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Impact of cognitive function on compliance with treatment in heart failure
Wpływ funkcji poznawczych na przestrzeganie zaleceń terapeutycznych w niewydolności serca

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Abstract:
In heart failure (HF) patients frailty syndrome and cognitive impairment (CI) affect outcome by decreasing the capability for performing self-care, adhering to the prescribed treatment regimen, monitoring symptoms.
The aim was to investigate whether CI affects the compliance to therapeutic regimens.
Methods: 170 with HF were included. We employed the Mini Mental State Examination (MMSE), for dementia and the Revised Heart Failure Compliance Scale to assess compliance.
Results: CI patients showed lower compliance in all domains: 2.8±1.0 vs 3.3±1.0 (keeping appointments), 2.8±0.9 vs. 3.4±0.9 (pharmaceutical compliance), 0.4±0.8 vs. 1.4±1.2 (regular body weight monitoring), 2.0±1.3 vs. 2.7±1.0 (reduced salt intake), 1.9±1.2vs. 2.9±1.0 (fluid intake restriction), and 0.5±0.8 vs. 1.7±1.1 (regular exercise). Multiple regression analysis showed cognitive function to be an independent predictor for regular body weight monitoring (β=1.223;$p<0.001$), fluid intake restriction (β=1.081;$p<0.001$), and regular exercise (β=1.237;$p<0.001$). In multivariate analysis, the stimulant variables for compliance with HF treatment were: education (β=1.124), being in a relationship (β=2.231), and lack of cognitive impairment (β=0.320); the number of hospitalizations due to HF was identified as a destimulant (β=-0.495).

Conclusion: Non-compliance is a major problem in elderly with HF. The cognitive function is an independent contributor to total compliance and to compliance with non-pharmaceutical recommendations. Being in a relationship and education are independent predictors of better compliance, while the number of rehospitalizations due to HF exacerbations is an independent predictor of worse compliance. Early detection of CI may offer an opportunity for intervention and a key strategy for improving clinical outcomes in older adults with HF.

Streszczenie:

U pacjentów z niewydolnością serca występowanie zespołu kruchości i zaburzeń funkcji poznawczych może wpływać na efekty leczenia, poprzez zmniejszenie możliwości samoopieki, przestrzegania ustalonych schematów terapeutycznych oraz upośledzenie monitorowania objawów.

Celem badania była ocena związku funkcji poznawczych z przestrzeganiem zaleceń terapeutycznych w leczeniu niewydolności serca.

Metody: Do badania włączono 170 pacjentów z rozpoznaną niewydolnością serca. W badaniu wykorzystano Mini Mental State Examination (MMSE) do oceny funkcji poznawczych oraz Revised Heart Failure Compliance Scale (RHFCS) do oceny przestrzegania zaleceń terapeutycznych ograniczania podaży sodu w diecie, ograniczenia płynów, codziennego ważenia i aktywności fizycznej.

Wyniki

Pacjenci z zaburzeniami funkcji poznawczych mają niższy poziom przestrzegania zaleceń w zakresie wszystkich domen kwestionariusza RHFCS, stosownie: przestrzeganie wizyt kontrolnych (2.8 ± 1.0 vs 3.3 ± 1.0), przestrzeganie zaleceń farmakologicznych (2.8 ± 0.9 vs. 3.4 ± 0.9), regularna kontrola masy ciała (0.4 ± 0.8 vs. 1.4 ± 1.2), ograniczenia spożycia soli (2.0 ± 1.3 vs. 2.7 ± 1.0), ograniczenia spożycia płynów (1.9 ±1.2 vs. 2.9 ±1.0), regularna aktywność fizyczna (0.5 ±0.8 vs. 1.7 ±1.1). Analiza regresji wielorakiej pokazała, że funkcje poznawcze są niezależnym predyktorem związanym z regularną kontrolą masy ciała (β=1.223; p<0.001), ograniczeniem płynów (β=1.081; p<0.001) i regularną aktywnością fizyczną (β=1.237; p<0.001). W analizie wieloczynnikowej niezależnymi predyktorami dostosowania do terapii niewydolności serca (stymulantami) okazały się: wykształcenie (β-1.124), życie w związku (β=2.231) i brak zaburzeń funkcji poznawczych (suma punktów kwestionariusza MMSE) (β=0.320) natomiast destymulantem - liczba hospitalizacji z powodu niewydolności serca. (β=-0.495)

Wnioski

1. Nieprzestrzeganie zaleceń terapeutycznych jest istotnym problemem wśród pacjentów z niewydolnością serca w wieku podeszłym.
2. Funkcje poznawcze są niezależnym predyktorem mającym związek z przestrzeganiem zaleceń terapeutycznych.
3. Życie w związku i wykształcenie są niezależnymi predyktorami zwiększającymi przestrzeganie zaleceń terapeutycznych, natomiast liczba rehospitalizacji z powodu zaostrzenia niewydolności serca jest niezależnym predyktorem obniżającym przestrzeganie zaleceń terapeutycznych.
4. Wczesne rozpoznawanie zaburzeń funkcji poznawczych może przyczyniać się do lepszego planowania interwencji i strategii zmierzającej do poprawy przestrzegania zaleceń i zwiększenia skuteczności leczenia.

