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# COPD is Associated with Cognitive Dysfunction and Poor Physical Fitness in Heart Failure

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## Abstract

**Objective—**To examine the associations among chronic obstructive pulmonary disease (COPD), cognitive function, and physical fitness in heart failure (HF).

**Background—**Cognitive impairment in HF in part stems from medical comorbidities and poor physical fitness. COPD, a frequent co-existing condition in HF, is a risk factor for cognitive impairment and a known cause of poor physical fitness. Yet, the interplay among COPD, cognition, and physical fitness has never been examined in HF.

**Methods—**191 HF patients completed a cognitive test battery and brief physical fitness assessment. Diagnostic history of COPD was ascertained via medical chart review.

**Results—**Regression analyses showed HF patients with COPD exhibited worse attention/ executive function and poorer fitness relative to their non-COPD counterparts. Worse fitness correlated with cognitive dysfunction.

**Conclusions—**COPD is associated with reduced cognition and worse fitness in HF. Longitudinal work that employs objective assessments of COPD is needed to determine directionality and clarify mechanisms.

### Keywords

COPD; heart failure; cognitive function; physical fitness



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**Conflict of Interest**

The authors declare no conflicts of interest.

## Introduction

Heart failure (HF) increases vulnerability to adverse neurological outcomes such as Alzheimer's disease [1]. Up to 80% of persons with HF also exhibit impairments on formal cognitive testing [2], including on tasks of attention/executive function and memory [3]. Cognitive impairment in HF is concerning in light of its key role in poor outcomes such as premature death [4].

Cognitive impairment in HF is most widely believed to stem from brain insult subsequent to alterations in cerebral blood flow [5]. However, the manifestation of cognitive impairment in this population appears to be complex and involves multiple physiological mechanisms. In particular, work from our group has previously shown that medical comorbidities that accompany HF, such as hypertension, diabetes, and sleep apnea, contribute to cognitive dysfunction in this population (for a review, see Alosco et al., 2013) [6]. Health-related factors also play a role in the development of cognitive impairment in HF, particularly poor physical fitness levels. Reduced fitness in HF is inevitable due to the combination of cardiac deficiency and high rates of physical inactivity in this population [7]. Extant evidence derived from our team indeed links poor fitness with significant impairment in multiple cognitive domains in HF such as attention, executive function, and memory [8].

Although not yet examined, chronic obstructive pulmonary disease (COPD) also likely contributes to cognitive impairment in HF. COPD is common in persons with HF, with a recent review showing prevalence rates in the literature range between 8–52% and likely hover around 20% [9]. COPD is an independent predictor of death and hospitalizations in persons with HF and has been suggested to confer greater risk for poor outcomes relative to other medical conditions in HF (e.g., hypertension, diabetes) [9]. Past research also documents the negative impact of COPD on cognition independent of HF. For example, mid-life COPD is associated with a twofold risk for mild cognitive impairment [10] and patients with COPD also exhibit greater impairments on neuropsychological testing relative to their healthy and demographically similar counterparts [11].

Poor physical fitness may represent one mechanism by which COPD increases risk for cognitive impairment in HF. Reduced fitness is a classic characteristic of COPD in light of the respiratory problems (e.g., airflow obstruction) that define this disease [12]. Moreover, a majority of persons with COPD also report failing to engage in recommended levels of physical activity [13]. This pattern of findings raises concern for heightened vulnerability to cognitive dysfunction in HF patients with COPD given the close association between poor fitness and cognitive dysfunction in both HF and COPD populations [14].

Despites these findings, the interplay among COPD, cognition, and poor physical fitness is not well understood, and no study has examined the impact of COPD on cognitive function in patients with HF. The purpose of the current study was to examine these possible associations and we hypothesized that a physician diagnosed history of COPD (as ascertained via medical chart review) would be associated with cognitive dysfunction and poorer physical fitness levels; worse fitness would in-turn predict decreased cognitive function.

