Molecular Crystals and Liquid Crystals

ISSN: 1542-1406 (Print) 1563-5287 (Online) Journal homepage: http://www.tandfonline.com/loi/gmcl20

Survival variables in old old patients (>85 years) with chronic heart failure

Antoniu Petriş, Gabriel Tatu-Chiţoiu, Irina Costache & Diana Ţînţ

To cite this article: Antoniu Petriş, Gabriel Tatu-Chiţoiu, Irina Costache & Diana Ţînţ (2016) Survival variables in old old patients (>85 years) with chronic heart failure, Molecular Crystals and Liquid Crystals, 628:1, 7-14, DOI: 10.1080/15421406.2015.1137411

To link to this article: http://dx.doi.org/10.1080/15421406.2015.1137411

Published online: 13 May 2016.

MOL. CRYST. LIQ. CRYST.
2016, VOL. 628, 7–14
http://dx.doi.org/10.1080/15421406.2015.1137411

Taylor & Francis
Taylor & Francis Group

Survival variables in old old patients (>85 years) with chronic heart failure

Antoniu Petriş[a], Gabriel Tatu-Chiţoiu[b], Irina Costache[a], and Diana Ţînţ[c]

[a]Faculty of Medicine, University of Medicine and Pharmacy "Grigore T. Popa" Iaşi, "St. Spiridon" County Emergency Hospital, Cardiology Clinic, Iaşi, Romania; [b]"Floreasca" Emergency Hospital, Bucureşti, Romania; [c]Faculty of Medicine, "Transilvania" University Braşov, ICCO Clinics Braşov, Romania

ABSTRACT

For the old old patients (pts) with congestive heart failure the use of combinations of drugs can easily lead to a sort of "evidence-based" polypragmasie. We analyzed a lot of 125 pts with congestive heart failure older than 85 years (mean 87.43 +/− 2.54 years), 53.6% male, enrolled consecutively between January 2011 – December 2012. We have compared some features of two subgroups: survivors' (S = 112 pts) vs deceased (D = 13 pts). The old old patients group included patients with length of hospitalization of 8.10+/−3.98 days and the rate of rehospitalization 6.4% and the death rate 10.4%. Number of drugs taken was 5.53+/−1.86 in S group vs 5.85+/−1.86 in D group (p = 0.560) and the length-of-stay was 8.18+/−3.79 in S group vs 7.38+/−5.53 in D group (p = 0.494). There were significant differences between group S vs D in: NYHA class, atrial fibrillation, hemoglobin level, blood urea nitrogen, and serum sodium. The number of drugs given to old old patients has not proven to reduce the length of stay, the rate of death and rehospitalization. Hyponatremia, anemia, increased BNP, blood urea nitrogen and serum uric acid are associated with increased mortality of old old patients.

KEYWORDS

Congestive heart failure; polypharmacy; hyponatremia

Introduction

The "oldest old" or "old old" patients, videlicet the individuals ≥85 years of age are a growing group in many countries. During the efforts to improve the life expectancy in older adults have been identified a number of relevant differences between the "young old" (65 to 74 years of age), the "older old" (75 to 84 years of age), and the "oldest old" (≥85 years of age) [1]. There are also the opinion that the heart failure (HF) patients between 70 and 74 years old should not be categorized as elderly because this does not add a differential value, keeping the category of 'oldest old patients' for those over 84 years old [2]. This follows a change of perception in modern society about the age's scales different from what we knew it before. Moreover, the estimation of the projections of life expectancy suggest that more than half of the people born since 2000 will live to be a 100 years old [3]. The patients older than 70 years are becoming more a more common in the admissions for acute pulmonary edema [4] or which are directed to ICU [5]. Two recent Italian surveys (TEMISTOCLE and CONFINE studies) found that the mean age of patients admitted for CHF increased from 77 years in

CONTACT Antoniu Petriş antoniu.petris@yahoo.ro
Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/gmcl.

Table 1. Baseline characteristics (S survival, D death).

