %, diabetes in 39 %, impaired renal function in 33 %, thyroid dysfunction in 12 %, and malignoma in 7 %. Sixty-eight percent of pts had a non-elective admission. Rhythm was sinus/atrial fibrillation or flutter/pacemaker in 64, 28 and 11 %, respectively. Median heart rate amounted to 80 bpm, median blood pressure to 122/74 mmHg. LBBB was present in 26 % of non-pacemaker pts. Eighteen percent had an ICD or CRT-D. Medication (admission vs. discharge) consisted of ACEI or ARB in 73 vs. 88 %, β-blocker in 71 vs. 89 %, mineral corticosteroid receptor antagonist (MRA) in 32 vs. 57 %, diuretics in 68 vs. 83 % ($p < 0.001$ for each). Forty-two percent of pts received a specific treatment procedure beyond pharmacotherapy, of

W. von Scheidt (✉) · P. Heidemann
I.Medizinische Klinik, Herzzentrum Augsburg-Schwaben, Klinikum Augsburg, Stenglinstr. 2, 86156 Augsburg, Germany
e-mail: wolfgang.scheidt@klinikum-augsburg.de

C. Zugck
Medizinische Klinik III, Kardiologie, Angiologie, Pulmonologie, Universitätsklinikum Heidelberg, Heidelberg, Germany

M. Pauschinger
Schwerpunkt Kardiologie, Med. Klinik 8, Klinikum Nürnberg Süd, Nürnberg, Germany

R. Hambrecht
Klinik für Kardiologie und Angiologie, Klinikum Links der Weser, gGmbH, Bremen, Germany

O. Bruder
Klinik für Kardiologie und Angiologie, Elisabeth-Krankenhaus Essen GmbH, Essen, Germany

A. Hartmann
Klinik für Kardiologie, Angiologie und Internistische Intensivmedizin, Klinikum St. Georg, Leipzig, Germany

M. Rauchhaus
Zentrum für Innere Medizin, Universitäres Herzzentrum Rostock, Universitätsklinikum Rostock, Rostock, Germany

R. Zahn
Medizinische Klinik B, Klinikum Ludwigshafen, Ludwigshafen, Germany

J. Brachmann
II. Medizinische Klinik, Klinikum Coburg, Coburg, Germany

U. Tebbe
Klinik für Kardiologie, Angiologie, Intensivmedizin, Klinikum Lippe-Detmold, Detmold, Germany

T. Neumann
Klinik für Kardiologie, Westdeutsches Herzzentrum, Universitätsklinikum Essen, Essen, Germany

R. H. Strasser
Klinik für Innere Medizin und Kardiologie, Herzzentrum Dresden, Technische Universität Dresden, Dresden, Germany

these 48 % revascularization, 39 % device therapy, 14 % electrical cardioversion, 5 % ablation procedures, 9 % valvular procedures, 6 % iv inotropes, 1.8 % IABP or LVAD implantation. At discharge, 33 % of survivors had ICD- or CRT-D implants. One-year mortality amounted to 16.8 %, and death or rehospitalization to 56 %. NYHA class III/IV was found in 30 % ($p < 0.001$ vs. index admission), general health status was improved in 45 % and unchanged in 36 % of patients. Eighty-five percent of pts took ACEI or ARB, 86 % β-blockers, 47 % MRA, and 78 % diuretics ($p < 0.001$ vs. index discharge for all).

Conclusion Patients with chronic heart failure and low ejection fraction represent an elderly and multimorbid population. While hospitalized, they experience a significant optimization of prognosis-relevant medication, revascularization and device therapy. After 1 year, mortality is moderate; drug adherence is high and NYHA status favourable. The EVITA-HF registry is able to reflect coherently the real-world management, efforts and follow-up in heart failure pts managed in tertiary care facilities.

Keywords Heart failure · Registry · Hospitalization · Treatment · Device therapy

Introduction

Heart failure is a frequent, serious and expensive syndrome; 1.5–2 % of Europeans suffer from overt (NYHA II–IV) heart failure, and another 1.5–2 % have asymptomatic (NYHA I) ventricular dysfunction [1]. The prevalence is rising because of the increasing life expectancy of the population and the increasing number of long-term survivors of large myocardial infarctions. On average, the annual mortality rate amounts to 12.5 %, and risk of death or rehospitalization to 40 % [1]. Almost 5 % of hospital admissions are due to heart failure, and about 2 % of health care costs in industrialized countries are caused by heart failure, mainly driven by hospital admissions [1]. Optimal, guideline-recommended management of heart failure may reduce adverse events and possibly the economic burden of this challenging disease.

M. Böhm
Innere Medizin III, Kardiologie, Angiologie, Intern. Intensivmedizin, Universitätsklinikum des Saarlandes, Homburg/Saar, Germany

S. Störk
Deutsches Zentrum für Herzinsuffizienz, Universität Würzburg, Würzburg, Germany

M. Hochadel · J. Senges
Stiftung Institut für Herzinfarktforschung Ludwigshafen, Ludwigshafen, Germany

Current treatment strategies are based on randomized clinical trials (RCTs). It is still unclear, whether these results can be translated into real-world situations with unselected, multimorbid patients. While RCTs evaluate the efficacy of a certain treatment modality under "experimental" conditions, registries evaluate the clinical effectiveness, i.e., the transferability and the transfer of RCT-generated data into clinical practice. Therefore, information from heart failure patients managed in real life is another important element of evidence complementing data derived from RCTs.

