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Cognitive Dysfunction Mediates the Effects of Poor Physical Fitness on Decreased Functional Independence in Heart Failure

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Abstract

Aim—Heart failure (HF) patients require assistance with activities of daily living (ADL). Poor physical fitness has recently been identified as a contributor to the high rates of disability in HF, though the mechanisms for such effects are unclear. Although not previously examined, decreased fitness may adversely impact ADLs in HF through its known association with cognitive impairment, a key correlate of self-care abilities in this population. We sought to test this possibility using a model-based approach.

Methods—197 patients with HF completed a physical fitness test and a neuropsychological test battery. A total ADL composite was derived from the Lawton Brody scale. Structural equation modeling tested whether cognitive function mediated the association between physical fitness and total ADLs.

Results—Fitness was reduced and cognitive dysfunction and impaired ADLs were prevalent. The initially significant association between fitness and total ADLs was attenuated when cognitive function was introduced as a mediator. This model demonstrated good fit (CFI = .91: *RMSEA* = .077) with a significant indirect pathway between physical fitness and total ADLs through cognitive function: Decreased physical fitness was associated with cognitive dysfunction (β = 0.35), which predicted greater assistance with ADLs (β = 0.22).

Conclusions—Poor physical fitness may lead to decreased functional independence in HF through its negative effects on cognitive function. Prospective studies are needed to confirm our findings, identify other mechanisms by which poor fitness impacts ADLs, and examine whether exercise interventions can improve cognition and help preserve ADL independence in HF.

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Keywords

Physical fitness; cognitive function; heart failure; activities of daily living

Introduction

Patients with heart failure (HF) are at risk for disability and often require assistance with many activities of daily living (ADL). As an example, approximately 80% of persons with HF have difficulties independently performing tasks such as housekeeping duties (e.g., cooking, cleaning), shopping, driving, and managing medications and finances.[1,2] Much attention has been paid to predictors of such impairments and a growing number of demographic (e.g., older age, being female) and clinical factors (e.g., dyspnea, reduced muscle strength, depression) have been identified.[3–5]

Reduced physical fitness is another likely contributor to the high rates of assistance with ADLs in patients with HF. Decreased fitness is a hallmark of HF and patients very rarely engage in any form of meaningful physical activity due to exercise intolerance.[6–8] Decreased cardiovascular fitness is a sensitive marker of increasing HF severity and thus a strong predictor of poor outcomes in this population such as heightened mortality risk.[9,10] Poorer fitness in HF has also been recently linked with decreased functional independence, including worse ability to ambulate, drive, and perform housekeeping duties.[2] Yet, the mechanisms for the adverse effects of poor fitness on ADLs remain poorly understood. Fatigue and reduced muscle strength may partially explain the fitness and ADL phenomenon, but it is likely more complicated given complex ADLs like driving and/or management of finances and medications do not require much physical exertion.

Although yet to be examined, decreased physical fitness may lead to poor ADL function in HF through its negative effects on cognitive function. Patients with HF are at risk for severe neurological conditions such as Alzheimer's disease and vascular dementia.[11] Impairments in cognitive function commence long before these conditions, as case controlled studies show HF patients exhibit deficits on tasks assessing memory and executive function, among others.[12] In persons with HF, cognitive impairment in these domains have indeed been linked with reduced ability to drive a car, manage medications, perform housekeeping duties, among other instrumental and basic ADLs.[2,13]

Decreased physical fitness is a known correlate of poorer cognitive function in HF, including of domains important for more complex ADLs such as medication management (e.g., executive function).[14,15] Despite these findings, no study has examined the interactions among physical fitness, cognitive function, and ADL performance in the context of a multivariate model. The purpose of the current study was to use a model-based approach to examine whether cognitive function mediates the effects of physical fitness on ADL performance in a sample of older adults with HF. We hypothesized that decreased physical fitness would adversely effect cognitive function to produce impairments in ADLs.

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Materials and Methods

Participants

The sample consisted of 197 persons with HF from a NIH-funded study examining neurocognitive function in older adults with HF. For inclusion, participants must have been between the ages of 50–85 years, English speaking, and had a diagnosis of New York Heart Association (NYHA) HF class II, III, or IV at the time of enrollment. All participants were recruited from outpatient cardiology clinics at Summa Health System in Akron, Ohio. NYHA class was determined during participants' routine clinical care prior to study entry and this information was ascertained by a thorough medical record review upon study enrollment. Potential participants were excluded for a history or current diagnosis of a significant neurological disorder (e.g. dementia, stroke), head injury >10 minutes loss of consciousness, severe psychiatric disorder (e.g. schizophrenia, bipolar disorder), substance abuse/dependence, and/or Stage 5 Chronic Kidney Disease.

