DEVICES

Frailty Syndrome in Heart Failure Patients who are Receiving Cardiac Resynchronization

AGNIESZKA MLYNARSKA, PH.D.,*,† RAFAL MLYNARSKI, M.D., PH.D.,† JOLANTA BIERNAT, M.D., PH.D.,† MACIEJ SOSNOWSKI, M.D., PH.D.,‡ and KRZYSZTOF S. GOLBA, M.D., PH.D.†,§

From the *Department of Internal Nursing, Chair of Internal Medicine, School of Health Sciences, Medical University of Silesia, Katowice, Poland; †Department of Electrocardiology, Upper Silesian Heart Centre, Katowice, Poland; ‡Unit for Noninvasive Cardiovascular Diagnostics, 3rd Chair of Cardiology, School of Medicine, Medical University of Silesia, Katowice, Poland; and §Department of Electrocardiology and Heart Failure, School of Health Sciences, Medical University of Silesia, Katowice, Poland

Background: *We hypothesized that patients with de novo cardiac resynchronization therapy (CRT) implantation had a more intense frailty syndrome when compared to the patients who qualified for a system upgrade.*

Methods: *One hundred and six patients aged ≥65 years were included. They were divided into two groups: de novo CRT implantation—74 patients and upgrade from standard right heart pacing—32 patients. A CRT was finally implanted in all of the patients. Frailty was evaluated using the Canadian Study of Health and Aging Clinical Frailty Scale (CSHA-CFS).*

Results: *The average results in CSHA-CFS were statistically higher (5.3 ± 0.8) in the de novo patients when compared to the patients who qualified for a system upgrade (4.9 ± 0.8); P = 0.027. Frailty syndrome was recognized in 81.1% of the patients in the de novo group and in 68.7% of the patients in the upgrade group; P = 0.164. Only one patient of the 106 had no attributes of frailty (or exposed ones) syndrome.*

Conclusions: *Frailty syndrome is a common phenomenon in patients with heart failure and over 65 years of age. The syndrome is most often recognized in patients who are de novo qualified for cardiac resynchronization. (PACE 2016; 39:370–374)*

frailty, heart failure, cardiac resynchronization therapy, pacemaker, cardioverter defibrillator

Introduction

According to its definition, frailty is a common geriatric syndrome that embodies an elevated risk of catastrophic declines in health and function among elderly patients. Frailty syndrome is combined with an increased risk of poor health outcomes including falls, incident disability, hospitalization, and mortality.[1–3] Frailty is a condition that has physical and cognitive domains that are related to the aging of the population, disability, and chronic disease with "reserve and resilience" as the hallmarks that are required to define and quantify it.[4]

Frailty stratification predicts a patient's risk of death or the need for institutional care.[5] In the last few years, some instruments have been developed to measure frailty. Examples of such methods are questionnaires such as, e.g., the Canadian Study Health and Aging Frailty Scale, Cardiovascular Health Study Scale (CHS), Edmonton Frail Scale (EFS), or Tilburg Frailty Indicator (TFI).[6–9] Although the frailty instruments were validated on a geriatric population, they have been identified as being potentially relevant for elderly patients with different cardiovascular diseases including heart rhythm disorders or heart failure.[10–12]

To date, there is a lack of complex research that examines the usefulness of frailty evaluation in patients with advanced heart failure who are being treated using invasive procedures such as cardiac resynchronization therapy (CRT). Cardiac resynchronization is a method that is used more frequently in elderly patients and frailty syndrome should probably be recognized in this group more often. Some of the patients who are qualified for CRT had a previously implanted standard pacing system (due to, e.g., sinus node dysfunction or atrioventricular blocks) and needed an upgrade for the CRT, while the others needed *de novo* CRT implantation. We hypothesized that patients with *de novo* CRT implantation had a more intense frailty syndrome, and therefore there would be the need for additional dedicated care.

Funding sources: None.
Conflict of Interest: None.