Key words: heart failure, compliance, cognitive function

Słowa kluczowe: niewydolność serca, przestrzeganie zaleceń, funkcje poznawcze

Introduction

Heart failure (HF) is a major epidemiological and clinical issue. The number of HF patients amounts to over 23 million cases worldwide i.e. the disease affects approximately 2–3% of the total population [1] and 10–20% of the elderly population (7.8% of men and 4.5% of women above 60, and 8.6% of men and 11.5% of women above 80 [2]).

Because over 80% of HF patients are aged 65 or over, they tend to suffer from a range of other concurrent diseases and clinical syndromes. Frequent comorbidities include frailty syndrome and cognitive impairment, which may significantly affect compliance with therapeutic regimens, and which are related to a higher number of hospitalizations and higher mortality in elderly HF patients [3,4].

Despite the high prevalence of frailty and cognitive impairment in the HF patients' population, these conditions are not routinely screened for in clinical settings and guidelines on optimal assessment strategies are lacking [5].

Most available studies estimate the prevalence of cognitive impairment in HF patients at 25% [6], but much higher rates have also been reported [7–12]. In a study by Cameron et al. on patients hospitalized for HF, moderate cognitive impairment was found in as many as 73% of participants [13]. Unfortunately, most studies of cognitive deficits in HF include small patient groups and use diverse definitions of cognitive impairment. Harkness et al. [14] stated that patients who had recently been hospitalized are likely to suffer from more severe cognitive impairment, while other studies have included similar reports about patients with severe left ventricular dysfunction [15].

Numerous studies indicate that patients with HF are at a higher risk of cognitive impairment than those without HF [8,10,11] or with other cardiovascular diseases [8].

Despite available treatment options, prognosis is poor. One in five patients is rehospitalized within the first month after discharge, and one in three within the next two months. 80% of HF hospitalizations are rehospitalizations due to exacerbation [16]. Statistics on 1-year and 5-year mortality from HF present similar findings [17]. One significant cause of rehospitalization is non-adherence to treatment. Medication adherence is one of a constellation of self-care behaviors (i.e. adherence to treatment regimens, symptom monitoring and symptom management) that can improve HF outcomes.

The World Health Organization defines compliance as "the extent to which the behavior corresponds with agreed recommendations from a health care provider" [11].

Among HF patients, the rates of adherence reported in studies vary between 10 and 98%, depending on the measurement instruments used [18-20].

Apart from pharmaceutical treatment, lifestyle changes are a significant part of HF patient care and management. Nieuwenhuis et al. [21] demonstrated in their study that 72% of HF patients comply

with four out of six therapeutic recommendations, including pharmaceutical treatment (98%), follow-up visits (95%), restrictions in salt (79%) and fluid intake (73%), and daily weighing (35%) [21]. Poor pharmaceutical compliance and lack of lifestyle changes are problems found in one in three HF patients.

According to patients, one of the most common causes of non-adherence is difficulty in complying with the physician's orders due to incomprehension. Patients also report difficulty obtaining prescription renewals, treatment side effects, financial barriers, and memory deficits [22]. The WHO also states that disability and cognitive impairment are more common in elderly patients and constitute the most frequent cause of non-adherence. Cognitive impairment may affect outcomes by impeding self-care in heart failure, adherence to medication, symptom monitoring, dietary compliance, and daily weighing. Cognitive impairment may interfere with any of these necessary tasks; for example, doses of diuretics may be missed, or changes in symptoms (dyspnea, weight gain) may not be recognized until they become severe.

However, few papers have as yet assessed the correlation between cognitive impairment and adherence to treatment in elderly heart failure patients.

Material and methods

The aim of this study was to investigate whether cognitive impairment affects the level of adherence to therapeutic regimens and treatment in HF patients. The study involved patients suffering from HF and treated with oral medication and lifestyle changes. The following questions were posed in this study:

1. Does adherence differ between patients with and without cognitive impairment?

2. Is there any correlation between social (sex, age, marital status, education) and clinical variables (cognitive impairment, NYHA class, duration of illness, prescribed pharmaceutical treatment, left ventricular ejection fraction, number of rehospitalizations), and adherence to pharmaceutical and non-pharmaceutical treatment in HF?

