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Cognitive deficits and health-related quality of life in chronic heart failure

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Abstract

Background—Patients with chronic heart failure (HF) have cognitive deficits in memory, psychomotor speed, and executive function and poor health-related quality of life (HRQL), but the association between cognitive deficits and HRQL is unknown.

Objectives—The objectives of this study were to 1) evaluate the relationship between heart failure (HF) severity, age, comorbidities, and cognitive deficits and health-related quality of life (HRQL) among patients with chronic HF; and 2) examine whether cognitive deficits mediated the relationship between HF severity and HRQL.

Design and Sample—This study was part of a larger explanatory study; 249 patients with HF completed face-to-face interviews.

Methods—Measures of HF severity, comorbidity (multiple comorbid conditions, hypertension, and depressive symptoms), cognitive function (domains of language, working memory, memory, psychomotor speed, and executive function), and HRQL were obtained. Clinical variables were abstracted from patients' records. Statistical analyses were conducted using descriptive statistics, Pearson's correlation coefficients, and multiple linear regression analyses.

Results—Overall, the HRQL of patients was moderately poor. Heart failure severity, age, depressive symptoms, and total recall memory explained 55% of the variance in HRQL, but the contribution of memory was minimal (1%). Patients with more severe HF, younger age, and more depressive symptoms had poorer HRQL. Other cognitive function variables, multiple comorbidity, and hypertension were not significant explanatory variables for HRQL. Cognitive deficits did not mediate the relationship between HF severity and HRQL.

Conclusions—Novel interventions targeted at improving HRQL continue to be urgently needed, particularly among younger patients and patients with depressive symptoms. Measures of HRQL are not sufficient as outcomes when investigating cognitive deficits in HF. Investigators need to include outcome measures of patients' actual abilities to perform daily activities and HF self-care.

Keywords

heart failure; health-related quality of life; quality of life; cognitive deficits; cognitive impairment

Despite improvements in medical therapies and care delivery, patients with heart failure (HF) continue to have poor health-related quality of life (HRQL) due to disabling symptoms.^{1,2} Investigators recently reported that the symptom burden among patients with HF was equivalent to that of patients with advanced pancreatic and lung cancer.³ Therefore, improving HRQL in HF care remains a priority. Many patients are affected because HF is at epidemic proportions in the United States. More than 5.7 million Americans have HF and over 670,000 new cases are reported annually among persons age 45 years and older.⁴

Health-related quality of life is a multidimensional concept that includes biological variables, symptom status, functional status, health perceptions, and overall well-being.⁵ In previous studies, better physical symptom status, older age, and fewer depressive symptoms were associated with better HRQL.^{6–8} In contrast, variables such as HF etiology and medical comorbidities were not associated with HRQL. Few researchers, however, have investigated whether there is a relationship between cognitive deficits and HRQL in HF.^{9,10}

Twenty-five to 50% of HF patients have cognitive deficits in working memory, memory, psychomotor speed, and executive function.^{9–11} In a recently completed study among 414 participants (249 HF patients, 63 healthy participants, and 102 participants with major medical conditions other than HF), HF patients had significantly poorer cognitive function than the other groups. Compared to the healthy and medical participants, the HF patients had more impairments in memory, psychomotor speed, and executive function. More HF patients (24%) were impaired in three or more cognitive domains compared to healthy (14%) and medical (12%) participants ($p = .02$).¹²

Patients with HF perceive that cognitive deficit symptoms diminish their quality of life, but studies have been limited by small samples and self-report measures of cognitive function.^{13,14} In HF, actual injury to brain structures appear to underlie the impaired cognition^{15,16} and there is evidence that increased HF severity is associated with more cognitive deficits.^{9–11} One reason that cognitive deficits may mediate the relationship between HF severity and HRQL is because persons with such deficits interpret and report symptoms and HRQL

differently than persons with intact cognition.¹⁷ Among 133 survivors of sudden cardiac arrest enrolled in a randomized trial to reduce mortality, several survivors who had the most severe cognitive impairment had the best quality of life scores and the lowest psychosocial distress scores.¹⁸