Address for reprints: Agnieszka Mlynarska, PH.D., Department of Internal Nursing, Upper-Silesian Medical Center, ul. Ziolowa 45/47, Poland. Fax: 48-32-2524098; email: agnieszkawlodyka@o2.pl

Received October 11, 2015; revised November 10, 2015; accepted December 7, 2015.

doi: 10.1111/pace.12800

Table I.

Evaluation of Frailty using the Canadian Study of Health and Aging Clinical Frailty Scale (CSHA-CFS)

Category of Frailty	Evaluation	Description of the Subject
1	Very fit	Robust, active, energetic, well-motivated, and fit; these people commonly exercise regularly and are in the fittest group for their age.
2	Well	Without any active disease, but less fit than people in category 1.
3	Well, with treated comorbid disease	Disease symptoms are well controlled compared to those in category 4.
4	Apparently vulnerable	Although not clinically dependent, these people commonly complain of being "slowed down" or have disease symptoms.
5	Mildly frail	With limited dependence on others for the instrumental activities of daily living.
6	Moderately frail	Help is needed with both the instrumental and noninstrumental activities of daily living.
7	Severely frail	Completely dependent on others for the activities of daily living or terminally ill.

Methods

One hundred and six patients aged ≥65 years (average age 74.9 ± 6.3; 18 women) who had qualified for CRT were included. Qualification for the implantation was based on the latest European Society of Cardiology guidelines, which were published in 2013.[13] All patients had: (1) ejection fraction evaluated by echocardiography (Simpson method) <35%, (2) left bundle branch block (LBBB), and (3) New York Heart Association (NYHA) Functional Classification ≥II.

Patients were retrospectively divided into two groups: (1) *de novo* CRT implantation—74 patients; and (2) upgrading from a standard right heart pacing system (DDD or VVI) to CRT—32 patients. A system upgrade was defined as changing the pacing mode from the standard right heart pacing (or implantable cardioverter defibrillator) to cardiac resynchronization-cardioverter defibrillator (CRT-D) by at least the implantation of a left ventricle lead and changing the device.

Finally in all of the patients, a cardiac resynchronization-pacemaker or CRT-D was implanted according to standard criteria. High-quality CRT devices were used and implantation was performed according to the institutional procedures.

Frailty Evaluation

Frailty was evaluated using the Canadian Study of Health and Aging Clinical Frailty Scale (CSHA-CFS). This scale is a seven-point scale that has a good predictive validity (regarding death and the need for institutional care) and its prognostic power relies on clinical judgment. Values ≥5 were recognized as frailty syndrome, while a value = 4 described patients who might be in danger of developing frailty syndrome. The precise CSHA-CFS scale is presented in Table I.

Statistical Analysis

The continuous data from CSHA-CFS are presented in points as mean values and their corresponding standard deviations. The Student's *t*-test was used for the statistical comparison of CSHA-CFS values. The Pearson's correlation coefficient r was used to correlate clinical and echocardiographic measurements with the level of frailty. A value of $P < 0.05$ was recognized as statistically significant. All calculations were performed using the Polish version of Statistica.

Results

The characteristics of the included patients are presented in Table II. Comparison of the levels of frailty for patients from both groups is presented in Figure 1. Only one patient out of the 106 had no attributes of frailty syndrome.

The average values in CSHA-CFS were statistically higher (5.3 ± 0.8) in the patients who had been qualified for *de novo* implantation when compared to the patients who had been qualified for an upgrade from a standard pacing system to the CRT (4.9 ± 0.8); $P = 0.027$. Frailty syndrome

Table II.

Characteristics of Patients who Were Included

Feature	*De novo* Implantation		Upgrade		P
	N	%	N	%	
CAD	64	86.49	21	65.62	0.01
Diabetes	32	43.24	14	43.75	0.96 NS
Hypertension	66	89.19	26	81.25	0.26 NS
Hyperlipidaemia	46	62.16	21	65.62	0.61 NS
Smoking	7	9.46	3	9.37	0.72 NS
Family history	13	17.57	4	12.5	0.71 NS
Obesity	6	8.11	4	12.5	0.71 NS
NYHA	2.81 ± 0.58		2.66 ± 0.6		0.22 NS

CAD = coronary artery disease; NYHA = New York Heart Association.

