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Neuropsychological Patterns Differ by Type of Left Ventricle Dysfunction in Heart Failure

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Abstract

Cognitive impairment is common among individuals with heart failure. The purpose of this study was to compare cognitive profiles of individuals with systolic and diastolic dysfunction. Eighty individuals with heart failure completed the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), Mini-Mental State Examination, Trail Making Test, and letter fluency. Approximately 25% of individuals with systolic dysfunction were impaired on the RBANS Total Scale score, compared with only 3% in the diastolic group. Additionally, individuals with systolic dysfunction scored lower than those with diastolic dysfunction on tests of immediate and delayed memory. The groups did not differ on tests of visuospatial skills, but there were mixed results on the RBANS Attention and Language subtests. Overall, the results of this study suggest that individuals with different types of cardiac dysfunction (systolic and diastolic dysfunction) demonstrate differential patterns of performance on neuropsychological tests. These findings have important clinical implications.

Keywords: Cardiovascular disease; Executive function; Learning and memory; Mild cognitive impairment; Assessment

Introduction

Heart failure (HF) is a progressive cardiovascular syndrome that affects one in five individuals over the age of 40 in the United States. It is the only major cardiovascular disorder that continues to increase in prevalence (Roger et al., 2012). As HF progresses, the heart is unable to pump enough blood to meet the body's oxygen demands, leading to a decreased supply of oxygen-rich blood to various tissues and organs and an accumulation of blood in the pulmonary and vascular systems. HF has diverse etiologies, but frequently develops after long-standing co-morbidities weaken and damage the heart (e.g., coronary artery disease or hypertension). Once initiated, there is no cure for the cardiovascular decline that occurs as a result of the HF syndrome.

HF is classified according to the type of left ventricular dysfunction as diastolic or systolic (Chatterjee & Massie, 2007). The left ventricle is stiff in diastolic dysfunction, so it does not fill adequately during diastole. Individuals with diastolic dysfunction generally have a normal cardiac output (i.e., the amount of blood pumped by the left ventricle every minute). However, because the left ventricle does not fill to capacity, receptors in the heart send signals to the brain that the heart is not receiving enough blood. This perceived decrease in blood signals the neuroendocrine system to conserve fluid, thus increasing the strain on the already stiff left ventricle. Clinically, fluid overload from diastolic dysfunction tends to present in the extremities with swelling. In contrast, systolic dysfunction is a state where the left ventricle of the heart is weakened and cannot pump with enough force. Individuals with systolic dysfunction experience a greatly diminished cardiac output, and fluid overload occurs most often in the lungs.

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Both types of left ventricular dysfunction cause symptoms such as fatigue, dyspnea and fluid retention and are associated with high mortality rates. Diagnosis of diastolic or systolic dysfunction is generally made on the basis of initial left ventricular ejection fraction (LVEF) (i.e., the percentage of blood that is pumped out of the left ventricle per heart beat) (Chatterjee & Massie, 2007). Individuals presenting with symptoms of HF and an LVEF of ≥50% are diagnosed with diastolic dysfunction, whereas individuals who present with symptoms of HF and an LVEF of <50% are diagnosed with systolic dysfunction. However, as HF progresses, LVEF decreases among both diastolic and systolic HF, and there is controversy regarding whether diastolic and systolic dysfunction represent separate HF phenotypes or two independent points on the disease continuum (Bronzwaer & Paulus, 2009). Regardless of the type of left ventricular dysfunction, approximately 50% of individuals die within 5 years of HF diagnosis (Roger et al., 2012).

Several studies suggest that 15–85% of HF patients exhibit cognitive impairment (Almeida & Tamai, 2001; Bornstein, Starling, Myerowitz, & Haas, 1995; Festa et al., 2011; Roman et al., 1997; Schall, Petrucci, Brozena, Cavarocchi, & Jessup, 1989; Trojano et al., 2003). The majority of studies examine cross-sectional data collected from a variety of clinical populations with a range of HF severity. In one of the first comprehensive studies, Trojano and colleagues (2003) administered seven neuropsychological tests to over 500 hospitalized individuals with HF. They found that 43% of individuals with mild HF and 58% of those with severe HF scored significantly lower than the matched controls on more than two neuropsychological tests. Other smaller studies involving individuals hospitalized with HF or awaiting heart transplantation reported similar prevalence rates (Almeida & Tamai, 2001; Bornstein et al., 1995; Festa et al., 2011; Roman et al., 1997; Schall et al., 1989). In contrast, studies of community-dwelling individuals with HF have yielded lower cognitive impairment rates that range from 15% to 25% (Bauer et al., 2012; Grubb, Simpson, & Fox, 2000; Pressler et al., 2010; Vogels, Oosterman, van Harten, Scheltens, et al., 2007). These findings suggest that prevalence rates are likely related to disease severity and source of participants. However, not all of the studies used comprehensive neuropsychological batteries, so it is difficult to estimate actual prevalence rates of cognitive impairment.