Therefore, the purpose of this study was to evaluate the relationship between cognitive deficits and HRQL in HF. The conceptual model guiding this study is presented in Figure 1.¹⁹ In the model, cognitive deficits are proposed to be related to HRQL and HF severity is proposed to be related to cognitive deficits and HRQL. Age and comorbid conditions are proposed to be related to cognitive deficits and thereby influence HRQL; covariates of education, gender, and medications also may influence cognitive deficits and thus HRQL. Cognitive deficits are proposed to mediate the relationship between HF severity and HRQL. Guided by the model, we hypothesized that: 1) HF severity, age, comorbidity (multiple comorbid conditions, hypertension, and depressive symptoms), and cognitive deficits explain HRQL among patients with HF, and 2) the relationship between HF severity and HRQL is mediated by cognitive deficits.

Methods

Procedures

This study was part of a larger comparative and explanatory study to evaluate cognitive deficits among patients with chronic HF compared to healthy participants and participants with major medical conditions other than HF. Patients were recruited from seven clinic sites in a Midwestern metropolitan area from September 2004 to May 2008. The institutional review boards at the sites approved the study. All patients provided written informed consent prior to data collection.

Patients completed face-to-face interviews in their homes or at the clinics where they received care, whichever they preferred. Two members of the research team completed each interview. The first research assistant was a graduate nursing student trained in assessment of NYHA class who collected the sociodemographic, HF severity, and comorbidity data. The second research assistant trained by the senior neuropsychologist collected the neuropsychological data. The time required to obtain consent and administer the questionnaires and tests was approximately 90 to 120 minutes.

Sample

Patients were eligible for the study if they had a medical diagnosis of chronic systolic HF with a left ventricular ejection fraction of 40% or lower documented by echocardiography, nuclear imaging, or cardiac catheterization within the past two years. Only patients with systolic dysfunction and left ventricular ejection fractions of 40% or lower were enrolled because these patients had documented episodes of low cardiac output. Patients were excluded if they had conditions known to cause cognitive deficits (e.g., stroke, major psychiatric condition) or had a terminal illness such as end-stage cancer. Of the HF patients invited to participate in the study, 80 declined because of lack of interest ($n = 43$) or time ($n = 12$), too sick ($n = 9$), family problems ($n = 2$), did not remember being invited to participate ($n = 1$), moving ($n = 1$), too many physician appointments ($n = 1$), needed to discuss with family ($n = 1$), approach at another visit ($n = 1$), other ($n = 4$), and unknown ($n = 5$).

Measures

Health-related quality of life—The Minnesota Living with Heart Failure Questionnaire was used to measure HRQL.^{20,21} This is a 21-item questionnaire on which patients rate how

HF has impacted their lives in the past month on 6-point response scales (0 = “not at all” to 5 = “very much”). Higher scores indicate poorer HRQL. Construct validity was supported using factor analysis¹ and reliability was supported with a Cronbach’s alpha of .95 among 211 HF patients¹ and .91 among 638 HF patients.² In the current study, the Cronbach’s alpha was .93.

Heart failure severity—Two measures of perceived physical functional capacity (New York Heart Association [NYHA] class and the Duke Activity Status Index) were used to evaluate the severity of HF symptoms and function because these symptoms vary widely among patients with similar echocardiographic findings. Perceived physical functional capacity is defined as the maximal capacity a person believes he or she has to perform specific physical tasks.²² The NYHA class²³ was measured during the interview. Scores range from 1 (no fatigue, palpitations, dyspnea, or angina with any activity) to 4 (fatigue, palpitations, dyspnea, or angina at rest). Validity and reliability were reported among 75 HF patients; the weighted kappa statistic was .41 and there was 56% agreement on the NYHA class between the patients’ physicians and a cardiologist.²⁴ The Duke Activity Status Index is a 12-item list of activities to which patients respond as to whether they can perform the activities; the range of responses is from 1 (“yes with no difficulty”) to 4 (“no cannot perform it for other reasons”).²⁵ Possible weighted scores range from 0 to 58.20, with higher scores representing better functional capacity. The Index was correlated with oxygen consumption ($r = .34$, $p < .0001$) and the 6-minute walk test ($r = .53$, $p < .0001$) among 119 patients with severe chronic obstructive pulmonary disease.²⁶ In this sample, the Cronbach’s alpha was .82.