# Methods

## Study Design

The current study was a cross-sectional analysis of the associations among COPD, physical fitness, and cognitive function.

## Human Subjects

This sample included a total of 191 participants with HF that were enrolled in a National Institutes of Health (NIH) study examining neurocognitive function in patients with HF. For study inclusion, participants must have been between 50–85 years of age, English as a primary language, and had a diagnosis of New York Heart Association (NYHA) class II, III, or IV. Participants were excluded for neurological disorders such as dementia, stroke, multiple sclerosis, etc., a head injury with >10 minutes loss of consciousness, severe psychiatric disorder (e.g. schizophrenia, bipolar disorder), past or current substance abuse/ dependence, and stage 5 chronic kidney disease. The current sample included participants with complete medical, cognitive, and physical fitness data.

## Variables and Measures

**Cognitive Function—**Participants were administered a neuropsychological test battery to examine cognitive function. The cognitive measures employed in this study are widely used in clinical settings, brief and easy to administer, and tap into distinct aspects of cognitive abilities. The domains and cognitive measures assessed include:

> **Attention/Executive Function:** The Trail Making Test A and B [15], Digit Symbol Coding [16], Frontal Assessment Battery [17], and Letter Number Sequencing [18] were used to examined attention/executive function. Trail Making Test A requires participants to connect a series of numbers in order as quickly as possible. It is a valid and reliable measure of visual attention and psychomotor speed. Trail Making Test B has participants connect both number and letters in an alternating (i.e., number then letter) ascending order as fast as possible. This measure is a valid and reliable indicator of executive functions such as multitasking and has a test-retest reliability of up to 0.89 [19,20].

For Digit Symbol Coding, there is a key with nine pairs of numbers and symbols. Participants are instructed to use this key to match symbols with the corresponding numbers as quickly as possible. This measure is a valid measure of attention, psychomotor speed, and working memory and has a strong test-retest reliability of $r = 0.84$ [21]. The Frontal Assessment Battery is a brief, but comprehensive, measure of several aspects of executive function, including lexical fluency, abstract reasoning, environmental autonomy, inhibition, sensitivity to interference, and higher-order motor programming. This measure has also been demonstrated to exhibit strong psychometric properties such as high internal consistency (Cronbach's alpha = 0.78) and good concurrent validity with gold measures of executive function (i.e., Wisconsin Card Sorting Test; $r = 0.87$) [17;22].

Lastly, Letter Number Sequencing is a task of working memory that has participants verbally order numbers and letter that are orally presented in an unordered sequence. This task exhibits a test-retest reliability of r = 0.75 [18].

**Memory:** The California Verbal Learning Test-II (CVLT-II) short and long delay free recall, and total recognition hits operationalized memory abilities [23]. Participants are asked to learn, recall, and then recognize a 16-item word list. This measure has strong test-retest reliability (r = 0.88) and good concurrent validity with other verbal memory measures (r = 0.63 to r = 0.96) [23].

**Language:** Boston Naming Test (BNT) [24] and Animal Fluency test [25] were administered to examine language functions. The Boston Naming Test consists of low to high familiar pictured objects that participants must correctly name. It is a task assessing confrontation naming and demonstrates high correlations with other measures of verbal abilities (r = 0.83) [26]. For the Animal Fluency Test, participants must name as many animals as possible within a 60-second time period.

**Physical Fitness—**All participants completed the 2-minute step test (2MST) in order to assess physical fitness [27]. For this task, participants are instructed to march 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. A higher step count reflects better physical fitness. An average step count over two minutes for healthy males between 60–85 years ranges from 71–115 and between 60–107 steps for females [27]. Below average 2MST according to the average age of males in this sample (mean = 68.58, SD = 9.36) is < 87 and for females with the average age of the current sample (mean = 68.41, SD = 8.27) is < 73 [27]. The 2MST is a valid measure of physical fitness, as it is highly correlated with metabolic equivalents [8,28].