This assessment can be achieved by a registry or a heart failure program. Registries, e.g., the ESC-HF-Pilot survey, the Euro Heart Failure Survey, the Swedish Heart Failure Registry, or the Italian Heart Failure Registry, gather and document information from a real life heart failure population [2–7]. Programs, e.g., Adhere, Optimize-HF, Improve-HF, HF-Action, intend to optimize a given situation by specific, pre-defined interventions [8–11]. These registries and programs, however, have certain shortcomings like selective instead of consecutive patient inclusion, heterogeneous populations with de novo or worsening heart failure, inclusion of both, systolic and diastolic heart failure, limited parameters checked, and mostly without or only very short-term follow-up.

The EVIdence based TreAtment in Heart Failure (EVITA-HF) registry was created to focus on a well-defined patient population covered by clear guideline recommendations, well-defined tertiary care heart centers, consecutive patient inclusion, a comprehensive assessment and a 1-year follow-up period. EVITA-HF evaluates demography, comorbidities, diagnostic and therapeutic measures, quality of life, adverse events during an index hospital stay or an index outpatient visit, and at a 1-year follow-up of patients treated for chronic heart failure and an ejection fraction below 40 %.

Here, we report on the characteristics, management modalities and follow-up of the hospitalized patients ($n = 1{,}853$) included in the first evaluation cohort (phase I cohort, January 2009 until June 2011) of EVITA-HF.

Methods

EVITA-HF was set up as a web-based registry using an electronic case report form (eCRF). Inclusion criteria were chronic heart failure since at least 3 months, and a documented ejection fraction of 40 % or less. Exclusion criteria were age younger than 18 years or missing consent of the patient. Patients were hospitalized (index hospitalization) in 1 of the 16 participating tertiary care heart centers. All centers offer the whole spectrum of diagnostic and treatment modalities in heart failure. Patients had to be included consecutively. Data management was

performed at the Institut für Herzinfarktforschung Ludwigshafen at the University of Heidelberg, Germany. The registry received approval by the institutional ethics committees. Each patient gave an informed written consent. The registry was supported by unrestricted grants from Medtronic, Novartis and Sanofi Aventis.

The eCRF collected baseline information on demographics, presentation, medical history, clinical evaluation and diagnostics, pharmacological treatment and non-pharmacological interventions, quality of life, and adverse events during index hospitalization. In a subset of participating centers, a representative one-year follow-up was performed by phone call and/or contact by the center or general practitioner. Thereby, information was obtained on vital status, adverse events and interventions since index discharge, current health status, pharmacological treatment, and quality of life. The follow-up information of survivors was regarded as 1-year status if obtained between 300 and 450 days after index discharge.

EVITA-HF was started in January 2009. As of June 2011, 1,853 hospitalized patients had been included. The 1-year follow-up as of February 2013 included 1,410 patients.

Statistical analysis

The patient population is described by absolute numbers and percentages with respect to categorical variables and medians with quartiles for continuous variables. The distribution of nominal categorical variables was compared between patient groups by Pearson Chi- square test and Mann–Whitney test, as appropriate. Prescription rates of medication and other binary states at discharge vs. admission and at 1-year FU versus discharge are shown for patients with documented information on both occasions and compared by McNemar's test.

One-year survival and event-free survival after index discharge were calculated by the product-limit method and demonstrated by Kaplan–Meier curves.

All tests were performed two-sided and p values ≤ 0.05 were considered significant. The computations were performed using the SAS system (release 9.3, SAS Institute, Inc., Cary, North Carolina).

Results

Baseline demographical data and comorbidities (Table 1)

Median age was 70 years; 24 % of patients were female. The two most frequent etiologies for heart failure were ischemic cardiomyopathy (CMP) in 56 % and dilated CMP in 27 %. A former hospitalization for heart failure was known in 65 % of pts, the first hospitalization being 4 years ago on median. Almost 40 % of pts had a history of myocardial infarction and of revascularization. An implanted device was present in 24 % of pts, in 18 % an ICD or CRT-D. History of hypertension was present in 76 % of pts, diabetes mellitus in 39 %, history of chronic kidney disease in 33 % (creatinine >1.5 mg/dl in 26 % of pts), COPD in 15 %, thyroid dysfunction in 12 %, peripheral artery disease in 10 %, h/o stroke in 9 %, active malignoma in 7 %. Reason for admission was non-elective (non-scheduled) in 68 %, and elective (scheduled) in 32 %. In-hospital mortality amounted to 2.1 %, median length of stay was 9 days (IQR 5–15).