Study design and sample

The study was conducted between January and August 2016, as a cohort study on a consecutive sample of 195 adults with a confirmed diagnosis of HF, enrolled from outpatient sites in the Lower Silesian Specialist Hospital. The study included patients scheduled for follow-up visits within the study period. The patients were recruited by a cardiologist on the basis of the relevant inclusion and exclusion criteria. Inclusion criteria were as follows: (1) age > 65 years, (2) clinically confirmed heart failure diagnosis, (3) the patient's written informed consent. Exclusion criteria were as follows: (1) age< 65, (2) requirement for intensive cardiac care, (3) history of stroke in the last six months, (4) inability to complete the questionnaires or lack of consent to participate in the study, (5) severe depression or terminal illness.

Ultimately, 25 patients were excluded. The study included 170 patients over 65 years of age, diagnosed with HF, receiving optimal treatment for at least six months. Questionnaires were distributed by a cardiac nurse. All patients were informed of the purpose and nature of our study, and provided written informed consent to participate. All patients completed all questionnaires.

Demographic and socio-demographic data (age, sex, years of education, marital status) were obtained from interviews performed by a cardiac nurse and from patient records. Clinical data, such as the New York Heart Association (NYHA) functional class, left ventricular ejection fraction (EF), number of rehospitalizations, and the medication taken were obtained from records and from personal interviews with the participants performed by a cardiac nurse.

Instruments

We used the Mini Mental State Examination (MMSE), developed by M. Folstein et al. It is a widely used screening test for dementia, whose advantages include speed of administration and simplicity of result interpretation [25]. The MMSE measures cognitive functions such as sense of direction, memory, attention, linguistic function, and visual–spatial abilities, as well as the ability to count, recall things, repeat, and carry out orders [25]. The possible score ranges from 0 to 30, with lower scores indicating more severe cognitive disorders. Patients with scores ≤23 are described as cognitively impaired [25].

Compliance with recommendations regarding a sodium-restricted diet, fluid restriction, exercise, and daily weighing was measured using the Revised Heart Failure Compliance Scale. Compliance was measured on a 5-point scale (0 = never; 1 = seldom; 2 = half of the time; 3 = mostly; 4 = always). Patients were asked to rate their compliance in the past week (medication, sodium-restricted diet, fluid restriction, and exercise), the past month (daily weighing), or the last 3 months (appointment keeping) before index hospitalization. Patients were defined as compliant when they followed a recommendation ‘always’ or ‘mostly’. Regarding daily weighing, patients were considered compliant when they weighed themselves daily or ≥3 times a week. Patients were considered to be “overall compliant” when they complied with ≥4 out of the 6 recommendations. The questionnaire has good psychometric properties — Cronbach’s alpha: 0.768, average inter-item correlation: 0.362.

The study was approved by the Bioethics Committee of the Wrocław Medical University, approval no. KB 67/2016.

Statistical analysis

1. The normality of the empirical distribution of quantitative variables was verified using the Shapiro–Wilk test. Mean values and standard deviations for the quantitative variables were calculated. The mean values were compared in three groups of patients using one-way analysis of variance (ANOVA). If the null hypothesis on the lack of differences between the groups was rejected, post hoc tests were performed (multiple comparison tests and the least significant difference (LSD) test).

2. Qualitative and ordinal variables were grouped into contingency tables, the values of these variables were summed (n_i), and percentages were calculated. The independence of the qualitative variables was verified using Pearson's chi squared test. The strength of correlations among variables was determined by calculating the Spearman's rank correlation coefficient (rho) and its significance (p). Findings were considered statistically significant at $p < 0.05$.
3. Multivariate linear regression analysis was used to assess the influence of independent variables on adherence. The forward stepwise approach was used to select variables. First, assumptions regarding the application of the least square method were verified, and analysis was performed to check for the presence of outliers. The standardized coefficients β and regression coefficients b were calculated for explanatory variables (MMSE and age). The statistical significance of particular variables in the model was verified using Student's t-test. The quality of the proposed linear multivariate regression model was evaluated by means of standard error of estimation (SE_e).
4. The statistical analysis was performed using the Statistica v. 10 software.

Results:

The survey included 170 patients with heart failure (90 female), aged 65 to 93 (mean M = 71.9±7.7 years). Participant characteristics were analyzed based on the patients' cognitive function scores. The basic socio-demographic characteristics of patients, broken down by cognitive function scores, are shown in the table. Patients in the cognitively impaired group were mostly female (69.7 % vs 42.3%), older (74 vs 68 y/o), single (71.2% vs 36.5%), and less educated (63.6% with primary education) (table 1).

Table 1. Socio-demographic characteristics of HF patients by cognitive function

Tabela 1. Charakterystyka socjo-demograficzna pacjentów z niewydolnością serca w zależności od wyniku kwestionariusza MMSE i zaburzeń funkcji poznawczych.