Measures

Activities of Daily Living—The self-report Lawton Brody Activities of Daily Living Scale assessed basic and instrumental ADLs.[16] Instrumental ADLs are operationalized by complex activities such as transportation, traveling, management of finances, telephone use, meal preparation, housekeeping, laundry, shopping, and medication maintenance. Basic ADLs include feeding, dressing, grooming, bathing, toileting, and ambulation. Instrumental ADL scores range from 0 to 16 and basic ADL scores range from 0 to 12. The sum of instrumental and basic ADLs is computed to yield a total ADL composite with scores ranging between 0–28. Any response that indicated receiving assistance was deemed impaired on that activity and a higher total score signifies better functionality. The Lawton Brody scale demonstrates strong inter-rater reliability (r = .85), and concurrent validity with other measures of functional status.[17]

Physical Fitness—The 2-minute step test (2MST) assessed physical fitness in the current sample.[18] The 2MST requires participants to step in place lifting his/her knees to a marked target set on the wall set at the midpoint between the kneecap and crest of the iliac for a 2-minute period. Greater step count reflects better physical fitness. Average step count for females between the ages of 50–85 ranges from 71–115 and between 60–107 steps for males. The 2MST has been correlated with metabolic equivalents derived from stress testing and is also a sensitive predictor of neurocognitive outcomes in HF.[14,15]

Cognitive Function—A series of neuropsychological measures were administered to assess cognitive function in multiple domains, including attention, executive function, and memory. All measures are widely used in medical populations and demonstrate excellent psychometric properties. The domains and their respective measures include:

Attention/Executive Function: Trail Making Test A and B,[19] Digit Symbol Coding,[20] and Letter Number Sequencing[21,22] were used to tap into attention and executive function. Trail Making Test A has participants connect numbers in sequential order as quickly as possible. For Trail Making Test B, participants connect a series of numbers and letters in alternating

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ascending order as fast as possible. In the Digit Symbol Coding task, participants must use a key to match symbols with corresponding numbers over a two-minute period. Letter Number Sequencing involves verbally ordering numbers and letters that are orally presented in an unordered sequence.

Memory: The California Verbal Learning Test-Second Edition (CVLT-II) long delay free recall[23] was administered to test memory function. The CVLT-II asks participants to learn and then recall a 16-item word list after a delay period.

Demographic and Medical History—Demographic and medical characteristics were ascertained through participant self-report and corroborated by medical record review.

Procedures

The local Institutional Review Board (IRB) approved the study procedures and all participants provided written informed consent prior to study enrollment. During a baseline assessment, participants completed demographic and psychosocial self-report measures, including the Lawton Brody Activities of Daily Living Scale. Participants completed the 2MST and were also administered a comprehensive cognitive test battery. All procedures were performed by a trained research assistant under the supervision of a licensed neuropsychologist.

Statistical Analyses

Structural equation modeling (SEM) was used to test the hypothesis driven model depicted in Figure 1. The model consists of one latent factor used to represent cognitive function. The five neurocognitive measures served as the indicators of cognitive function. All of the cognitive tests were transformed to T-scores (a distribution with a mean of 50 and a standard deviation of 10) using normative data in order to maintain directionality among scales and account for the influence of demographic factors, including age, and gender in the case of the CVLT-II. The parameter of a single indicator was fixed at 1 in order to correct for scaling. 2MST and total ADLs served as the manifest predictor and mediator variables, respectively.