Two studies administered comprehensive neuropsychological batteries to relatively large community-dwelling HF samples and found lower performance on verbal (but not visual) memory and conflicting results on the tests of executive function, psychomotor speed, and verbal fluency (Pressler et al., 2010; Vogels, Oosterman, van Harten, Scheltens, et al., 2007). For example, both studies reported that individuals with HF had poorer performance on delayed memory recall using two common tests of verbal list learning. Both studies used Controlled Oral Word Association (COWA) as a measure of verbal fluency; while Vogels and colleagues documented that individuals with HF scored lower than healthy controls, Pressler and colleagues did not find group differences. Several smaller studies also documented impairment in memory, but the results on tests of executive function (e.g., TMT B) and psychomotor speed were mixed (Gunstad et al., 2005; Hoth, Poppas, Moser, Paul, & Cohen, 2008; Tanne et al., 2005). It is important to note that on measures of global cognition, individuals with HF (regardless of severity) frequently score lower than controls, but their scores generally do not fall below the cut-off point for dementia (Pressler et al., 2010; Vogels, Oosterman, van Harten, Scheltens, et al., 2007). Thus, the mild degree of impairment may contribute to the inconsistent results. Longitudinal data are needed to better understand these inconsistencies and identify possible underlying mechanisms for cognitive impairment in HF.

LVEF is often used as a measure of HF severity. A few studies reported that LVEF is a significant predictor of cognitive impairment in HF (Festa et al., 2011; Hoth et al., 2008; van den Hurk et al., 2011); therefore, the prevalence of cognitive impairment may also be related to HF severity. Festa and colleagues (2011) assessed a sample of 207 individuals with HF who were awaiting transplantation and found that an LVEF of <30% was the strongest predictor of lower memory scores. Hoth and colleagues (2008) reported that decreased LVEF was associated with lower scores of attention and executive function in individuals with moderate-to-severe HF (defined as LVEF ≤40%). Similarly, a large prospective cohort study ($n = 2{,}484$) of community-dwelling individuals with impaired glucose metabolism and Type 2 diabetes reported that an LVEF of <50% was related to cognitive decline (attention and executive function) in the 313 individuals who developed HF over the course of the 9-year follow-up. The New York Heart Association (NYHA) classification is also considered a measure of HF severity, and studies have reported a relationship between NYHA classification and cognitive impairment. For example, in a study involving 369 individuals with HF, Incalzi and colleagues (2003) reported a significant negative relationship between NYHA classification and scores on the Rey Auditory Verbal Learning Test. In this sample of individuals hospitalized with HF, 58% of NYHA class II patients were impaired on the measures of verbal memory recall; the prevalence increased to 85% among individuals in the NYHA class IV group (Incalzi et al., 2003).

The majority of studies reviewed previously have focused on individuals with systolic dysfunction. Few studies have included both diastolic and systolic dysfunction, and none has compared cognitive profiles in the two groups (Almeida & Tamai, 2001; Vogels, Oosterman, van Harten, Scheltens, et al., 2007). Two small neuroimaging studies documented medial temporal lobe atrophy in individuals with systolic dysfunction (Vogels, Oosterman, van Harten, Gouw, et al., 2007; Woo, Kumar, Macey, Fonarow, & Harper, 2009). In addition, Vogels and colleagues found a correlation between medial temporal

lobe atrophy and memory performance. This relationship has not been explored in individuals with diastolic dysfunction. Therefore, the purpose of this study is to recruit individuals from both groups (i.e., diastolic and systolic dysfunction) and compare cognitive profiles. Based on the literature, we hypothesized that individuals with systolic dysfunction will perform lower than expected on tests of memory, while individuals with diastolic dysfunction will have preserved memory function.

Methods

Participants

Participants were recruited prospectively from a community-based tertiary HF clinic that serves as a referral center for Western Iowa, South Dakota, and Nebraska. One hundred and two potential participants were approached to participate in the study. Fifteen declined participation because of time constraints. Three declined participation stating that they were "too tired" or "just not feeling up to testing." Finally, four participants were excluded because of history of stroke or other neurological conditions. The final sample consisted of 80 patients who were treated between January and May 2009. The University of Nebraska Institutional Review Board approved the study. Fourteen staff cardiologists at the clinic diagnosed participants with either systolic or diastolic HF, based on American Heart Association (AHA) criteria (Roger et al., 2012). Each patient was discussed during a case conference to insure a consensus for the diagnosis of diastolic or systolic dysfunction.