Comorbidity—The Charlson Comorbidity Index was used to measure multiple comorbidity.²⁷ To complete the Index, patients are asked whether they have a history of medical problems in 12 areas; responses are “yes” or “no”. The items are weighted by severity of the medical condition and each rating is worth 1, 3, or 6 points. A higher score represents more and/or more severe comorbid conditions. Among patients with chronic medical conditions, the Index categories were predictive of 1-year mortality and health care costs.²⁸

Hypertension—During the interview, blood pressure was measured using the American Heart Association recommended protocol.²⁹ The definition of hypertension was blood pressure higher than 140/90 mm Hg (130/80 mm Hg for patients with diabetes mellitus).³⁰

Depressive symptoms—The Patient Health Questionnaire-8 (PHQ-8)³¹ was used to measure depressive symptoms. This questionnaire was originally developed as the PHQ-9 based on the nine depression criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition. Item 9, which requires that participants respond to whether they have had suicidal ideation, is removed from the PHQ-8 because it is not necessary to use when assessing nonpsychiatric populations.³¹ Possible scores range from 0 to 24. Scores of 1 to 4 indicate no depressive symptoms; 5 to 9 mild depressive symptoms; 10 to 14 moderate depressive symptoms, 15 to 19 moderately severe depressive symptoms; and 20 to 24 severe depressive symptoms. Validity and reliability have been reported, with Cronbach’s alpha .89 among 3000 patients in primary care and .86 among 3000 obstetrical and gynecological patients.³² The Cronbach’s alpha in the current sample was .82.

Covariates—Variables that may influence cognitive function were evaluated as covariates. Selected medications have known effects on cognitive function. Medications evaluated were those with a primary indication for central nervous system disorders and those with major adverse effects on the central nervous system. These included major tranquilizers or anti-

psychotic medications, anti-depressants including lithium, Alzheimer disease medications (cholinesterase inhibitors), atropine and scopolamine, steroid hormones, beta-adrenergic antagonists, narcotic analgesics, and barbiturates.³³ Patients were categorized into two groups: receiving and not receiving a medication known to alter cognitive function.

Educational level and premorbid intellect influence cognitive function; the neuropsychological tests are sensitive to these variables. Therefore, education and premorbid intellect (measured by the Wechsler Test Adult Reading) were included as covariates in the models. Gender was included as a covariate because in past studies, elderly women who received hormone replacement therapy had poorer cognitive function than women who did not receive it.³⁴ Oxygen saturation, assessed by pulse oximetry, was used as a covariate for severe resting decompensation.

Cognitive deficits—Cognitive deficits were measured using a valid, reliable neuropsychological test battery (Table 1) designed to assess the domains most often included in a neuropsychological examination for vascular cognitive disorders.³⁵ To evaluate patients' general mental status, the Mini-Mental State Examination³⁶ was administered. This is a brief 30-point screening measure commonly used to screen for cognitive deficits; higher scores indicate better mental status. To estimate premorbid intellect, the Wechsler Test of Adult Reading (WTAR)³⁷ was administered. In this test, persons are asked to pronounce a list of words aloud that are phonologically irregular. The test yields a standard score (mean = 100, standard deviation = 15, without adjusting for education). The WTAR was used as a covariate in the analyses.