A measurement model was first performed in order to examine model fit among the latent factor cognitive function and its indicators. An initial regression analysis tested the strength of the relationship between the 2MST and total ADL. A structural model then tested model fit for cognitive function as a possible mediator between the exogenous variables 2MST and total ADLs. Diagnostic history of hypertension and type 2 diabetes mellitus (T2DM) served as covariates for cognitive function in the current model. These are two of the more prevalent comorbid conditions in HF that are well established to negatively impact cognitive function in this population. EQS software using maximum likelihood approach tested the SEM. Goodness of fit was evaluated by comparative fit index (CFI), and the root mean-square error of approximations (RMSEA), using commonly accepted values of these indices (e.g., CFI ≥ .90; RMSEA ≤ .08).[24,25] RMSEA and CFI provide the best evaluation of overall model fit and while the χ^2 value is reported it was not used to determine fit given the sensitivity of this index to factors such as sample size and normality.[26–28]

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Results

Demographic and Medical Characteristics

See Table 1 for demographic and medical characteristics of the sample. Participants averaged 68.07 (SD = 8.94) years of age, were 35.5% female, and 83.2% Caucasian. Bivariate correlations showed a significant association between age and 2MST performance ($r(-0.18$, $p = 0.01)$, but not total ADLs. A medical record review indicated that the sample had an average left ventricular ejection fraction of 40.25 (SD = 14.41). Of the sample, 83.8% had an NYHA class II and only 3 participants were NYHA class IV. Comorbid medical conditions were common, with many participants having hypertension, T2DM, a history of myocardial infarction, elevated total cholesterol, and coronary artery disease. Of participants with known medication history (N = 179), 77.2% were prescribed beta-blockers. There were no between medication group differences on the 2MST, total ADLs, or any of the cognitive variables ($p > 0.05$ for all).

ADLs and Physical Fitness

Refer to Table 1 for medical and demographic characteristics of the current sample. The mean total ADL composite was 25.34 (SD = 3.20). HF patients most frequently reported requiring assistance with shopping (26.9%), food preparation (31.5%), laundry (38.0%), housekeeping duties (36.6%), and physical ambulation (15.2%). Although less common, participants also reported difficulties with independence in transportation, and managing medications and finances. See Table 2. In terms of physical fitness, both males and females demonstrated decreased levels of fitness, as 2MST performance for females fell in the below average range and in the low average end of the normative range for males.

Cognitive Function

Relative to normative data, participants performed in the average range on measures of attention, and memory, and low average on a task assessing executive function (i.e., Trail Making Test B). When using a T-score cutoff of 35 (1.5 SD below the mean of normative standards), >20% of the sample exhibited impairments in executive function. Of the sample, 11.2% demonstrated impairments on Trail Making Test A, 10.2% on Digit Symbol Coding, and 3.6% exhibited impaired performances on Letter Number Sequencing.

Measurement Model

A measurement model first examined fit of the indicators of the latent construct cognitive function. Digit symbol coding was fixed at 1.0. The measurement model demonstrated good fit: $\chi^2(5, 197) = 11.89$, $p = 0.04$, *CFI* = 0.97, *RMSEA* = 0.08 (90% CI = 0.02, 0.15). All neuropsychological measures significantly loaded on to the cognitive function latent factor ($\beta = .36$ to .79, $p < .05$ for all).

Structural Model

Table 3 shows the covariance matrix among the variables. An initial model, without cognitive function, revealed that poorer 2MST performance demonstrated a significant direct effect on poorer total ADL function ($\beta = 0.19$, $p < 0.01$). To clarify this finding,

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follow-up partial correlations controlling for hypertension and T2DM showed that the 2MST demonstrated specific associations with the following ADLs: Shopping ($r(193) = 0.14$, $p = 0.048$, independence in transportation $r(193) = 0.26$, $p < 0.001$), feeding ($r(193) = 0.16$, $p = 0.02$), and physical ambulation ($r(193) = 0.28$, $p < 0.001$). In each case, lower 2MST was associated with poorer ADL function.

The relationship between the 2MST and total ADLs was attenuated and became non-significant ($\beta = 0.09$, $p > 0.05$) when the mediator cognitive function was introduced. Specifically, the model with cognitive function as the mediator between the 2MST and total ADL performance demonstrated good fit: $\chi^2(26, 197) = 55.90$, $p < 0.01$, CFI = .91: *RMSEA* = .077 (90% CI = .05, .10). Structural pathways showed that decreased performance on the 2MST was associated with worse cognitive function, and in turn, poorer cognitive function predicted greater dependence in ADLs ($p < 0.05$). Sobel test revealed that there was a significant indirect effect of the 2MST on total ADL performance through cognitive function ($p < .05$). Taken together, these findings suggest the presence of partial mediation. See Figure 1 for standardized parameter estimates.