A chart review was performed to determine eligibility for the study. We included participants who were age 50 or older, who had a history of HF for at least 6 months prior to study enrollment, and had a stable AHA guideline-based medication regimen for at least 4 weeks (Roger et al., 2012). Participants were excluded if they had a previous diagnosis of dementia or neurological disease (e.g., Alzheimer's disease, Parkinson's disease, epilepsy, or stroke); history of substance abuse/treatment; hepatic insufficiency [aspartate aminotransferase (AST) >40 units per liter for men or >72 units per liter for women, or an alkaline phosphatase (ALP) >200 units per liter]; severe renal failure (serum creatinine >2.5 mg/dl); anemia; implantable device (e.g., pace maker or defibrillator); or history of a myocardial infarction, unstable angina, coronary artery bypass surgery, or percutaneous transluminal coronary angioplasty within 3 months of study enrollment. Participants completed the Mini-Mental State Examination (MMSE) to rule out dementia and were excluded for scores <25.

Participants were interviewed to collect demographic information (age, gender, and years of education). In addition, a chart review was done to collect additional clinical variables, including duration of HF disease (months), LVEF value, NYHA classification (I, II, III, or IV) (Levin, Dolgin, Fox, & Gorlin, 1994), number of co-morbid illnesses, and number of medications. Participants completed a number of questionnaires designed to explore other potential confounders of cognition; specifically, the Charlson Co-morbidity Index (Deyo, Cherkin, & Ciol, 1992), the Patient Health Questionnaire (PHQ)-8 (Corson, Gerrity, & Dobscha, 2004; Kroenke & Spitzer, 2002), the Duke Activity Status Index (DASI) (Hlatky et al., 1989), the Lawton & Brody Instrumental Activities of Daily Living (IADL) questionnaire (Lawton & Brody, 1969), and the Epworth Sleepiness Scale (ESS) (Johns, 1991). Finally, participants in the study completed a series of neuropsychological tests designed to measure multiple cognitive domains.

Measures

The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) is a widely used neuropsychological battery that measures multiple cognitive domains and takes approximately 30 min to administer (Randolph, 1998). The relatively brief administration time is ideal because fatigue is common among HF patients. The RBANS has good reliability and validity and has previously been used with HF patients (Bauer et al., 2012; Hoth et al., 2008; Wolfe, Worrall-Carter, Foister, Keks, & Howe, 2006). The RBANS contains 12 subsets (list learning, story memory, figure copy, line orientation, picture naming, semantic fluency, digit span, coding, list recall, list recognition, story memory, and figure recall) that contribute to 5 Index scores (immediate memory, visual/spatial construction, language, attention, and delayed memory) and a Total Scale score (global cognitive function). For this study, Randolph's (1998) norms were used. The RBANS Index scores are adjusted for age and have an average of 100 and a standard deviation (*SD*) of 15.

Additional measures of executive function were included because the medical management of HF symptoms relies on executive function, and prior studies found impairment on tests of executive function in patients with HF (Bauer et al., 2012; Hoth et al., 2008; Vogels, Oosterman, van Harten, Scheltens, et al., 2007). The Trail Making Test (TMT) (Parts A and B) (Reitan & Wolfson, 1985) was used as a measure of processing speed and switching. The time to complete TMT was recorded, and a difference score (Part B minus Part A) was also calculated. The number of D words (1 min) was used as a measure of phonemic fluency (Kramer et al., 2003). Finally, the MMSE was used as a measure of global cognitive function (Folstein, Folstein, &

McHugh, 1975). Neuropsychological test scores that were greater than 1.5 *SD* below the published means for age were classified as impaired.

Statistical Analysis

Group differences in demographic and clinical variables and neuropsychological test results were compared using independent *t*-tests or χ^2 tests depending on the distribution of the data. The effect size for group differences in neuropsychological test scores was calculated using Cohen's *d*. Multiple linear regression modeling was performed to examine the unique contribution of systolic versus diastolic dysfunction on RBANS Index Scores (Immediate and Delayed Memory, Attention) and RBANS Total Scale score. Potential confounding variables for the model were identified as those variables that differed significantly between the groups (i.e., age, gender, number of comorbid illnesses, and LVEF). Education was also included as a potential confounding variable in the regression models because of its strong association with many neuropsychological tests. All six independent variables (age, gender, education, number of comorbid illnesses, LVEF, and systolic vs. diastolic group) were simultaneously entered into the linear multiple regression model in one step in order to evaluate each independent variable's unique contribution to the respective neuropsychological test score, while controlling for the other five. SPSS for Windows (version 19.0, SPSS, Inc., Chicago, IL). Significance for all statistical tests was set at alpha = .05.