**Demographic and Medical History—**Self-report and a medical chart review were used to ascertain demographic and medical characteristics. Specifically, participants first completed a medical history questionnaire to self-report demographic information and history of medical conditions. A medical chart review was then performed to supplement and corroborate participant’s self-report and to ascertain physician-diagnosed history of comorbid medical conditions. Through these methods, a physician-diagnosed history of COPD (i.e., positive or negative diagnostic history) for all participants was obtained along with a history of hypertension, diabetes, sleep apnea (central or obstructive), and depression. For all medical conditions, any history at all was deemed to be a positive diagnostic history. Participants also completed a self-report questionnaire that asked participants to indicate the number of cigarettes smoked per week.

## Procedures

The Summa Health System and Kent State University Institutional Review Board (IRB) approved the study procedures and all participants provided written informed consent prior to study enrollment. Participants first completed demographic and medical history self-report measures and a medical chart review was performed. A trained research assistant then administered a neuropsychological test battery to each participant in order to assess attention/executive function, memory, and language. Finally, participants completed the 2MST under the instruction of the trained research assistant and their height and weight were measured to calculate their body mass index according to the standard formula. A licensed neuropsychologist supervised all study procedures.

### Statistical Analyses

Neuropsychological raw scores were converted to T-scores (a distribution with a mean of 50, and a standard deviation of 10) using normative data that adjusts for age, and gender for measures of memory. This conversion was performed in order to facilitate clinical interpretation and maintain directionality across scales. Attention/executive function, memory, and language composite scores consisted of the mean of the T-scores of cognitive measures that make-up their respective domain. Consistent with clinical convention, a T-score $< 35$ was used to define cognitive impairment. This score represents 1.5 SD below the normative mean and has been shown to be sensitive to the detection of cognitive impairment [29].

Independent samples *t*-tests and chi-square analyses were used to examine differences in demographic and medical characteristics between HF patients with and without COPD. A series of separate hierarchical regression analyses were performed to determine the interplay among COPD, cognitive dysfunction, and reduced physical fitness in HF. The dependent variables included attention/executive function, memory, language, and the 2MST. Block 1 included covariates known to influence cognitive function and physical fitness, including age, sex (1 = males; 2 = females), years of education, LVEF, diagnostic history of hypertension, diabetes, sleep apnea, and depression (1 = positive diagnostic history; 0 = negative diagnostic history), as well as cigarette smoking, and BMI. Diagnostic history of COPD (1 = positive history; 0 = negative history) was then entered in block 2 to determine the independent association between COPD and cognitive function and physical fitness. Finally, partial correlations controlling for the above listed demographic and medical variables, as well as COPD, then examined the association between the 2MST and cognitive function in each domain.

## Results

### Sample Characteristics

See Table 1 for a summary of the sample demographic and medical characteristics. Of the sample, 24.6% (n = 47) of patients with HF had a comorbid history of COPD. Independent samples *t*-tests and chi-square analyses revealed that there were no between group differences for demographic variables (i.e., age, sex) or medical and health factors, including LVEF, BMI, smoking status, or history of hypertension, diabetes, or depression ($p > 0.05$ for all). However, HF patients with COPD were more likely to have fewer years of education and a history of sleep apnea versus those without COPD ($p < 0.05$). See Table 1.

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### Cognitive Test and Physical Fitness Performance in the Overall Sample

Table 2 displays cognitive test performance. Impairments in cognitive function were common in the overall sample, most notably on tasks of attention/executive function and memory. When using a T-score cutoff of 35, (i.e., 1.5 SD below the normative mean), 16.2% demonstrated impaired performance on CVLT-II recognition hits and 19.4% and 25.1% scored below a T-score of 35 on Trail Making Test B and the Frontal Assessment Battery, respectively. Impairments in language were also evident, but not as common.

