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The effects of sensorial and mobility frailty on the overall and domain-specific cognition performance of Chinese community-dwelling older adults

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Abstract

This study aimed to investigate the different impacts of sensorial and mobility frailty on overall and domain-specific cognitive function. Further, the independent associations between other intricate capacity (IC) dimensions, including vitality and psychological dimensions, and overall and domain-specific cognitive function were investigated. A total of 429 participants (mean age, 72.91 ± 7.014 years; 57.30% female) underwent IC capacity assessment. Other covariates, such as demographics, health-related variables were also assessed. Overall or domain-specific cognitive impairment was used as a dependent variable in logistic regression analyses adjusted for demographic, health-related, and psychosocial confounders. After adjustment for demographic, health-related, and psychosocial confounders, individuals with sensorial frailty (odds ratio [OR] = 0.435; 95% confidence interval [CI] = 0.236–0.801; $P = .008$) had a significantly lower risk of mild cognitive impairment (MCI), marginally low delayed memory impairment (OR = 0.601, 95% CI = 0.347–1.040; $P = .069$), and language impairment (OR = 0.534, 95% CI = 0.305–0.936; OR = 0.318, $P = .029$; OR = 0.318,95% CI = 0.173–0.586; $P < .001$) by Boston naming and animal fluency tests than did those with both sensorial and mobility frailty or mobility frailty only. Depressive symptoms had a significant negative influence on executive function. Cardiovascular disease and non-skin malignancy were independent determinants of MCI, and diabetes mellitus was independently associated with processing speed, attention, and executive function. Sensorial and mobility frailty were independent risk factors for cognitive impairment. Mobility frailty had a greater negative influence on the overall cognitive function and memory and language function than did sensorial frailty. The reserve decline in the psychological dimension of IC and chronic diseases also had a significant adverse influence on overall and domain-specific cognition function.

Abbreviations: AD = Alzheimer disease, ARHL = age-related hearing loss, CI = confidence interval, CVD = cardiovascular disease, FAQ = Functional Assessment Questionnaire, HVLT-R = Hopkins Verbal Learning Test-Revised, IC = intricate capacity, MCI = mild cognitive impairment, MMSE = mini-mental state examination, OR = odds ratio, TMT = trail making test.

Keywords: cognitive function, mild cognitive impairment, mobility frailty, neuropsychological test, pre-mild cognitive impairment, sensorial frailty

1. Introduction

Age-related multiple sensory impairment, particularly hearing and/or vision impairment, is defined as sensorial frailty.[1] Motor dysfunctions, including slowness and/or weakness, are a subtype of physical frailty referred to as mobility frailty.[2,3] Both age-related multiple sensory impairments and motor dysfunction are also important domains of intricate capacity (IC).[4,5] The sensory and locomotion domains are the physical

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

This study was approved by Huadong Hospital Ethics Committee for Human Research (Approval No. Ref 2018K055). All participants provided written informed consent before enrollment. All methods were performed in accordance with the relevant guidelines and regulations (Declaration of Helsinki).

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dimensions of IC. The influence of the physical dimension of IC on the cognitive domain has been investigated in many previous studies, and it is reported that sensory and motor dysfunction may precede the cognitive symptoms of Alzheimer disease (AD) by several years and significantly increase the risk of AD.[6] Age-related multiple sensory impairment, particularly hearing and/or vision, is a dementia-modifiable risk factor.[1,7–9] Cumulative evidence from previous cross-sectional and longitudinal studies confirmed that age-related hearing loss (ARHL),[1,7,10,11] vision impairment,[9,12] and dual sensory impairment[13–17] are independently associated with cognitive decline and different domains of cognitive functions, including episodic memory, executive function, and language fluency. Moreover, dual sensory impairment is associated with greater cognitive difficulties and more extensive impairment in specific domains than is single vision or hearing impairment.[18,19] Individuals with dual sensory impairment at baseline had a higher risk of possible cognitive impairment and probable dementia than those with no sensory impairment.[14,20] Thus, age-related decline in visual function and/or ARHL may be a functional marker of cognitive decline.

