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Cognitive Function Does Not Impact Self-Reported Health-Related Quality of Life in Heart Failure Patients

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Abstract

Introduction—Adults with heart failure (HF) often demonstrate impairment across multiple domains of cognitive functioning and report poor health-related quality of life (HRQoL).

Surprisingly, cognitive deficits were generally not associated with HRQoL in a carefully evaluated sample (Pressler, Subramanian, & Kareken, 2010). The exception was memory, which was only weakly associated with HRQoL. However, cognitive deficits interfere with self-care and disease self-management, which could be expected to affect HRQoL.

Objective—We sought to verify this counter-intuitive finding in a large well-characterized sample of HF patients using a well-validated neuropsychological battery.

Method—Participants were 302 adults (63% male) predominately Caucasian (72.5%) HF patients (68.7 ± 9.6 years) recruited from two medical centers. Self-reported HRQoL was assessed using the Kansas City Cardiomyopathy Questionnaire (KCCQ). Participants completed a neuropsychological battery examining attention, executive function, memory, and visuospatial functioning. Hierarchical multiple linear regression was used for analyses.

Results—Mild global cognitive impairment was observed in 29.5% of the sample (Modified Mini-Mental State Examination score < 90). Controlling for gender, depression, HF severity, premorbid IQ, comorbidities, and education, only executive function predicted HRQoL, $\beta = .17$, $p < .05$. However, executive function only accounted for .6% of the variance in HRQoL.

Conclusion—Cognitive function generally did not predict HRQoL in HF patients, consistent with Pressler et al. (2010). The correlates of HRQoL in HF do not appear to include mild cognitive impairment. Other factors may play a bigger role such as disease severity, age and depressive

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symptoms (Pressler et al., 2010). Future studies should investigate modifiable determinants of HRQoL in HF patients, toward the goal of finding interventions that preserve HRQoL during this chronic illness.

Keywords

heart failure; cognition; health-related quality of life

Introduction

In the United States, over 5 million adults have heart failure (HF) [1]. HF is accompanied by burdensome somatic symptoms including dyspnea, fatigue, and edema [2,3], and depression is common [4, 5]. These factors contribute to many HF patients reporting poor health related quality of life (HRQoL) [2]. Independent predictors of poor HRQoL include age, gender, HF severity, depressive symptoms, socioeconomic status, and the presence of two or more co-morbidities [6–10]. Moreover, patients with poor HRQoL evidence poor prognosis, including more frequent hospitalizations and increased mortality [11–13].

Cognitive deficits interfere with self-care and disease self-management, which could in turn affect HRQoL. Evidence indicates that 30–50% of HF patients demonstrate impairment across multiple domains of cognitive functioning, including attention, executive function, and memory, [14–16]. Bennett, Sauvé, and Shaw [17] developed a conceptual frame work based on empirical data to guide examination of cognitive impairment in HF based on the assumption that physiological changes resulting from HF contribute to cognitive impairment, which then leads to diminished HRQoL. The model suggested that cognitive impairment, particularly deficits in memory and attention, contribute to poor HRQoL by interfering with disease self-management and, thus, contributing to worsening symptomology, and increasing morbidity and mortality [17]. Although intuitive and empirically-driven, this conceptual framework has not been conclusively demonstrated by later reports using objective, neuropsychological assessment of cognitive function.

In HF patients, early reports suggested a relationship between QoL and self-reported cognitive function [11,18]. However, these studies were restricted by limited sample sizes and lacked objective assessment of cognitive function. Reports of other cardiovascular disease samples also demonstrated associations between cognitive function and QoL. In patients enrolled in cardiac rehabilitation, poorer baseline cognitive performance was associated with lower baseline QoL and smaller improvements in QoL following cardiac rehabilitation [19]. Similarly, another study reported that poorer cognitive function was associated with lower QoL 5 years following cardiac surgery [20]. In addition, it has been reported that cognitive decline restricts improvement in QoL following coronary artery bypass graft surgery [21].