Table 1 Baseline demographics and comorbidities of 1,853 EVITA-HF patients

n	1,853
Age, years, median (IQR)	70 (61–77)
Female, % (*n*)	24.3 (450/1,853)
Ischemic CMP, % (*n*)	55.6 (1,025/1,845)
Dilated CMP, % (*n*)	27.0 (499/1,845)
Heart failure for >1 year, % (*n*)	63.7 (1,120/1,758)
Previously hospitalized for heart failure, % (*n*)	64.6 (1,192/1,844)
Years since first hospitalization for heart failure, median (IQR)	4 (1–10)
H/o myocardial infarction, % (*n*)	40.0 (740/1,849)
H/o revascularization, PCI and/or CABG, % (*n*)	38.2 (703/1,841)
H/o PCI, % (*n*)	29.8 (548/1,841)
H/o CABG, % (*n*)	17.2 (316/1,841)
H/o valve surgery, % (*n*)	4.1 (75/1,839)
H/o atrial fibrillation, % (*n*)	39.2 (726/1,850)
H/o cardioversion, % (*n*)	9.4 (172/1,839)
H/o stroke, % (*n*)	9.3 (172/1,849)
Peripheral artery disease, % (*n*)	10.2 (188/1,854)
Hypertension, % (*n*)	75.8 (1,403/1,852)
COPD, % (*n*)	14.6 (270/1,852)
Chronic kidney disease, % (*n*)	33.4 (618/1,851)
Diabetes mellitus, % (*n*)	38.7 (716/1,852)
Thyroid dysfunction, % (*n*)	12.1 (222/1,850)
Active malignoma, % (*n*)	6.8 (126/1,851)
Implanted device (ICD, CRT-D, CRT-P, PM), % (*n*)	23.5 (433/1,846)

H/o history of, *CMP* cardiomyopathy, *PCI* percutaneous catheter intervention, *CABG* coronary artery bypass graft, *COPD* chronic obstructive pulmonary disease

Clinical and technical findings at index presentation (Table 2)

Median BMI amounted to 27.1 kg/m^2. Blood pressure amounted to 122/74 mmHg, and heart rate to 80 bpm.

Table 2 Clinical and technical findings at presentation

n	1,853
BMI, kg/m^2, median (IQR)	27.1 (24.3–30.9)
Systolic BP, mmHg, median (IQR)	122 (110–140)
Diastolic BP, mmHg, median (IQR)	75 (65–80)
Heart rate, bpm, median (IQR)	80 (68–95)
NYHA class, % (*n*)	
I	8.2 (152/1,846)
II	28.7 (530/1,846)
III	44.8 (827/1,846)
IV	18.3 (337/1,846)
Rhythm, % (*n*)	
Atrial fibrillation/flutter	28.1 (520/1,849)
Sinus rhythm	63.8 (1,179/1,849)
Paced	11.2 (207/1,849)
QRS width, ms, median (IQR)	110 (92–140)
LBBB, % (*n*) (PM pts excluded)	26.4 (431/1,634)
Ejection fraction, median (IQR)	30 (25–35)
Ejection fraction ≤30 %, % (*n*)	60.8 (1,127/1,853)
Mitral regurgitation present, % (*n*)	53.5 (991/1,851)
Pulmonary hypertension present, % (*n*)	29.6 (470/1,589)

Table 3 Laboratory data

n	1,853
Median (IQR)	
Hemoglobin, g/dl	13.4 (11.9–14.5)
Creatinine, mg/dl	1.2 (1.0–1.6)
GFR (MDRD formula), ml/min	60.3 (43.4–77.3)
Sodium, mmol/l	139 (136–141)
Potassium, mmol/l	4.2 (3.9–4.6)
C-reactive protein, mg/dl	1.1 (0.5–3.4)
Cholesterol, mg/dl	169 (135–201)
NT-pro BNP, pg/ml (measured in 52 % of pts)	4,330 (1,750–9,408)

NYHA classes were 8 % class I, 29 % in class II, 45 % in class III, and 18 % in class IV. Heart rhythm was sinus in 64 %, atrial fibrillation or flutter in 28 %, and pacemaker stimulation in 11 %. Median QRS width was 110 ms, left bundle branch block was found in 26 % of pts. Median ejection fraction amounted to 30 %. Mitral regurgitation was present in 53 %, pulmonary hypertension in 30 % of pts.

Laboratory data (Table 3)

Median values for hemoglobin (13.4 g/dl), creatinine (1.2 mg/dl), GFR (60 ml/min, MDRD formula), sodium (139 mmol/l), potassium (4.2 mmol/l) and cholesterol (169 mg/dl) were in the normal or near-normal range. Median C-reactive protein was elevated with 1.1 mg/dl. NT-proBNP (measured in 52 % of pts) amounted to 4,330 pg/ml.

Table 4 Medication and device status at admission and discharge in patients discharged alive

	Admission	Discharge	*p* value
n	1,803	1,803	
ACEI/ARB	73.0%	89.6%	<0.001
β-Blocker	71.0%	90.4%	<0.001
MRA	31.8%	58.2%	<0.001
Diuretics	68.0%	83.6%	<0.001
Digitalis	15.5%	20.0%	<0.001
Amiodarone	9.0%	14.2%	<0.001
Ivabradin	1.0%	1.0%	1.0
ASS	50.4%	62.1%	<0.001
ADP-antagonists	14.6%	28.1%	<0.001
Oral anticoagulants	24.4%	30.9%	<0.001
Statins	48.8%	64.7%	<0.001
Oral antidiabetics	17.3%	17.3%	0.92
Insulin	14.3%	15.2%	0.049
Antidepressants	6.7%	6.8%	0.78
Implanted device	23.2%	39.4%	<0.001
ICD or CRT-D	17.8%	32.9%	<0.001

McNemar test used

Medication (Table 4)