In addition to sensory impairment, mobility frailty is associated with poorer prognosis and adverse outcomes, including poor cognitive function, overall health, and survival.[2,3] Gait abnormality has been confirmed as an independent predictor of cognitive decline in healthy elderly adults[21] and non-AD dementia in individuals aged >75 years who did not have dementia at baseline.[22] Motor dysfunction is also associated with specific domains related to cognitive function. Slow gait was independently associated with decline in cognitive domains, including attention, memory, verbal fluency, language, visuospatial ability, and executive function.[23,24] Further, slow gait speed and subjective memory complaint or mild cognitive impairment (MCI) commonly co-occur, referred as Motoric Cognitive Risk Syndrome, which predicts the risk of cognitive decline or dementia is stronger than either slow gait speed or cognitive impairment alone.[25–27] Older individuals with stronger handgrip strength have better cognitive function.[28] Older individuals with reduced handgrip strength at baseline showed a significant decline in global cognitive function[29,30] and an increased risk of MCI over a 3.6-year follow-up period.[29] Furthermore, self-reported upper extremity function and gait demonstrated the strongest association with executive function.[23,24,31] However, the different effects of sensorial and mobility frailty, and concurrent sensorial and mobility frailty on overall and domain-specific cognitive performance remain elusive. Understanding these influences will facilitate the personal screening and integrated care of older people.

Other domains of IC, including psychological and vitality domains,[4,5] may also affect cognitive performance. Psychological capacity is typically reflected by depressive symptoms, which have been reported to affect cognitive function. Older people with lower scores on the Epidemiological Studies Depression Scale had significantly poorer global cognition and lower scores on mini-mental state examination (MMSE) items such as orientation, memory, attention and computation, and language.[32] Depression is independently associated with poor cognitive performance and increased comorbid metabolic dysregulation-induced cognitive impairment in middle-aged adults.[33] Non-demented individuals with elevated depressive symptoms had lower cognitive performance, and those with concurrent APOE4 allele positivity had poorer visual short- and long-term memory performance.[34] Older adults with a trajectory of subthreshold depressive symptoms also exhibited accelerated cognitive decline.[35] However, compared with other dimensions, the interaction between vitality and cognition remains elusive.

The primary purpose of this study was to investigate the different effects of other 4 IC domains, including sensorial and mobility frailty (sensorial and location domains), psychological and vitality domains on overall and domain-specific cognitive performance. The primary research objective was to clarify the effects of sensorial and mobility frailty on overall and domain-specific cognitive performance. The secondary objective was to clarify the effects of other IC domains, including psychological and vitality domains, and chronic diseases on overall and domain-specific cognitive performance.

2. Methods

2.1. Participants

In total, 429 community-dwelling elderly Chinese adults without dementia or handicaps (mean age, 72.91 ± 7.014 years; 57.30% female) were recruited from a population-based cross-sectional study of health promotion for older adults with frailty.[36] The inclusion and exclusion criteria were reported in detail in several previous studies.[3,10,37] In brief, 429 eligible volunteers of 5175 subjects were recruited from 20 communities in the Zhoujiaqiao Primary Health Service area, Shanghai, via face-to-face communication in each community from September 2018 to June 2019.[36] Among 429 eligible volunteers from total 474 volunteers, the prevalence of mobility frailty is 15.9%.[3] Of 45 ineligible volunteers from total 474 volunteers were excluded because of the following conditions: clinically profound hearing or vision loss, mental retardation, psychosis, disability, and dementia (including AD) with Clinical Dementia Rating Scale (CDR) > 0.5 or a score of the Rapid Cognitive Screen (RCS) < 6.[36] This study was approved by the Ethics Committee of Huadong Hospital and was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent.

2.2. Sensorial and mobility frailty assessment

Briefly, sensorial frailty was defined as age-related hearing and/or vision decline. Hearing decline was diagnosed based on a pure-tone average of ≤ 25 dB in the better ear based on 0.5, 1, 2, and 4 kHz thresholds using pure-tone audiometry. Those with hearing decline associated with tinnitus were also accepted. Vision decline was diagnosed based on self-reported fair or poor even eyesight with glasses or corrective lenses using a 5-item Likert-type scale with eyesight scored as excellent, very good, good, fair, or poor.[38] Mobility frailty was diagnosed when gait and/or handgrip strength was below the Chinese reference values.[39]