Surprisingly, studies of patients with HF produced different conclusions. Cognitive deficits (domains of language, working memory, memory, psychomotor speed, and executive function) generally were not associated with HRQoL in 249 HF patients in a carefully evaluated sample [14]. The exception was that total recall memory was weakly associated with HRQoL. The authors noted that 24% of the sample demonstrated cognitive

impairments in at least three domains and suggested that HRQoL and cognitive deficits may be separate constructs in patients with HF, exhibiting little or no overlap. However, a smaller study reported that cognitive impairment, defined as a Mini-Mental State Examination (MMSE) score below 25, was associated with poorer QoL in a sample of 136 hospitalized HF patients in Serbia [7]. However, in multivariate analyses cognitive impairment did not remain an independent correlate of QoL, as only the presence of depressive symptoms, NYHA class, income, and duration of HF remained independently related to QoL[7]. Ultimately this report also suggested that factors other than cognitive impairment may be the strongest correlates of HRQoL in HF.

The complex nature of the relationship between HRQoL and cognitive function could result in conflicting reports. For example, Bennet et al. [17] suggested that a curvilinear relationship may exist. However, Pressler et al. [14] found no indication of a curvilinear relationship.

These findings that cognitive function is unrelated to HRQoL in HF are somewhat counter intuitive. We sought to replicate these reports in a large, well-characterized sample of HF patients using a well-validated, comprehensive neuropsychological battery to assess global cognitive functioning, executive function, attention, memory, and visuospatial ability. In keeping with recent reports [14], we hypothesized that only a weak relationship, if any, would be observed between HRQoL and cognitive performance. Furthermore, we tested curvilinear effects.

Method

Participants

The sample consisted of 302 older adults with HF enrolled in the larger, ongoing Heart Failure Adherence, Behavior, and Cognition Study (Heart ABC) (22). Study eligibility requirements were as follows: (1) Aged 50–85 years at enrollment, (2) Documented systolic HF diagnosis within 36 months of study enrollment, (2) Physician-documented New York Heart Association class II or III 3 months duration, (3) No cardiac surgery within last 3 months, (4) No history of neurological disorder or injury (e.g., Alzheimer's disease, dementia, stroke, seizures), (5) No history of moderate or severe head injury, (6) No past or current history of psychotic disorders, bipolar disorder, learning disorder, developmental disability, renal failure requiring dialysis, or untreated sleep apnea, (7) No current substance abuse or within the past 5 years, and (8) No current use of home tele-health monitoring program for HF. Participants with complete data on the measures of HRQoL and cognitive function were selected for analysis.

Measures

Self-Reported HRQoL—The Kansas City Cardiomyopathy Questionnaire (KCCQ) was used to measure self-reported HRQoL[23]. The KCCQ demonstrates good psychometric properties [24, 25]. It is more contemporary and has a better factor structure than the Minnesota Living with Heart Failure Questionnaire. The KCCQ asks the patient to self-report on any physical limitations and symptoms (ankle swelling, chest pain, and shortness

of breath) and how any of these may affect the patient's satisfaction and enjoyment of life [25]. Higher scores represent better health status. Although the overall summary score has also been used in other studies to measure HRQoL, the quality of life (QoL) score was used in the current analyses. The QoL domain has good reliability (Chronbach's $\alpha = .78$) and validity (moderate to strong correlation with the general health perception scale of the SF-36, $r = 0.46$; strong correlation with NYHA class, $r = -0.64$) [24, 25].

Cognitive Function—Cognitive function across multiple domains was measured using a comprehensive neuropsychological test battery, the gold standard for detecting cognitive impairment. The battery consisted of tests with strong psychometric properties and assessed the following four cognitive domains:

Attention—Stoop Word and Color subtests [26, 27], Letter-Number Sequencing (LNS) [28], and the Trail Making Test A (TMT-A)[29]. The Stroop Word and Color subtests assess attention and processing speed through the first two of three tasks. In the first task, individuals say the names of colors printed in black ink. In the second task, the participant must state the color of the ink regardless of the written word. Test-retest reliability is adequate for both tasks (Word = .88; Color = .79) [27]. LNS assesses working memory by asking participants to verbally reorganize numbers and letters that are presented in an unordered sequence. Test-retest reliability is estimated to be $r = 0.75$ [28]. TMT-A evaluates psychomotor speed and complex visual attention by asking individuals to draw lines to connect 25 numbered circles in ascending order as quickly as possible. Estimated test-retest reliability is $r = 0.79$ [29].