Results

Demographics and Clinical Characteristics

Table 1 summarizes the demographics and clinical characteristics of the participants. The sample included 47 individuals with systolic dysfunction and 33 individuals with diastolic dysfunction. Compared with the group with diastolic dysfunction, the systolic group was significantly older (68 vs. 75 years, $p = .015$). There were no group differences in education. As expected, participants with systolic dysfunction were predominantly men (79% vs. 42%, $p = .001$), had lower LVEFs ($p = .028$), and higher NYHA classifications ($p = .058$). Participants with systolic dysfunction had higher scores on the Charlson Comorbidity Index than those with diastolic dysfunction ($p = .019$). The number of medications and HF duration did not differ significantly between the groups. There were no group differences on the measures of depressive symptoms ($p = .267$), physical activity ($p = .170$), daytime sleepiness ($p = .513$), or IADLs ($p = .051$). Of note, none of the participants were excluded for an MMSE score of <25.

Neuropsychological Test Scores

Group performance on the neuropsychological tests is presented in Table 2. The RBANS Index Scores, MMSE, letter fluency, and TMT scores were normally distributed. Participants with systolic dysfunction scored significantly lower on the RBANS Total Scale compared with the diastolic dysfunction group. When considering the five overall RBANS Index

Table 1. Demographic and clinical characteristics of study participants by cardiac dysfunction type: mean (*SD*)

	Systolic dysfunction ($n = 47$)	Diastolic dysfunction ($n = 33$)	t	p
Age (years)	74.7 (8.9)	68.1 (14.6)	2.493	.015
Education (years)	13.8 (3.1)	13.9 (2.1)	−0.099	.921
Comorbid illnesses (#)	4.8 (2.5)	3.6 (2.0)	2.387	.019
LVEF (%)	35.3 (10.7)	40.8 (10.8)	−2.238	.028
Medications (#)	11.5 (3.5)	10.0 (3.3)	1.986	.051
Disease duration (months)	92.8 (86.2)	79.4 (59.0)	0.775	.441
PHQ-8 total score	3.34 (3.06)	4.38 (4.70)	−1.120	.267
ESS total score	5.95 (3.94)	5.38 (3.01)	0.658	.513
Lawton IADL total score	6.68 (1.64)	7.45 (1.50)	−1.995	.051
DASI total score	6.73 (2.95)	7.72 (2.95)	−1.386	.170
			χ^2	p
Gender—women (%)	10 (21%)	19 (58%)	11.054	.001
NYHA classification I/II (%)	17 (36%)	19 (58%)	3.589	.058

Note: LVEF = left ventricular ejection fraction; PHQ-8 = Patient Health Questionnaire—8; ESS = Epiworth Sleepiness Scale; IADL = Instrumental Activities of Daily Living; DASI = Duke Activity Status Index; NYHA = New York Heart Association.

Table 2. Neuropsychological test score comparisons by HF dysfunction: mean (*SD*)

	Systolic dysfunction ($n = 47$)	Diastolic dysfunction ($n = 33$)	t	p	d
RBANS indexes					
Total scale	90.1 (15.8)	98.5 (13.9)	−2.455	.016	0.541
Immediate memory	86.5 (17.8)	96.9 (14.6)	−2.774	.007	0.603
Visuospatial/constructional	102.4 (18.0)	102.4 (16.7)	0.005	.996	0.000
Language	93.3 (9.1)	97.5 (12.6)	−1.757	.083	0.388
Attention	90.2 (19.3)	96.1 (15.4)	−1.451	.151	0.330
Delayed memory	91.1 (16.8)	103.2 (11.7)	−3.556	.001	0.756
RBANS subtests					
List learning trial 1	3.5 (1.4)	4.1 (1.1)	−1.981	.051	0.474
List learning trial 2	5.2 (1.6)	5.9 (1.4)	−2.035	.045	0.442
List learning trial 3	6.0 (1.8)	7.0 (1.3)	−2.724	.008	0.588
List learning trial 4	6.3 (1.8)	7.6 (1.5)	−3.271	.002	0.730
List learning total	21.0 (5.6)	24.5 (5.2)	−3.071	.003	0.652
Story memory	14.5 (4.2)	17.8 (4.2)	−3.397	.001	0.731
Figure copy	18.0 (2.0)	18.6 (2.0)	−1.262	.211	0.302
Line orientation	16.1 (3.6)	16.0 (3.4)	0.198	.844	0.029
Picture naming	9.8 (0.5)	9.6 (0.7)	0.987	.327	0.346
Semantic fluency	15.5 (3.8)	18.7 (5.6)	−3.054	.003	0.660
Digit span	9.1 (2.3)	10.0 (2.7)	−1.585	.117	0.359
Coding	34.0 (10.5)	41.2 (11.4)	−2.896	.005	0.633
List recall	3.6 (2.3)	6.0 (3.0)	−4.041	<.001	0.838
List Recognition	18.3 (2.1)	19.2 (1.1)	−2.300	.024	0.508
Story recall	7.1 (2.7)	9.2 (2.2)	−3.774	<.001	0.780
Figure recall	11.0 (4.8)	14.1 (3.7)	−3.116	.003	0.667
MMSE	27.6 (1.9)	29.0 (1.2)	−3.526	.001	0.780
Letter fluency (“D” words in 1-min)	9.0 (4.6)	10.3 (4.6)	−1.137	.259	0.280
TMT A (s)	52.5 (24.2)	43.4 (20.4)	1.757	.083	0.395
TMT B (s)	134.0 (68.5)	98.7 (61.5)	2.340	.022	0.522
TMT B—TMT A	81.5 (50.8)	55.3 (47.8)	2.297	.024	0.514