2MST, Cognitive Function, ADL Performance

After adjusting for hypertension and T2DM, the 2MST was correlated with scores on Trail Making Test A ($r(193) = 0.25$, $p < 0.001$) and B ($r(193) = 0.28$, $p < 0.001$), and Digit Symbol Coding ($r(193) = 0.31$, $p < 0.001$); there was a trend for Letter Number Sequencing ($r(193) = 0.13$, $p = 0.07$). In each case, decreased performance on the 2MST correlated with worse cognitive function. No such pattern emerged for the CVLT-II Long Delay Free Recall ($p > 0.10$).

Performance on many of the attention and executive function measures predicted ADLs such as shopping, laundry, bathing, and physical ambulation, even after controlling for hypertension and T2DM. Notably, better attention and executive function correlated with increased reported ability to manage medications and independence in transportation ($p < 0.05$). Performance on the CVLT-II Long Delay Free Recall was not associated with any of the ADLs ($p > 0.05$ for all). See Table 4.

Discussion

Reduced physical fitness, cognitive dysfunction, and heightened assistance with ADLs were all common in this sample of HF patients. In HF, decreased fitness is associated with poor outcomes, including reduced functional independence.[2] Findings from the current study suggest this relationship may partly stem from the negative effects of poor fitness on cognitive function. Many aspects of these findings warrant further discussion.

We found that reduced cognitive function mediated the association between poor physical fitness and a need for greater assistance with ADLs in older adults with HF. Exercise intolerance and physical limitations often accompany HF due to the inability of the heart to meet the blood supply demands of the muscles.[8] Consequently, HF patients exhibit poor fitness levels that worsen with increasing HF severity. A vast literature demonstrates the adverse impact of poor fitness and inactivity on cognitive function in many patient (e.g.,

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Alzheimer's disease) and healthy samples.[29–31] Decreased physical fitness is also a significant risk factor for cognitive impairment across multiple domains in patients with HF, including frontal systems deficits.[15] This pattern is unfortunate, as cognitive impairment contributes to decreased functional independence in HF, with emphasis noted on the role of executive dysfunction.[2,13] Indeed, deficits in executive function were found in >20% of this sample and emerged as a significant predictor of important ADLs with potentially harmful repercussions (e.g., management of medications, driving). These tasks require complex cognitive processes and executive deficits likely preclude patients' abilities to organize, plan, and monitor their behavior.[32] Taken together, the directionality of the proposed associations between physical fitness, cognitive function, and ADLs is strongly supported by the literature; however, prospective studies are much needed to confirm and clarify our findings.

Improved fitness is a key treatment target in HF and may serve as a possible avenue for preserved cognition and functional independence. The mechanisms for poor physical fitness and subsequent cognitive impairment likely involves the detrimental effects of decreased fitness on vascular health such as endothelial dysfunction, exacerbated cardiac dysfunction, and cerebral hypoperfusion–the most commonly proposed mechanism of cognitive impairment in HF.[8,33–38] Fortunately, fitness in HF is modifiable[39] and increased fitness can improve vascular function, including higher cerebral perfusion levels.[40] Interestingly, cardiac rehabilitation has been linked with better cerebral perfusion and cognitive function in cardiovascular disease patients[41] and daily activity has been suggested to reduce the risk of dementia.[42] The cognitive benefits of exercise may ultimately translate to increased self-care abilities in HF. As an example, exercise in Alzheimer's disease patients has recently been shown to benefit cognitive function and lead to better ADL function.[43] Evidence also suggests cognitive interventions among patients with Alzheimer's disease promote preservation of complex instrumental ADLs.[44] Future studies should investigate whether participation in exercise programs (e.g., cardiac rehabilitation) improves neurocognitive function in HF and subsequently preserves functional independence.

Identification of interventions that can improve cognitive function and ADLs in HF would likely prove to have significant societal, health, and economic benefits. Poor self-care abilities in HF (particularly, medication non-adherence) have been shown to increase mortality risk and lead to recurrent hospital readmissions possibly due to worsening HF symptoms.[45–48] Interestingly, improving medication adherence in other medical populations (e.g., diabetes) by as a little as 20% has been suggested to reduce health care costs by > $1,000 per patient[49] and this pattern likely generalizes to HF. Lastly, the current findings and other emerging studies suggest HF patients may be at risk for impaired driving due to deficits in cognitive function.[50] Cognitive impairment significantly raises risk for vehicle crashes[51] and case controlled studies are needed to determine whether HF patients are at risk for harm to themselves or others while on the road. Likewise, tightly designed longitudinal studies are needed to empirically test the health and psychosocial benefits of improved ADLs in older adults with HF.