To measure the language domain, the Boston Naming Test³⁸ was administered. Patients are asked to name line drawings of common objects for this test, with higher scores indicating more ability (possible raw score may range from 0 to 60). To measure working memory, the Wechsler Adult Intelligence Scale, 3rd edition (WAIS-3), Digit Span Subtest³⁹ was administered. Scores included the raw forward (possible range 0 to 14) and raw backward (possible range 0 to 16). The raw span scores were analyzed separately and a scaled score (mean = 1-, SD = 3) was created by transformation of the total score.³⁹ To measure verbal learning and memory, the Hopkins Verbal Learning Test⁴⁰ was administered. For this test, patients are presented a 12-word list over three trials and are asked to recall the words after each list presentation. Following a 20-minute delay, they are asked to recall the 12 words. Scores analyzed are the total learning over the three trials (possible score 0 to 36 for summed recall of trials) and delayed recall (possible score 0 to 12). To measure visuospatial abilities, the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Figure Copy and Figure Memory measures were used.³⁵⁻⁴¹ Five figures that increase in complexity (circle, diamond, intersection, rectangle, and cube) are shown to patients and they are asked to draw a copy of each figure. Possible scores (Figure Copy) range from 0 to 11, with higher scores indicating greater abilities. After a 20-minute delay, patients are asked to remember and draw the figures again; possible scores (Figure Memory recall) range from 0 to 14.

To measure psychomotor speed, the Digit Symbol Subtest³⁹ and the Trail Making Test Part A⁴² were administered. In the Digit Symbol Subtest, patients are asked to use a key that shows individual pairings of numbers with symbols to match a series of numbers with the symbols. The scaled score (from the WAIS-3 standardization sample, mean = 10, standard deviation = 3) is the measure of analysis with higher scores being better. In the Trail Making Test Part A, patients are asked to connect the numbered circles displayed on a page as quickly as possible. The measure of analysis is the number of seconds to complete the test; higher scores (longer time) reflect slower psychomotor speed.

To measure executive function, the Trail Making Test Part B⁴² and the Controlled Oral Word Association⁴³ were administered. For the Trail Making Test Part B, patients are asked to connect numbered and lettered circles sequentially in alternate alpha-numeric order as fast as possible. The measure of analysis is the number of seconds to complete the test, with higher scores being worse. In the Controlled Oral Word Association test, the speed with which patients can search and retrieve a word from their mental lexicon is measured. A letter of the alphabet is given to patients and they are asked to name as many words as they can that begin with that letter. The number of words generated in 90 seconds for each letter is the measure of analysis.

Statistical Analysis

Descriptive statistics were computed for study variables. For the neuropsychological tests, Z-scores were constructed using neuropsychological test scores obtained from a local sample of 63 education-matched healthy individuals. These Z-scores were used to perform statistical analyses. Cognitive deficit cutoff scores were defined from the healthy individuals' Z-scores using the 7th percentile. Patients who performed at or below the 7th percentile cutoff were regarded as being cognitively impaired in that domain.⁴⁴ Pearson's product-moment correlation coefficients were computed to assess multicollinearity and to examine relationships between the continuous study variables and HRQL. The ANOVA and t-test were computed to examine differences in HRQL by NYHA class and hypertension, respectively. A series of multiple linear regression analyses were conducted with HRQL (Living with Heart Failure Questionnaire) entered as the dependent variable. Explanatory variables were HF severity (NYHA and Duke Activity Status Index), age, multiple comorbidity (Charlson Comorbidity Index), hypertension, depressive symptoms (PHQ-8), and cognitive deficits (each neuropsychological test entered in separate equations to examine the cognitive domains individually). Covariates entered were medications that influence cognitive function, education, premorbid intellect, gender, and oxygen saturation. A quadratic term for each cognitive function variable was included to test for a non-linear effect between cognitive deficits and HRQL. Mediation of each cognitive function variable on the relationship between HF severity and HRQL was assessed by estimating the indirect effect using a bootstrap algorithm.⁴⁵ The sample size was based on the comparative aim of the study to compare HF patients to healthy and medical participants¹² and was sufficient for this analysis.⁴⁶