At admission, pts were treated with ACE inhibitors (ACEI) or angiotensin receptor blockers (ARB), β-blockers and mineral corticosteroid receptor antagonists (MRA) in 73, 71 and 32 %, respectively. Diuretics were taken by 68 % of pts. Treatment with digitalis was found in 16 % of pts, amiodarone in 9 %. Ivabradin was used very rarely (1 %). Half of the pts were taking aspirin, 15 % ADP-antagonists, and 24 % were anticoagulated. Statins were used in 49 %, oral antidiabetics in 17 %, insulin in 14 %, and antidepressant drugs in 7 %. The discharge medication differed significantly from the medication at admission. The number of pts treated with ACEI/ARB, β-blockers, mineral corticosteroid receptor antagonists and diuretics increased significantly, Table 4. At discharge, 90 % of pts received ACEI/ARB, 90 % β-blockers, 58 % MRA, and 84 % diuretics ($p < 0.001$ vs. admission for each). The use of digitalis, amiodarone, aspirin, ADP-antagonists, oral anticoagulants, and statins also increased significantly ($p < 0.001$).

Non-pharmacological treatment (Fig. 1)

In 768 of 1,843 pts (42 %), 940 specific, i.e., non-pharmacological procedures were performed: 369 (48 % of the 768 pts) revascularization procedures (PCI 82 %, CABG 18 %), 297 (39 % of pts) device therapies (ICD 62 %,

CRT-D 28 %, CRT-P 3 %, pacemaker 7 %), 111 (14 % of pts) cardioversions due to atrial fibrillation or flutter, 36 (5 % of pts) ablation procedures, 68 (9 %) valvular procedures, 14 (1.8 %) IABP or implantation of an assist device, and 45 (6 %) iv inotropes. The device status changed significantly from admission to discharge. At admission, 18 % of hospitalized pts had an ICD or CRT-D implanted, at discharge 33 % ($p < 0.001$; Table 4).

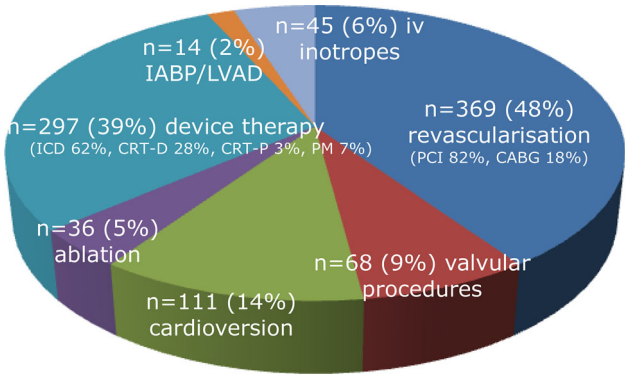

Fig. 1 In 42 % of patients (768/1,843), 940 specific procedures (1.22 per patient) beyond oral heart failure medication were performed during the index hospitalization. *N* absolute number of procedures, % refers to the 768 patients

One-year follow-up (Tables 5, 6; Fig. 2)

One-year mortality was 16.8 %, death or rehospitalization amounted to 56 %. Death, myocardial infarction or stroke occurred in 18 %. The NYHA status in survivors was significantly improved at follow-up compared to index admission: 30 % in NYHA class III or IV vs. 58 % at baseline ($p < 0.0001$). During 1-year follow-up, 2.5 % of pts underwent PCI, 1.5 % bypass surgery, 2.4 % valvular surgery or intervention, 1.6 % cardioversion, and 1.7 % ablation procedures. Compared to baseline, general health status, as assessed by the visual analogue scale, was improved in 45 % and unchanged in 36 % of subjects. 42 % had an ICD or CRT device implanted at 1-year follow-up. 6 % of pts had received an ICD or CRT implantation during the 1-year follow-up.

Adherence to medication after 1 year was significantly lower compared to discharge, but remained high with 85 % (−7 % compared to discharge) of patients taking ACEI/ARB, 86 % (−6 %) β-blockers, 47 % (−13 %) mineral

Table 5 Demographics and findings in patients with complete 1-year follow-up (FU)

	Baseline	Follow-up	*p* value
Participating in FU, (*n*)		1,433	
FU available, (*n*)		1,410	
FU, months, median (IQR)		12.0 (10.8–12.9)	
1-year mortality (KM)		16.8 %	
Death or rehospitalization (KM)		55.9 %	
Death, myocardial infarction or stroke (KM)		18.3 %	
FU survivors, (*n*)		1,152	
Rehospitalization, % (*n*)		45.2 (433/957)	
NYHA status, % (*n*)			
I/II	42.2 (310/735)	70.3 (517/735)	<0.001
III/IV	57.8 (425/735)	29.7 (218/735)	<0.001
Procedures during FU, % (*n*)			
PCI		2.5 (24/964)	
CABG		1.5 (14/964)	
Valvular		2.4 (23/897)	
Cardioversion		1.6 (15/964)	
Ablation		1.8 (17/964)	
Implanted device, % (*n*)	41.4 (474/1,146)	48.4 (555/1,146)	<0.001
ICD or CRT-D, % (*n*)	35.8 (410/1,146)	41.8 (479/1,146)	<0.001
Planned HTX, % (*n*)		2.7 (23/852)	
General health status (VAS), % (*n*)			
Improved		44.8 (360/803)	
Unchanged		35.7 (287/803)	
Worse		19.4 (156/803)	

