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ORIGINAL RESEARCH

Bridging Pain and Motoric Cognitive Risk Syndrome: Mediating Effect of Handgrip Strength

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Background: Motoric cognitive risk syndrome (MCR) is a preclinical stage of dementia that strongly predicts future cognitive deterioration and dementia development. Although research has advanced in exploring MCR's epidemiological aspects, the association between pain, handgrip strength (HGS), and MCR remain insufficiently studied.

Methods: This cross-sectional study analyzed baseline data from the 2015 China Health and Retirement Longitudinal Study (CHARLS), restricted to participants aged ≥45 years. MCR cases were identified through self-reported cognitive complaints combined with objectively measured gait slowing, excluding subjects with existing dementia. Using multivariable-adjusted logistic regression, we investigated associations between chronic pain, HGS, and MCR prevalence. Mediation analysis further assessed whether HGS mediated the pain-MCR relationship. Stratified analyses evaluated effect modification across key demographic strata.

Results: This research encompassed a cohort of 4,795 individuals, displaying an average age of 67.3 ± 6.5 years, comprising 4,648 non-MCR and 147 MCR individuals. In the non-MCR group, 70.3% had no pain, 4.8% had one pain, and 25.3% had two or more pains. In the MCR group, 51% had no pain, 10.2% had one pain, and 38.8% had two or more pains ($p < 0.001$). The mean HGS was 29.1kg ± 9.0kg in the non-MCR group, significantly higher than the MCR group's 21.7kg ± 8.4kg ($p < 0.001$). Pain was positively associated with MCR, increasing its likelihood by 1.9 times per unit increase (OR = 1.90, 95% CI: 1.29–2.80, $p = 0.001$). Conversely, HGS was negatively associated, reducing MCR likelihood by 9% per unit increase (OR = 0.91, 95% CI: 0.88–0.93, $p < 0.001$). HGS's indirect effect on the pain-MCR link was 2.58×10^{-3} ($p < 0.001$), explaining 24.87% of the total effect variation.

Conclusion: The study found that pain is positively associated with MCR, while HGS is negatively associated with MCR, and HGS mediates the relationship between pain and MCR.

Keywords: pain, handgrip strength, motoric cognitive risk syndrome, CHARLS, cross-sectional study

Introduction

The global aging population has precipitated a steady rise in age-related neurodegenerative conditions, with dementia and cognitive impairment representing particularly pressing public health challenges. China currently bears the world's largest dementia burden and, given demographic projections, may account for nearly 50% of global cases by 2050.[1,2] Within this context, motoric cognitive risk (MCR) syndrome has emerged as a critical predementia marker, operationally defined by coexisting subjective cognitive complaints and objectively measured gait slowing in older adults without dementia.[3] MCR demonstrates significant predictive validity for multiple adverse outcomes including incident falls,[4] functional disability,[5] dementia,[5] cardiovascular events,[6] and premature mortality.[7] Identifying modifiable risk factors for MCR could inform targeted prevention strategies, potentially mitigating both the personal suffering and substantial socioeconomic costs associated with dementia progression.

Pain represents a complex multidimensional experience encompassing both sensory and affective components, classically defined as an unpleasant sensation associated with actual or potential tissue damage.[8] This prevalent

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health concern affects a substantial proportion of adults globally, with many experiencing persistent or chronic manifestations.[9] In the Chinese context, pain-related conditions generate annual healthcare expenditures exceeding ¥1 trillion,[10] while simultaneously contributing to substantial disease burden through increased disability-adjusted life years (DALYs). Beyond its economic impact, chronic pain frequently precipitates numerous adverse health outcomes including mobility limitations, anxiety disorders, and depressive symptoms.[11] Studies have demonstrated that chronic pain may intensify cognitive decline, potentially contributing to the development of conditions such as MCR. However, the pathophysiological mechanisms linking pain to the progression of MCR are not well understood, necessitating further mechanistic research.