Executive function—Trail Making Test B (TMT-B)[29], the Stroop Color Word subtest [26, 27], and the Frontal Assessment Battery [30, 31]. TMT-B measures executive dysfunction by instructing participants to draw lines to connect circled numbers and letters in ascending order, alternating between numbers and letters. Estimated test-retest reliability is $r = 0.89$ [29]. The Stroop Color Word subtest assesses selective attention, cognitive flexibility, and processing speed through the final of three tasks. Test-retest reliability is estimated at $r = .71$ [27]. Participants are asked to read a list with written color names that differ from the word color ink they are printed in. The FAB briefly assesses executive functioning through six subtests designed to measure abilities related to conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy. The FAB demonstrates good test-retest reliability ($r = .85$) [30, 31].

Memory—Rey Auditory Verbal Learning Test (RAVLT) Learning Over Time, True Hits, Short Delay, and Long Delay scores [32]. The RAVLT measures verbal memory by asking participants to recall as many words as possible from a list read five times. The Learning Over Time score provides the total numbers of words recalled over the course of the 5 presentations of the list. The True Hits measure reflects the number of items correctly identified on a recognition task. The Short Delay score is the total items recalled following an interference trial. The Long Delay Score is the sum of items recalled following a delay [32].

Visuospatial Ability—Rey Complex Figure Copy Task (ROCF)[33, 34]. The ROCF assesses visuospatial activity by asking participants to reproduce a complex drawing by hand. Scores are calculated based on accuracy and placement of details of the figure, with higher scores reflecting better visuospatial abilities.

Raw scores were converted into age-adjusted T-scores for the cognitive tests in each domain to facilitate interpretation. Composite scores were calculated for each domain by averaging the subtest T-scores of each domain. AT-score of 35 or lower (1.5 standard deviations below the normative sample's mean) indicated cognitive impairment [35]. Of note, the neuropsychological assessment was used for research purposes only and was not diagnostic of clinical impairment.

Covariates—The following variables were included as covariates/potential confounders of any observed relationship between cognitive function and HRQoL: highest education level achieved, Charlson Comorbidity Index (CCI) score [36], HF severity (as estimated by NYHA class [37], depression (PHQ-9 Total Score) [38], estimated IQ (based on AMNART) [39], and gender (0 = male, 1 = female). The CCI is a summary score of comorbid medical conditions (e.g., diabetes, peripheral vascular disease, myocardial infarction, etc.) [36]. New York Heart Association (NYHA) levels of HF severity [37] range from Class I (no symptoms) and Class II (Mild) to Class III (Moderate) and Class IV (Severe). NYHA class was documented by physicians prior to enrollment and confirmed by a trained research assistant who assessed self-reported HF symptoms and limitations. The PHQ-9 [38] consists of 9 items assessing depressive symptoms, with higher scores indicating more severe depression. The PHQ-9 demonstrates good reliability and validity [38]. Estimated IQ was determined using the North American Adult Reading Test (AMNART) [39]. The AMNART asks participants to read irregularly pronounced words. The test provides a reliable IQ estimate for medical populations [39].

Procedure

Study participants were recruited from inpatient and/or outpatient cardiology practices in northeast Ohio and provided informed consent to participate. The Institutional Review Boards of Kent State University, Summa Health Systems, Inc., and Case Western Research University approved all study procedures. Following consent, a trained research assistant administered the series self-report questionnaires and neuropsychological testing.