Note: MMSE = Mini-Mental Status Exam; TMT A = Trail Making Test Part A; TMT B = Trail Making Test Part B; TMT B–TMT A = Trail Making Test Part B minus Trail Making Test Part A.

scores, the systolic dysfunction group scored significantly lower on the RBANS Immediate and Delayed Memory Indices than the participants with diastolic dysfunction ($t = -2.774$, $p = .007$ and $t = -3.556$, $p = .001$, respectively). Cohen’s d statistic ranged from .541 to .756 for the RBANS Index scores and .442 to .838 for the RBANS subtests and MMSE, letter fluency, and TMT scores, indicating a medium to large effect size of group differences. In contrast, there were no group differences on the RBANS visuospatial/constructional, Language, or Attention Index scores.

The participants with systolic dysfunction performed significantly lower than those with diastolic dysfunction on all verbal and visual memory subtests. As expected, there were no differences on the visuospatial subtests (figure copy or line orientation). While there were no differences on the picture naming subtest, the systolic dysfunction group performed significantly lower than the diastolic function group on semantic fluency ($t = -3.054$, $p = .003$). Similarly, there were no group differences on the digit span subtest, but the systolic dysfunction group performed significantly lower than the diastolic dysfunction group on the coding subtest ($t = -2.896$, $p = .005$). With regards to the additional neuropsychological tests, there were no group differences on phonemic fluency; however, the systolic dysfunction group performed significantly lower on the MMSE ($t = -3.526$, $p = .001$) and both TMT B ($t = 2.340$, $p = .022$) and the TMT difference score ($t = 2.297$, $p = .024$).

Table 3 summarizes the proportion of individuals in each group who scored in the impaired range on the RBANS Index and Total Scale scores, letter fluency, and TMT A and B. Overall, the impairment rates on the RBANS Index and Total Scale scores ranged from 2% to 34%. Impairment rates on letter fluency ranged from 42% to 60% and impairment rates on TMT A and B ranged from 3% to 13%. Participants with systolic dysfunction had a significantly higher proportion of participants who scored in the impaired range on RBANS Total Scale score compared with individuals with diastolic dysfunction (23% vs. 3%). In addition, the prevalence was also significantly different for two RBANS Index scores: Delayed Memory and Attention. There was a non-significant trend for the groups to differ on the RBANS Immediate Memory Index. There were no group differences on the Language and Visuospatial/constructional Indices, letter fluency, and TMT A and B.

Results from the multiple regression models are presented in Tables 4–7. The models accounted for 24%–30% of the variance in scores on the RBANS Immediate Memory, Delayed Memory, and Attention Indices, as well as the RBANS Total Scale

Table 3. Prevalence of individuals who scored in the impaired range on RBANS

RBANS index	Systolic dysfunction ($n = 47$) (%)	Diastolic dysfunction ($n = 33$) (%)	χ^2	p
Total scale score	23	3	6.312	.012
Immediate memory	32	15	2.906	.088
Delayed memory	19	3	4.605	.032
Attention	34	9	6.665	.010
Language	2	9	1.979	.159
Visuospatial/constructional	9	6	0.168	.682
Letter fluency ("D" words in 1-min)	60	42	2.287	.130
TMT A	9	6	0.159	.690
TMT B	13	3	2.191	.139

Note: TMT A = Trail Making Test Part A; TMT B = Trail Making Test Part B.

Table 4. Predictors of RBANS total scale score

Source	R^2	B	95% CI	R^2 change	*df* (*F*)	p
Overall	.299				6, 73 (5.180)	<.001
Constant		41.458	13.522 to 69.394			.004
Age		0.142	−0.134 to 0.418	.010		.310
Gender		−2.391	−9.449 to 4.668	.004		.502
Education		2.555	1.396 to 3.714	.186		<.001
Comorbid		0.088	−1.330 to 1.506	<.001		.902
LVEF		0.082	−0.205 to 0.370	.003		.570
SD/DD		9.706	2.446 to 16.966	.068		.009

Note: LVEF = Left ventricular ejection fraction; SD/DD = Systolic dysfunction/diastolic dysfunction.

score. As expected, education was a significant positive predictor of scores across all four models, accounting for 4%–19% of the total variance. Systolic dysfunction was a significant predictor of the RBANS Total Scale score (B = 9.706, $p = .009$) as well as Immediate and Delayed Memory (B = 10.688, $p = .012$ and B = 13.221, $p = .001$). Systolic dysfunction was the strongest predictor of scores for the RBANS Delayed Memory Index, accounting for 12% of the variance in scores. Interestingly, age, gender, number of comorbid conditions, and LVEF were not significant predictors of scores in any of the four regression models performed for this study.