Handgrip strength (HGS) serves as a robust objective measure of overall physical capability and a validated predictor of current and future health status.[12] Emerging evidence indicates that chronic pain may contribute to accelerated biological aging processes, potentially compromising musculoskeletal integrity and reducing muscular strength.[13] Mechanistic evidence suggests that chronic pain may precede declines in physical capacity. Specifically, persistent nociceptive signaling can induce neuromuscular inhibition and disuse atrophy, leading to reduced muscle strength including HGS.[13,14] Concurrently, pro-inflammatory states associated with chronic pain may accelerate sarcopenia, further compromising HGS.[15] Epidemiological studies consistently demonstrate an inverse relationship between pain prevalence and HGS in middle-aged and older populations.[16] Notably, diminished HGS shows significant associations with both functional disability and cognitive impairment.[17,18] This relationship is particularly evident in longitudinal research involving Chinese elderly populations, where greater baseline HGS predicted slower rates of cognitive decline.[19] From a neurophysiological perspective, HGS reflects integrated nervous and motor system function,[20] and the deterioration of these systems represents a key pathway in age-related cognitive deterioration.[21] Cognitive function is vital to MCR, but limited research on HGS and MCR leaves their connection unclear, necessitating further study. Given that HGS is a robust biomarker of neuromuscular integrity and cerebral health,[20,22] it may constitute a critical pathway linking pain to cognitive-motor deficits in MCR. Thus, we hypothesize that HGS mediates the association between pain and MCR.

Utilizing data obtained from the 2015 China Health and Retirement Longitudinal Study (CHARLS), this research investigated the relationship between pain, HGS, and MCR in individuals aged 45 years and older. A mediation analysis framework was employed to evaluate the potential mediating role of HGS in the association between pain and MCR.

Study Methodology

Data Collection

The present analysis employed a cross-sectional design, leveraging data sourced from the CHARLS. Conducted as a longitudinal, nationally representative survey targeting Chinese adults ≥ 45 years older, CHARLS was designed to create a comprehensive, publicly accessible micro-level dataset that is both reliable and representative of middle-aged and elderly populations. A multistage probability-proportional-to-size (PPS) sampling strategy was employed across 28 provincial-level regions to ensure demographic diversity. Comprehensive methodological details regarding CHARLS have been extensively documented in previous research.[23] The CHARLS study was approved by the Ethics Review Committee of Peking University (approval number: IRB00001052-11015). All methods were carried out in accordance with relevant guidelines and regulations, and all participants signed informed consent forms when participating. The inaugural national data collection occurred in 2015 with an initial cohort of 21,095 respondents. For analytical rigor, exclusion criteria were applied sequentially: individuals below 45 years (n=7,105), those with incomplete MCR assessments (n=8,929), undocumented pain (n=129), unspecified HGS data (n=66), and missing covariate information (n=71) were omitted. This selection process yielded a final analytical cohort of 4,795 middle-aged and elderly participants, with the complete exclusion pathway illustrated in Figure 1.