Results

Demographic and clinical data are presented in Table 2. The sample included 249 patients with chronic HF. The mean age of patients was 62.9 years (standard deviation $\pm$ 14.6, range = 20 to 93), 63% were men, and 56% were married. Patients reported race as White (67%), African American (32%), Asian (1%), and American Indian or Alaskan Native (<1%) and ethnicity as 100% non-Hispanic. The mean education level was 12.9 years. The NYHA class of patients was: I = 15%; II = 34%; III = 39%; and IV = 12%. The patients had a mean left ventricular ejection fraction of 28%; 41% had implantable cardioverter-defibrillators and 22% had biventricular pacemakers. The average HF duration was 7.5 years (standard deviation = 7.5 years).

Table 3 presents the descriptive statistics for the study variables. Overall, the HRQL of patients was moderately poor and HF severity was high with low perceived physical functional capacity. Patients had moderate to moderately high numbers of comorbid conditions. Mean blood pressure and depressive symptoms were within normal range, but 17% had hypertension and 26% had high depressive symptoms (PHQ-8 total score equal to or greater than 10). Mean scores on the neuropsychological tests were within normal limits. However, the Z-score analysis indicated that patients had deficits in memory (Hopkins total

recall, 23%), psychomotor speed (Digit Symbol, scaled, 19%), and executive function (Trail Making Test B, 19% and Controlled Oral Word Association, 16%). Twenty-four percent had cognitive deficits in three or more domains. The sample size varies slightly across analyses because a few patients were unable to complete the full neuropsychological test battery.

The Pearson's correlation coefficients demonstrated that depressive symptoms ($r = .68, p < .0001$) and perceived functional capacity (Duke Activity Status Index) ($r = -.58, p < .0001$) were strongly associated with HRQL. The associations between age and HRQL ($r = -.31, p < .001$) and multiple comorbidity and HRQL ($r = .21, p = .001$) were moderate. Patients with higher HF severity (NYHA class) had significantly poorer HRQL ($F = 39.4, p < .0001$). Means and standard deviations of the HRQL scores for the four NYHA classes were: I, 21.5 ± 15.5 ; II, 36.7 ± 18.7 ; III, 55.9 ± 23.7 ; and IV, 63.9 ± 18.2 . All means were significantly different from each other after Tukey adjustment except for classes III and IV. There was no difference in HRQL by hypertension status ($t = .44, p = .66$). Three cognitive function variables were significantly negatively associated with HRQL: psychomotor speed as measured by Digit Symbol, scaled ($r = -.28, p < .0001$), working memory as measured by Digit Span, scaled ($r = -.15, p = .02$), and executive function as measured by Trail Making Test B ($r = -.14, p = .03$). All other correlations between the cognitive function variables and HRQL were lower than .12 and not significant.

In the regression models, memory (Hopkins Verbal Learning Test total recall) was the only cognitive function variable associated with HRQL. Measures of psychomotor speed (Digit Symbol) and executive function (Trail Making B) approached significance. The hypothesis that HF severity, age, comorbid conditions (depressive symptoms), and cognitive deficits in memory explain HRQL was supported. Heart failure severity (NYHA class and Duke Activity Status Index), age, the comorbid condition of depressive symptoms, and memory were all significant and accounted for most of the unique variance in HRQL (Table 4). Younger patients with more severe functional limitations and poorer perceived functional capacity, more depressive symptoms, and poorer memory had worse HRQL. Although significant, memory accounted for only 1% of the variance in HRQL. Age, HF severity (Duke Activity Status Index), and depressive symptoms contributed most to the HRQL variance (5%, 6%, and 10%, respectively, for unique variance). Covariates of medications that influence cognitive function, years of education, gender, and oxygen saturation were not associated with HRQL while premorbid intellect was. In total, the significant explanatory variables (HF severity, age, depressive symptoms, and memory) explained 55% while the covariates, hypertension, and multiple comorbidity explained 11% of the variance but were not significant.