KM Kaplan–Meier estimates at 366 days after discharge, *VAS* visual analogue scale, *HTX* heart transplantation

Table 6 Medication at 1-year follow-up

	Discharge	Follow-up	*p* value
n (alive at 1 year)	857	857	
ACEI/ARB	91.4%	84.5%	<0.001
β-Blocker	91.8%	85.9%	<0.001
MRA	59.9%	47.0%	<0.001
Diuretics	83.3%	77.7%	<0.001
Digitalis	17.0%	18.2%	0.25
Amiodarone	15.6%	14.5%	0.31
Ivabradin	1.2%	0.8%	0.37
ASS	61.4%	53.9%	<0.001
ADP-antagonists	26.2%	13.7%	<0.001
Oral anticoagulants	32.9%	34.2%	0.40
Statins	65.0%	59.9%	<0.001
Oral antidiabetics	17.9%	19.2%	0.19
Insulin	15.4%	14.0%	0.12
Antidepressants	5.2%	6.0%	0.34

McNemar test, generalized estimating equations

ACEI angiotensin-converting enzyme inhibitors, *ARB* angiotensin receptor blockers, *MRA* mineral corticosteroid receptor antagonist

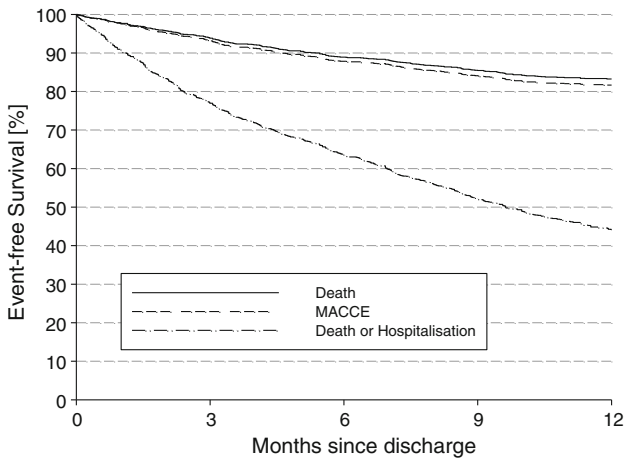

Fig. 2 Kaplan–Meier curves for all cause death, MACCE (death, myocardial infarction, stroke), and combined endpoint of death or rehospitalization during the 1-year follow-up

corticosteroid receptor antagonist, and 78 % (−6 %) diuretics ($p < 0.001$ vs. baseline for all, Table 6).

Discussion

The EVITA-HF registry coherently reflects the contemporary real-world management of chronic heart failure patients with reduced EF treated in tertiary care heart center facilities. The EVITA-HF sample is typical for heart failure, representing an elderly and multimorbid population. During hospital stay these patients received a remarkable optimization of the prognosis-relevant medication. Revascularization and device therapy were the leading specific non-pharmacological procedures performed. At discharge, guideline-recommended drug- and device-therapy was significantly improved. The 1-year follow-up showed a moderate mortality rate, a high drug adherence and a sustained improvement of the NYHA status.

Heart failure registries

There are numerous observational heart failure registries or surveys [2–7, 12–21], heart failure programs [8, 11, 22, 23, 24, 25] and large administrative data sets [26] with published results. However, they differ in the populations included and the clinical situations studied, making comparisons difficult. Most registries included chronic (outpatient) and acute (hospitalized) heart failure patients with both, de novo or worsening heart failure [2, 3, 6, 7, 14]. All except one [11] registry or program included systolic and diastolic heart failure patients [2–8, 12–19, 22, 23, 24]. Thus, a heterogeneous spectrum of heart failure patients is represented in these registries. Follow-up data are sparse and limited to mortality and hospitalization, thus lacking information about NYHA status, drug adherence, or device status [3–5, 9, 23]. The EVITA-HF registry aimed at addressing a very homogeneous, well-defined group of heart failure patients, for which unequivocal guideline recommendations are available, i.e., chronic systolic heart failure with an ejection fraction of 40 % or less. This allows to investigate how institutions may close the gap between guideline recommendations and the real-world setting.

Baseline demographics and clinical findings

Baseline demographics in EVITA-HF reveal a median age of 70 years in hospitalized patients, which is comparable to the average age of 69–73 years reported by other registries [2–9], but differs markedly from the median age of 60–65 years in seven heart failure, landmark randomized controlled trials (RCTs) [27–34]. Despite different inclusion criteria, other heart failure registries revealed similar proportions as those of EVITA-HF regarding ischemic etiology, comorbidities and h/o atrial fibrillation [2–4, 6–9]. Multimorbidity in heart failure patients included in registries is much more prevalent than in RCTs, owing to the higher age and the less restrictive exclusion criteria. Admission may be driven by heart failure, or by another condition (e.g., ischemia, atrial fibrillation or diabetes) with HF being a "comorbidity" (as in Euro Heart Failure Survey, [4, 5]). In the scenario of multimorbidity, heart failure is one condition only among a variety of others determining symptoms, mortality and rehospitalization. In

addition, with an increasing number of accompanying diseases, more contraindications to recommended therapies have to be observed (e.g. renal dysfunction and MRA, very old age or frailty and ICD), as well as more drug interactions. Thus, the penetrance of guideline recommendations in real life has other potential limits than suboptimal patient management solely.