Discussion

Overall, the results of this study suggest that individuals with different types of cardiac dysfunction (diastolic and systolic dysfunction) demonstrate different patterns of performance on neuropsychological tests. Approximately 25% of individuals with systolic dysfunction were impaired on the RBANS Total Scale score, compared with only 3% in the diastolic group. Additionally, individuals with systolic dysfunction scored lower than those with diastolic dysfunction on tests of immediate and delayed memory. The groups did not differ on tests of visuospatial skills, letter fluency, or TMT A and B, but there were mixed results on the RBANS Attention and Language subtests. The regression analysis suggested that even after adjusting for disease severity and demographics (age, gender, and education), systolic dysfunction accounted for a significant amount of variability in RBANS Total Scale score and RBANS Immediate and Delayed Memory Indices.

Individuals with systolic dysfunction had significantly lower scores on the tests of global cognition (RBANS Total Scale score and MMSE) than individuals with diastolic dysfunction. Approximately 25% of individuals with systolic dysfunction scored in the impaired range on the RBANS Total Scale score versus only 3% of individuals with diastolic dysfunction. It is important to note that none of the participants were excluded for an MMSE of <25. Therefore, in the context of an outpatient HF clinic, the cognitive impairment associated with HF may be more appropriately classified as "mild cognitive impairment" (MCI) (Petersen et al., 1999; Winblad et al., 2004) that primarily affects the domains of memory and executive function. However, no studies have used published MCI criteria to classify individuals with HF. The current findings suggest that individuals with diastolic dysfunction may have a lower prevalence of memory and global cognitive impairment and this argues for considering the type of cardiac dysfunction when examining cognitive impairment in HF.

When considering specific cognitive domains, memory was the most commonly impaired among individuals with systolic dysfunction. Approximately one-third of individuals with systolic dysfunction were impaired on tests of verbal and visual

Table 5. Predictors of RBANS immediate memory index score

Source	R^2	B	95% CI	R^2 change	*df* (*F*)	*p*
Overall	.258				6, 73 (4.238)	.001
Constant		36.216	4.325 to 68.107			
Age		0.101	−0.214 to 0.417	.004		.524
Gender		1.901	−6.157 to 9.959	.002		.640
Education		2.553	1.230 to 3.877	.151		<.001
Comorbid		0.761	−0.858 to 2.380	.009		.352
LVEF		0.096	−0.232 to 0.424	.003		.560
SD/DD		10.688	2.400 to 18.976	.067		.012

Note: LVEF = Left ventricular ejection fraction; SD/DD = Systolic dysfunction/diastolic dysfunction.

Table 6. Predictors of RBANS delayed memory index score

Source	R^2	B	95% CI	R^2 change	*df* (*F*)	*p*
Overall	.262				6, 73 (4.327)	.001
Constant		57.428	27.911 to 86.945			<.001
Age		0.083	−0.209 to 0.375	.003		.572
Gender		−5.363	−12.821 to 2.095	.021		.156
Education		1.258	0.034 to 2.483	.042		.044
Comorbid		0.235	−1.264 to 1.734	.001		.756
LVEF		0.286	−0.017 to 0.590	.036		.064
SD/DD		13.221	5.550 to 20.892	.119		.001

Note: LVEF = Left ventricular ejection fraction; SD/DD = Systolic dysfunction/diastolic dysfunction.

Table 7. Predictors of RBANS attention index score

Source	R^2	B	95% CI	R^2 change	*df* (*F*)	*p*
Overall	.237				6,73 (3.778)	.002
Constant		46.845	13.270 to 80.421			.007
Age		0.120	−0.212 to 0.452	.005		.474
Gender		−3.243	−11.727 to 5.240	.006		.449
Education		2.734	1.341 to 4.127	.160		<.001
Comorbid		−0.649	−2.354 to 1.056	.006		.450
LVEF		0.016	−0.330 to 0.361	<.001		.927
SD/DD		6.747	−1.979 to 15.472	.025		.128

Note: LVEF = Left ventricular ejection fraction; SD/DD = Systolic dysfunction/diastolic dysfunction.