There was no evidence that cognitive deficits mediated the relationship between HF severity (NYHA class) and HRQL. The quadratic effects between cognitive deficits and HRQL were not significant at the .05 level and therefore, a curvilinear relationship was not supported.

Discussion

This is one of the first studies to examine the influence of cognitive deficits on HRQL in a carefully characterized and diverse sample of HF patients. Importantly and as hypothesized, HF severity, age, depressive symptoms, and memory explained HRQL in these patients, accounting for 55% of the variance. Although memory was a significant variable, it accounted for only 1% of the HRQL variance. The finding that HF severity, age, and depressive symptoms explained HRQL is consistent with other studies and supports the critical role that HF symptoms, physical function, and depressive symptoms play in diminishing HRQL in HF.⁶⁻⁸ The majority of patients in this sample were receiving optimized medical therapies, yet they had moderately poor HRQL, highlighting the

challenges of providing care to these vulnerable patients with complex needs. Novel interventions directed at ameliorating symptoms and improving HRQL continue to be urgently needed.

The low associations between the cognitive function variables and HRQL are consistent with some past research with other perceptual variables. For example, among 50 HF patients, cognitive impairment was not associated with depressive symptoms or positive affect.⁴⁷ The low associations between cognitive function and HRQL suggest that they are two distinct constructs with little shared variance. In contrast to past research that used self-report measures of cognitive deficits,^{13,14} no evidence was found to support that cognitive deficits measured by neuropsychological tests mediated the relationship between HF severity and HRQL. Given the low associations between the cognitive function variables and HRQL, it would be unlikely to find a mediation effect. In this sample, 24% of the patients had cognitive deficits in three or more domains¹² which may have contributed to the low associations with HRQL. Patients with cognitive deficits do not consistently report poor HRQL and as the deficits become worse, they sometimes report better HRQL.^{17,18} It is appropriate to measure HRQL as a perception, but when investigating cognitive deficits in HF, other outcomes also need to be evaluated. Patients' abilities to perform daily activities and HF self-care may be compromised and need to be evaluated. The inability to perform instrumental activities of daily living (IADLs) was associated with cognitive deficits among patients awaiting cardiac transplant.⁴⁸ Patients with HF and cognitive deficits reported difficulties in performing IADLs (e.g., maintaining a checkbook, managing personal finances) that lead to emotional distress and sense of loss.⁴⁹ In future studies, investigators need to examine associations between cognitive deficits and performance of IADLs and HF self-care in order to design testable interventions for improving cognitive function and outcomes.

Enrollment of a carefully characterized sample of HF patients and representative numbers of women and minority (African-American) patients were strengths of this study. Valid, reliable measures were administered to evaluate cognitive deficits and HRQL. Comorbid conditions common to HF were included as variables. The cross-sectional nature of the study limited the ability to fully examine associations between HF severity, cognitive deficits, and HRQL over time. Investigators need to conduct longitudinal studies that would provide useful information about the associations among the variables and how they change over time as part of the HF trajectory of illness. The measures of HF severity and cognitive deficits were limited by the fewer numbers of patients with NYHA class IV who participated. However, this was expected because class IV patients are symptomatic at rest and may refuse participation because of fatigue or other factors. Results are only applicable to patients with chronic systolic HF with left ventricular ejection fractions of 40% and lower.

In conclusion, HF severity, age, and depressive symptoms explained HRQL. Cognitive deficits were not associated with HRQL nor did they mediate the relationship between HF severity and HRQL. Health-related quality of life and cognitive deficits represent distinct constructs. Future studies are needed to design and test novel interventions targeted at improving HRQL and at improving the daily lives of patients. Studies continue to be needed to more thoroughly understand the mechanisms responsible for the memory loss, psychomotor slowing, and decreased executive function in HF and to identify testable interventions to prevent or delay cognitive decline.