2.3. Cognitive assessment

Global cognition was assessed using the MMSE test. Dementia (including AD) with Clinical Dementia Rating Scale (CDR) > 0.5 or the score of the Rapid Cognitive Screen (RCS) < 6 [36]. Cognitive performance was assessed using the normative z-scores of a neuropsychological test battery, including 2 tests in each of the attention or executive (trail making test A and B [TMT A and B]), language (Boston naming and animal fluency tests), and memory domains (Hopkins Verbal Learning Test-Revised [HVLT-R] test). The stratification of cognitive performance was based on our previously reported criteria.[3,37] Process z-scores or total z-scores above 1 standard deviation (the norm on TMT A, TMT B, and intrusion errors), or below 1 standard deviation (the norm on other measures) were considered as dysfunction. Pre-MCI was classified as follows: 2 impaired process scores, 1 impaired process score and 1 impaired total score, impaired total score on 2 measures across different cognitive domains, and a Functional Assessment Questionnaire (FAQ) score of 6 to 8. MCI was classified as an impaired total score on 2 measures in the same domain, 1 impaired score in each of the 3 cognitive

domains, or an FAQ score of ≥ 9. The digit symbol test was used to assess the processing speed/attention/executive domain.

2.4. Vitality and psychological domain assessment

Vitality decline of IC was assessed using 3 parameters: fatigue, low physical activity, and abnormal weight based on an abnormal body mass index. Fatigue and low physical activity were assessed according to the Fried frailty criteria with Chinese reference values.[39,40] Vitality decline was diagnosed when 2 or more of the above 3 parameters were abnormal. The psychological domain dysfunction of IC was based on depressive symptoms, which were assessed using the 15-item short form of the Geriatric Depression Scale.[41]

2.5. Covariates

The covariates included self-reported smoking, alcohol intake, and 13 chronic comorbidities.[3,37] The number of comorbidities was categorized as 0, 1, 2, and > 2. Several common chronic diseases, such as diabetes mellitus, cardiovascular disease (CVD), stroke, and non-skin malignancies, were also considered as covariates. Neuropsychiatric symptoms and social dysfunction were assessed using a brief version of the self-report Neuropsychiatric Inventory Questionnaire (NPI-Q) and the 21-item Social Dysfunction Rating Scale.[3,37]

2.6. Statistical analysis

The Null Hypothesis (H0) of the analyses of the study was set as there is no effect of sensorial and mobility frailty on overall and domain-specific cognitive performance. Accordingly, the Alternative Hypothesis (Ha) was that there is significant effect of sensorial and mobility frailty on overall and domain-specific cognitive performance. The Alpha level ($P \leq .05$, 2 sides) was set to reject H0 and accept Ha. In this observational study, we included all eligible patients during the study period in the analysis. But we did not estimate in advance the sample size required to reject H0. Continuous variables are expressed as medians and quartiles and categorical data are expressed as proportions. Bivariate correlations of continuous variables were analyzed using Spearman test for non-normally distributed variables and Pearson test for normally distributed variables. Categorical data were compared using the X^2 test. The differences in continuous variables between the groups were analyzed using a univariate analysis of variance. Univariate correlations were analyzed using the Mann–Whitney *U* test when the homogeneity of variables was inappropriate. In order to understand the independent impact of different covariates, the associations between sensory frailty, mobility frailty, other domains of IC, or covariates and overall cognitive performance and specific cognitive domains were assessed using multiple regression analyses adjusted for demographic factors, including age, sex, and education level; other health-related variables, including smoking, drinking, vitality, chronic diseases, and number of comorbidities; and psychosocial factors, including social dysfunction, depression symptoms, and neuropsychiatric symptoms. The multiple regression analyses were run for overall cognitive performance and then separately for each specific cognitive domain, which were used as dependent variables. All statistical analyses were performed using SPSS version 18.0, and statistical significance was set at $P < .05$.

3. Results

3.1. Participant characteristics

The demographic characteristics and health-related factors, including smoking, alcohol intake, and the number of comorbidities, of the 429 participants are reported in our recently published paper (Supplementary Table 1, http://links.lww.com/MD/M790).[42] In the present paper, the proportion of chronic diseases, domain-specific cognitive impairment scores, NPI-Q scores, and global cognitive and social dysfunction scores among all groups are presented in Table 1. Significant differences among groups were observed in MMSE, Boston naming, animal fluency, digit span forward, social dysfunction scores, and the proportion of diabetes mellitus and stroke.