Reduced physical fitness was also prevalent in the overall sample of HF patients. Specifically, relative to normative data for men and women between 65 and 69 years of age, both men (mean (SD) = 64.12 (23.45) steps) and women (mean (SD) = 56.23 (21.71) steps) in this sample exhibited well below average performances on the 2MST. In fact, 83.6% of men fell in the below average range (i.e., < 87 steps) and 73.9% of women also exhibited below average fitness (i.e., < 73 steps).

### COPD and Cognitive Function

Chi-square analyses showed HF patients with COPD exhibited significantly greater impairments in cognitive function. In particular, impairments were more prevalent in HF patients with COPD versus those without for Trail Making Test B ($\chi^2$ ($N$ = 191, df = 1) = 6.28, $p$ = 0.01; odds ratio = 2.60, 95% CI = 1.21, 5.58), Frontal Assessment Battery ($\chi^2$ ($N$ = 191, df = 1) = 4.04, $p$ = 0.04; odds ratio = 2.07, 95% CI = 1,01, 4.22), and on Digit Symbol Coding ($\chi^2$ ($N$ = 191, df = 1) = 5.89, $p$ = 0.02; odds ratio = 3.17, 95% CI = 1,20, 8.37). See Table 2.

Table 3 presents regression analyses examining the associations among COPD, cognitive function, and physical fitness. Hierarchical regressions showed that COPD demonstrated a significant association with attention/executive function ($\beta = -0.14$, $p$ = 0.04), even after controlling for demographic, medical, and clinical variables. HF patients with COPD exhibited poorer performance in this domain relative to HF participants without such history. This pattern did not emerge for memory or language abilities ($p > 0.05$).

### COPD and Physical Fitness

All men with COPD and all women with COPD fell in the below average range for the 2MST performance, as according to normative data based on 2MST performances in men and women between 65 and 69. In contrast, many men (21.3%) and women (36.0%) HF patients without COPD had 2MST performances in the average range. ANOVA analyses showed men ($F$(1, 120) = 10.47, $p < 0.01$) and women ($F$(1, 67) = 10.49, $p < 0.01$) HF patients with COPD exhibited worse performance on the 2MST then their non-COPD counterparts.

Regression analyses controlling for age, sex, education, LVEF, diagnostic history of hypertension, diabetes, sleep apnea, and depression, cigarette smoking, and BMI revealed a significant association between COPD and the 2MST ($\beta = -0.23$, $p < 0.01$). Specifically, HF participants with COPD exhibited worse physical fitness levels than HF patients without COPD.

### Poor Physical Fitness and Cognitive Dysfunction

Poor physical fitness was associated with worse cognitive function in this sample. Partial correlations controlling for age, sex, education, LVEF, hypertension, diabetes, sleep apnea, COPD, depression, smoking status, and BMI showed significant association between the 2MST and attention/executive function ($r(178) = 0.25$, $p < 0.01$) and language abilities ($r(178) = 0.17$, $p = 0.02$). In each case, poorer physical fitness was associated with worse cognitive function. No such pattern emerged for memory ($p > 0.10$).

## Discussion

COPD, cognitive dysfunction, and poor fitness were all prevalent in this sample of patients with HF. Past work shows that medical (e.g., hypertension, diabetes) and health factors (e.g., reduced fitness) play an important role in the manifestation of cognitive impairment in HF. This study extends these findings and identifies COPD, a prevalent comorbid condition in HF, as another correlate of cognitive dysfunction in this population and this relationship may involve reduced physical fitness.