This study has important clinical implications. Clinicians need to identify patients most at risk for poor HRQL: patients with more severe HF, younger patients, and patients with high depressive symptoms. These patients are in need of more individualized educational and

care interventions to help them manage in their daily lives. Cognitive deficits in memory, psychomotor speed, and executive function are common and patients need to be evaluated for these deficits; the plan of care needs to be modified accordingly. Treatment of depressive symptoms is indicated. It is essential that clinicians involve family caregivers in the plan of care for patients with severe HF and those with cognitive deficits.

Summary and Implications

Heart failure severity, age, and depressive symptoms explained HRQL. Patients with more severe HF, young patients, and patients with more depressive symptoms had poorer HRQL. Cognitive deficits were not associated with HRQL nor did they mediate the relationship between HF severity and HRQL.

Clinicians need to identify patients most at risk for poor HRQL: patients with more severe HF, younger patients, and patients with high depressive symptoms. These patients need individualized educational and care interventions to help them manage in their daily lives. Evaluation of patients for deficits in memory, psychomotor speed, and executive function are needed and the plan of care should be modified accordingly. Treatment of depressive symptoms is indicated. It is essential that family caregivers be involved in the care patients with severe HF, poor HRQL, and cognitive deficits.

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Figure 1.
 Conceptual Model of Cognitive Deficits and Health-Related Quality of Life in Chronic Heart Failure¹⁹
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Table 1**Cognitive Domains and Neuropsychological Tests^a**

Cognitive domains	Neuropsychological tests and scoring
Global cognitive function	Mini-mental State Examination; raw score
Premorbid intellect	Wechsler Test of Adult Reading; standard score of mean = 100 and standard deviation = 50
Language	Boston Naming Test; raw score of line drawings named
Working memory	Digit Span; raw scores for forward and backward spans; scaled score total mean = 10 and standard deviation = 3
Declarative verbal memory	Hopkins Verbal Learning Test; total recall of 12-word lists presented three times; delayed recall of list after 20 minutes
Visuospatial ability	Figure Copy from the CERAD battery; total copy is drawing 5 figures; Figure Memory (recall) is drawing the figures after 20 minutes
Psychomotor speed	Digit Symbol; scaled score (mean = 10, standard deviation = 3) Trail Making Test Part A; raw score is time in seconds
Executive function	Trail Making Test Part B; raw score is time in seconds Controlled Oral Word Association; raw score is the number of words generated over 90 seconds

^a A battery of neuropsychological tests was used (available from the author) known to measure language, working memory, memory, psychomotor speed, and executive function reliably and validly.

Table 2

Demographic and Clinical Variables (n=249)

Variable	
Age (Mean, SD ^a)	62.9 + 14.6
Sex (n, %)	
Men	158 (63%)
Women	91 (37%)
Race (n, %)	
African American	79 (32)
Asian	2 (1)
White	167 (67)
American Indian/Alaskan Native	1 (< 1)
Other	0 (0)
Ethnicity (n, %)	
Hispanic	0 (0)
Non-Hispanic	248 (100)
Missing/Not Reported	1 (<1)
Marital status (n, %)	
Married	140 (56)
Not married	109 (44)
Economic status (n, %)	
Comfortable	123 (49)
Just enough to make ends meet	81 (33)
Not enough to make ends meet	44 (18)
Missing/Not Reported	1 (< 1)
Education, years (mean ± SD)	12.9 ± 2.8
Premorbid intellect ^b (mean ± SD)	94.3 ± 17.0
NYHA class ^c (n, %)	
I	38 (15)
II	85 (34)
III	97 (39)
IV	29 (12)
Ejection fraction (mean ± SD)	28.2 ± 10.3
Implantable cardioverter-defibrillator (n, %)	103 (41)
Bi-ventricular pacemaker (n, %)	55 (22)
Heart failure duration (mean ± SD)	7.5 ± 7.5

^aStandard deviation^bWechsler Test of Adult Reading, standard score; nationally standardized sample (mean = 100, SD ± 15)^cNew York Heart Association = NYHA