Data Analyses

Although the current study is ongoing, data from the baseline assessment were used in the current, cross-sectional analyses. Means, standard deviations, and frequencies were calculated to describe the sample. Hierarchical multiple linear regression was conducted with the following covariates entered into Block 1: gender, depression, HF severity, premorbid IQ, comorbidities, and highest educational level achieved. Domains of cognitive functioning were entered as continuous variables into Block 2. A separate hierarchical multiple linear regression was performed to assess potential curvilinear relationships between HRQoL and cognitive performance. In this analysis, variables entered into Blocks 1

and 2 remained the same. A quadratic term for each cognitive domain was included in Block 3. All data analyses were conducted using IBMSPSS version 20.0 statistical software.

Results

Participants

The sample consisted of predominantly older (68.70 ± 9.55 years), male (62.6%), white (72.5%), HF patients (see Table 1). The average 3MS score was 91.9 (SD = 6.1). The following percentages of patients had impairments on individual domains (composite T-score ≥ 35): Attention: 11.9% ($n = 36$); Executive Function: 54.0% ($n = 163$); Memory: 6.3% ($n = 19$); Visuospatial Ability: 11.6% ($n = 35$). Mean composite scores for each cognitive domain are presented in Table 1.

Cognitive Domains and Quality of Life

Hierarchical multiple linear regression analyses were conducted to examine the relationship between cognitive domains and HRQoL. In the first step, the linear combination of demographic and medical control variables accounted for 50.2% of the variability in HRQoL, $F(7, 294) = 49.50$, $p < .001$. Specifically, more depressive symptoms ($\beta = -.49$, $p < .001$) and NYHA class ($\beta = -.33$, $p < .001$) were associated with worse HRQoL. Highest education level achieved, Charlson score, estimated IQ, and gender were not related to HRQoL. In the second step, the final model accounted for 51.2% of the variability in HRQoL, $F(11, 290) = 30.59$, $p < .001$. Executive function was the only cognitive domain associated with HRQoL ($\beta = .17$, $p < .05$). Although significant, executive dysfunction accounted for only .6% of the variance in HRQoL. There was no evidence of a curvilinear relationship between HRQoL and any domain of cognitive function. Bivariate correlations between HRQoL and demographic and medical covariates are presented in Table 2. See Table 3 for a full summary of hierarchical regression analyses.

Discussion

The current study investigated whether cognitive function was associated with HRQoL in a sample of patients with HF. Cognitive function generally was not related to HRQoL in HF patients. Only performance on tasks of executive function were associated with HRQoL, and then only weakly. Additionally, no evidence of a curvilinear relationship between any cognitive domain and HRQoL emerged.

Our findings were largely consistent with Pressler et al.'s [14] report that, with the exception of memory, cognitive function generally did not predict HRQoL. However, we found that executive function, not memory, was the only cognitive domain associated with HRQoL, and approximately half of the sample demonstrated impairment in executive function. Similar to Pressler et al.'s findings regarding memory, executive function explained a small amount of variability in HRQoL. Although abilities associated with executive function—planning meals and organizing medications—would be expected to impact HRQoL by interfering with disease management, depressive symptoms and disease severity appear to be stronger, more consistent predictors of HRQoL. Similarly, Erceg et al. [7] reported that the association between cognitive impairment and HRQoL in elderly HF patients was attenuated after

adjusting for depressive symptoms, NYHA class, income, and HF duration. This is also consistent with other literature suggesting that depressive symptoms interfere with medication adherence, are associated with a greater number of distressing physical symptoms, and increase mortality risk [5, 40–42]. Similarly, worsening disease severity adversely impacts QoL as patients' physical limitations increase and functional capacity declines[43].