Characteristic	Total		Cognitive function				p test result
			normal MMSE score (>23)		MMSE score indicating impairment (≤23)		
	N = 170		N = 104		N = 66		
Age (years):							
Me (Q_1; Q_2)	70 (65; 77)		68 (65; 73)		74 (69; 82)		<0.001
Min – Max	61 – 93		61 – 93		63 – 87		
Sex:	n	%	n	%	n	%	
Male	80	47.1%	60	57.7%	20	30.3%	<0.001
Female	90	52.9%	44	42.3%	46	69.7%	
Residence:	n	%	n	%	n	%	
Urban	136	80.0%	85	81.7%	51	77.3%	0.609
Rural	34	20.0%	19	18.3%	15	22.7%	
Education:							
Primary	73	42.9%	31	29.8%	42	63.6%	<0.001
High school	57	33.5%	40	38.5%	17	25.8%	
College/University	40	23.5%	33	31.7%	7	10.6%	
Relationship status:							
Single	85	50.0%	38	36.5%	47	71.2%	<0.001
In a relationship	85	50.0%	66	63.5%	19	28.8%	

MMSE-Mini Mental State examination, Me-median,

The patients studied also had different clinical characteristics. Cognitively impaired patients had had HF longer (mean duration of illness 6.0 vs 5.6 years), were diagnosed with NYHA class IV more often (33.3% vs 15.3%) and had had more hospitalizations due to HF exacerbations in the previous six months (Me = 3 vs 2) than those with normal cognitive function (table 2).

Table 2. Clinical characteristics of HF patients by cognitive function

Tabela 2. Charakterystyka kliniczna pacjentów z niewydolnością serca w zależności od wyniku kwestionariusza MMSE i zaburzeń funkcji poznawczych.

Characteristic	Total		Cognitive function				p test result
	N = 170		normal MMSE score (>23)		MMSE score indicating impairment (≤23)		
Duration of illness in years							
Me (Q_1; Q_2)	5.8 (3; 7)		5.6 (3; 6)		6.0 (4; 7)		0.013
Min – Max	1 – 31		1 – 31		1 – 15		
Comorbidities:	n	%	n	%	n	%	
Ischemic heart disease	88	51.8%	55	52.9%	33	50.0%	0.834
Arterial hypertension	37	21.8%	23	22.1%	14	21.2%	0.959
Valvular heart disease	28	16.5%	21	20.2%	7	10.6%	0.153
Cardiomyopathy	29	17.1%	18	17.3%	11	16.7%	0.920
Diabetes mellitus	39	22.9%	21	20.2%	18	27.3%	0.377
NYHA class							
II°	93	54.7%	72	69.3%	21	31.8%	<0.001
III°	51	30.0%	28	26.9%	23	34.8%	
IV°	26	15.3%	4	3.8%	22	33.3%	
Medication used:							
ACE inhibitors	135	79.4%	86	82.7%	49	74.2%	0.257
Diuretics	150	88.2%	88	84.6%	62	93.9%	0.087
Glycosides	23	13.5%	18	17.3%	5	7.6%	0.115
Beta-blockers	80	47.1%	43	41.3%	37	56.1%	0.086
CCBs	2	1.2%	1	1.0%	1	1.5%	1.000
Ejection fraction (EF %)							
Me (Q_1; Q_2)	40 (35; 50)		45 (35; 55)		40 (35; 50)		0.208
Min – Max	20 – 70		20 – 70		20 – 60		
Number of hospitalizations							<0.001
Me (Q_1; Q_2)	2.5 (1; 4)		2 (1; 3)		3 (2; 4)		
Min – Max	0 – 8		0 – 8		0 – 7		

NYHA- New York Heart Association, Me-median, CCB Calcium channel blockers, ACE angiotensin-converting-enzyme inhibitor, EF- Ejection fraction

Scoring of compliance with heart failure treatment using the Revised Heart Failure Compliance Scale in groups of patients identified based on their cognitive function demonstrated that

cognitively impaired patients (MMSE≤23) showed lower compliance in all domains of the questionnaire, i.e.: 2.8 ± 1.0vs 3.3 ± 1.0 for keeping follow-up appointments, 2.8 ± 0.9 vs. 3.4 ± 0.9 for pharmaceutical compliance, 0.4 ± 0.8 vs. 1.4 ± 1.2 for regular body weight monitoring, 2.0 ± 1.3 vs. 2.7 ± 1.0 for reduced salt intake, 1.9 ±1.2 vs. 2.9 ± 1.0 for fluid intake restriction, and 0.5 ± 0.8 vs. 1.7 ± 1.1 for regular exercise. With the total compliance scores calculated, a statistically significant difference was found between the two groups. The cognitively impaired group obtained a total compliance score of 10.4 ± 4.0 points, while patients with normal cognitive function obtained 15.3 ± 3.6 points (table 3).

Table 3. Compliance with heart failure treatment as scored using the Revised Heart Failure Compliance Scale in groups of patients identified based on cognitive function — comparison results
Tabela 3. Analiza porównawcza przestrzegania zaleceń terapeutycznych kwestionariuszem Revised Heart Failure Compliance Scale w zależności od wyniku kwestionariusza MMSE i zaburzeń funkcji poznawczych.