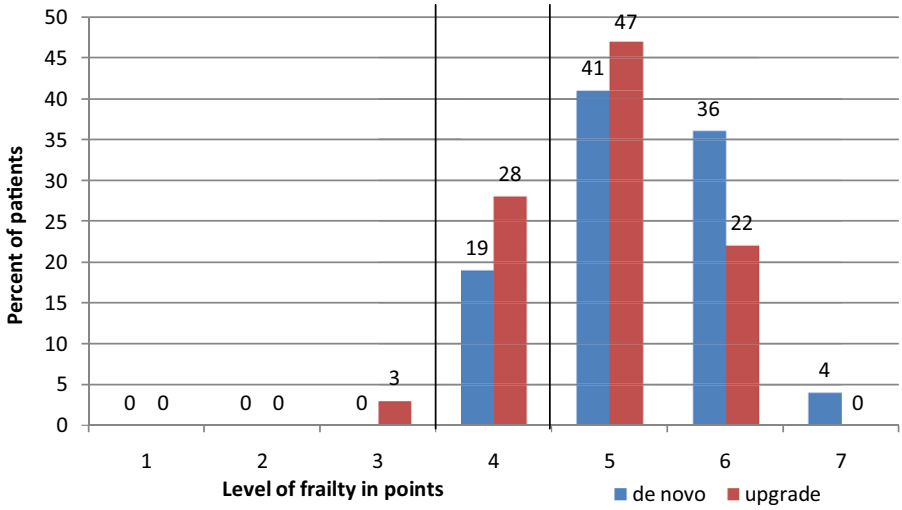

Figure 1. *Comparison of the levels of frailty in % for patients from both groups.*

was recognized in 81.1% of the *de novo* qualified patients and in 68.7% of the patients who had been qualified for an upgrade. Patients were at a risk for frailty (value on CSHA-CFS scale = 4) were identified as follows: *de novo*—18.9% versus upgrade—28.1%; P = 0.164. After dividing the group of included patients, accordingly age statistical difference (P = 0.025) was found in patients with more than 75 years. The relation in the group of 65–75 years was not statistical. The exact results are presented in Tables III and IV.

The next step was a comparison of frailty between the groups according to the gender of the patients. The women who had qualified for the *de novo* implantation had statistically (P = 0.048) higher values of frailty on the CSHA-CF scale (5.4 ± 0.9) when compared to the women who had qualified for an upgrade from a standard pacing system to a CRT (4.4 ± 0.9). A similar relationship was found in men (5.2 ± 0.8) who had qualified for *de novo* implantation versus (4.9 ± 0.8) for men who had qualified for an upgrade from a standard

Table III.

Average Values in CSHA-CFS in the Subgroups According to Age

	De novo	Upgrade	P
Entire group	5.3 ± 0.8	4.9 ± 0.8	0.027
Patients 65–75 years	5.1 ± 0.7	4.9 ± 0.9	0.453
Patients > 75 years	5.5 ± 0.8	4.8 ± 0.7	0.025

CSHA-CFS = Canadian Study of Health and Aging Clinical Frailty Scale.

Table IV.

Category of Frailty in CSHA-CFS in the Subgroups According to Age

	Age 65–75 years (Number of Patients)		Age > 75 years (Number of Patients)	
Score	**Upgrade**	***De novo***	**Upgrade**	***De novo***
3	1	0	0	0
4	1	10	3	9
5	9	13	3	20
6	7	10	6	12
7	0	0	3	0

CSHA-CFS = Canadian Study of Health and Aging Clinical Frailty Scale.

pacing system to a CRT; however, the difference was not statistically significant (P = 0.148).