Characteristics	S (n = 112)	D (n = 13)	p
Age (years) - mean (SD)	87.35 (2.44)	88.15 (3.28)	0.282
Female (%)	47.3	38.5	0.548
Urban area (%)	46.4	69.2	0.127
Nr. of years of evolution of heart failure - mean (SD)	4.36 (5.16)	3.75 (4.34)	0.818
Nr. of hospital addmissions in the last 12 months - mean (SD)	1.20 (0.46)	1.08 (0.27)	0.364

2002 to 79 years in 2008 and that the number of very old patients (>85 years) was substantial and increasing year-by-year [6]. Although the incidence and prevalence of over 85-year-old HF patients in 'real-life' is increasing they have many issues still doubtful, primarily due to the exclusion of elderly people from most randomized controlled trials on HF [7]. Octogenarians HF patients are managed despite the fact that clinical benefits at this age of some drugs are not clear proven [8]. For the old old patients (pts) with congestive HF the use of combinations of drugs can easily lead to a sort of "evidence-based" polypragmasie.

Methods

In this study we used data of a single center database on 125 pts with symptomatic congestive heart failure older than 85 years screened consecutively between January 2011 – December 2012 in an academic hospital from Iaşi, Romania. The recruited patients are admitted with dyspnoea, the verification of HF based on the presence of symptoms and signs of HF being done by the investigators according to the guidelines on acute and chronic HF published by the European Society of Cardiology [9]. Clinical history, symptoms, signs, cardiovascular and associated comorbidities, standard biology, chest X-ray and echocardiographic data, and medications were recorded (Tables 1, 2, 3). The creatinine clearance was calculated according to the Cockcroft and Gault formula. Hypertension was defined as systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg. An assessment of preserved left ventricular systolic function was given by echocardiography left ventricular ejection fraction (EF) ≥45%.

Table 2. Cardiovascular and associated comorbidities (S survival, D death).

Characteristics	S (n = 112)	D (n = 13)	p
Hypertension (%)	76.8	76.9	0.991
Ischaemic heart disease (%)	59.8	38.5	0.142
Previous stroke (%)	16.1	15.4	0.950
Atrial fibrillation (%)	58	38.5	0.021
Peripheral arterial disease (%)	11.6	0	<0.001
Venous insufficiency (%)	19.6	15.4	0.715
Smoker (%)	10.7	30.8	0.165
Chronic alcoholism (%)	28.6	15.4	0.258
Diabetes (%)	15.2	23.1	0.466
COPD (%)	20.5	23.1	0.832
Renal failure* (%)	40.2	53.8	0.348
Liver failure (%)	9.8	23.1	0.307
Cancer history (%)	14.3	15.4	0.916

* Defined as creatinine clearance < 30 mL/min calculated from serum creatinine values using the Cockcroft and Gault formula; COPD, chronic obstructive pulmonary disease.

Table 3. Treatment on admission/discharge (S survival, D death).

Characteristics	S (n = 112)	D (n = 13)	p
Furosemide (%)	56.3	76.9	0.133
Spironolactone (%)	27.7	46.2	0.170
Indapamide (%)	8.9	7.7	0.883
Statin (%)	12.5	0	<0.001
Dopamine (%)	4.5	46.2	<0.014
Digoxin (%)	21.4	30.8	0.449
Anticalcics (%)	25	23.1	0.880
ACE-inhibitors (%)	53.6	38.5	0.306
Angiotensin receptor blockers (%)	4.5	0	0.441
Betablockers (%)	57.1	69.2	0.406
Amiodarone (%)	3.6	15.4	0.284
Aspirine (%)	64.3	15.4	<0.001
Clopidogrel (%)	25.0	23.1	0.880
Antivitamin K (%)	17.9	38.5	0.178
Nitrats (%)	65.2	53.8	0.424
Trimetazidine (%)	32.1	23.1	0.508
Aminophylline (%)	51.8	76.9	0.072
Neurologic drugs ((%)	14.3	23.1	0.407
Antidiabetic drugs (%)	11.6	23.1	0.304

Ethics

This study was conducted in accordance with the Declaration of Helsinki. Patient data were extracted from the observation charts with respect of their confidentiality and anonymity. On admission, each patient signed an informed consent form according to the regulations of the Rules of Procedure of the Emergency County Hospital 'St. Spiridon' Iaşi, Romania.