Adherence to heart failure treatment (RHFCS questionnaire)	Total N = 170	Cognitive function		p test result
		normal MMSE score (>23)	MMSE score indicating impairment (≤23)	
1. Follow-up appointment keeping				
M ± SD	3.1 ± 1.0	3.3 ± 1.0	2.8 ± 1.0	<0.001
Me (Q_1; Q_3)	3 (2; 4)	4 (3; 4)	3 (2; 4)	
Min – Max	0 – 4	0 – 4	1 – 4	
2. Taking medication as prescribed				
M ± SD	3.1 ± 0.9	3.4 ± 0.9	2.8 ± 0.9	<0.001
Me (Q_1; Q_3)	3 (2; 4)	4 (3; 4)	2 (2; 4)	
Min – Max	0 – 4	0 – 4	2 – 4	
3. Daily weighing				
M ± SD	1.0 ± 1.1	1.4 ± 1.2	0.4 ± 0.8	<0.001
Me (Q_1; Q_3)	1 (0; 2)	2 (0; 2)	0 (0; 1)	
Min – Max	0 – 3	0 – 3	0 – 3	
4. Reduced sodium intake				
M ± SD	2.4 ± 1.2	2.7 ± 1.0	2.0 ± 1.3	0.003
Me (Q_1; Q_3)	3 (2; 3)	3 (2; 3)	2 (1; 3)	
Min – Max	0 – 4	0 – 4	0 – 4	
5. Restricted fluid intake				
M ± SD	2.5 ± 1.2	2.9 ± 1.0	1.9 ± 1.2	<0.001
Me (Q_1; Q_3)	3 (2; 3)	3 (2; 4)	2 (1; 3)	
Min – Max	0 – 4	0 – 4	0 – 4	
6. Regular exercise				
M ± SD	1.2 ± 1.2	1.7 ± 1.1	0.5 ± 0.8	<0.001
Me (Q_1; Q_3)	1 (0; 2)	2 (1; 3)	0 (0; 1)	
Min – Max	0 – 4	0 – 4	0 – 3	
Total compliance score (points)				
M ± SD	13.4 ± 4.5	15.3 ± 3.6	10.4 ± 4.0	<0.001
Me (Q_1; Q_3)	14 (10; 17)	16 (13; 18)	11 (7; 14)	
Min – Max	4 – 23	7 – 23	4 – 18	

RHFCS- Revised Heart Failure Compliance Scale, Me-median, SD- standard deviation, M-average

A very strong correlation was found between the total score in the MMSE cognitive function questionnaire and the total score in the RHFCS compliance questionnaire (r = 0.753). (fig. 1).

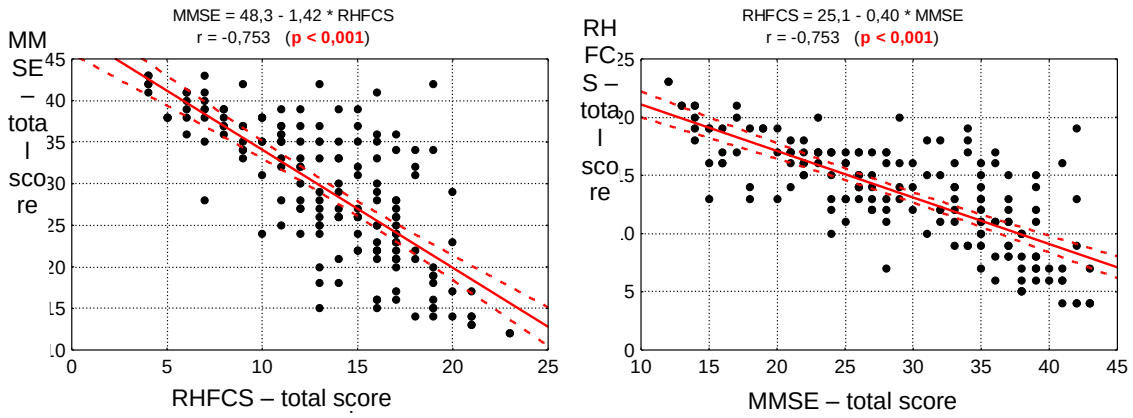

Fig. 1. Correlation diagram for cognitive function (MMSE score) and compliance with treatment (RHFCS score) in patients with HF

Fig. 1. Diagram korelacyjny pomiędzy zaburzeniami funkcji poznawczych (MMSE) a stosowaniem się do zaleceń lekarskich (RHFCS) pacjentów z niewydolnością serca

Analysis of correlations between cognitive function scores and compliance with treatment — Spearman's rho

Correlation analysis (Spearman's rho) and simple regression (b) results for total MMSE score and the RHFCS compliance domains show a statistically significant correlation between cognitive function and compliance with treatment in all domains studied: follow-up appointment keeping (rho=0.212; p=0.006), medication taking (rho=0.331; p<0.001), body weight monitoring (rho=0.516; p<0.001), salt restriction (rho=0.253; p=0.001), fluid intake restriction (rho=0.431; p<0.001), and regular exercise (rho=0.533; p=<0.001), as well as total compliance scores (rho=0.555; p<0.001). Simple regression analysis showed a similar association between MMSE scores and total RHFCS scores. The results are shown in table 4.