3.2. The effects of sensorial and mobility frailty on overall cognition

Participants lacking sensorial and mobility frailty had a significantly lower risk of pre-MCI after adjustment for demographic confounders (odds ratio [OR] = 0.371; 95% confidence interval [CI] = 0.155–0.892; $P = .027$) and adjustment for demographic and health-related confounders (OR = 0.356, 95% CI = 0.138–0.917; $P = .032$) than did those with sensorial and mobility frailty. However, the significance disappeared after adjustment for all confounders (OR = 0.437, 95% CI = 0.164–1.168; $P = .099$) (Table 2). Those with sensorial frailty had a lower risk and those with mobility frailty had a higher risk of pre-MCI in all models than did those with both sensorial and mobility frailty. However, these differences were not significant. Individuals lacking sensorial and mobility frailty (OR = 0.076, 95% CI = 0.017–0.336, $P = .001$; OR = 0.080, 95% CI = 0.018–0.357, $P = .001$; OR = 0.048, 95% CI = 0.006–0.377, $P = .004$) and with sensorial frailty only (OR = 0.450, 95% CI = 0.266–0.759, $P = .003$; OR = 0.466, 95% CI = 0.268–0.809, $P = .007$; OR = 0.435, 95% CI = 0.236–0.801, $P = .008$) had a significantly lower risk of MCI after adjustment for demographic confounders, demographic and health-related confounders, and all confounders. There was no significant difference between those with mobility frailty only (OR = 0.397, 95% CI = 2.087, $P = .275$; OR = 0.443, 95% CI = 0.081–2.424, $P = .348$; OR = 1.131, 95% CI = 0.166–7.725, $P = .900$) and those with both sensorial and mobility frailty after adjustment for 3 kinds of confounders.

3.3. The other determinators of overall cognition

Education level and CVD were independent risk factors for pre-MCI and MCI (Table 2). Those with a high education level had a significantly lower risk of pre-MCI (OR = 0.893, 95% CI = 0.833–0.958, $P = .002$) and MCI (OR = 0.830, 95% CI = 0.771–0.894, $P < .001$) after adjustment for demographic factors, pre-MCI (OR = 0.876, CI = 0.813–0.945, $P = .001$) and MCI (OR = 0.816, 95% CI = 0.754–0.883, $P < .001$) after adjustment for demographic and health-related factors, and pre-MCI (OR = 0.879, 95% CI = 0.811–0.954, $P = .002$) and MCI (OR = 0.818, 95% CI = 0.750–0.892, $P < .001$) after adjustment for all confounders. Individuals without CVD had a significantly lower risk of pre-MCI (OR = 0.440, 95% CI = 0.255–0.758, $P = .003$) and a marginally lower risk of MCI (OR = 0.578, 95% CI = 0.331–1.011; $P = .055$) after adjustment for demographic and health-related factors, and significantly lower risk for pre-MCI (OR = 0.468, 95% CI = 0.264–0.830, $P = .009$) and MCI (OR = 0.520, 95% CI = 0.279–0.969, $P = .039$) after adjustment for all confounders.

3.4. The effects of sensorial and mobility frailty on domain-specific cognition

The multiple regression analysis indicated that the significantly different effects of sensorial and mobility frailty on domain-specific cognition were evident in the memory, language, attention and executive domains (Tables 3). Individuals with only

Table 1

Cognitive characteristics of study participants.

	Total sample	Lack of sensory and mobility impairment (n = 40)	Sensory impairment (n = 208)	Mobility impairment (n = 15)	Sensory and mobility impairment (n = 164)	F/χ^2 value	*P*
Global cognition							
MMSE	417	28.240 ± 1.731	27.460 ± 1.690	27.270 ± 2.086	27.010 ± 1.991	5.044	.002
Domian-specific cognition status							
TMT A	414					3.653	.301
Normal	310	34	149	11	116		
Dysfunction	104	5	51	4	44		
TMT B	413					4.737	.192
Normal	351	37	172	12	130		
Dysfunction	62	2	28	3	29		
Delay recall	418					5.202	.158
Normal	316	32	159	13	112		
Dysfunction	102	7	45	2	48		
Recognition	419					3.761	.288
Normal	347	35	170	14	128		
Dysfunction	72	4	34	1	33		
Boston naming	419					16.122	.001
Normal	323	36	163	13	111		
Dysfunction	96	2 (5.263%)	40 (19.074%)	2 (13.333%)	52 (31.902%)		
Animal fluency	419					17.762	.000
Normal	334	35	173	10	116		
Dysfunction	85	3 (7.895%)	29 (14.356%)	5 (33.333%)	48 (29.268%)		
Digit span forward	418					8.126	.043
Normal	364	37	180	14	133		
Dysfunction	54	1 (2.632%)	23 (11.330%)	1 (6.667%)	29 (17.901%)		
Digit span backward	418					0.482	.923
Normal	372	35	180	13	144		
Dysfunction	46	3	23	2	18		
Digit symbol	412					3.760	.289
Normal	359	35	174	15	135		
Dysfunction	53	3	26	0	24		
Social dysfunction	363	27.13 ± 6.637	30.20 ± 8.855	31.92 ± 15.130	32.020 ± 9.654	2.677	.047
NPI-Q	401					37.179	.871
0	256	23	136	6	91		
≥1	145	14	58	7	66		
Chronic diseases							
CVD	426					5.633	.131
No	173	16	95	7	55		
Yes	253	24	113	8	108		
Diabetes mellitus	426					13.086	.004
No	350	37	180	10	123		
Yes	76	3 (7.500%)	28 (13.462%)	5 (33.333%)	40 (24.540%)		
Stroke	426					12.150	.007
No	384	37	197	13	137		
Yes	42	3 (7.500%)	11 (5.288%)	2 (13.333%)	26 (15.951%)		
Non-skin malignancy	426	40	208	15	163	1.261	.738
No	395	37	195	13	150		
Yes	31	3	13	2	13		