Statistical analysis

For continuous variables, mean, standard deviation (SD), median, minimum and maximum were assessed. For non-continuous variables, the frequency distribution was considered. In this analysis was used the independent-samples t-test to compares the means between two unrelated groups on the same continuous, dependent variable. All statistical analyses were two-tailed with a threshold for significance set at a P value <0.05. The Pearson product-moment correlation coefficient (r) was used as measure of the strength and direction of association that exists between two variables measured on at least an interval scale. All final analyses were conducted using SPSS software, version 20 (SPSS Inc, Chicago, Illinois, USA).

Results

We have analyzed a lot of 125 patients with congestive heart failure, older than 85 years (mean 87.43 +/− 2.54 years, median 87 year, range 85–99) (Figure 1), 53.6% male, enrolled consecutively between January 2011 - December 2012. The old old patients group included patients with length of hospitalization of 8.10+/−3.98 days and the rate of rehospitalization 6.4% and the death rate 10.4%. We have compared some features of two groups: survivors' (S = 112 pts) vs deceased (D = 13 pts). Heart failure etiology in this groups (S vs D) was: ischemic dilated cardiomyopathy 52 pts (46.4%) vs 5 pts (38.5%), alcoholic cardiomyopathy 4 pts (3.6%) vs 0, hypertensive cardiopathy 33 pts (29.5%) vs 5 pts (38.5%) and mixed in 23 pts (20.5%) vs 3 pts (23.1%). The New York Heart Association (NYHA) class distribution (S-group vs D-group) was the following: in NYHA class II 59 pts (52.7%) vs 2 pts (15.4%), in

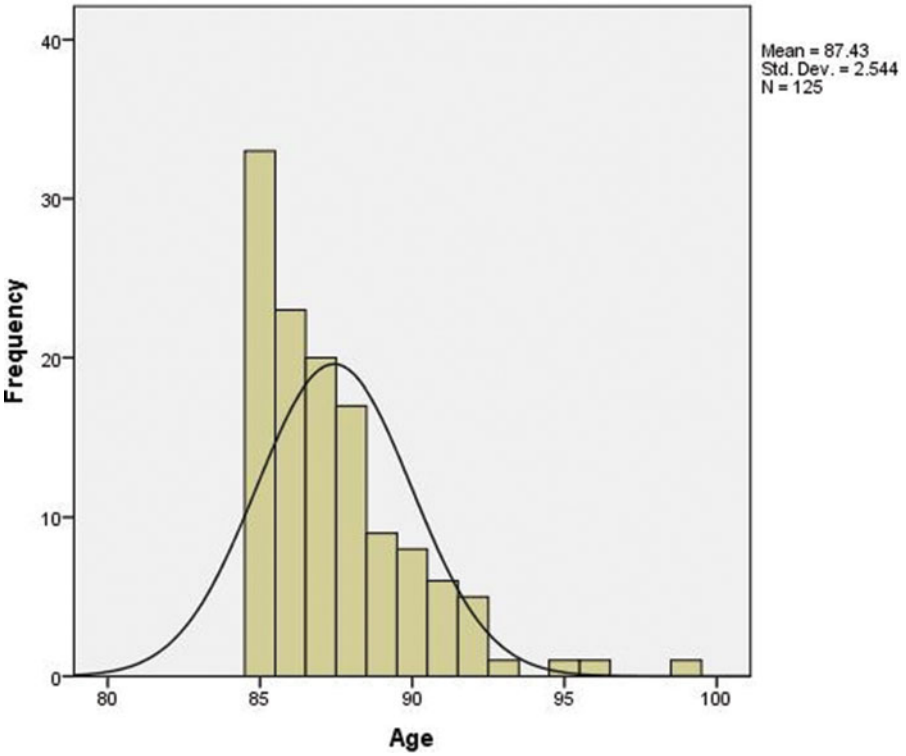

Figure 1. Distribution of the analyzed cohort according to age.

