Association between motoric cognitive risk syndrome and frailty among Chinese older adults

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Research article

Keywords: cognitive complaints, slow gait, frailty, older adult

Posted Date: October 1st, 2019

DOI: https://doi.org/10.21203/rs.2.15390/v1

Version of Record: A version of this preprint was published at BMC Geriatrics on March 19th, 2020. See the published version at https://doi.org/10.1186/s12877-020-01511-0.

Abstract

Background: Motoric cognitive risk syndrome (MCR) is a newly proposed pre-dementia syndrome incorporating subjective cognitive complaints and slow gait. Previous studies have shown that subjective cognitive complaints and slow gait are reported to be associated with frailty in cognitively unimpaired older adults, but little is known giving attention to the link between MCR and frailty in older adults. Therefore, the aim of the study was to explore the associations of MCR and its components and frailty in Chinese older adults.

Methods: In an observation cross-sectional study, a total of 429 older adults aged 60 years and older were admitted to the geriatric department. According to MCR criteria, all participants were classified to 4 groups: 1) MCR group; 2) subjective cognitive complaints group; 3) slow gait group; 4) healthy control group. Physical frailty was assessed by Clinical Frailty Scale (CFS). The multivariate logistic regression analysis was used to examine the association between MCR and frailty in older adults.

Results: The prevalence of subjective cognitive complaints, slow gait and MCR was 15.9%, 10.0% and 4.0%, respectively. After adjusting for confounding variables, the logistic regression analysis showed that slow gait (odds ratio [OR] 3.40, 95% confidence interval [CI] 1.40-8.23, P=0.007) and MCR (odds ratio [OR] 5.53, 95% confidence interval [CI] 1.46-20.89, P=0.012) were independently associated with frailty, but not subjective cognitive complaints.

Conclusions: MCR and slow gait were significantly associated with frailty in Chinese older adults. Further study should prospectively determine the causal relationship between MCR and frailty.

Introduction

Accelerated population aging and extended average life expectancy in China is further expected to increase age-associated pathological conditions, such as cognitive impairment and frailty. Motoric cognitive risk syndrome (MCR) is a pre-dementia syndrome which is characterized by the simultaneous presence of subjective cognitive complaints and slow gait in older individuals without dementia or mobility disability [1]. The reported prevalence of MCR ranged from 2% to 18% [2–6]. MCR was found to be associated with adverse clinical outcomes in older individuals, such as dementia, falls, disability and mortality [1,7–10]. A prospective cohort study based in the Einstein Aging Study showed that older adults with MCR were at more than 3-fold risk of developing dementia and over 12-fold risk of vascular dementia[1]. While a recent study from Japanese community-dwelling sample of older adults reported that MCR was a risk factor of future dementia (HR = 2.49) and disability (HR = 1.69) [7]. Kumai and colleagues found that the rate of conversion to dementia in the MCR group was 1.38 times higher than the non-MCR group, and both slow gait and lower scores in executive tests were reported to be predictive of higher rate of conversion to dementia [11]. In addition, due to screening MCR avoiding complex neuropsychological tests or neuroimaging examinations, it is more conducive to increase accessibility of

clinical dementia risk assessment and implement appropriate prevention strategies. Therefore, MCR has gained extensive research and clinical attentions.

Frailty is a common geriatric syndrome that is partly reversible and characterized by age-related decline in physiologic reserves and function of multiple systems, resulting in increasing vulnerability triggered by minor stressor events and further leading to negative health outcomes, including falls, disability, hospitalization and mortality [12–14]. Growing body of evidences showed that cognitive impairment and frailty are closely related in advancing aging in that they may share similar etiologies. For example, frail status may raise the risk of cognitive decline, incident mild cognitive impairment and dementia [15–19]. Alternatively, cognitive impairment also increases the risk of frailty [20,21] Frailty and cognitive impairment often coexist [22,23], so the construct of cognitive frailty was proposed, which is also described as a risk factor of dementia [24,25].