CVD = cardiovascular disease, GDS = the Geriatric Depression Scale, MMSE = Mini-Mental Status Exam, NPI-Q = Self-report Neuropsychiatric Inventory Questionnaire, TMT A and B = trail making test A and B. **P* < .05; ***P* < .01; and ****P* < .001.

sensorial frailty had a marginally lower risk of delayed recall impairment than did those with both sensorial and mobility frailty after adjustment for demographic and health-related confounders (OR = 0.603, 95% CI = 0.361–1.006; *P* = .053) and adjustment for all cofounders (OR = 0.601, 95% CI = 0.347–1.040; *P* = .069) (Table 3). The highest risk of memory impairment was observed in the group of patients with both sensory and mobility frailty using delayed memory and recognition tests, but the difference was not significant between the sensorial and mobility frailty group and the mobility frailty group, or the lack of sensorial and mobility frailty groups. The results of both the Boston naming and animal fluency tests indicated that those with mobility frailty or both sensorial and mobility frailty had significant impairment in the language domain (Table 3). Individuals lacking sensorial and mobility frailty had the lowest risk of language domain impairment after adjustment for demographic factors (OR = 0.121, 95% CI = 0.028–0.522, *P* = .005; OR = 0.212, 95% CI = 0.062–0.725, *P* = .013), adjustment for demographic and health-related confounders (OR = 0.071, 95% CI = 0.009–0.535, *P* = .010; OR = 0.231, 95% CI = 0.067–0.798, *P* = .020), and adjustment for all confounders (OR = 0.088, 95% CI = 0.012–0.674, *P* = .019; OR = 0.172, 95% CI = 0.039–0.763, *P* = .021). Those with only sensorial frailty also had a lower risk of language domain impairment after adjustment for demographic factors (OR = 0.539, 95% CI = 0.332–0.875, *P* = .024; OR = 0.417, 95% CI = 0.247–0.703, *P* < .001), adjustment for demographic and health-related confounders (OR = 0.555, 95% CI = 0.333–0.927, *P* = .024; OR = 0.372, 95% CI = 0.213–0.648, *P* < .001), and adjustment for all confounders (OR = 0.534, 95%

CI = 0.305–0.936, $P = .029$; OR = 0.318, 95% CI = 0.173–0.586, $P < .001$) by aforementioned tests. Although there was a low possibility of high risk for processing speed/attention/executive function (by TMT A and digit symbol tests) domain impairment, and executive function impairment (by TMT B test) were observed in individuals lack of sensorial and mobility frailty after adjustment for all confounders, only those with sensorial frailty had a low trend of high risk for processing speed/attention/executive function impairment (by digit symbol test) after adjustment for all confounders. No significant differences in processing speed/attention/executive function impairment were observed among the 4 experimental groups.

Table 2

Association between sensory and/or mobility frailty and overall cognition using multiple nominal regression adjusted for demographic factors, other health-related variables, and psychosocial factors.

	Pre-MCI	MCI
Variables	**OR (95%CI)**	**OR (95%CI)**
Sensory and mobility stratification (refer: Sensory and mobility impairment)		
No sensory and mobility impairment	0.437 (0.164, 1.168)	0.048 (0.006, 0.377)**
Sensory impairment	0.836 (0.468, 1.495)	0.435 (0.236, 0.801)**
Mobility impairment	2.284 (0.454, 11.485)	1.131 (0.166, 7.725)
Education level	0.879 (0.811, 0.954)**	0.818 (0.750, 0.892)***
CVD (refer: With CVD)	0.468 (0.264, 0.830)**	0.520 (0.279, 0.969)*

CI = confidence intervals, CVD = cardiovascular disease, GDS = the Geriatric Depression Scale, NPI = self-report Neuropsychiatric Inventory Questionnaire, OR = odds ratios. The association is adjusted for demographic factors (age, sex, education), other health-related variables (self-reported smoking, alcohol intake, vitality, chronic diseases, and number of comorbidities), and psychological factors (GDS, NPI, and social dysfunction).