NYHA class III 46 pts (41.1%) vs 9 pts (69.2%) and in NYHA class IV 59 pts (6.3%) vs 2 pts (15.4%).

Chest X-ray was performed in 89.3% cases (S-group) vs 76.9% in D-group (p 0.572) and echocardiogram in 100% cases (S-group) vs 84.6% in D-group (p 0.165). Nor difference between cardio-thoracic index (on chest X-ray) in S-group (0.54+/−0.06) and D-group (0.51+/−0.06) (p 0.363), left and right ventricular diameters (echocardiogram) (for left ventricle diameter 52.56+/−9.72 mm in S-group and 53.00+/−8.08 mm in D-group, p 0.886; for right ventricle diameter 34.77+/−8.92 mm in S-group and 38.40+/−7.97 mm in D-group, p 0.223). There was a significant difference in the left ventricle ejection fraction between the two groups (44.36+/−13.12% in S-group and 38.33+/−5.59% in D-group, p 0.015). BNP values are 524.49+/−116.87 vs 2480.75+/−951.99 pg/ml, p = 0.131.

Number of drugs taken was 5.53+/−1.86 in S-group vs 5.85+/−1.86 in D-group (p = 0.560) and the length-of-stay was 8.18+/−3.79 in S group vs 7.38+/−5.53 in D group (p = 0.494) (figure 2). There were significant differences between group S vs D in: NYHA class (p = 0.011), atrial fibrillation (p = 0.021), left ventricle ejection fraction (p = 0.015), hemoglobin level (12.57+/−1.92 vs 11.20+/−1.87 g/dl, p = 0.017), blood urea nitrogen (58.38+/−28.92 vs 77.30+/−47.99 mg/dl, p = 0.04) and serum sodium (139.97+/−4.55 vs 136.69+/−7.12 mg/dl, p = 0.024).

Evolution (survival vs death) was correlated with presence of atrial fibrillation (r = 0.207*), NYHA class (r = 0.228*), smoker status (r = 0.183*), BUN level (r = 0.183*), uric acid level (r = 0.322**), serum sodium level (r = −0.206*), brain natriuretic peptide (BNP) level (r = 0.658**), and with administration of dopamine (r = 0.449**) and aspirin (r = −0.304**, a negative relation: more aspirine administrated in the survival group) but not

