



# Association between frailty and a measure of cognition: a cross-sectional study on community-dwelling older adults

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## Abstract

**Background** Frailty is a geriatric syndrome that is generally represented as a universal issue in the aging population and may lead to adverse health-related events. The most widely used definition of frailty was proposed by Fried et al., wherein frailty is characterized by low physical activity, involuntary weight loss, exhaustion, poor muscle strength, and slow gait speed. The concept of “cognitive frailty” (simultaneous occurrence of both cognitive impairment and physical frailty) has recently been proposed. The Alzheimer’s Disease 8 (AD8) is a brief questionnaire used to differentiate normal aging from dementia. We hypothesized a positive correlation between frailty and AD8 scores in community-dwelling older adults.

**Methods** Individuals over 65 years who visited a medical center in Taipei city during May, 2012 to April, 2013 for an annual check-up were eligible. The final sample comprised 205 older adults (average age =  $75.5 \pm 7.6$  years). Frailty status was determined according to the Fried frailty criteria. Multiple logistic regression analyses were used to estimate the odds of frailty among individuals with AD8 scores of 2 or more.

**Results** After adjusting for age, gender and health-related behaviors, the odds ratio of frailty for individuals with AD8 scores  $\geq 2$  was 5.3 ( $p = 0.008$ ). This positive relationship remained even after adjustment for additional correlates.

**Conclusion** The findings have important implications for the early identification of frailty risk, provided that longitudinal studies can identify the directionality of the relationship between AD8 scores and frailty.

**Keywords** Frailty · Alzheimer’s Disease 8 · Taiwan · Older people

## Introduction

Frailty is a geriatric syndrome that is generally represented as a universal issue in the aging population. It may have adverse health effects, including hospitalization,

institutionalization, falls, and mortality [1]. Fried et al. [2] proposed the most widely used frailty model, wherein frailty is characterized by low physical activity, involuntary weight loss, exhaustion, poor muscle strength, and slow gait speed.

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Cognitive impairment may cause clinical vulnerabilities among aging people, and can be used to predict several adverse health effects. There is considerable evidence of the positive correlation between cognitive impairment and frailty [3–6]. However, researchers, including Fried et al., have only considered distinct effect models of physical frailty, without regard for the complexity of the syndrome. Kelaiditi et al. proposed the concept of “cognitive frailty” in the aging population [7]. Cognitive frailty refers to the simultaneous occurrence of both cognitive impairment and physical frailty and complement further deficiencies in the conventional definition of frailty. Several screening tests [8] such as the Mini-Mental State Examination (MMSE) [9], Cognitive Abilities Screening Instrument [10], and General Practitioner Assessment of Cognition [11], can be used to detect dementia. However, these have various limitations: The MMSE is subject to ceiling effects; consequently, early signs of dementia are not easily detected using this tool, especially in highly educated individuals [12]. The Cognitive Abilities Screening Instrument and General Practitioner Assessment of Cognition generally can be administered only by well-trained professional staff, and these often take too long to implement in practice. These disadvantages are overcome in the Alzheimer’s Disease 8 (AD8) [13–16], a screening tool containing eight questions to differentiate individuals with and without dementia. In contrast to the Mini-Cog and MMSE, the AD8 is sensitive to early signs of dementia regardless of etiology, and it is capable of assessing intra-individual changes across several cognitive domains compared to previous levels of function. Furthermore, the AD8 is short, efficient, and culturally sensitive. Therefore, the AD8 is an ideal instrument for use in primary care practice for both research and annual wellness visits.

Given previous evidence of the positive association between cognitive impairment and frailty, we hypothesize a positive association between frailty and AD8 scores in community-dwelling older adults.

## Methods

### Study design and participants

This study was conducted in the Tri-Service General Hospital (TSGH), Taipei, and was approved by the TSGH Ethics Committee in accordance with the Declaration of Helsinki (TSGHIRB 100-05-257). All participants provided written informed consent.

The enrollment period was from May, 2012 to April, 2013. Individuals eligible for enrollment had to be over 65 years of age and to have participated in an annual routine check-up in one medical center in Taipei city. The

final sample comprised 205 participants. We collected data using structured questionnaires administered by trained interviewers as well as physical tests.

### Definition of frailty

We assessed the following characteristics, defined by Fried et al. [2], to determine frailty status. *Weakness* This is assessed in terms of grip strength, tested via a dynamometer. Weight was adjusted for body mass index and gender based on criteria used in the Cardiovascular Health Study [2]. *Slowness* This was determined using the completion time for a 15-foot walk [17]. The cut-off level was based on the slowest 20% of the study population. *Exhaustion* Participants were presented with two items that they had to respond to with reference to the previous week: (a) “I felt that everything I did was an effort” and (b) “I could not get going.” These items were taken from the Center for Epidemiologic Studies Depression Scale (CES-D) [18]. Possible responses were 0 (rarely or never, < 1 day), 1 (some or sometimes, 1–2 days), 2 (a moderate amount of the time, 3–4 days), or 3 (most of the time). People who chose “2” or “3” for either statement were classified as “positive”. *Weight loss* This was defined as unintentional weight loss of more than 5% of total body weight or 3 kg in the past year. *Low activity* The International Physical Activity Questionnaire Short Form–Taiwan Edition [19, 20] was used to calculate energy expenditure. Participants meeting three or more of the above criteria were considered as frail.