*$P < .05$;

**$P < .01$; and

***$P < .001$.

3.5. Other determinants of domain-specific cognition

Other independent determinants affecting different domain-specific cognitive functions included age, education level, depressive symptoms, diabetes mellitus, and smoking status (Table 3). Education level was independently associated with delayed recall on the HVLT-R, with language function on the Boston naming and animal fluency tests, and with processing speed/attention/executive function as measured by the TMT A. Individuals with a high education level had a significantly lower risk of delayed memory impairment (OR = 0.893, 95% CI = 0.831–0.961, $P = .002$), language impairment as measured by the Boston naming test (OR = 0.898, 95% CI = 0.834–0.968, $P = .005$) and animal fluency test (OR = 0.906, 95% CI = 0.839–0.977, $P = .011$), and speed/attention/executive function impairment (OR = 0.885, 95% CI = 0.818–0.956, $P = .002$) after adjustment for all confounders. Age was an independent risk factor for processing speed/attention/executive function as assessed by the TMT A, but not by digit symbol tests, and for executive function as indicated by the TMT B test. Older individuals had a significantly higher risk of processing speed/attention/executive

Table 3

Association between sensory and/or mobility dysfunction and low cognitive function in memory, language, attention and executive domains using multiple regression adjusted for demographic factors, other health-related variables, and psychosocial factors.

	Delay recall	Recognition	Boston naming test	Animal fluency	TMT A	Digital Symbol	TMT B
Variables	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Sensory and mobility stratification (refer: Sensory and mobility impairment)							
No sensory and mobility impairment	0.446 (0.156, 1.269)	0.557 (0.179, 1.731)	0.088 (0.012, 0.674)*	0.172 (0.039, 0.763)*	0.641 (0.172, 2.391)	0.368 (0.075, 1.809)	0.244 (0.029, 2.208)
Sensory impairment	**0.601 (0.347, 1.040)**	0.730 (0.404, 1.319)	0.534 (0.305, 0.936)*	0.318 (0.173, 0.586)***	1.512 (0.842, 2.716)	0.961 (0.471, 1.959)	1.193 (0.604, 2.358)
Mobility impairment	0.648 (0.125, 3.360)	0.435 (0.052, 3.625)	0.334 (0.040, 2.821)	2.098 (0.518, 8.487)	1.622 (0.350, 7.514)	-	1.766 (0.375, 8.329)
Age					1.065 (1.022, 1.110)**		1.061 (1.011, 1.114)*
Sex (refer male)							
Education level	0.893 (0.831, 0.961)**		0.898 (0.834, 0.968)**	0.906 (0.839, 0.977)*	0.885 (0.818, 0.956)**		
GDS15 score							0.860 (0.754, 0.980)*
Diabetes mellitus (refer: With diabetes mellitus)					0.418 (0.225, 0.776)**	0.401 (0.192, 0.835)*	0.334 (0.164, 0.682)**
Smoking (refer: Current smokers)							
Never smokers						0.306 (0.112, 0.834)*	
Ever smokers						0.975 (0.237, 4.002)	

The association is adjusted for demographic factors (age, sex, education), other health-related variables (self-reported smoking, alcohol intake, vitality, chronic diseases, and number of comorbidities), and psychological factors (GDS, NPI, and social dysfunction).

CI = confidence intervals, GDS = the Geriatric Depression Scale, OR = odds ratios.