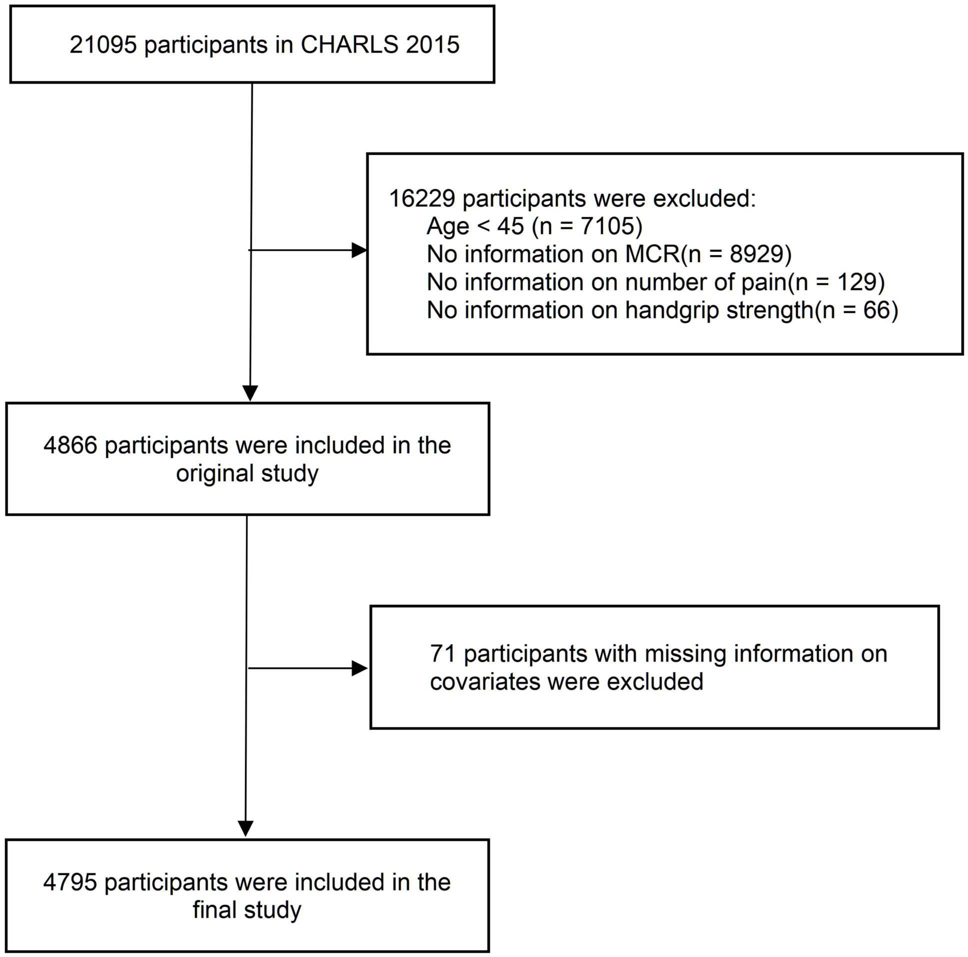

Figure 1 Flowchart of the participants selection process.
Abbreviations: CHARLS, China health and retirement longitudinal study; MCR, Motoric cognitive risk syndrome.

Assessments

MCR

We employed the established diagnostic framework for MCR, which requires the concurrent presence of: (1) subjective cognitive complaints and (2) objectively measured slow gait speed (GS), in individuals without dementia.[24] Dementia identification is detailed in the Supplementary Methods.

Subjective cognitive complaints were evaluated through a standardized single-item question: "How would you describe your current memory function?" Participants responded using a 5-point ordinal scale:

1. Excellent
2. Very good
3. Good
4. Fair
5. Poor

Responders selecting "Fair" (4) or "Poor" (5) were operationally classified as exhibiting clinically significant cognitive complaints.

GS was objectively measured using infrared sensor technology during a 2.5-meter walk at self-selected usual pace. Three trials were conducted with adequate rest periods between measurements. Slow GS was defined using population-based normative data, with the following age- and sex-specific thresholds [>1 standard deviation (SD) below mean values]:[25]

- Male participants:
  - Aged <75 years: ≤0.44 m/s
  - Aged ≥75 years: ≤0.35 m/s

- Female participants:
  - Aged <75 years: ≤0.41 m/s
  - Aged ≥75 years: ≤0.33 m/s

Pain

A self-report questionnaire was administered by the CHARLS investigators in each wave of data collection to obtain information regarding body pain. The questionnaire commenced with the inquiry, "Are you often troubled by any pain in your body?" Based on the participants' responses, pain was categorized as a binary variable (yes/no). Pain locations were identified across 15 specific sites and subsequently grouped into three primary regions: head and neck; trunk (encompassing the chest, stomach, back, waist, or buttocks); and limbs (including shoulders, arms, wrists, fingers, legs, knees, ankles, or toes). Pain data for this study were obtained from CHARLS 2015.

HGS

HGS was assessed during baseline evaluations utilizing a hydraulic grip strength dynamometer. Each participant underwent two consecutive measurements for both the left and right hands. The highest value recorded across all four trials was selected as the continuous variable for subsequent analysis.[26,27]

Control Variables

The baseline investigation examined a range of demographic and health-related variables. These encompassed age, sex, geographic residency (urban or rural), and marital status—classified as married and living with a spouse or married but living without a spouse or single, divorced, and windowed. Additional covariates included the count of chronic conditions (none, single, or multiple), smoking status (smoker or non-smoker), drinking status (non-drinker, drink but less than once a month, or drink more than once a month), highest educational attainment (elementary school or below or middle school or above), body mass index (BMI), and sleep quality (good, fair or poor). Chronic disease prevalence was ascertained through self-reported diagnoses of fourteen non-communicable conditions: hypertension, diabetes, dyslipidemia, chronic pulmonary disease, hepatic disorders, renal disease, cardiovascular events (myocardial infarction, stroke), malignancies, arthritis, asthma, gastrointestinal ailments, cognitive impairment, mental health conditions, and musculoskeletal disorders.