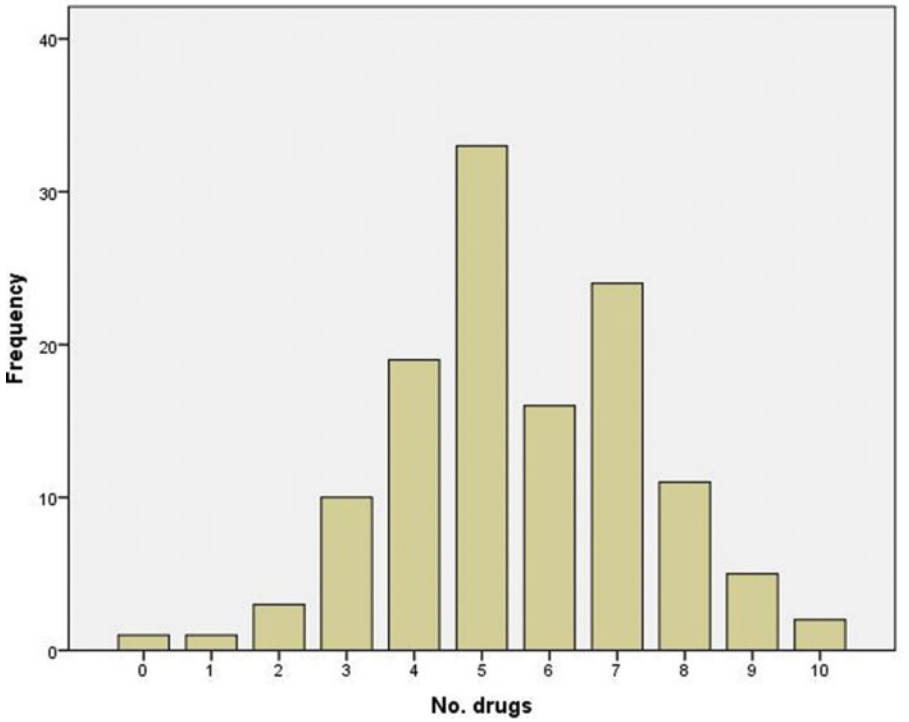

Figure 2. Distribution of the number of drugs administrated per patient.

with the number of drugs administrated per patient (r = 0.053) or length-of-stay (r = −0.062) (Figure 3). Length-of stay was correlated with the number of drugs administrated per patient (r = 0.182*), age (r = −0.209*), NYHA class (r = 0.192*), nr. of admission in the last 12 months (r = 0.234**), smoker status (r = −0.185**), GPT value (r = −0.207*) and the left ventricle ejection fraction (r = −0.331**). The number of drugs administrated is correlated with the length-of stay (r = 0.182*), systolic blood pressure (r = 0.218*), history of HBP (r = 0.176*), left ventricle ejection fraction (r = −0.321**), and some drug administration: furosemid (r = 0.430**), spironolactone (r = 0.249**), indapamide (r = 0.226*), statin (0.317*), digoxin (r = 0.231**), anticalcics (r = 0.246**), angiotensin receptor blockers - ARB (r = 0.247*), beta-blockers (r = 0.220*), clopiudogrel (r = 0.286**), nitrats (r = 0.389**), trimetazidine (r = 0.235**), aminophylline (r = 0.329**), neurologic drugs (r = 0.341**), antidiabetic drugs (r = 0.245**).

Legend: *correlation is significant at the 0.05 level (2-tailed); **correlation is significant at the 0.01 level (2-tailed).

Discussion

The median survival in Mogansen et al. study [11] was 20 months for patients >85 years and 50 months for the other age groups (<85 years) combined. In a study on octogenarians the in-hospital mortality was 10.9% and mean 12 and 24-months survival 62.3% and 48.2% [8]. In a multivariate model, a significant association with the composite of all-cause mortality or cardiovascular hospitalization, or all-cause mortality alone was found for a higher NYHA class, higher uric acid level, lower body mass index, prior myocardial infarction, and larger