Among the influences of coexisting diseases that were analyzed, only diabetes and arterial hypertension had a significant influence on frailty. In patients with diabetes (n = 46), similar values of frailty were found (*de novo* patients [5.3 ± 0.9] vs patients who had qualified for an upgrade [5.1 ± 0.8]) although the difference was not statistically significant (P = 0.528). Patients without diabetes who had qualified for an upgrade from a standard pacing system to a CRT had a statistically (P = 0.015) lower level of frailty (4.7 ± 0.8) when compared to the *de novo* implanted patients (5.2 ± 0.8).

A similar observation was found among patients with arterial hypertension (n = 92). Frailty was statistically (P = 0.043) more intense in the *de novo* population (5.3 ± 0.8) versus the population that had qualified for an upgrade (4.9 ± 0.7). Obesity and atrial fibrillation had no significant influence on the values of frailty.

Discussion

Due to the aging and increasingly complex nature of our patients, frailty has become a high-priority element of cardiovascular medicine.[14] Recognition of frailty should be a part of the evaluation of elderly adults with cardiovascular disease because it is a biological syndrome that reflects a state of decreased physiological reserve and vulnerability to stressors.[14]

The prevalence of frailty ranges from 10% to 60%, depending on the type of cardiovascular disease as well as the tool and sometimes the cutoff that is chosen to define frailty. In some research, it was documented that frailty correlated with mortality and morbidity of a full spectrum of cardiovascular diseases including heart failure.[14]

Frailty is also an important prognostic indicator in heart failure. McNallan et al.[15] examined 223 individuals with heart failure in southeastern Minnesota between 2007 and 2011. After correction for age, sex, and ejection fraction, patients who were categorized as frail by the biological phenotype had a twofold increased risk of death compared to those with no frailty, whereas a 0.1 unit increase in the deficit index was associated with a 44% increase in the risk of death. The authors concluded that the deficit index and the biological phenotype can predict mortality equally.

Khan et al.[16] assessed the association between frailty syndrome and the risk for heart failure in elderly patients. In this research, frailty was evaluated using the Health ABC Short Physical Performance Battery (HABC Battery) and the Gill index in 2,825 participants aged 70–79 years. The authors concluded that frailty is independently associated with a risk of heart failure (HF) in older adults.

One of the most effective heart failure therapies is CRT. In this method, a special implanted device (pacemaker or cardioverter defibrillator) with three leads, including right atrium (if appropriate), right ventricle, and left ventricle, is needed.[13,17] According to the latest European guidelines, patients with II-IV NYHA functional class, LBBB, wide QRS complex, and ejection fraction <35% can obtain advantages from this method. It is estimated that approximately 2% of the adult population in developed countries has heart failure; most of the patients are 70 years or older. Based on the current guideline criteria, only 5–10% patients with HF are indicated for CRT.[13]

One of the numerous researches, a paper by Dominguez-Rodriguez et al.[18] discusses the subject of cardiac resynchronization and frailty syndrome. The authors analyzed frailty and clinical data from 102 patients with nonischemic cardiomyopathy before CRT defibrillator implantation. The authors used the Fried and Walston

questionnaire in the research. The authors concluded that frailty is a strong predictor of an adverse postimplantation outcome in patients with nonischemic cardiomyopathy who are undergoing CRT-D. The authors performed the analysis during 12 months of follow-up. The cited paper is the first in which the influence of frailty on response to cardiac resynchronization was analyzed. In our research, we compared patients qualified for the cardiac resynchronization and to the upgrade from standard right heart pacing. It is difficult to compare the results of both of the researches; however, both papers stressed that an analysis of frailty syndrome in patients with cardiac resynchronization could be a valuable add-on to the standard patient care.

The role of frailty in advanced heart failure that is treated using implantable cardiac devices is still not fully explored and more research is necessary to confirm the role of frailty. The results of our research as well as the other research cited by us appear to confirm the necessity of an evaluation of frailty in patients with heart failure.

In our opinion, patients who meet the criteria, especially aged ≥65 years, should be screened for frailty. The criteria for the implantation of pacemakers including CRT are clearly defined and the evaluation of any of the additional factors including frailty will not change the decision about implantation. However, this knowledge is important during follow-up visits in which we can, for e.g., prescribe additional care. Intense and more holistic care should improve the entire care regimen and could even improve the quality of life. Furthermore, more studies are necessary in order to understand the relationship between heart failure and frailty and to create the best care strategies for such patients.