However, the current findings do not support Bennett et al.'s [17] model proposing a role of cognitive deficits in worsening QoL in HF. Although Bennet et al.'s model was based on early empirical reports of self-reported cognitive function, at this time little evidence supports a direct or indirect relationship between objective cognitive functioning and HRQoL in HF patients. In addition, our findings contradict prior qualitative reports that patients with cognitive impairment do experience reduced QoL. Importantly, the current study utilized performance-based assessment of cognitive impairment, which may have contributed to differences between the current findings, as well as Pressler et al.'s, and previous reports relying on subjective measurement. Some studies, though not all, have suggested that patients demonstrate little awareness of their cognitive declines. For example, Gunstadand colleagues [44] demonstrated a stronger relationship between depressive symptoms and self-reported cognitive deficits than between neuropsychological test performance and self-reported cognitive deficits in older adults with cardiovascular disease. In addition, reduced QoL was a contributor [44]. Similarly, Humphreys et al. [45] reported that the relationship between neuropsychological assessment and self-reported cognitive functioning was attenuated after adjusting for psychological distress in adults with atherosclerotic vascular disease. Although some prior research on the topic is mixed, a recent large, community-based sample also found that depressive symptoms were related to subjective cognitive complaints after controlling for demographic and psychosocial variables, whereas no relationship between subjective cognitive complaints and an objective measurement emerged following adjustment for covariates [46].

Age may also have influenced findings, although not included in primary analyses due to the use of age-adjusted test scores. A small, positive correlation was observed between age and HRQoL. Pressler et al. [14] also reported that younger age was related to poorer HRQoL. Younger HF patients tend to report more depressive symptoms[47]. It is likely that younger HF patients are more likely to experience depressive symptoms in response to the limitations and burdens of chronic illness[47]. Similarly, younger HF patients may be more likely to report poorer HRQoL given the greater perceived physical and social limitations.

In the current sample, HRQoL was high (KCCQ: $M = 71.3$, $SD = 24.6$). Allen et al. previously reported that KCCQ overall summary scores <45 at 1 and 24 weeks post-discharge following hospitalization predict 6-month mortality or chronically low HRQoL in a large sample of HF patients [48]. According to Allen et al., one week post-discharge, higher NYHA class was negatively correlated with KCCQ scores, with patients classified as NYHA class III demonstrating a median KCCQ score of 45 (interquartile range: 33 to 60) [48]. In the current sample, only 9.6% ($n = 29$) of participants demonstrated overall summary scores below 45. This represents a much smaller proportion than reported by Allen

et al. Assessing HRQoL at the time of hospitalization or shortly following discharge may yield different findings.

Additionally, others have also reported lower HRQoL scores in HF outpatients > 60 years of age (KCCQ clinical summary: median = 54; interquartile range: 38 to 74) [6] and > 65 years of age (KCCQHRQoL: M = 60, SD = 25) [43]. The current sample primarily comprised of outpatients classified as class II or III and possibly represents patients with well-controlled HF who are closely followed by their cardiologists. This may have contributed to higher self-reported HRQoL as opposed to other HF studies.

Limitations of the current study should be noted. The cross-sectional design restricts the ability to draw firm conclusions. An experimental design may yield different findings or may provide more definitive confirmation of the current results. Our findings may have been stronger in samples with poorer HRQoL, as the current sample of volunteers included few NYHA Class IV patients. Also, the current study did not examine potential longitudinal changes in cognitive impairment and HRQoL. It is possible that cognitive impairment predicts more rapid decline in HRQoL or that changes in cognitive performance predict changes in HRQoL.

Although only a small number reported very low HRQoL in our study, many reported reductions in HRQoL associated with HF. Self-reported HRQoL does not appear to be strongly influenced by cognitive impairment; other factors play a bigger role such as disease severity and depressive symptoms. The current study expands previous work by providing evidence using an objective, comprehensive neuropsychological battery in a well-characterized sample of HF patients and by exploring the possibility of curvilinear relationships. Future studies should investigate modifiable determinants of HRQoL in HF patients, toward the end of finding interventions that preserve HRQoL during this chronic illness.

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Summary and Implications

What's New?