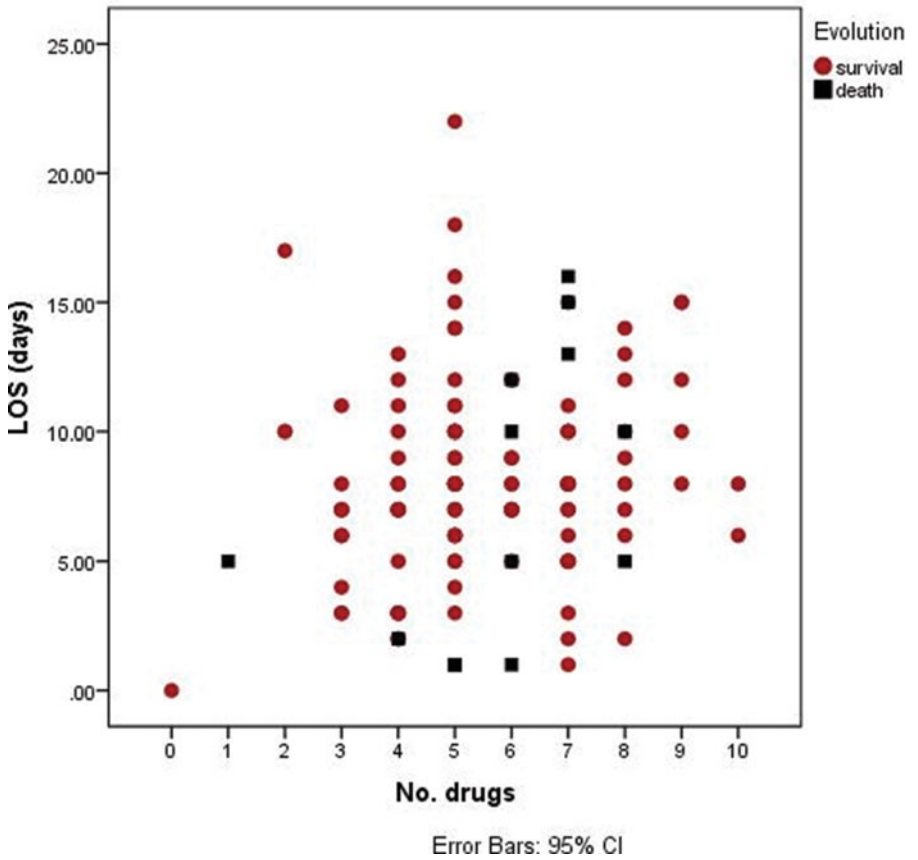

Figure 3. Distribution of the number of drugs administrated per patient and lenght-of-stay (LOS) analyzed according S or D group.

left atrial (LA) dimension [12]. In our study, the patient evolution (survival vs death) was correlated with presence of atrial fibrillation, NYHA class, smoker status, BUN, uric acid, serum sodium and brain natriuretic peptide (BNP) level, and with administration of dopamine and aspirin.

Barsheshet et al. [13] recently concluded that mortality risk in the older population is not decreased in those with preserved LVEF. In our study, the length-of stay and the number of drugs administrated was correlated with the left ventricle ejection fraction ($r = -0.331$, respectively $r = -0.321$).

The contemporary Guidelines [9] mentions as established therapy of chronic left heart failure the following main classes of drugs: diuretics, angiotensin converting enzyme inhibitors (ACEi) /angiotensin receptor blockers (ARB), beta-blockers (BB), mineralocorticoid receptor antagonists (MRA) and digitalis (low doses). In Mahler study [10] the mean number of drugs per patient with congestive heart failure (at the first visit) differs depending on the analyzed country: 4.80 drugs in Germany, 4.86 drugs in Spain, 5.40 drugs in France, 5.51 drugs in UK, 5.54 drugs in Italy and 5.64 drugs in Nederland. Euro Heart Failure II notice in the elderly patients an underuse and underdosage of medications recommended for heart failure [14]. The optimal treatment (association of ACEi/ARB+BB+MRA) was used in only 5% of patients at discharge in a cohort study in the French national healthcare insurance database [8]. In our study they are 6.4% of patients treat with this drug triad. In the study cited above on

multivariate analysis the associations ACEi/ARB+BB+MRA ($p = 0.01$) and ACEi/ARB+BB ($p < 0.001$) were associated with improved survival.

Limitations

Our survey was an observational study conducted only in patients hospitalized with HF in a single center. The follow-up duration was also limited to the in-hospital period, but the present database has enough subjects to examine the relationship between several classes of medication and short-term outcomes in a real-life LOS.

Conclusions

There were significant differences between group S vs D in NYHA class, atrial fibrillation, hemoglobin level, blood urea nitrogen, and serum sodium. The number of drugs given to old old patients has not proven to reduce the length of stay, the rate of death and rehospitalization. Hyponatremia, anemia, increased BNP, blood urea nitrogen and serum uric acid are associated with increased mortality of old old patients.

References

[1] Aronow, W.S., Fleg, J.L., Pepine, C. J., Artinian, N.T., Bakris, G., Brown, A.S., Ferdinand, K.C., Forciea, M.A., Frishman, W.H., Jaigobin, C., Kostis, J.B., Mancia, G., Oparil, S., Ortiz, E., Reisin, E., Rich, M.W., Schocken, D.D., Weber, M.A., & Wesley D.J. (2011). *J. Am. Coll. Cardiol.*, *57*, 2037–2114.