Statistical Analysis

Sample characteristics were summarized with means and SD for continuous variables and frequencies with percentages for categorical variables. Secondly, we used Spearman correlation to evaluate the relationships between the main variables. The study used the Baron and Kenny mediation model.[28] The analytical framework evaluated the intermediary effect of HGS measured at baseline in the association between pain and MCR. Linear regression analyses were conducted to: (1) explore the association between pain and HGS, (2) examine the link between pain and MCR, and (3) investigate the pain-MCR relationship with HGS as a mediator. The odds ratio (OR) quantified the association's magnitude between variables. We utilized a nonparametric bootstrap approach with 1000 resamples to assess both the total and indirect effects.[29] Stratified subgroup analyses explored effect heterogeneity across predefined demographic and health-related categories. Covariates accounted for in the analyses encompassed age, sex, educational attainment, marital status, geographic residence, smoking status, drinking status, sleep quality, BMI, and the number of diagnosed chronic diseases. Statistical significance for mediation effects was determined using bias-corrected accelerated bootstrap 95% CI, with effects deemed significant if the interval excluded zero. All statistical analyses were performed with R (v4.3.2), using a significance level of $p < 0.05$.

Result

Study Participants' Baseline Traits

The study cohort was divided into non-MCR and MCR subgroups, with their demographic and clinical characteristics detailed in Table 1. The analysis included 4,795 participants, with an average age of 67.3 ± 6.5 years. Of these, 2,416 were female (50.4%) and 2,379 were male (49.6%). There were 4,648 in the non-MCR group and 147 in the MCR group. The mean age of non-MCR group was 67.2 ± 6.4 years, and 2,322 (50%) were women and 2,326 (50%) were men. The mean age of MCR group was 71.5 ± 8.1 years. There were 94 females (63.9%) and 53 males (36.1%). A significant

Table 1 Baseline Characteristics of the Study Participants with and Without Motoric Cognitive Risk Syndrome

Variables	Total n = 4795	Non-MCR n = 4648	MCR n = 147	P-Value
Age, Mean ± SD	67.3 ± 6.5	67.2 ± 6.4	71.5 ± 8.1	< 0.001
Sex, n (%)				< 0.001
Female	2416 (50.4)	2322 (50)	94 (63.9)	
Male	2379 (49.6)	2326 (50)	53 (36.1)	
Residence, n (%)				0.697
Rural	3009 (62.8)	2919 (62.8)	90 (61.2)	
Urban	1786 (37.2)	1729 (37.2)	57 (38.8)	
Marital status, n (%)				< 0.001
Married and living with a spouse	3781 (78.9)	3683 (79.2)	98 (66.7)	
Married but living without a spouse	121 (2.5)	119 (2.6)	2 (1.4)	
Single, divorced, and windowed	893 (18.6)	846 (18.2)	47 (32)	
Education Status, n (%)				0.026
Elementary school or below	3679 (76.7)	3555 (76.5)	124 (84.4)	
Middle school or above	1116 (23.3)	1093 (23.5)	23 (15.6)	
Smoking Status, n (%)				0.842
Smoker	2473 (51.6)	2396 (51.5)	77 (52.4)	
Non-smoker	2322 (48.4)	2252 (48.5)	70 (47.6)	
Drinking Status, n (%)				0.005
Drink but less than once a month	377 (7.9)	366 (7.9)	11 (7.5)	
Drink more than once a month	1219 (25.4)	1198 (25.8)	21 (14.3)	
Non-drinker	3199 (66.7)	3084 (66.4)	115 (78.2)	
Sleep quality, n (%)				0.215
Good	2555 (53.3)	2480 (53.4)	75 (51)	
Fair	1267 (26.4)	1233 (26.5)	34 (23.1)	
Poor	973 (20.3)	935 (20.1)	38 (25.9)	
BMI, Mean ± SD	24.6 ± 37.6	24.5 ± 36.5	29.5 ± 64.0	0.114
Number of chronic conditions, n (%)				0.001
0	834 (17.4)	822 (17.7)	12 (8.2)	
1	1207 (25.2)	1176 (25.3)	31 (21.1)	
≥2	2754 (57.4)	2650 (57)	104 (70.7)	
Number of pain, n (%)				< 0.001
0	3344 (69.7)	3269 (70.3)	75 (51)	
1	236 (4.9)	221 (4.8)	15 (10.2)	
≥2	1215 (25.3)	1158 (24.9)	57 (38.8)	
Hand grip strength(kg), Mean ± SD	28.9 ± 9.0	29.1 ± 9.0	21.7 ± 8.4	< 0.001