The current study is not without limitations. As previously mentioned, the extant literature supports the proposed directionality modeled in Figure 1, but prospective studies are needed to validate our findings. Similarly, full mediation among variables rarely occurs and other

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unexamined factors (e.g., dyspnea, fatigue) may also help to explain the effects of poor fitness on ADL function. However, it is noted that while physical symptoms may contribute to the association between poor fitness and basic ADLs such as ambulation, they likely do not account for performance of instrumental ADLs (e.g., medication management, independence in transportation). Nevertheless, future work is needed to identify the differential risk factors of impaired basic and instrumental ADLs in HF. Similar to this notion, decreased fitness in HF is associated with reduced brain volume and thinner cortex[52] and future studies should also use model based approaches to determine whether such brain changes contribute to impairments in ADLs via cognitive dysfunction. ADLs were operationalized using self-report and future studies that use more objective and informant assessments of functional independence in HF are needed to fully elucidate our findings. We also examined HF as a broad disease entity and did not investigate the specific types of HF (i.e., diastolic vs. systolic) as it relates to physical fitness, cognitive function, and ADLs. The nature by which the different etiologies of HF affects these factors may be distinct[53] and future work should examine the associations among fitness, cognition, and ADLs across HF types. Finally, neuropsychological measures were scored using normative data to account for demographic variables and we also controlled for the most prevalent comorbid medical factors (i.e., hypertension, T2DM) well known to impact neurocognitive outcomes in HF. However, large randomized controlled trials are needed to confirm our findings by fully accounting for possible confounding medical and demographic variables such as age, gender, medical status, and medication therapy.

In brief summary, the current study suggests that cognitive dysfunction may explain the effects of poor physical fitness on reduced functional independence in HF. Prospective studies are needed to confirm directionality and determine whether exercise interventions can improve cognitive function in HF to help preserve self-care abilities.

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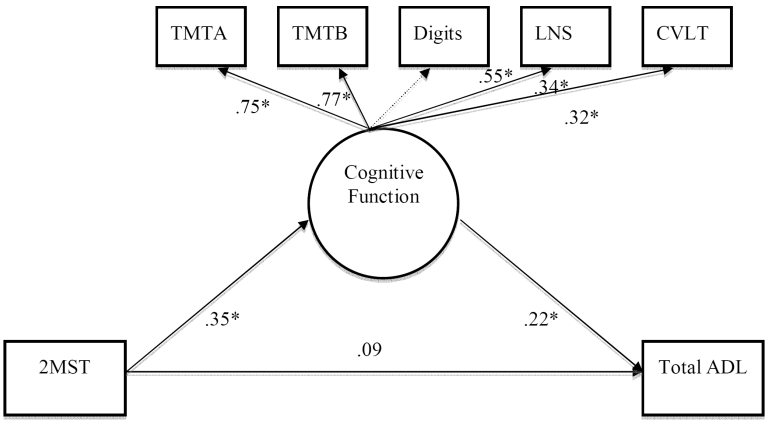

Figure 1. Cognitive Function Mediates the Effects of Physical Fitness on ADL Function in Patients with Heart Failure (N = 197)

Notes. The pathway between cognitive function and Digits was fixed. Standardized parameters estimates are presented in the model; significance levels for these paths are based on the unstandardized estimates. Pathways connected hypertension (β = −0.17) and type 2 diabetes mellitus (β = −0.21) demonstrated significant effects on the latent construct cognitive function. They were not included in the Figure for ease of presentation. Abbreviations—2MST = 2 minute step test; TMTA = Trail Making Test A; TMTB = Trail Making Test B; Digits = Digit Symbol Coding; LNS = Letter Number Sequencing; CVLT= California Verbal Learning Test Long Delay Recall; ADL = Activities of Daily Living *$p < .05$