Compared with the operational definition of cognitive frailty, MCR focuses more on subjective cognitive complaints but not mild cognitive impairment (MCI) [26]. Subjective cognitive complaints with normal objective cognitive tests indicate the presence of subjective cognitive decline [27]. Subjective cognitive decline has been reported to be predictive of incident MCI [28], as well as dementia [29]. Thus, MCR might represent an earlier stage of preclinical dementia. Additionally, although subjective cognitive decline and slow gait are reported to be associated with frailty in cognitively unimpaired older adults [24,25,30], little is known giving attention to the link between MCR and frailty in older adults. With aging, older adults with MCR were hypothesized to exhibit the higher risk of frailty when comparing with any component of MCR. Therefore, we conducted this study to elucidate the associations of MCR and its components and frailty in Chinese older adults.

Methods

Participants

Anobservation cross-sectional study was carried out with a total of 935 potential participants from the geriatric department of Zhejiang Hospital in China, and the baseline assessments were done from October 2014 to September 2018. Inclusion criteria in this study were aged 60 years and older, ability to understand and communicate Chinese. Participants with a history of Parkinson's disease or Parkinson's syndrome (n = 29), dementia (n = 93), MCI defined as those who scored less than 24 on the Mini-Mental State Examination (MMSE) (n = 187) or mobility disability (n = 104) who are inability to ambulate with or without walking aids were excluded. Participants who had incomplete data (n = 93) used to diagnose MCR were also excluded. After exclusions, 429 cases were eligible. Data including demographic variables, medical history and functional assessments were collected by a trained geriatric physician and nurse via computer-aided hospital-based comprehensive geriatric assessment.

Approval for this study was granted by medical ethical committees of Zhejiang Hospital and written informed consent was obtained from each participant.

MCR diagnosis

Based on MCI criteria [31,32], MCR was defined as both the presence of subjective cognitive complaints and slow gait in those without dementia or mobility disability [1]. Subjective cognitive complaints were obtained by face-to-face interview based on response to one of item in 15-item geriatric depression scale (GDS–15) [33]. The standardized question on “Do you feel you have more problems with memory than most?” was asked by a well-trained nurse. A positive response “yes” on this question was recorded by subjective cognitive complaints. Gait speed (m/s) at normal pace was timed by four-meter usual gait speed test. Slow gait was defined as gait speed one standard deviation below age- and sex-specific means. The cut-off values of slow gait in this study were: males 60–74 years at 0.91 m/s, males ≥75 years at 0.69 m/s, females 60–74 years at 0.80 m/s, females ≥75 years at 0.66 m/s.

According to MCR criteria, all participants were classified to 4 groups: 1) MCR group; 2) subjective cognitive complaints group; 3) slow gait group; 4) healthy control group.

Frailty assessment

Based on the Canadian study on Health and Aging, frailty was assessed by the Clinical Frailty Scale (CFS) which grading from 1 (very fit) to 7 (severely frail) [34]. The evaluator recorded the level of frailty by clinical judgment using available clinical information. In this study, a score of CFS greater than four was defined as the presence of frailty [35].

Other covariates

Demographic variables including age, sex, educational level, marriage status, cigarette smoking and alcohol use were obtained. The body mass index (BMI) was calculated by height and weight. Physician diagnosed medical diseases including diabetes mellitus, cerebrovascular diseases, hypertension and coronary artery disease were recorded. Comorbidities were defined as coexisting five kinds or more diseases. Participants who took five or more oral prescription medications were considered as polypharmacy. A history of falls in the past year was also recorded. Grip strength was measured three times using a hand dynamometer. The maximum of the three trials was recorded for the final analysis. Depression symptoms were evaluated using GDS–15 [33] and cognitive functioning using MMSE [36].

Statistical analysis

Normal distributions of continuous variables were presented as the means± standard deviation (SDs), and categorical variables were expressed as number (percentage). The One-way ANOVA test (for normally distributed continuous data), the chi-square test (for categorical data) were used to compare the statistical differences among the control, subjective cognitive complaints, slow gait and MCR groups.

Furthermore, the association of MCR with frailty was analyzed using the multivariate logistic regression models and expressed in odds ratios (ORs) and 95% confidence intervals (CIs). The multivariate logistic regression models were conducted 3 models. Model 1 was started with the unadjusted covariate, Model 2 was tested after adjusting for age, sex and education, and Model 3 was analyzed adjusting for marriage status, BMI, comorbidities, polypharmacy, fall history, grip strength, depressive symptom and MMSE scores, other than adjusting for those in Model 2. The variables were analyzed by using the SPSS 18.0 software (SPSS, Chicago, IL, USA). All significance tests were two-tailed, and statistical significance was assumed as $P<0.05$.