*$P < .05$;

**$P < .01$; and

***$P < .001$; bold values denote marginally statistical significance.

function impairment after adjustment for demographic factors (OR = 1.309, 95% CI = 1.002–1.076, *P* = .037), adjustment for demographic and health-related confounders (OR = 1.045, 95% CI = 1.007–1.084, *P* = .020), and adjustment for all confounders (OR = 1.065, 95% CI = 1.022–1.110, *P* = .003) (Table 3); and for executive function by TMT B test after adjustment for demographic factors (OR = 1.049, 95% CI = 1.006–1.093, *P* = .025), adjustment for demographic and health-related confounders (OR = 1.056, 95% CI = 1.011–1.103, *P* = .014), and adjustment for all confounders (OR = 1.061, 95% CI = 1.011–1.114, *P* = .017) (Table 3). Individuals lacking depressive symptoms (OR = 0.860, 95% CI = 0.754–0.980, *P* = .024) had a significantly lower risk of executive function impairment after adjustment for demographic, health-related, and psychosocial confounders (Table 3). Those without diabetes mellitus had a significantly lower risk of speed/attention/executive function impairment as measured by the TMT A (OR = 0.418, 95% CI = 0.225–0.776, *P* = .006) and digit symbol test (OR = 0.401, 95% CI = 0.192–0.835, *P* = .012), and of executive function impairment (OR = 0.334, 95% CI = 0.164–0.682, *P* = .003) after adjustment for all confounders (Table 3). In addition, never smokers had a significantly lower risk of speed/attention/executive function impairment as measured by the digit symbol test after adjustment for demographic and health-related confounders (OR = 0.266, 95% CI = 0.099–0.721, *P* = .009) and all confounders (OR = 0.306, 95% CI = 0.112–0.834, *P* = .021) (Table 3).

4. Discussion

This study aimed to investigate the different impacts of sensorial and mobility frailty on overall and domain-specific cognitive function. Further, the independent associations between multimorbidity, chronic diseases, and other IC dimensions, including vitality and psychological dimensions, and overall and domain-specific cognitive function were investigated. Our findings indicated that mobility frailty or both sensorial and mobility frailty had a more significant impact than other IC dimensions on overall cognition and some domain-specific cognitive functions, including delayed memory and language function, according to the z-scores of the neuropsychological test battery. Two other dimensions of IC, both psychological dimensions, referred to as depressive symptoms, were independent determinants of executive function, and vitality had no influence on overall and domain-specific cognitive function. Moreover, chronic diseases, including CVD and diabetes mellitus, also had independent negative influences on overall and domain-specific cognitive function.

Both sensorial frailty and mobility frailty were included in the different frailty models. Sensorial and mobility frailty are the components of the multidimensional model and the deficit accumulation model,[43–46] and mobility frailty was included in the most popular frailty model, known as the physical frailty phenotype.[40] The results of the current study indicated that individuals with sensorial frailty had a lower risk of MCI than did those with mobility frailty, but a higher risk of MCI than those lacking sensorial and mobility frailty. Furthermore, patients with sensorial frailty had a lower risk of delayed memory and language impairment than did those with mobility frailty. Our results were similar to those of previous studies showing that the functional decline of age-related sensory organs[13–20,47] or locomotion impairment, including handgrip strength[28–31] and gait,[21–24] were closely associated with overall and domain-specific cognitive decline. However, we did not find a significant impact of sensorial and mobility frailty on executive function. A locomotion impairment only was present in 15 participants (Supplementary Table 1, http://links.lww.com/MD/M790), which limits the conclusions concerning the influence of locomotion (mobility) frailty alone on cognition. In addition, the visuospatial domain was not assessed in the present study. This may be due to the small sample size, particularly small sample regarding each cognitive domain. Regardless, our results provide important evidence for the construct of the frailty multidimensional model and the deficit accumulation model. Since both sensorial and mobility frailty significantly influence cognitive function, sensorial and mobility frailty should be considered as important components of the frailty deficit accumulation model and frailty multidimensional model. The more significant influence of mobility than sensory domain on cognitive function also provided rationality for the construction of the physical frailty phenotype, which is more simple, rapid, and valid in clinical practice. A growing body of epidemiological evidence demonstrates that physical frailty may increase the risk of future cognitive decline and dementia.[44,45,48] Therefore, integrating interdisciplinary care and personal assessment, and finding evidence-based interventions for patients with multiple sensory and locomotion impairments will be beneficial for the healthy aging of older adults.[49–51] Frailty syndrome is dynamic and might progressively involve in the decline in multiphysiological systems. Mobility frailty in combination with cognitive impairment, defined as Motor Cognitive Risk Syndrome, in which individuals with concurrent motor and cognitive dysfunction had more adverse outcomes.[25–27,52] However, the effect of sensorial frailty in combination with cognitive impairment, including subjective cognitive decline or MCI on adverse prognosis, such as the risk of further cognitive decline, and quality of life, remains elusive. we should also monitor these patients with concurrent sensory and cognitive dysfunction, referred to as sensory cognitive risk syndrome, and further investigate whether the syndrome has a more severe influence on the healthy aging of older adults than does sensory dysfunction.