SBP in our population was well controlled and considerably lower than in other registries (122 mmHg vs. 129–144 mmHg, [2, 3, 7, 8, 22]), probably explained by the higher drug adherence. Whether this translates into a better outcome is debatable recognizing the U-shaped distribution between systolic blood pressure and mortality [35]. However, in the study of Lee et al., the quintile of systolic heart failure patients (ejection fraction of less than 40 %) with the lowest mortality had systolic blood pressure values between 120 and 139 mmHg [35]. Current guidelines recommend a target heart rate of less than 70 bpm at rest, as higher heart rate is a risk factor in heart failure with reduced EF [36]. Although in EVITA-HF, median heart rate was lower than in other registries (80 vs. 82–89 bpm, [2, 3, 7, 22]), only 27 % of our patients had a heart rate of 70 bpm or less. Thus, heart rate seems to be an underrecognized target for improvement. This should be achieved by either uptitrating the dosage of β-blocker, or adding ivabradin in patients with sinus rhythm [1, 33, 36].

Medication on admission and discharge

At discharge, the percentage of pts treated with ACEI or ARB/BB/MRA was increased highly significant in EVITA-HF to 90 %/90 %/58 %, which is clearly superior to five other registries reporting data from pts with reduced EF. In these populations 68–86 %/41–87 %/21–38 % received ACEI or ARB/BB/MRA, respectively at discharge [5, 6, 8, 15, 22]. The most recent ESC-HF-Pilot registry reports a prevalence for the discharge medication of 78 %/81 %/54 % for the three drug classes, respectively [2, 3]. 20–30 % of patients reveal renal dysfunction as a relative or absolute contraindication for use of MRA. To which extent non-use is due to contraindications or side effects, or due to suboptimal transfer of recommendations remains an unresolved issue and requires further analysis. Use of diuretics increases considerably during hospital stay in all registries and amounts to 82–95 % of pts at discharge [2, 3, 5–8]. Prescription of digitalis is rare in EVITA-HF compared to other registries with 20 vs. 30–43 % [5, 6, 8, 22]. Data for the use of amiodarone are missing in nearly all registries, which is noteworthy, since 14 % of our pts were treated with this drug. Anticoagulation is not well documented in HF registries. For the Adhere International Registry, a considerable underuse of anticoagulation in HF pts with atrial fibrillation was reported [38]. The 30 % rate of anticoagulation in our registry corresponds very well to the 34 % rate of pts with a history of atrial fibrillation or flutter.

A very high prevalence of prognostically relevant drugs at discharge is documented in EVITA-HF. This may explain the very high follow-up drug adherence at 1 year. For ACEI/ARB and for BB the rate of discontinuation over 1 year is 7 and 6 % only, indicating a very stringent compliance of the pts. For MRA only a discontinuation rate of 13 % is noticed. The reasons denote further evaluation. It may reflect the fact that MRA therapy is more complex, most probably due to side effects or unstable renal function leading to discontinuation of the drug. There are reports doubting about a net clinical benefit of MRAs in real life HF pts [14, 37].

Specific treatment procedures during hospital stay

A unique feature of EVITA-HF is the evaluation of specific, non-pharmacological treatment modalities during the hospital stay. In nearly half of the pts more than recompensation or optimization of medical treatment was performed. Leading procedures are revascularization (in most cases PCI) and device implantation in 48 and 39 % of patients receiving more than drug treatment (20 and 16 % of the whole cohort). An EF of 35 % or less was present in 75 % of our pts. Primarily these patients are potential candidates for ICD implantation according to current guidelines [1]. About 60 % of non-ICD patients in our population did not have an indication according to the guidelines, or had a contraindication such as terminal heart failure or frailty.

The high number of specific procedures performed during one index hospital stay reflects the modern treatment modalities in heart failure, focusing more and more on intervention- and device-based therapies in patients receiving near optimal pharmacotherapy already. The indication for an ICD or CRT-D, ablation procedures or a valvular intervention may be found and for the first time discussed during the index admission, but performed later on. This is reflected by the increasing number of pts with an ICD or CRT-D from admission (18 %) to discharge (33 %) to the 1-year follow-up (42 %), and another 10 % of pts receiving revascularization, valvular or electrophysiological procedures between discharge and 1-year follow-up. The penetrance for guideline-recommended ICD therapy in published registries is far from being optimal. In the ESC-HF Pilot survey 33 % of potential candidates did have an ICD [2, 3]. Twenty-one percent of pts hospitalized for worsening heart failure in the IN-HF registry are carrier of an ICD, and 12 % in S-HFR patients with an EF of less than 40 % [6, 7]. Of note, only 4 % of patients included in the randomized, controlled SHIFT study (inclusion criterion EF 35 % or less) had an ICD or

CRT device [33]. Given the prevalence of 23-36 % of a LBBB in our registry and others [2, 3, 6] CRT or CRT-D is even more underutilized as a guideline-recommended device therapy and needs improvement.