Results

Prevalence and characteristics of the total sample

Of the total participants, the prevalence of subjective cognitive complaints, slow gait and MCR was 15.9%, 10.0% and 4.0%, respectively.

The characteristics of the total 429 participants are presented in Table 1. Mean age of the participants was 76.7 (±7.7) years; 59.9% were male, 34.0% achieved high school and above of educational level and 79.3% were married. The mean BMI was 23.7(±3.2) kg/m^2. More than half (60.4%) of the participants reported 5 or more comorbid conditions, and hypertension (75.8%) was the most common chronic disease. Nearly half of the participants (46.2%) accounted for polypharmacy. About 15% of participants were classified as physical frailty.

Comparing variables between groups

As shown in Table 1, significant differences were observed among the four groups (i.e., the control, subjective cognitive complaints, slow gait and MCR groups) with regard to BMI, polypharmacy, grip strength, four-meter gait speed, GDS–15 scores, MMSE scores and physical frailty (all P for trend <0.05). There were no significant differences in age, sex, educational level, marriage status, smoke history, drink history, comorbid diseases (such as diabetes mellitus, cerebrovascular diseases, hypertension and coronary artery disease) and fall history in the past year among the groups (all P for trend >0.05).

The association between MCR and frailty

Table 2 shows the results of the multivariate logistic regression analysis on the association between MCR and frailty. Crude Model 1 showed that slow gait (OR 4.81, 95% CI 2.35–9.85) and MCR (OR 7.22, 95% CI 2.61–19.99) were associated with frailty. Model 2, after adjusting for age, sex and education, showed that slow gait (OR 4.36, 95% CI 1.94–9.80) and MCR (OR 9.98, 95% CI 2.88–34.59) remained associated with frailty. In the fully adjusted Model 3, the results still unchanged, slow gait (OR 3.40, 95% CI 1.40–

8.23) and MCR (OR 5.53, 95% CI 1.46–20.89) increased risk of frailty. However, no significant difference was found between subjective cognitive complaints and frailty.

Discussion

In this study, MCR and slow gait were both significantly associated with frailty in older adults in geriatric department, but not subjective cognitive complaints. These associations remained unchanged after adjusting for the potentially confounding variables. These results revealed the association between MCR and frailty was significantly observed with slow gait, and the combination of subjective cognitive complaints and slow gait may have more predictive value than the single component in order to explain their common mechanisms with frailty.

The primary finding of this study is that MCR was associated with frailty in elder population. This finding is in accordance with a cross-sectional study from France [37], which showed that physical frailty and in particular slow gait speed were associated with cognitive impairment, indirectly reflecting slow gait and cognitive impairment often coexist with MCR, and suggesting that MCR and frailty interact with each other with aging. Subjective cognitive complaints and slow gait are common condition in aging process, and have been considered as early clinical indicators of cognitive impairment and dementia during the preclinical stages. Cognitive impairment is a longitudinal process that begins with minor alterations in certain domains and slowly progresses to multiple changes in many domains [38]. The accumulation of cerebral amyloid deposition and neurofibrillary tangles plays a critical role in progression of Alzheimer's disease neuropathology [39,40]. In addition, brain regions alterations including motor cortices, striatum and substantia nigra are often involved [39,40]. Studies have shown that MCR had a wider involvement of brain regions not limited to the hippocampus, which is a key brain region for memorization and spatial navigation processes [41–43]. It was characterized by smaller volumes of total gray matter, total cortical gray matter, premotor cortex, prefrontal cortex especially dorsolateral segment, but no significant differences were obtained in terms of the volumes of hippocampal and white matter [44,45], which are in concordance with these results as the two components of MCR controlling cognitive complaints and slow gait. MCR related brain regions reduction contributes to predict cortical neurodegenerative dementia more than subcortical dementia such as vascular dementia [44]. A study by Wang and colleagues found that frontal lacunar infarcts was associated with slow gait, poor memory function and MCR, but not with cognitive complaints [46], revealing that this brain area might result in MCR by disrupting frontally based neural networks facilitating memory and gait functions [47,48]. On the other hand, the accumulation of common brain pathologies and related brain areas alterations may also contribute to progressive frailty [49,50]. Cerebral amyloid-beta deposition and neurofibrillary tangles were associated with the symptoms of frailty including slower gait speed and lower body mass index in dementia free elders [51,52]. Thus, the association between MCR and frailty could be explained by the aboved mechanisms. Slow gait as a common manifestation, we also could well understand why slow gait is linked with frailty. However, the lack of longitudinal prospective studies about the casual associations between MCR and frailty prevents from drawing conclusions.