We found that HF patients with COPD exhibited worse attention/executive function relative to HF patients without COPD. In non-HF samples, COPD is an independent predictor of impairments on neuropsychological testing [10,11]. COPD may contribute to cognitive impairment in HF via additive reductions in cerebral oxygenation and resulting brain damage. Reduced cerebral blood flow in HF patients is suggested to disturb oxygen supply to the brain to result in cerebral injury (e.g., white matter hyperintensities) and subsequent cognitive impairment [5]. Cerebral hypoperfusion and brain metabolic abnormalities are also common in COPD patients and correlated with cognitive dysfunction in this population [30–32]. The physiological effects of COPD (e.g., low blood oxygenation due to airflow obstruction) may interact with cardiac dysfunction to exacerbate structural brain alterations in HF [30]. Indeed, brain abnormalities in COPD are particularly common in the frontal cortex, which is consistent with the observed impact of COPD on frontal lobe mediated cognitive functions (e.g., attention/executive function) in this study. In contrast, COPD was not associated with memory or language abilities in this sample and the exact reason for this pattern is unclear. One possibility is that the brain regions largely responsible for these mental functions (e.g., medial temporal lobe) may not have been injured beyond a necessary threshold to yield clinically meaningful impairments in this specific sample. However, it is also possible that the cognitive tests employed in this study may also account for the differential findings. The assessment of memory and language in this sample may have been inadequate to detect impairments in memory and language in patients with HF and COPD. In contrast, the more comprehensive assessments of attention/executive function was likely sufficient to capture impairment in this domain. Prospective studies that employ neuroimaging are much needed to elucidate brain changes and corresponding disturbances in cognitive function over time in HF patients with and without COPD.

Our findings suggest that poor physical fitness may be involved in COPD-related cognitive deficits in HF patients. Persons with HF are known to exhibit reduced fitness due to exercise intolerance secondary to the inability of the heart to meet the demands of the skeletal muscles [33]. Poor fitness is a key contributor to cognitive impairment in HF and COPD may contribute to cognitive dysfunction in this population due to its association with poor fitness stemming from diminished pulmonary ventilation and increased rates of physical inactivity [7,13,14]. Poor physical fitness is linked with vascular abnormalities (e.g., endothelial dysfunction) that negatively impact cerebral blood flow [34,35] and this pattern may translate to insult to the cerebral morphometry [34]. Indeed, reduced fitness is associated with smaller total and regional brain volume in patients with HF [36], as well as among older adults and in patients with Alzheimer's disease [37–39]. Longitudinal studies are needed to determine whether the negative impact of COPD on physical fitness levels accelerates brain atrophy and increases risk for neurodegenerative conditions in HF.

The current findings are limited in several ways, most notably the lack of objective measures of COPD. A physician-diagnostic history, as ascertained through medical records, operationalized COPD. While this methodology may tap into the long-term impact of COPD, objective assessment of lung function such as spirometry would be a more reliable and sensitive approach. Objective assessments of pulmonary function would allow for examination of COPD severity along a continuum and thus determine whether there is a dose-response relationship between COPD and cognition. As an example, cognitive impairment has been found in COPD patients with and without hypoxemia, suggesting that even subclinical levels of low blood oxygenation may alter neurocognitive outcomes [31]; however, we were unable to test this possibility. This is unfortunate, as subclinical effects of COPD on the cognition are particularly likely in this sample of patients with relatively mild HF (e.g., LVEF of approximately 40%). In this context, the lack of sensitive objective COPD assessments (as well as of other medical conditions) and mild disease status of the sample may indeed partially explain the relatively modest effects observed and the reduced prevalence rates of COPD and other medical comorbidities (e.g., sleep apnea) in this sample.

Several other limitations of the current study deserve further discussion. The cross-sectional study design limits any type of causal inferences and the directionality between COPD, physical fitness, and cognition remains unclear. For example, it is also possible that participants with cognitive impairment may be less likely to participate in physical activity and thus limit physical fitness levels in these individuals. Longitudinal cohort studies are much needed in this area. In addition, symptoms of HF often involve ventilatory defects and thus COPD may be over- or misdiagnosed in this population [10]. Prospective studies that utilize measures sensitive to both cardiac function (e.g., echocardiography) and COPD (e.g., pulmonary function tests) will also help to differentiate symptoms manifesting from HF versus COPD and thus elucidate the distinct impact of these diseases on cognitive function.