Table 4. Correlation analysis (Spearman's rho) and simple regression (b) results for total MMSE score and the RHFCS compliance domains

Tabela 4.Wyniki analizy korelacji (rho Spearmana) i regresji prostej (b) pomiędzy sumą punktów kwestionariusza MMSE a domenami compliance kwestionariusza RHFCS oceniające dostosowanie się do zaleceń terapeutycznych.

Compliance with HF treatment domains (RHFCS question number)	Correlation analysis		Regression analysis	
	rho	p	b	p
Follow-up appointment keeping	0.212	0.006	0.041	0.010
Taking medication as prescribed	0.331	<0.001	0.057	<0.001
Daily weighing	0.516	<0.001	0.113	<0.001
Reduced sodium intake	0.253	0.001	0.071	<0.001
Restricted fluid intake	0.431	<0.001	0.110	<0.001
Exercise	0.533	<0.001	0.127	<0.001
Total compliance score	0.555	<0.001	0.519	<0.001

RHFCS- Revised Heart Failure Compliance Scale, MMSE-Mini Mental State Examination, rho- Spearman's rho

Multiple-factor analysis

Subsequently, multiple-factor analysis was performed for associations between cognitive function and the RHFSC compliance domains. Multiple regression analysis showed cognitive function to be an independent predictor for regular body weight monitoring (β=1.223; $p<0.001$), fluid intake restriction (β=1.081; $p<0.001$), and regular exercise (β=1.237; $p<0.001$). The model was found to be statistically significant: $F(3.166) = 39.1$; $p<0.001$ (table 5).

Table 5. Pearson's linear regression coefficients (b) for cognitive impairment (MMSE) and RHFCS questions assessing compliance with treatment

Tabela 5. Wartości współczynników regresji liniowej Pearsona (b) pomiędzy zaburzeniami funkcji poznawczych (MMSE) a domenami kwestionariusza RHFCS oceniającego stosowanie się do zaleceń lekarskich

RHFCS questions	Simple regression		Multiple regression	
	b	p	beta	p
Regular follow-ups in the past 3 months	+0.940	0.010	0	NS
Pharmaceutical compliance	+1.584	<0.001	0	NS
Daily weighing	+2.129	<0.001	+1.223	<0.001
Reduced sodium intake	+1.153	<0.001	0	NS
Restricted fluid intake	+1.922	<0.001	+1.081	<0.001
Regular exercise	+2.179	<0.001	+1.237	<0.001
Total compliance score	+0.607	<0.001	0	NS

RHFCS- Revised Heart Failure Compliance Scale, MMSE-Mini Mental State Examination

Linear correlation analysis for compliance with treatment and selected predictors

Linear correlation analysis included the socio-demographic and clinical variables that differed between the patient groups studied (tables 1 and 2).

Univariate analysis showed that total compliance scores were positively affected by: education (b=2.449), being in a relationship (b=2.449) and MMSE scores (b=0.519); and negatively affected by: age (b=-0.126), NYHA class (b=-2.671) and the number of hospitalizations due to HF (b=-1.066). In multivariate analysis, the following predictors (stimulant variables) for compliance with heart failure treatment were identified: education (β=-1.124), being in a relationship (β=2.231) and lack of cognitive impairment as measured by the MMSE questionnaire (β=0.320); the number of hospitalizations due to HF was identified as a destimulant (β=-0.495) — table 6. The model was found to be adequate: $F(4.165) = 36.2$; $p<0.001$.

Table 6. Multivariate linear correlation coefficients for compliance with treatment (total RHFCS score) and the predictors analyzed

Tabela 6. Wartości współczynnika korelacji liniowej pomiędzy stosowaniem się do zaleceń lekarskich (zsumowana ocena compliance wg kwestionariusza RHFCS) a analizowanymi predyktorami.