Conclusions

Frailty syndrome is a significant part of the life of patients with heart failure who are older than 65 years. It is most often recognized in patients who are *de novo* qualified for cardiac resynchronization as compared to patients with a previously implanted standard pacing system. The relation of frailty is age-dependent—it is more intense in patients who are more than 75 years of age. Diabetes and arterial hypertension appear to have a significant influence on frailty in patients with advanced heart failure.

References

1. Campbell AJ, Buckner DM. Unstable disability and the fluctuations of frailty. Age Aging 1997; 26:315–318.
2. Rockwood K. What would make a definition of frailty successful? Age Aging 2005; 34:432–434.
3. Ferruci L, Guralnik JM, Studenski S, Fried LP, Cutler GB Jr, Walston JD. Designing randomized aimed at preventing or delaying functional decline and disability in frail, older persons: A consensus report. J Am Geriatr Soc 2004; 52:625–34.
4. Varadhan R, Seplaki CL, Xue QL, Bandeen-Roche K, Fried LP. Stimulus-response paradigm for characterizing the loss of resilience in homeostatic regulation associated with frailty. Mech Ageing Dev 2008; 129:666–670.
5. Rockwood K, Mitnitski A, Song X, Steen B, Skoog I. Long-term risks of death and institutionalization of elderly people in relation to deficit accumulation at age 70. J Am Geriatr Soc 2006; 54:975–979.
6. Koller K, Rockwood K. Frailty in older adults: Implications for end of life care. Cleve Clin J Med 2013; 80:168–174.
7. Fried L, Tangen C, Walston J, Newman A, Hirsch C, Gottdiener J, Seeman T, et al. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56:146—156.
8. Rolfson D, Majumdar S, Tsuyuki R, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. Age Ageing 2006; 35:526–529.
9. Gobbens R, van Assen M, Luijkx K, Schols J. The predictive validity of the Tilburg Frailty Indicator: Disability, health care utilization and quality of life in a population at risk. Gerontologist 2012; 52:619–631.
10. Singh M, Alexander K, Roger LV, Rihal CS, Whitson HE, Lerman A, Jahangir A, et al. Frailty and its potential relevance to cardiovascular care. Mayo Clin Proc 2008; 83:1146–1153.
11. Hubbard RE, O'Mahony MS, Woodhouse KW. Characterising frailty in the clinical setting: A comparison of different approaches. Age Ageing 2009; 38:115–119.
12. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, et al. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56:146–156.
13. Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA, Cleland J, et al. 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy: The Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Eur Heart J 2013; 34:2281–2329.
14. Afilalo J, Alexander K, Mack M, Maurer M, Green P, Allen LA, Popma J, et al. Frailty assessment in the cardiovascular care of older adults. J Am Coll Cardiol 2014; 63:747–762.
15. McNallan S, Chamberlain A, Gerber Y, Singh M, Kane R, Weston S, Dunlay S, et al. Measuring frailty in heart failure: A community perspective. Am Heart J 2013; 166:768–774.
16. Khan H, Kalogeropoulos A, Georgiopoulou V, Newman A, Harris T, Rodondi N, Bauer D, et al. Frailty and risk for heart failure in older adults: The health, aging and body composition study. Am Heart J 2013; 166:887–894.
17. Doltra A, Bijnens B, Tolosana JM, Gabrielli L, Castel MÁ, Berruezo A, Brugada J, et al. Effect of cardiac resynchronization therapy on left ventricular diastolic function: Implications for clinical outcome. J Card Fail 2013; 19:795–801.
18. Dominguez-Rodriguez A, Abreu-Gonzalez P, Jimenez-Sosa A, Gonzalez J, Caballero-Estevez N, Martín-Casañas F, Lara-Padron A, et al. The impact of frailty in older patients with non-ischaemic cardiomyopathy after implantation of cardiac resynchronization therapy defibrillator. Europace 2015; 17:598–602.