Although unable to be determined from the current findings, past work raises the possibility that cognitive impairment in HF and COPD populations may be partially reversible. For instance, cardiac rehabilitation in HF patients has been shown to confer long-term improvements in attention/executive function and memory and such gains were suggested to involve increases in physical fitness [40]. Pulmonary rehabilitation has also been linked with cognitive benefits in multiple domains in patients with COPD [41]. Prospective studies are strongly encouraged to determine the most effective behavioral and medical interventions that may be able to reduce risk for poor neurocognitive outcomes in HF patients with and without COPD.

## Conclusions

COPD is associated with reduced cognitive function in older adults with HF and this relationship may in part involve physical fitness. Future research that utilizes objective measures of COPD and advanced neuroimaging is needed to determine directionality and clarify possible brain-based mechanisms.

## Acknowledgments

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## Abbreviations

| | |
|---|---|
| **COPD** | Chronic obstructive pulmonary disease |
| **HF** | Heart failure |

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## Table 1

Demographic and Medical Characteristics of Heart Failure Patients with and without COPD

| Demographic Characteristics | Total Sample | Heart Failure w/ COPD | Heart Failure w/o COPD | $\chi^2/t$ statistic |
|---|---|---|---|---|
| *N* | 191 | 47 | 144 | -- |
| Age, mean (SD) years | 68.52 (8.96) | 69.57 (8.68) | 68.17 (9.06) | 0.93 |
| Sex (% Women) | 36.1 | 40.4 | 34.7 | 0.50 |
| Education, mean (SD) years | 13.48 (2.72) | 12.74 (2.34) | 13.73 (2.80) | −2.17* |
| **Medical Characteristics** | | | | |
| LVEF, mean (SD) | 40.46 (14.44) | 39.89 (17.01) | 40.64 (13.56) | −0.28 |
| Hypertension (%) | 69.1 | 72.3 | 68.1 | 0.31 |
| Type 2 diabetes mellitus (%) | 36.1 | 31.9 | 37.5 | 0.48 |
| Sleep Apnea (%) | 25.7 | 42.6 | 20.1 | 9.33* |
| Depression (%) | 18.8 | 21.3 | 18.1 | 0.24 |
| Number of cigarettes per week | 2.18 (11.39) | 2.09 (10.44) | 2.22 (11.72) | −0.07 |
| BMI | 30.56 (7.33) | 31.47 (8.91) | 30.27 (6.75) | 0.85 |

*Note*. LVEF = Left ventricular ejection fraction; COPD = Chronic obstructive pulmonary disease; BMI = Body mass index;

* $p < .05$

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## Table 2

Cognitive Test Performance (N = 191)