### Screening for cognitive impairment

The AD8 is a simple, reliable, and valid screening tool that is sensitive and predictive in detecting early cognitive changes from many dementing diseases, including Alzheimer’s disease, vascular dementia, Lewy body dementia, and frontotemporal dementia. The AD8 has eight questions, which examine memory, judgment, daily activity, and orientation. It can be self-administered or completed by the caregiver either in person or over the phone. The AD8 has a very brief scoring system, with more than two “yes” answers implying that further diagnostic tests are necessary (sensitivity > 84%, specificity > 80%) [13].

### Covariates

Data on age, smoking status, and alcohol intake were obtained via self-report. Positive smoking status was determined if participants had ever smoked in their lives. Alcohol consumption was dichotomized and defined as drinking at least once per week. Individuals with a self-reported doctor’s diagnosis of hypertension, those taking

antihypertensive medications, or those with an average blood pressure of  $\geq 140/90$  mmHg were considered to have hypertension. Diabetes mellitus was defined by self-report of a physician's diagnosis, fasting plasma glucose  $\geq 126$  mg/dL, or the use of diabetic medications (including insulin injection or oral hypoglycemic agents). Medical history of coronary artery disease, stroke, chronic obstructive pulmonary disease, and arthritis were verified by self-report. The 5-item Brief Symptom Rating Scale (BSRS-5) and the AD8 were administered within an organized questionnaire. The BSRS-5 [21] has been frequently used to screen for possible depression. It contains five psychopathology items. Participants who recorded above six on the BSRS-5 were considered to have possible depression.

### Statistical analyses

Descriptive statistics of continuous and categorical covariates were represented with mean  $\pm$  SD and  $N$  (%) as appropriate. Differences between groups were examined using independent sample  $t$  test and Chi-square tests. Logistic regression analysis was used to estimate the odds of frailty between participants scoring less than 2 or 2 or more on the AD8. Model 1 was adjusted for age, gender, alcohol consumption, and smoking history. Model 2 was further adjusted for hypertension, diabetes mellitus, stroke, coronary artery disease, chronic obstructive pulmonary disease, and arthritis. Model 3 was further adjusted for body mass index, Brief Symptom Rating Scale 5, white blood cell count, hemoglobin, low-density lipoprotein, and albumin. Model 4 was further adjusted for myostatin, and follistatin. Statistical analyses were performed with SPSS 18 software.

## Results

### Characteristics of study population

Participants ( $n = 205$ ) had an average age of  $75.5 \pm 7.6$  years. Women accounted for more than half of participants ( $n = 107$ , 52.2%). Fourteen participants met the criteria for frailty. Compared to those with  $AD8 < 2$ , participants with  $AD8 \geq 2$  tended to have higher BSRS-5 scores and more chronic diseases, such as hypertension, diabetes mellitus, and coronary artery disease (Table 1).

### Association between AD8 and frailty

Table 2 shows the relationship between AD8 scores and frailty. After adjusting for gender, age, alcohol intake, and smoking history (Model 1), the odds ratio (OR) of frailty

for those with  $AD8 \geq 2$  was 5.3 (95% confidence interval [CI] 1.5–17.9,  $p = 0.008$ ). After adjusting for other covariates in Models 2–4, the positive relationship between AD8 scores and frailty remained. For Models 2–4, the ORs of frailty for those with  $AD8 \geq 2$  were 7.1, 11.8, and 12.2, respectively.

## Discussion

Our results show higher scores on the AD8 increased the odds of frailty among community-dwelling older adults. This relationship remained after adjusting for basic demographics, chronic disease, albumin, and some potential inflammatory biomarkers. This finding suggests that cognitive impairment even in the early stage may have a positive correlation with frailty.

Frailty is a common syndrome among older individuals. It is related with functional losses in at least one of many domains, including physical ability, cognition, mood, and sociality [22]. An accumulation of evidence has demonstrated an association between physical frailty and cognitive impairment [4]. As a result, a new notion of “cognitive frailty” has emerged, which refers to the presence of both physical frailty and cognitive impairment. However, tests used to evaluate cognitive function in most studies could only identify this in patients with more obvious cognitive impairment—patients characterized by frailty for which it is too late to intervene. Further, completion of these screening tests usually takes significant time and requires well-trained administrators, making them a costly endeavor. The AD8 is a simple, valid, and reliable informant-based measure that is sensitive and predictive in discriminating older adults without dementia from those with even mild forms of dementia from all causes. It does so in an efficient, inexpensive, culturally sensitive, and socially acceptable manner that is also generalizable and translatable to the community. To the best of our knowledge, this is the first study to demonstrate a positive relationship between AD8 scores and frailty among older individuals.