Association between subjective cognitive complaints and frailty failed to observe in this study sample. It was inconsistent with previous studies such as the Hellenic Longitudinal Investigation of Aging and Diet study [30] and the Healthy Aging Longitudinal Study in Taiwan [24] revealing that subjective cognitive decline was associated with increased likelihood for frailty in cognitively unimpaired elderly individuals. Self-reported subjective cognitive decline complaints were adopted, but the discrepancy results were obtained due to the differences in frailty assessment criteria to quantify frailty status. In addition, the characteristics of the enrolled study sample were also inconsistent. The potential neurobiological explanations for the association between subjective cognitive decline and frailty lies in that both two factors increased risk of future cognitive decline [15,16,28,29] and Alzheimer's disease pathology [53–56].

An important advantage of this study lies in all the enrolled older participants who underwent a comprehensive geriatric assessment focusing on the functional status of the elderly, such as daily activities of life, cognitive and frailty. Indeed, in our geriatric department, we have a trained team for comprehensive geriatric assessment, and all the assessments are designed to be a professional software system. Thus, the validity and consistency of the evaluations are guaranteed. Another advantage is that MCR and CFS-defined frailty screening in this study are relatively simple and easy to be implemented in other clinical settings, such as community health service centers and other primary medical centers. CFS was reported to reflect the dynamic and reversible changes of frailty, and well associate with frailty index. Thus, it can similarly predict adverse outcomes for elder patients [34,57]. On the contrary, this study also has some limitations. First, although this study is first to report the association between MCR and frailty, the cross-sectional study precluded us from elucidating the causal relationships. Second, due to a monocentric study, there are a selection bias and a representativeness bias in this study. Third, although these study participants were at normal MMSE range, some participants with mild hidden dementia might be undiagnosed. Finally, the standard definition of MCR is also a limitation in this study. The definition of slow gait is already standardized, but subjective cognitive complaints have different choices. Subjective cognitive complaints are defined as by one item of GDS–15 in this study according to the standard reported in most studies. Furthermore, the accuracy of self-reported cognitive complaints may be affected by the disease, emotional and environmental factors. Thus, the generalization of the study results could not be ignored because it is less sensitive for non-demented older adults.

Conclusions

Our results support the idea of that MCR and slow gait were associated with frailty in older adults without dementia or mobility disability. Further study is needed to better explicit the pathophysiological, behavioral and environmental variables in order to prospectively determine the causal relationship between MCR and frailty in the multicenter study with a large sample. More researches are also necessary to be done to develop new interventions and preventative strategies for improving quality of life and reducing or reversing cognitive impairments and frailty in older adults.

Abbreviations

MCR: motoric cognitive risk; CFS: Clinical Frailty Scale; MCI: mild cognitive impairment; BMI: body mass index; MMSE: Mini-Mental State Examination; GDS–15: 15-item Geriatric Depression Scale; SD: standard deviation; OR: odds ratio; CI: confidence interval.

Declarations

Acknowledgements

We would like to acknowledge the other staff from the geriatric department of Zhejiang Hospital for their positive involvement in this study.

Funding

This study was supported by innovation disciplines of Zhejiang Province, Science Technology Department of Zhejiang Province (2014C33241), Zhejiang Medical Science and Technology Project (2016ZDB001, 2018ZH001) and “1530”personnel training project from Zhejiang Hospital (2018–30–09).

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors’ contributions

SS and CX participated in study design, coordination and data analyses. SS wrote the original manuscript, and all the authors participated in interpreted the results, revised and approved the final manuscript.