| | Total Sample | | | HF w/ COPD | | | HF w/o COPD | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Raw Score Mean (SD)** | **T-Score Mean (SD)** | **% T < 35** | **Raw Score Mean (SD)** | **T-Score Mean (SD)** | **% T < 35** | **Raw Score Mean (SD)** | **T-score Mean (SD)** | **% T < 35** |
| **Attention/Executive Function** | | | | | | | | | |
| Trail Making Test A | 41.72 (16.09) | 49.55 (10.89) | 10.5 | 45.89 (17.75) | 46.71 (13.05) | 12.8 | 40.36 (15.33) | 50.48 (9.97) | 9.7 |
| Trail Making Test B | 128.12 (75.52) | 43.65 (18.27) | 19.4 | 157.04 (87.36) | 38.26 (18.81) | 31.9 | 118.67 (68.98) | 45.40 (17.80) | 15.3 |
| Frontal Assessment Battery | 15.73 (2.50) | 43.50 (21.47) | 25.1 | 14.87 (3.20) | 37.63 (23.78) | 36.2 | 16.01 (2.16) | 45.42 (20.38) | 21.5 |
| Digit Symbol Coding | 49.76 (14.14) | 47.51 (9.29) | 9.9 | 43.47 (12.39) | 43.64 (8.41) | 19.1 | 51.82 (14.11) | 48.76 (9.24) | 6.9 |
| Letter Number Sequencing | 8.74 (2.48) | 50.33 (9.03) | 4.2 | 8.38 (2.54) | 48.32 (10.12) | 6.4 | 8.86 (2.46) | 50.98 (8.58) | 3.5 |
| Memory | | | | | | | | | |
| CVLT-II LDFR | 7.86 (3.41) | 46.78 (10.67) | 8.4 | 8.00 (3.83) | 47.23 (12.72) | 12.8 | 7.82 (3.28) | 46.63 (9.96) | 6.9 |
| CVLT-II SDFR | 7.43 (3.20) | 47.30 (10.47) | 6.3 | 7.26 (3.33) | 46.70 (11.00) | 6.4 | 7.49 (3.17) | 47.50 (10.33) | 6.3 |
| CVLT-II recognition hits | 13.48 (2.32) | 44.32 (15.28) | 16.2 | 13.66 (2.09) | 44.89 (12.70) | 17.0 | 13.42 (2.40) | 44.13 (12.70) | 16.0 |
| Language | | | | | | | | | |
| Boston Naming Test | 53.22 (6.27) | 48.83 (15.28) | 14.7 | 51.02 (7.62) | 43.48 (17.15) | 21.3 | 53.94 (5.60) | 50.57 (14.25) | 12.5 |
| Animal Fluency | 19.47 (4.92) | 54.85 (11.06) | 2.6 | 18.28 (4.50) | 52.74 (10.30) | 2.1 | 19.86 (5.00) | 55.53 (11.24) | 2.8 |

*Note*. CVLT = California Verbal Learning Test; LDFR = Long delay free recall; SDFR = Short delay free recall

## Table 3

The Associations Among COPD, Cognitive Function, and Physical Fitness in Heart Failure (N = 191)

| | **Attention/ Executive Function** | **Memory** | **Language** | **2MST** |
|---|---|---|---|---|
| | β | β | β | β |
| *Block 1* | | | | |
| Age (year) | 0.05 | −0.09 | 0.02 | −0.30** |
| Sex (1 = male; 2 = female) | 0.00 | −0.05 | −0.07 | −0.12 |
| Education (years) | 0.32** | 0.13 | 0.29** | 0.21** |
| LVEF | 0.11 | 0.07 | 0.07 | 0.07 |
| Hypertension (1 = yes; 0 = no) | −0.13 | 0.07 | −0.02 | −0.02 |
| Diabetes (1 = yes; 0 = no) | −0.09 | 0.00 | 0.01 | −0.01 |
| Sleep Apnea (1 = yes; 0 = no) | −0.15* | 0.03 | −0.14 | −0.17* |
| Depression (1 = yes; 0 = no) | −0.04 | −0.08 | −0.07 | 0.03 |
| Cigarette Smoke | −0.06 | −0.06 | 0.00 | −0.09 |
| BMI | −0.07 | −0.11 | −0.12 | −0.24** |
| F | 5.80** | 0.83 | 3.74** | 6.02** |
| $R^2$ | 0.24 | 0.04 | 0.17 | 0.25 |
| *Block 2* | | | | |
| COPD (1 = yes; 0 = no) | −0.14* | 0.05 | −0.11 | −0.23 |
| Model F-statistic | 5.78** | 0.78 | 3.67** | 6.86** |
| F change | 4.47* | 0.36 | 2.58 | 11.72** |
| $R^2$ | 0.26 | 0.05 | 0.18 | 0.30 |
| $R^2$ Change | 0.02 | 0.002 | 0.01 | 0.05 |

*Note*.

*$p < 0.05$;

**$p < 0.01$.

LVEF = Left ventricular ejection fraction; COPD = chronic obstructive pulmonary disease; 2MST = 2-minute step test.

β = Standardized beta coefficient