[2] Formiga, F., Aramburu-Bodas, O., & Pérez-Calvo, J. I. (2013). *Eur. J. Heart Fail.*, *15*, 1075.

[3] Christensen, K., Doblhammer, G., Rau, R., & Vaupel, J.W. (2009). *Lancet*, *374*, 1196–1208.

[4] Chioncel, O., Ambrosy, A.P., Bubenek, S., Filipescu, D., Vinereanu, D., Petriş, A., Christodorescu, R., Macarie, C., Gheorghiade, M., & Collins, S.P. (2014). *J. Cardiovasc. Med. (Hagerstown)* doi:10.2459/JCM.0000000000000192.

[5] Chioncel, O., Ambrosy, A.P., Filipescu, D., Bubenek, S., Vinereanu, D., Petriş, A., Collins, S.P., Macarie, C., & Gheorghiade, M. (2015). *J. Cardiovasc. Med. (Hagerstown)*, *16*, 331–40.

[6] Biagi, P., Nardi, R., Baldo, C. I., Scanelli, G., Panuccio, D., Bonanome, A., Miserocchi, F., Lusiani, L., Bonizzoni, E., Campanini, M., Nozzoli, C., & Vescovo, G., on behalf of the FADOI-CONFINE Study Group. (2014). *Italian Journal of Medicine*, *8*, 19–28.

[7] Heiat, A., Gross, C.P., & Krumholz, H.M. (2002). *Arch. Intern. Med.*, *162*, 1682–1688.

[8] Vorilhon, Ch., Chenaf, C., Mulliez, A., Pereira, B., Clerfond, G., Authier, N., Jean, F., Motreff, P., Citron, B., Eschalier, A., Lusson, J. R., & Eschalier, R. (2015). *Archives of Cardiovascular Diseases Supplements*, *7*, 30.

[9] McMurray, J.J.V., Adamopoulos, S., Anker, S.D., Auricchio, A., Böhm, M., Dickstein, K., Falk, V., Filippatos, G., Fonseca, C., Gomez-Sanchez, M.A., Jaarsma, T., Køber, L., Lip, G.Y.H., Maggioni, A.P., Parkhomenko, A, Pieske, B.M., Popescu, B.A., Rønnevik, P.K., Rutten, F.H. Schwitter, J., Seferovic, P., Stepinska, J., Trindade, P.T., Voors, A.A., Zannad, F., & Zeiher, A. (2012). *Eur. Heart J.*, *33*, 1787–1847.

[10] Komajda, M., Lapuerta, P., Hermans, N., Gonzalez-Juanatey, J.R., van Veldhuisen, D.J., Erdmann, E., Tavazzi, L., Poole-Wilson, Ph., & Le Pen, C. (2005). *Eur. Heart J.*, *26*, 1653–1659.

[11] Mogensen, U. M., Ersbøll, M., Andersen, M., Andersson, Ch., Hassager, Ch., Torp-Pedersen, Ch., Gustafsson, F., & Køber, L. (2011). *Eur. J. Heart Fail.*, *13*, 1216–1223.

[12] Manzano, L., Daphne, B., Roughton, M., Shibat, M., Anker, S. D., Ghio, S., van Veldhuisen, D., Cohen-Solal, A., Coats, A. J., Poole-Wilson Ph, P. A., & Flather, M. D. on behalf of the SENIORS Investigators. (2011). *Eur. J. Heart Fail.*, *13*, 528–536.

[13] Barsheshet, A., Shotan, A., Cohen, E., Garty, M., Goldenberg, I., Sandach, A., Behar, S., Zimlichman, E., Lewis, B. S., & Gottlieb, S. for the HFSIS Steering Committee and Investigators. (2010). *Eur. J. Heart Fail.*, *12*, 833–840.
[14] Komajda, M., Hanon, O., Hochadel, M., Lopez-Sendon, J.L., Follath, F., Ponikowski, P., Harjola, V.P., Drexler, H., Dickstein, K., Tavazzi, L., & Nieminen, M. (2009). *Eur. Heart J.*, *30*, 478–486.