Table 3

Means, Standard Deviations, and Ranges of Variables (n = 249)

Variable	Mean $\pm$ SD ^a	Actual range
Health-related quality of life (Living with Heart Failure Questionnaire)	45.0 (24.6)	0-100
Perceived functional capacity (Duke Activity Status Index)	15.1 $\pm$ 12.5	0 – 58
Oxygen saturation	95.7 $\pm$ 1.9	82 – 99
Comorbidity (Charlson)	3.1 $\pm$ 1.8	1 – 10
Depressive symptoms (PHQ-8)	6.5 $\pm$ 5.5	0 – 24
Systolic blood pressure	116.9 $\pm$ 18.2	80 – 183
Diastolic blood pressure	68.6 $\pm$ 11.6	45 – 116
Mini-Mental State Examination	27.6 $\pm$ 2.2	15 – 30
Language (Boston Naming Test # correct)	52.0 $\pm$ 7.4	18 – 60
Working memory (Digit Span)		
Forward	6.2 $\pm$ 1.3	3 – 9
Backward	4.3 $\pm$ 1.1	2 – 8
Scaled	9.7 $\pm$ 2.9	4 – 19
Memory (Hopkins Verbal Learning Test; raw scores)		
Total recall	20.0 $\pm$ 5.8	1 – 32
Delayed recall	6.8 $\pm$ 2.9	0 – 12
Visuospatial ability (Figure Copy and Memory, raw scores)		
Figure Copy total	8.7 $\pm$ 1.5	0 – 11
Figure Memory recall	7.5 $\pm$ 2.7	0 – 14
Psychomotor speed		
Digit Symbol, scaled	8.5 $\pm$ 2.9	3 – 16
Trail Making Test A (time in seconds)	48.8 $\pm$ 24.1	16 – 190
Executive function		
Trail Making Test B (time in seconds) Controlled Oral Word	133.4 $\pm$ 69.8	30 – 300
Association (raw scores)	30.1 $\pm$ 11.9	4 – 65

^aStandard deviation = SD

Table 4

Multiple Linear Regression Model Explaining Health-Related Quality of Life (Living with Heart Failure Questionnaire) (n = 237)

Variables	b^a	SE^a	$t(F)^b$	p^c	s^2d	Cumulative R^2	bivariate r or point biserial
Cognitive medications ^e	1.23	2.01	.61	.54	.00	.01	.09
Gender (women) ^e	-1.59	2.12	-.75	.45	.00	.01	.04
Education (years) ^e	.39	.46	.84	.41	.00	.06	-.20
Premorbid intellect ^e	-.23	.07	3.15	.002	.02	.08	-.25
Oxygen saturation ^e	-.09	.54	-.17	.87	.00	.08	-.12
Multiple comorbidity	-.18	.55	-.33	.74	.00	.11	.21
Hypertension	-1.07	2.63	-.41	.68	.00	.11	-.03
Age	-.39	.07	-5.51	<.0001	.05	.20	-.31
Perc. functional capacity	-.75	.12	-6.45	<.0001	.06	.51	-.58
Depressive symptoms	1.74	.21	8.25 (3.59)	<.0001 (.01)	.10	.64	.68
NYHA class (Reference: Class IV)							
Class I	-6.63	5.36	-1.24	.22	.00	.64	--
Class II	-10.64	3.88	2.74	.01	.01	.65	--
Class III	-4.30	3.54	1.22	.22	.00	.65	--
Memory (total recall)	-1.99	.82	-2.42	.02	.01	.66	-.11

Total $R^2 = .66$; total adjusted $R^2 = .64$ ^a beta coefficient and standard error.^b t reported for individual variables, F also reported for overall NYHA effects.^c p -value reported for testing individual variables equal to 0, and also overall for NYHA effects only.^d squared semi-partial correlation coefficient (Type II). The squared semi-partial correlation for an explanatory variable can be interpreted as the proportion of variance in the dependent variable (HRQL) uniquely associated with that explanatory variable.^e Covariates.