Just like the healthy population, those exhibiting early cognitive impairment behaviors can be identified in the community. Using the AD8, we can quickly identify those who might have early cognitive impairment ( $AD8 \geq 2$ ). Given our findings, we would reasonably suspect these individuals to be more likely to become frail, or to already be frail. For these people, early interventions could be provided to prevent or postpone the occurrence or worsening of frailty and dementia.

Some important limitations to this study must be considered. First, this was a cross-sectional study, and thus it is not appropriate to use the findings to predict that those with higher AD8 scores will be more likely to become frail.

**Table 1** Participant characteristics by AD8 scores

Characteristic	AD8 score < 2	AD8 score ≥ 2	Total	<i>p</i> value
Continuous variables, mean (SD)				
Age (years)	75.1 (7.3)	77.0 (8.5)	75.5 (7.6)	0.158
BMI (kg/m <sup>2</sup> )	24.2 (2.9)	24.0 (3.5)	24.2 (3.0)	0.800
Brief Symptom Rating Scale 5	1.8 (2.4)	4.1 (3.8)	2.2 (2.8)	< 0.001
Hb (g/dL)	13.6 (1.3)	13.7 (1.3)	13.6 (1.3)	0.817
WBC (1000 cells/μL)	5.3 (1.5)	5.5 (1.3)	5.4 (1.5)	0.720
LDL (mg/dL)	118.4 (32.2)	118.9 (27.0)	117.8 (31.4)	0.929
Albumin (mg/dL)	4.5 (0.2)	4.5 (0.2)	4.5 (0.2)	0.106
Myostatin (pg/mL)	21.4 (12.9)	20.0 (10.4)	21.1 (12.3)	0.545
Follistatin (pg/mL)	1412.8 (726.8)	1538.1 (816.6)	1468.0 (758.2)	0.362
Categorical variables, <i>n</i> (%)				
Men	82 (48.5)	16 (44.4)	98 (47.8)	0.792
Hypertension	84 (49.7)	25 (69.4)	109 (53.2)	0.023
Diabetes mellitus	20 (11.8)	8 (22.2)	28 (13.7)	0.045
Stroke	6 (3.6)	3 (8.3)	9 (4.4)	0.226
CAD	13 (7.7)	8 (22.2)	21 (10.2)	0.018
COPD	18 (10.7)	7 (19.4)	25 (12.2)	0.158
Arthritis	57 (33.7)	16 (44.4)	73 (35.6)	0.258
History of smoking	24 (14.2)	4 (11.1)	28 (13.7)	0.898
With weekly alcohol consumption	9 (5.3)	2 (5.6)	11 (5.4)	0.760

Differences between groups were examined via *t* test and Chi-square test

*BMI* body mass index, *Hb* hemoglobin, *WBC* white blood cell count, *LDL* low-density lipoprotein, *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease

**Table 2** Logistic regression for the association between frailty and AD8 scores

Model	OR (95% CI)	<i>p</i> value
Model 1	5.3 (1.5–17.9)	0.008
Model 2	7.1 (1.6–31.7)	0.010
Model 3	11.9 (1.9–76.3)	0.009
Model 4	12.3 (1.7–87.7)	0.013

Adjusted covariates: Model 1 = age, gender, alcohol consumption, smoking history. Model 2 = Model 1 + (hypertension + diabetes mellitus + stroke + coronary artery disease + chronic obstructive pulmonary disease + arthritis). Model 3 = Model 2 + (body mass index + Brief Symptom Rating Scale 5) + (white blood cell count + hemoglobin + low-density lipoprotein + albumin). Model 4 = Model 3 + (myostatin + follistatin)

*OR* odds ratio, *CI* confidence interval

Second, this was a hospital-based health examination program study, and older people who visit hospitals are considered to be healthier than the general aging population. Thus, the frailty rate in this study may have been underestimated. The main concern is that our ability to test the associations of AD8 scores and frailty may be underpowered. However, the differences in AD8 scores between these patients were striking. Third, some criteria of frailty were examined using self-reported data, which are subject to bias. Despite these limitations, the strength in the study

is that enrollment among healthy adults signify the association of frailty and early cognitive impairment.

This study investigated the relationship between AD8 and frailty, finding that higher AD8 scores is associated with frailty among community-dwelling older Taiwanese. It merits prospective study design to clarify the potential role of the AD8 in preventative measures and interventions for frailty among community-dwelling older population.

## Compliance with ethical standards

**Conflict of interest** There is no conflict of interest for any of the authors related to the study.

**Ethical approval** This study was conducted in the Tri-Service General Hospital (TSGH), Taipei, and was approved by the TSGH Ethics Committee in accordance with the Declaration of Helsinki (TSGHIRB 100-05-257).

**Informed consent** All participants provided written informed consent.

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