Sensorial and mobility frailty are also the vulnerability increase of 2 important dimensions of IC. To the best of our knowledge, this study is the first to investigate the impact of other IC dimensions on the cognitive dimension. Sensorial and mobility frailty have been found to have a synergic impact on the physical dimension of health-related quality of life. Sensorial frailty mainly affects the domains of senses, and mobility affects the domains of independent living and pain.[42] In this study, our results indicated that both sensorial and mobility frailty had a significant influence on overall and domain-specific cognitive function, even if the influence of mobility frailty was stronger than that of sensorial frailty. Thus, in order to unify the dimensions of frailty and IC, we suggest that sensory and mobility dimensions of IC should be integrated into the physical frailty phenotype to facilitate clinical research and healthcare, and improve the sensitivity of physical frailty screening instrument. Corresponding to other dimensions, cognitive and psychosocial frailty phenotypes can also be constructed. Depressive symptoms, referred to as the psychological dimension of IC, have been reported to affect overall and domain-specific cognitive function.[32–35] However, our results showed that depressive symptoms were only significantly associated with a high risk of executive function impairment. In addition to sample size, other factors, such as APOE4 positivity, could have affected our results.[34] In our previous study, we found that depression had a significant negative impact on overall health-related quality of life; the domains of independent living and pain in the physical dimension but not the senses domain; and all domains of the psychosocial dimension, including mental health, happiness, self-worth, coping, and relationships. [42]

Although vitality decline had an extensive negative impact on health-related quality of life, including overall health-related quality of life, the domains of senses and pain in the physical dimension, and the domains of mental health and relationships in the psychosocial dimension after adjustment for demographic, health-related, and psychological confounders, [42] we did not find an adverse impact of vitality on overall

and domain-specific cognitive function. The impact of vitality on cognitive function needs to be investigated using a longitudinal cohort with a large sample and validated assessment tools of vitality. However, the absence of a consensus about vitality definition leads to vitality capacity is a physiological state resulting from the interaction between multiple physiological systems, reflected in the level of energy and metabolism, neuromuscular function, and immune and stress response functions of the body.[5] Vitality capacity is the core domain and the basis of other IC domains.[4,5] Self-perceived fatigue, malnutrition or nutrition, and body composition is the top candidate attributes for vitality.[5] The parameters for the screening vitality vulnerability in our study come from these top candidate attributes, which increases the strength of our reported results. Self-perceived fatigue/exhaustion, might also be the first physical component of frailty.[53] Therefore, we proposed that the vulnerability of vitality might be the pre-frailty status, and different frailty phenotypes could be created based on IC. Vulnerability in other IC domains together with the vulnerability of vitality (pre-frailty) will construct different frailty phenotypes, such as physical (including sensorial and mobility), cognitive, and psychosocial frailty phenotypes.

Age, education level, and lifestyle habits, such as smoking, were common causes of cognitive impairment. Multimorbidity and chronic diseases have been reported to be risk factors for cognitive impairment. Our results indicated that the number of comorbidities did not affect overall and domain-specific cognitive function. Indeed, we found that the number of multimorbidities only had an independently negative effect on health-related quality of life in the independent living domain of the physical dimension after adjustment for demographic, health-related, and psychological confounders.[29] However, some chronic diseases have a significant influence on cognitive function. CVD had independent negative effects on overall cognitive function. In addition, diabetes mellitus had significant negative effects on processing speed/attention/executive function as measured by both the TMT A and digit symbol test, as well as executive function as measured by the TMT B. Due to the small sample of patients with non-skin malignancy, we did not include this variable in the multiple regression models when we analyzed the independent risk factors for domain-specific cognitive function. The small sample size also had a limitation for the evaluation of the severity of chronic diseases, which could be more appropriate than the number of comorbidities to investigate their impact on cognitive performance. Moreover, the participants' feelings about the diseases (e.g., worry) or their perceptions (e.g., pain) could have itself an impact on the cognitive performance. These factors all rely on the presence of multiple diseases but have not been directly investigated in this study.

5. Conclusion

Individuals with concurrent sensorial and mobility frailty or mobility frailty had a significantly higher risk of overall cognitive impairment and delayed memory and language domain impairment than those with only sensorial frailty. The reserve decline in the psychological dimension of IC had a significant adverse effect on executive function. Chronic diseases, such as CVD were independent determinants of MCI, and diabetes mellitus had an independent negative influence on domain-specific cognitive function, including processing speed, attention, and executive function.

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