Predictor	Univariate analysis		Multivariate analysis	
	b	p	b	p
Age	-0.126	0.004	0	NS
Male	0.460	0.506	0	NS
Education	2.449	<0.001	1.124	0.002
Relationship status — in a relationship	3.941	<0.001	2.231	<0.001
Duration of illness	0.014	0.853	0	NS
NYHA class	-2.671	<0.001	0	NS
Number of hospitalizations	-1.066	<0.001	-0.495	0.002
MMSE – total score	0.519	<0.001	0.320	<0.001

RHFCS- Revised Heart Failure Compliance Scale, MMSE-Mini Mental State Examination, NYHA- New York Heart Association

RHFCS = 4.16 + 1.124 × Education + 2.231 × Not lonely – 0.495 × No of hosp. + 0.320 × MMSE

Discussion:

An improved understanding of the determinants associated with adherence to medication and health behaviors has become an important factor in management strategies for HF. The ability to identify indicators of low medication adherence is crucial for both improving clinical care and determining the targets of intervention for the prevention of complications in HF and for HF treatment. The purpose of the study was to assess the impact of cognitive function on compliance with treatment. In the present study, cognitive impairment was found in 38.8% of patients, whose mean age was 70 y/o, with cognitively impaired patients 6 years older on average than patients with normal cognitive function.

The prevalence of cognitive impairment observed in our sample is similar to previous studies, which have reported rates of cognitive impairment of 17%–75% in patients with HF, dependent on the severity of HF, intensity of symptoms, and comorbidities [9, 14, 26–30]. The high rate of cognitive impairment among patients with HF, consistently reported across studies, highlights the importance of cognitive screening in this high-risk population.

A study by Huynh et al. demonstrated that even mild cognitive impairment was negatively associated with 30-day readmission or mortality rates, independently of other factors [28].

In the present study, cognitively impaired patients had higher NYHA classes and numbers of hospitalizations for HF exacerbations than patients with normal cognitive function. Published studies often report a correlation between disease severity evidenced by NYHA classes III–IV and functional or cognitive deficits [12, 31], and describe a positive impact of HF treatment and of cognitive function improvement [32].

The connection between poor adherence to therapy and cognitive function is not well documented in clinical practice, while the few existing reports bring conflicting findings. In some studies, impaired cognitive function in HF patients predicted poorer overall adherence [33] and self-care behaviors [34], but other studies did not support these findings [24].

In a study by Evangelista et al., elderly people were more compliant with diet and exercise recommendations than their younger counterparts. There was no difference in terms of other health-related behaviors [35].

In the present study, statistically significant differences in compliance with treatment were found between cognitively impaired patients and those with normal cognitive function. Patients with cognitive deficits obtained lower scores in all individual domains of the RHFCS questionnaire, and lower total scores. In single-factor correlation analysis and simple regression analysis, statistically significant correlations were found between cognitive function scores and all compliance questionnaire domains. Multiple-factor and multiple regression analyses showed cognitive function to be an independent predictor of compliance, particularly in the daily weighing, exercise, and fluid intake restriction domains. After adjusting for other variables, multiple-factor analysis showed that better cognitive function is a significant independent determinant of higher total compliance scores.

Dolansky et al. analyzed the correlation between cognitive impairment and compliance with sodium intake restrictions. Their results showed that cognitively impaired patients experienced difficulties in correctly collecting urine samples for analyses, but cognitive function was not found to be correlated with sodium intake in daily diet [36]

In a study by Cameron et al., mild cognitive impairment was significantly correlated with symptom monitoring capabilities, but not with adherence to sodium intake restrictions [13]. Contrary to these findings, Dickson et al. found that cognitive function significantly predicted self-care maintenance behaviors, specifically including following sodium intake recommendations [11].

Reported compliance with sodium-restricted diet varies from 50% [37] to 88% [38, 39], and the conflicting findings may result from the variety of questionnaires used for assessing both cognitive function and compliance. The present study used a compliance assessment questionnaire, while the authors cited mainly used self-care questionnaires [11, 13].

In the present study, regular exercise was complied with by a significantly lower percentage of patients in the cognitively impaired group, and was one of the least frequently followed recommendations, second to body weight monitoring. Moreover, multiple-factor analyses showed cognitive function to be an independent predictor of regular exercise. Published studies emphasize the fact that as many as 30% of patients stop exercising immediately after HF diagnosis [38], and 41%–58% do not comply with daily exercise and rest recommendations [35, 37].

Older adults with heart failure are known to have a much lower exercise tolerance, largely due to a 50%–75% decrease in aerobic capacity in addition to well-known alternations in peripheral musculoskeletal performance that contribute to fatigue and greater symptom severity [5]. In the study by Evangelista, 51% of patients above 70 y/o reported some degree of difficulty complying with exercise recommendations [35]. According to Meirelles, lower rates of hospitalization, improved physical function, and enhanced health-related quality of life are found in HF patients who routinely exercise [40]. Elderly patients who exercised at least 3 times a week were diagnosed with dementia less frequently than those who exercised less often [41].

In the present study, apart from cognitive function, factors such as age, disease severity, number of hospitalizations, education, and being in a relationship were found to have a significant impact on compliance with treatment.