One-year follow-up

Detailed 1-year follow-up data beyond mortality and morbidity is another unique feature of EVITA-HF. 45 % of pts report an improved general health status compared to baseline, only 19 % deteriorated. The NYHA status is persistently improved with 30 % of pts only remaining in NYHA III or IV, compared to 58 % at index admission. Most probably the high drug compliance is at least one reason for the lasting stabilization of this population. Nevertheless, the rate of rehospitalization is 45 % at 1 year. This is comparable to the 44 %in the ESC-HF-Pilot survey [2, 3]. Other reported rehospitalization rates are higher with 25–36 % in a 4–12 week follow-up [5, 9, 24]. Almost 17 % of our patients received a specific procedure during follow-up (7 % device implantation, 9.8 % non-device procedure, e.g. PCI or CABG, Table 5). The specific reasons for rehospitalization in the other 28 % of our population, e.g. decompensation, comorbidities or independent causes require a further detailed analysis. In-hospital mortality and mortality rates during follow-up are available for several registries. In-hospital mortality of 2.1 % in EVITA-HF compares favourably with 2.5–4.1 % in the OPTIMIZE-HF population with reduced EF [9], 3.2 % in Adhere [8], and 3.3 % in the US-National Inpatient Sample 2009 [26]. The Euro Heart Failure Survey reported in 2003 a 3-month mortality of 13 % [5]. The 1-year mortality in EVITA-HF amounts to 16.8 %. In ESC-HF-Pilot the 1-year mortality for hospitalized patients with reduced EF was 18.6 % [2]. In S-HFR the 1-year mortality in 18.852 patients (both hospitalized and outpatients) with an EF of 40 % or less and a median age of 71 years amounted to 17 % [14]. Independent from the specific causes of mortality, which will be analyzed separately, a 1-year mortality of 16–19 % in an elderly population suffering from moderate to severe systolic heart failure is most probably what we can obtain realistically in a real-world situation even with optimal medical and non-medical therapy.

Limitations

We restricted our inclusion criteria to chronic systolic heart failure, thus excluding de novo heart failure, as well as heart failure with preserved EF. Data are restricted to tertiary care hospitals, and may differ from those of facilities not able to provide the full spectrum of management options. Several issues will be addressed in ongoing analyses of the EVITA-HF registry, e.g. subgroup evaluation for age, sex, renal function, and type of admission. In addition, detailed evaluation of the dosage of prognostically relevant medications and reasons for limited ICD- and CRT-penetrance will be analyzed.

Summary

In conclusion, the EVITA-HF registry confirms clinical epidemiology of existing heart failure registries. Importantly, it adds valuable new information regarding effectiveness of in-hospital management and guideline adherence and offers a detailed 1-year follow-up in patients with chronic systolic heart failure. EVITA-HF is a comprehensive data base evaluating the quality of care in real life for this well-defined population with unequivocal guideline recommendations.

References

1. McMurray JJV, Adamopoulos S, Anker SD et al (2012) ESC-Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Eur Heart J. doi:10.1093/eurheartj/ehs104
2. Maggioni AP, Dahlstroem U, Filippatos G et al (2010) EU-RObservational research programme: The Heart Failure Pilot Survey (ESC-HF Pilot). Eur J Heart Fail 12:1076–1084
3. Maggioni AP, Dahlstroem U, Filippatos G et al (2013) EU-RObservational research programme: regional differences and 1-year follow-up results of the Heart Failure Pilot Survey (ESC-HF Pilot). Eur J Heart Fail 15:808–817
4. Cleland JG, Swedberg K, Follath F et al (2003) The EuroHeart failure survey programme—a survey on the quality of care among patients with heart failure in Europe. Part 1: patient characteristics and diagnosis. Eur Heart J 24:442–463
5. Komajda M, Follath F, Swedberg K et al (2003) The EuroHeart failure survey programme—a survey on the quality of care among patients with heart failure in Europe. Part 2: treatment. Eur Heart J 24:464–474
6. Jonsson A, Edner M, Alehagen U et al (2010) Heart failure registry: a valuable tool for improving the management of patients with heart failure. Eur J Heart Fail 12:25–31
7. Oliva F, Mortara A, Cacciatore G et al (2012) Acute heart failure patient profiles, management and in-hospital outcome: results of the Italian Registry on Heart Failure Outcome. Eur J Heart Fail 14:1208–1217
8. Fonarow GC, Heywood JT, Heidenreich PA et al (2007) Temporal trends in clinical characteristics, treatments, and outcomes for heart failure hospitalizations, 2002 to 2004: findings from Acute Decompensated Heart Failure National registry (ADHERE). Am Heart J 153:1021–1028
9. Fonarow GC, Abraham WT, Albert NM et al (2008) Factors identified as precipitating hospital admissions for heart failure and clinical outcomes. Findings from Optimize-HF. Arch Intern Med 168:847–854
10. Yancy CW, Fonarow GC, Albert NM et al (2009) Influence of patient age and sex on delivery of guideline-recommended heart