Ethical approval and consent to participate

Medical ethical committees of Zhejiang Hospital approved the whole study and written informed consent was obtained from each participant.

Consent for publication

Not applicable.

Competing interest

All the authors declare no potential conflicts of interest in this study.

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Tables

Table 1 Characteristics and comparing among the four groups

	Total (n=429)	Healthy control (n=301)	Subjective cognitive complaints (n=68)	Slow gait (n=43)	MCR (n=17)	*P*-value
s (mean ± SD)	76.7±7.7	76.6±7.6	75.7±7.8	79.1±7.7	76.7±8.7	0.156
)	257(59.9)	189(62.8)	34(50.0)	27(62.8)	7(41.2)	0.092
ol and above, n (%)	146(34.0)	207(68.8)	40(58.8)	28(65.1)	8(47.1)	0.150
ı (%)	340(79.3)	239(79.4)	58(85.3)	29(67.4)	14(82.4)	0.154
r former smoker, n	100(23.3)	73(24.3)	15(22.1)	9(20.9)	3(17.6)	0.885
r former drinker, n	99(23.1)	74(24.6)	13(19.1)	9(20.9)	3(17.6)	0.710
n ± SD, kg/m^2)	23.7±3.2	23.7±3.0	22.8±3.1	24.5±3.8	24.4±4.5	0.032
diabetes, n (%)	101(23.5)	76(25.2)	8(11.8)	13(30.2)	4(23.5)	0.079
cerebrovascular ı (%)	129(30.1)	86(28.6)	19(27.9)	15(34.9)	9(52.9)	0.160
hypertension, n	325(75.8)	223(74.1)	52(76.5)	36(83.7)	14(82.4)	0.500
coronary artery (%)	141(32.9)	93(30.9)	24(35.3)	15(34.9)	9(52.9)	0.273
ities (≥ 5 drugs), n	259(60.4)	176(58.5)	42(61.8)	29(67.4)	12(70.6)	0.542
ıacy (≥ 5 drugs), n	198(46.2)	132(43.9)	27(39.7)	27(62.8)	12(70.6)	0.014
y in the past year,	69(16.1)	50(16.6)	10(14.7)	8(18.6)	1(5.9)	0.643
gth, (mean ±	30.6±9.4	31.8±9.2	29.7±8.8	26.8±9.7	23.0±6.8	<0.001
r usual gait speed D, m/s)	1.0±0.3	1.1±0.2	1.1±0.2	0.6±0.1	0.6±0.2	<0.001
e symptoms from nean ± SD, scores)	2.2±2.4	1.6±2.0	4.0±2.7	2.7±2.4	5.1±2.9	<0.001
ean ± SD, scores)	27.4±1.9	27.6±1.8	27.2±1.8	26.9±2.0	25.7±1.7	<0.001
CFS≥ 5, n (%)	64(14.9)	33(11.0)	7(10.3)	16(37.2)	8(47.1)	<0.001

Abbreviations: BMI, body mass index; GDS-15, 15-item Geriatric Depression Scale; MMSE, Mini-Mental State Examination; CFS, Clinical Frailty Scale.

Table 2 Multivariate analysis of the association between MCR and physical frailty

	Model 1		Model 2		Model 3	
	OR(95%CI)	*P*-value	OR(95%CI)	*P*-value	OR(95%CI)	*P*-value
Healthy control	1.00	-	1.00	-	1.00	-
Subjective cognitive complaints	0.93(0.39-2.21)	0.873	1.03(0.41-2.56)	0.952	0.76(0.26-2.26)	0.619
Slow gait	4.81(2.35-9.85)	<0.001	4.36(1.94-9.80)	<0.001	3.40(1.40-8.23)	0.007
MCR	7.22(2.61-19.99)	<0.001	9.98(2.88-34.59)	<0.001	5.53(1.46-20.89)	0.012

Abbreviations: OR, odd ratio; CI, confidence interval; BMI, body mass index.

Notes: Model 1: crude model; Model 2: adjusted for age, sex and education; Model 3: adjusted for Model 2 plus BMI, comorbidities, polypharmacy, grip strength, depressive symptom and MMSE scores.