- Cognitive deficits are generally not associated with Quality of Life in patients with Heart Failure. Executive function was the only cognitive element to have a weak association with Quality of Life.
- Using a larger sample size, this study validates the robust findings of Pressler et al. (2010).
- Disease severity and depressive symptoms are greater determinants of HRQoL in patients with Heart Failure.

Table 1Characteristics of Participants (*N* = 302)

	<i>M(SD) or N(%)^a</i>
<i>Demographic and Medical Factors</i>	
Age	68.7(9.6)
Male	189(62.6)
Race	
American Indian/Alaska Native	2(.7)
Asian	1(.3)
African American	80(26.5)
White	219(72.5)
Education Level	
8 th Grade or Less	7(2.3)
9–11 th Grade	26(8.6)
High School	86(28.5)
Technical or Trade School	33(10.9)
Some College	81(26.8)
Bachelor's Degree	39(12.9)
Master's Degree	30(9.9)
Married	175(57.9)
Myocardial Infarction	149(49.3)
Diabetes Mellitus	132(43.7)
Charlson Comorbidity Index	3.3(1.7)
Ejection Fraction	31.46(10.97)
Pacemaker	86(28.5)
Automated Implantable Cardioverter-Defibrillator(AICD)	110(36.4)
Months since HF diagnosis	105.01(108.21) ^b
NYHA	
Class I	31(10.3)
Class II	65(21.5)
Class III	191(63.2)
Class IV	15(5.0)
PHQ-9 Total	4.6(4.9)
KCCQoL	71.3(24.6)
<i>Cognitive Factors</i>	
Estimated IQ	109.9(10.4)
3MS Score	91.9(6.7)
Attention Composite T-Score	44.2(7.5)
Executive Function Composite T-Score	34.3(6.8)
Memory Composite T-Score	47.8(7.5)
Visuospatial T-Score (Rey COPY)	50.6(10.4)

^aMeans and standard deviations are presented for continuous variables. Sample size and percentages are presented for categorical variables.

^b As individuals with heart failure typically have heart disease for several years prior to diagnosis of heart failure and heart failure is only definitively diagnosed following diagnostic documentation, self-reported months since diagnosis likely does not provide an accurate representation of time since heart failure onset.

Abbreviations HF = heart failure; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PHQ-9, Patient Health Questionnaire-9.

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Table 2

Correlations between demographic and medical variables and QoL (N=302).

	Age	Highest Education Level Achieved	Total Charlson Score	NYHA Classification	PHQ-9	Estimated Premorbid IQ	LVEF	HRQoL
Age	---	.06	.13*	-.04	-.14*	.17**	.01	.22***
Highest Educational Level Achieved		---	-.10	-.14*	-.18**	.61***	-.03	.13**
Total Charlson Score			---	.07	.04	-.03	.08	.03
NYHA Classification				---	.37***	-.09	-.05	-.42***
PHQ-9					---	-.19**	-.03	-.65***
Estimated Premorbid IQ						---	.06	.15**
LVEF							---	.01

* $p < .05$;** $p < .01$;*** $p < .001$.

Abbreviations: KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; NYHA, New York Health Association; PHQ-9, Patient Health Questionnaire-9.

Table 3

Hierarchical Multiple Linear Regression Predicting KCCQ scores (N=302).

KCCQ					
Variable	B	SE B	t	β	p
Block 1					
Highest Educational Level Achieved	.226	.697	.325	.017	.746
Total Charlson Score	-.357	.483	-.739	-.031	.460
NYHA Classification	-9.123	1.233	-7.399	-.329	.000
PHQ-9 Total Score	-2.039	.188	-10.830	-.487	.000
Estimated Premorbid IQ	.163	.102	1.601	.083	.110
Sex	-.835	1.803	-.463	-.020	.643
Block 2					
Visuospatial Ability	-.118	.088	-1.339	-.060	.182
Executive Function	.525	.221	2.373	.174	.018
Memory	-.051	.126	-.402	-.019	.688
Attention	-.209	.182	-1.148	-.077	.252

Abbreviations: KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA, New York Health Association; PHQ-9, Patient Health Questionnaire-9.