Relationship status (being in a relationship) was a significant independent predictor of better compliance. The present findings are consistent with preliminary reports from other authors. In a study by Wu et al. [42], social support and financial status were significant predictors of dose count and dose-days, but were not correlated with the correct amount of doses taken at the right time. Sayers et al. observed a correlation between adherence to treatment and emotional support, but not instrumental support [43]. Dunbar et al. [44] confirm better adherence and compliance, fewer rehospitalizations, and fewer depressive symptoms for patients supported by their families and friends. Those enjoying social support maintained a proper diet, exercised regularly, complied with medication, and were able to recognize symptoms of decompensation [45]. Similarly, in a study by Ni [46], living alone and lacking knowledge were significantly correlated with poor compliance with daily weighing and fluid restriction.

Associations between education and compliance are seldom discussed in published studies. The few papers available report no correlation between education and compliance [35, 42], though knowledge has been confirmed to be correlated with better non-pharmaceutical compliance [46].

Murray et al. [47] noted that the frequency of rehospitalizations among HF patients who did not follow their therapeutic regimen was three times higher. In the present study, rehospitalizations for exacerbations and disease severity were independent predictors of worse compliance. Mockler et al. [48] demonstrated that discontinuation of the prescribed treatment was an independent predictor of rehospitalization for HF. Non-adherence to therapy was an independent factor associated with higher

mortality rates among the participants of the Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity (CHARM) trial program [49]. Old age, frailty syndrome and comorbidity may contribute to non-adherence among HF patients, consequently leading to more frequent rehospitalizations, institutionalization and ultimately, death [50].

Published evidence for the relationship between functional status (NYHA class) and adherence was rated inconsistent due to conflicting evidence. The study by Wu showed that patients with higher NYHA classes had lower adherence in terms of the percentage of days that the correct doses were taken. However, this study did not find a significant relationship between NYHA class and adherence calculated as the percentage of doses taken or the percentage of doses taken on schedule [42]. In a study by Rodgers et al., patients with higher NYHA classes had lower non-adherence levels [51], but reports also exist that do not indicate a significant correlation between the two variables [52, 53]. Jones emphasized that patients adhering to daily weight monitoring are less frequently rehospitalized for HF exacerbations, and in the present study, cognitively impaired participants had particularly low levels of compliance with the daily weighing recommendation, while their numbers of hospitalizations were higher, compared to respondents with normal MMSE scores. Non-adherence can be explained by polypharmacy, drug interactions, and adverse effects [20].

In summary, poorer cognitive function is associated with lower reported adherence among older adults with HF. Such findings may help account for the elevated mortality risk in HF patients with cognitive impairment. If replicated, clinician assessment of cognitive function among HF patients may provide key insight into patients' ability to adhere to treatment recommendations. Prospective studies that objectively measure treatment compliance (i.e. electronic monitoring) are much needed to clarify the relationship between cognitive function and HF patients' actual (as opposed to perceived) ability to adhere to treatment regimens [54].

Conclusion

Non-compliance is a major problem in elderly patients with HF cognitively impairment.

The cognitive function is an independent contributor to total compliance and to compliance with non-pharmaceutical recommendations (daily weighing, exercise, and fluid intake restrictions) in older adults with HF.

Being in a relationship and education are independent predictors of better compliance, while the number of rehospitalizations due to HF exacerbations is an independent predictor of worse compliance with treatment.

Early detection of CI may offer an opportunity for intervention and a key strategy for improving clinical outcomes in older adults with HF

Implications for practice

Cognitive impairment is a common comorbidity of HF that may affect patients' capabilities for adhering to prescribed treatment and lifestyle changes.

Simple memory screening may help identify patients with HF in need of assistance in accomplishing optimal self-care and adherence to pharmaceutical and non-pharmaceutical treatment. Cognitive function should also be assessed routinely in patients with heart failure, particularly when first diagnosed, when changes in treatment regimen occur, and with worsening disease severity, since these events have been shown to precede changes in cognitive function. Incorporating geriatric performance-based measures in heart failure management would allow for more treatment strategies aimed at improving physical function, cognitive outcomes, and quality of life. The role of family and social support in contributing to informed and active participation in the treatment process should also be emphasized.

Study limitations

We are well aware of the potential limitations of this study. The most important limitation is the fact that the study sample was recruited from a single center. Another limitation is that no other methods of adherence monitoring were used besides the self-assessment questionnaire. Studies using self-reported questionnaires may yield different results than those measuring adherence using a Medication Event Monitoring System. Another problem of using self-reported measures of sodium restriction, fluid restriction, and daily weighing adherence is the possible bias present when patients lack knowledge on the optimum amounts of sodium and fluids in their daily diet.

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Availability of data and materials

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Ethics approval and consent to participate

The study protocol was approved by the Independent Bioethics Committee of the Wroclaw Medical

University (decision no. KB 67/2016). All participants gave written informed consent after thorough explanation of the procedures involved. The study was carried out in accordance with the tenets of the Declaration of Helsinki.

Consent for publication

All co-authors have agreed to the submission and publication of this manuscript.

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