failure care in the outpatient cardiology practice setting: findings from IMPROVE HF. Am Heart J 157:754–762
11. Albert NM, Fonarow GC, Yancy CW et al (2010) Influence of dedicated heart failure clinics on delivery of recommended therapies in outpatient cardiology practices: findings from the registry to improve the use of evidence-based heart failure therapies in the outpatient setting (IMPROVE HF). Am Heart J 159:238–244
12. Tavazzi L, Senni M, Metra M et al (2013) Multicenter prospective observational study on acute and chronic heart failure: one year follow up results of IN-HF (Italian Network on Heart Failure) outcome registry. Circ Heart Fail 6:473–481
13. Stalhammar J, Stern L, Linder R et al (2012) Resource utilization and cost of heart failure associated with reduced ejection fraction in Swedish patients. J Med Econ 15:938–946
14. Lund LH, Svennblad B, Melhus H et al (2013) Association of spironolactone use with all-cause mortality in heart failure: a propensity scored cohort study. Circ Heart Fail 6:174–183
15. Choi DJ, Han S, Jeon ES et al (2011) Characteristics, outcomes and predictors of long-term mortality for patients hospitalized for acute heart failure: a report from the Korean heart failure registry. Korean Circ J 41:363–371
16. Youn YJ, Yoo BS, Lee JW et al (2012) Treatment performance measures affect clinical outcomes in patients with acute systolic heart failure: report from the Korean Heart Failure Registry. Circ J 76:1151–1158
17. Parenica J, Spinar J, Vitovec J et al (2013) Long-term survival following acute heart failure: the Acute Heart Failure Database Main registry (AHEAD Main). Eur J Intern Med 24:151–160
18. Hamaguchi S, Kinugawa S, Tsuchihashi-Makaya M et al (2013) Characteristics, management, and outcomes for patients during hospitalization due to worsening heart failure—a report from the Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD). J Cardiol 62:95–101
19. Sato N, Kajimoto K, Keida T et al (2013) Clinical features and outcome in hospitalized heart failure in Japan (from the ATTEND Registry). Circ J 77:944–951
20. Waldum B, Westheim AS, Sandvik L et al (2012) Baseline anemia is not a predictor of all-cause mortality in outpatients with advanced heart failure or severe renal dysfunction. Results from the Norwegian Heart Failure Registry. J Am Coll Cardiol 59:371–378
21. Fruhwald FM, Ulmer H, Pacher R et al (2011) Heart rate and functional impairment are predictors of outcome in heart failure patients in the real world. Data from the Austrian Heart Failure registry. Wien Klin Wochenschr 123:378–383
22. Fonarow GC, Abraham WT, Albert NM et al (2008) Dosing of beta-blocker therapy before, during, and after hospitalization for heart failure (from organized program to initiate lifesaving treatment in hospitalized patients with heart failure). Am J Cardiol 102:1524–1529
23. Gheorghiade M, Vaduganathan M, Fonarow GC, Bonow RO (2013) Rehospitalization for heart failure. Problems and perspectives. J Am Coll Cardiol 61:391–403
24. Kociol RD, Peterson ED, Hammill BG et al (2012) National survey of hospital strategies to reduce heart failure readmissions: findings from the Get with the Guidelines-Heart Failure registry. Circ Heart Fail 5:680–687
25. Fonarow GC (2011) Improving quality of care and outcomes for heart failure. Circ J 75:1783–1790
26. Chen J, Dharmarajan K, Wang Y et al (2013) National trends in heart failure hospital stay rates, 2001 to 2009. J Am Coll Cardiol 61:1078–1088
27. Lechat P, Cibis-II Investigators (1999) The cardiac insufficiency bisoprolol study II (CIBIS-II): a randomised trial. Lancet 353:9–13
28. Fagerberg B, Merit-HF Study Group (1999) Effect of metoprolol CR/XL in chronic heart failure: metoprolol CR/XL randomised intervention trial in congestive heart failure (MERIT-HF). Lancet 353:2001–2007
29. Pitt B, Zannad F, Remme W et al (1999) The effect of spironolactone on morbidity and mortality in patients with severe heart failure. N Engl J Med 341:709–717
30. Packer M, Coats AJS, Fowler MB et al (2001) Effect of carvedilol on survival in severe chronic heart failure. N Engl J Med 344:1651–1658
31. Pitt B, Remme W, Zannad F et al (2003) Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med 348:1309–1321
32. Bardy GH, Lee KL, Mark DB et al (2005) Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 352:225–237
33. Swedberg K, Komajda M, Boehm M et al (2010) Ivabradine and outcomes in chronic heart failure (SHIFT): a randomized placebo-controlled study. Lancet 376:875–885
34. Lenzen MJ, Boersma E, Scholte op Reimer WJM et al (2005) Under-utilization of evidence-based drug treatment in patients with heart failure is only partially explained by dissimilarity to patients enrolled in landmark trials: a report from the Euro Heart Survey on Heart Failure. Eur Heart J 26:2706–2713
35. Lee DS, Ghosh N, Floras JS et al (2009) Association of blood pressure at hospital discharge with mortality in patients diagnosed with heart failure. Circ Heart Fail 6:616–623
36. Boehm M, Swedberg K, Komajda M et al (2010) Heart rate as a risk factor in chronic heart failure (SHIFT): the association between heart rate and outcomes in a randomized placebo-controlled trial. Lancet 376:886–894
37. Frankenstein L, Katus HA, Grundtvig M et al. (2013) Association between spironolactone added to beta-blockers and ACE inhibition and survival in heart failure patients with reduced ejection fraction: a propensity score-matched cohort study. Eur J Clin Pharmacol [Epub]
38. Suarez J, Piccini JP, Liang L et al (2012) International variation in use of oral anticoagulation among heart failure patients with atrial fibrillation. Am Heart J 163:804–811