memory. Individuals with systolic dysfunction scored lower across RBANS Immediate and Delayed Memory Indices and respective subtests, compared with those with diastolic dysfunction. These findings are congruent with other studies that have included community-dwelling samples with primarily systolic dysfunction. Other studies have reported that approximately 25% of community-dwelling individuals with HF exhibit verbal memory impairment when compared with other chronic illness groups (i.e., individuals with other chronic illnesses, but no HF) and healthy controls (Bauer et al., 2012; Pressler et al., 2010; Vogels, Oosterman, van Harten, Scheltens, et al., 2007). Furthermore, the Vogels and colleagues (2007) and Pressler and colleagues' (2010) samples were also men, similar to our systolic group. Findings from the current study suggest that gender was not a significant contributor to memory impairment in individuals with systolic dysfunction, although the current study may be underpowered to address this issue.

The biological mechanisms for cognitive impairment in HF are not yet known. Two possible biological mechanisms have been reported in the HF literature. A study by Alves and colleagues (2005) reported a decreased blood flow to right lateral temporoparietal and posterior cingulate cortices and the right and left precuneus and cuneus using single photon emission computed tomography (SPECT) (Alves et al., 2005). Additional studies documented decreased whole brain volume (Paul et al., 2005), as well as decreased volume in areas of the brain related to cognition including the hippocampus and frontal cortex (Vogels, Oosterman, van Harten, Gouw, et al., 2007; Woo et al., 2009; Woo, Macey, Fonarow, Hamilton, & Harper, 2003).

These changes in the hippocampus and frontal cortex may be related to memory and executive function impairment in HF. The changes in the brain are thought to be due to hypoxia, but other mechanisms have not been ruled out. In addition, the white matter watershed areas of the brain (e.g., medial temporal lobe) are highly sensitive to changes in overall blood flow. The findings of the current study suggest that systolic and diastolic dysfunction may affect the brain through different biological mechanisms. It is possible that lower systemic perfusion and diminished cerebral auto regulation associated with lower LVEF selectively targets medial temporal lobe structures (Alves et al., 2005; Georgiadis et al., 2000). However, additional research is needed to understand the possible biological mechanisms for the differential patterns of memory performance.

In addition, other factors, such as co-morbid medical conditions, may influence cognitive performance. Individuals with HF commonly experience several co-morbid conditions including hypertension, coronary artery disease, hypercholesterolemia, and diabetes. The prevalence of co-morbid conditions is similar between the systolic and diastolic groups, with only minor differences in the rates of hypertension and coronary artery disease (Roger et al., 2012). Riegel, Lee, Glaser, & Moelter (2012) found a relationship between a higher number of co-morbid conditions and measures of simple and complex attention (Riegel et al., 2012). However, another study did not find this relationship (Pressler et al., 2010). Although the current study collected the number of co-morbid conditions, we did not specify the type of co-morbid conditions. This is a limitation of the current study that should be investigated in future studies.

While there were no group differences of the RBANS Attention and Language Indices, there were mixed results for the subtests. With regards to attention, approximately one-third of individuals with systolic dysfunction scored >1.5 *SD* below the mean on the RBANS Attention Index compared with $<10\%$ of individuals with diastolic dysfunction. In samples composed primarily of individuals with systolic dysfunction, Hoth and colleagues (2008) and Wolfe and colleagues (2006) reported similar levels of impairment on attention using the RBANS Attention Index. In this study, the systolic group scored significantly lower than the diastolic group on the coding subtest, but not the digit span subtest. This may be in part due to the complexity of these two subtests. In factor analyses studies of the RBANS, digit span and coding load on different components. Digit Span consistently loads on components related to verbal processing/memory, while coding loads on components related to visuomotor processing/memory (Duff et al., 2006; Garcia, Leahy, Corradi, & Forchetti, 2008; Wilde, 2006). Coding requires, not only sensory processing but also visuomotor coordination. In contrast, the digit span test in the RBANS battery only assesses forward digit span and requires only sensory processing. Therefore, it is not surprising that the digit coding test may be more sensitive than the digit forward test in detecting subtle impairment in this sample of individuals with HF. This pattern was also evident on TMT. The systolic group performed significantly lower on TMT B, which is a measure of set shifting and involves visuomotor coordination, but not TMT A, which is a simpler measure of visuomotor tracking. Even after accounting for the psychomotor speed, in the TMT difference score, there were still significant group differences on the TMT difference score. In conclusion, it appears that individuals with systolic dysfunction are more likely to be impaired on the tests of complex attention versus the tests of simple attention. Neuroimaging studies of HF patients, primarily with systolic dysfunction, document structural changes in the prefrontal cortex (volume loss and white matter hyperintensities) (Vogels, Oosterman, van Harten, Gouw, et al., 2007; Woo et al., 2003, 2009). The changes in the prefrontal cortex may be related to impairment of complex attention (Stuss, 2011), but more studies are needed.