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Table 1

Demographic and Clinical Characteristics

DEMOGRAPHIC CHARACTERISTICS	
Age, mean (SD)	68.07 (8.94)
Years of Education, mean (SD)	13.56 (2.72)
Female (%)	35.5
Race (% Caucasian)	83.2
MEDICAL AND CLINICAL CHARACTERISTICS	
Overall Sample LVEF, mean (SD) (N = 188)	40.25 (14.41)
NYHA Class (% I; II;III,;IV)	0.5;83.8;14.2;1.5
Diabetes (% yes)	36.0
Hypertension (% yes)	68.0
History of Myocardial Infarction (% yes)	56.9
Elevated Total Cholesterol (% yes)	66.0
Sleep Apnea (% yes)	24.9
Coronary Artery Disease (% yes)* (N = 192)	79.2
Angina (% yes)* (N = 192)	31.0
Atrial Fibrillation (% yes)* (N = 192)	29.9
Overall Sample 2MST, mean (SD)	61.72 (23.45)
Males 2MST, mean (SD)	65.04 (23.28)
Females 2MST, mean (SD)	55.70 (22.69)
COGNITIVE TEST PERFORMANCE, mean (SD)	
Trail Making Test A	49.42 (11.68)
Trail Making Test B	43.42 (18.22)
Digit Symbol Coding	47.36 (9.36)
Letter Number Sequence	50.61 (8.99)
CVLT-II LDFR	47.16 (10.29)

Note.

LVEF = Left Ventricular Ejection Fraction; 2MST = two minute step test; CVLT-II LDFR = California Verbal Learnin) Test Long Delay Free Recall; Sample size for LVEF is 188 due to missing data.

*Sample sizes reduced for these variables due to missing data.

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Table 2

Reported ADL performance (*N* = 197)

	Mean (SD)
Total ADL, mean (SD)	25.34 (3.20)
Instrumental ADL, mean (SD)	13.64 (2.81)
Basic ADL, mean (SD)	11.70 (0.80)
	% Impaired
Telephone Use	1.5
Shopping	26.9
Food Preparation	31.5
Housekeeping	36.6
Laundry	38.0
Driving	7.1
Medication Management	6.1
Finances	10.1
Toileting	4.6
Feeding	1.0
Dressing	3.6
Grooming	4.1
Physical Ambulation	15.2
Bathing	1.5

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Table 3

Bivariate Covariance Matrix

	2MST	Total ADL	HTN	T2DM	CVLT-II	TMT A	TMT B	Digits	LNS
2MST	549.77	--	--	--	--	--	--	--	--
Total ADL	13.92	10.21	--	--	--	--	--	--	--
HTN	−2.34	−0.12	0.22	--	--	--	--	--	--
T2DM	−2.13	−0.32	0.03	0.23	--	--	--	--	--
CVLT-II	−0.11	2.74	0.08	0.01	105.91	--	--	--	--
TMT A	85.03	9.69	−1.20	−1.21	34.35	136.49	--	--	--
TMT B	143.67	8.17	−2.05	−1.90	54.26	124.65	331.96	--	--
Digits	79.53	5.67	−0.71	−1.28	18.03	63.16	94.47	87.08	--
LNS	35.72	4.15	−0.60	−0.46	27.90	38.04	79.29	35.95	80.81

Note. 2MST = 2-minute step test; HTN = hypertension; T2DM = type 2 diabetes mellitus; TMT A = Trail Making Test A; TMT B = Trail Making Test B; Digits = Digit Symbol Coding; LNS = Letter Number Sequencing; CVLT-II = California Verbal Learning Test-II Long Delay Recall; ADL = Activities of Daily Living

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Table 4

Correlations Examining Cognitive Function and Specific ADL Performance

	TMT A	TMT B	Digits	LNS	CVLT-II LDFR
Telephone	.02	.14 (p = .06)	.01	−.01	−.01
Shopping	.18*	.09	.13 (p = .07)	.08	.07
Food Preparation	.09	.04	−.02	.10	.02
Housekeeping	.11	.06	.08	.11	.08
Laundry	.15*	−.05	.03	.05	.07
Transportation	.22**	.14*	.19**	−.01	.09
Medications	.18*	.08	.13 (p = .07)	.15*	.07
Finances	.03	.01	.05	−.02	−.05
Toileting	.09	.12	.00	.11	.01
Feeding	−.01	−.01	.06	.03	.00
Dressing	.09	.06	.08	.07	.08
Grooming	.09	.08	.13 (p = .07)	.08	.12
Physical Ambulation	.25**	.18*	.27**	.13	.08
Bathing	24**	.07	.13 (p = .06)	.09	.09

Note.

TMT A = Trail Making Test A; TMT B = Trail Making Test B; Digits = Digit Symbol Coding; LNS = Letter Number Sequencing; CVLT-II = California Verbal Learning Test-II Long Delay Recall; ADL = Activities of Daily Living

* $p \leq 0.05$;

** $p < 0.01$;