With regards to the language domain, there were no group differences on the mean index scores or prevalence of cognitive impairment. However, the systolic group performed significantly lower on category fluency compared with the diastolic group. It is important to note that $<10\%$ of individuals in both groups scored in the impaired range on the RBANS Language Index. The RBANS Language Index includes picture naming and category fluency. Category fluency is a particularly sensitive test of cognitive impairment for older adults (Duff et al., 2003) so it is not surprising that there were group differences on category fluency. In addition, the RBANS picture naming subtest has been noted to have ceiling effects (Duff et al., 2003), so the naming task that is part of the RBANS battery may not be sensitive enough to detect subtle impairment in object naming. In contrast, the performance on letter fluency did not differ between the groups, but both cardiac dysfunction groups scored within the lower normal to impaired range when comparing the scores with an independent sample of healthy older adults (Kramer et al., 2003). This underscores the need to include matched controls in future studies. Therefore, tests of verbal fluency may be more sensitive than object naming for detecting subtle impairment of language among individuals with HF.

As noted earlier, there were no group differences on the measures of visuospatial function, and fewer than 10% of individuals in either group had impaired scores on the RBANS Visuospatial/constructional Index. It appears that visuospatial function, as measured by figure copy and line orientation, is preserved in individuals with either type of cardiac dysfunction. This finding is similar to other HF studies that have found normal performance on visuospatial tasks (Bauer et al., 2012; Vogels, Oosterman, van Harten, Scheltens, et al., 2007). In addition, neuroimaging studies have not found changes in the more posterior brain regions associated with visuospatial function (Vogels, Oosterman, van Harten, Gouw, et al., 2007; Woo et al., 2003). However, visuospatial tasks have not been routinely included in other studies involving individuals with HF (Bauer, Johnson, & Pozehl, 2011).

It is important to note that there are several methodological limitations of this study to consider. The data are cross sectional, which limits the ability to assess the degree of change that may occur across the HF disease trajectory. The current study collected the number of co-morbid conditions but did not specify the type of co-morbid conditions; therefore, differences in co-morbidities such as hypertension, hypercholesterolemia, coronary artery disease could not be compared between the groups. The current study utilized published norms (Randolph, 1998) to determine the prevalence of impairment; however, this may limit the generalizability of the findings. Data in the current study were collected in the Midwest; therefore, ethnicity of the sample is limited to Caucasians. No measure of premorbid intellect was obtained, so it is difficult to examine the impact of premorbid intelligence on neuropsychological scores in this sample. Although we excluded patients with current psychiatric illness, we did not conduct a clinical psychiatric assessment to account for the presence of major depression in this sample. Of note, there were no group differences on the PHQ-8.

In conclusion, results from this study suggest that the type of cardiac dysfunction (i.e., systolic vs. diastolic) affects cognition in different ways. The biological underpinnings of this are not yet understood and should be the focus of future studies. However, the findings from this study have important clinical implications. HF is a complex disease to manage because it involves high-level decision-making and awareness of symptoms. For example, patients need to monitor their weight, ease of breathing, and level of fatigue on a daily basis in order to adjust medication dosages. Twenty-five percent of HF patients discharged from the hospital are readmitted within 30 days (Bennett, Pressler, Hays, Firestine, & Huster, 1997; Happ, Naylor, & Roe-Prior, 1997; Naylor, Stephens, Bowles, & Bixby, 2005). The most common reasons for readmission include difficulty following complex medical regimens and diminished recognition of worsening symptom status (Dickson, Deatrick, & Riegel, 2008; Naylor et al., 2005). It is possible that high readmission rates and difficulty managing HF symptoms are related to a decline in cognitive abilities. However, few studies have explored this relationship. Further, the cognitive impairment associated with HF is subtle and may not be easily detected during routine clinic visits. The results from this study strongly support the use of cognitive screening in clinical settings. In particular, a neuropsychological screening instrument that is brief, yet sensitive to mild changes in cognition, particularly in memory and executive function, is needed, and currently there is no recommended screening instrument for use in the clinic setting. It would also be useful to apply standard clinic criteria to help classify the MCI subgroups in HF. In addition, Bauer and colleagues (2012) documented that scores of IADLs were significantly correlated to scores of the RBANS Immediate Memory Index, RBANS Total Scale score, TMT B, and letter fluency. More studies are needed to explore the relationship between neuropsychological test scores and the impact of cognitive impairment on functional measures. Individuals with systolic dysfunction may need more comprehensive treatment plans that take into account possible memory impairment and decreased global cognition. Most importantly, future studies should attempt to determine the biological mechanisms that contribute to cognitive impairment in HF.

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Conflict of Interest

None declared.

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