Abbreviations: BMI, body mass index; MCR, motoric cognitive risk syndrome.

proportion of participants lived in rural areas (62.8%) and were married and cohabiting with their spouses (78.9%). Significant variations emerged across demographic and health-related variables—including age, gender distribution, educational attainment, marital status, alcohol intake, and chronic disease prevalence—with statistical significance maintained across all measures ($p < 0.01$). Notably, in the non-MCR group, 32.67 participants (70.3%) had no pain, 221 (4.8%) had one pain, and 1215 (25.3%) had two or more pain. In the MCR group, 75 participants (51%) had no pain, 15 (10.2%) had one pain, and 57 (38.8%) had two or more pain. ($p < 0.001$). Similarly, the mean HGS in the non-MCR group was 29.1kg ± 9.0 kg, which significantly differed from the mean HGS of 21.7 kg ± 8.4 kg in the MCR group ($p < 0.001$).

Associations of Pain and HGS with MCR

Table 2 displays associations between pain, HGS, and MCR. The analysis examined the association of pain with MCR across 4,795 participants. Unadjusted analyses showed a statistically significant positive association between pain at one site and MCR, with an OR of 2.96 (95% CI: 1.67–5.24; $P < 0.001$). After adjusting for covariates in Model 1, the effect size attenuated slightly (OR = 2.71, 95% CI: 1.51–4.84; $p = 0.001$). Further adjustments in Model 2 (OR = 2.81, 95% CI: 1.56–5.06; $p = 0.001$) and Model 3 (OR = 2.76, 95% CI: 1.53–4.99; $p = 0.001$). Unadjusted analyses showed a significant link between pain at multiple sites and MCR (OR = 2.15; 95% CI: 1.51–3.05; $P < 0.001$). Adjustments in Models 1, 2, and 3 slightly reduced the effect size but maintained significance: Model 1 (OR = 2.02; 95% CI: 1.40–2.91; $P < 0.001$), Model 2 (OR = 2.08; 95% CI: 1.42–3.04; $P < 0.001$), and Model 3 (OR = 1.90; 95% CI: 1.29–2.80; $P = 0.001$). This consistency indicates that, despite the adjustment for covariates, pain remains positively associated with MCR.

HGS demonstrated a significant inverse association with MCR in the analysis (OR = 0.90, 95% CI: 0.88–0.92; $p < 0.001$). This relationship retained statistical significance across sequential adjustments: Model 1 (OR = 0.90, 95% CI: 0.88–0.92; $p < 0.001$), Model 2 (OR = 0.90, 95% CI: 0.88–0.93; $p < 0.001$), and Model 3 (OR = 0.91, 95% CI: 0.88–0.93; $p < 0.004$). After adjusting for covariates, the robustness of the negative association between HGS and MCR persisted.

Table S1 presents the results of a subgroup analysis examining the relationship between pain and MCR, demonstrating consistent associations across all subgroups (interaction P>0.05). Table 3 highlights that sleep quality significantly affects the link between HGS and MCR (interaction P=0.028).

HGS Mediated the Association Between Pain and MCR

Table 4 illustrates the associations among baseline pain, HGS, and MCR. Pain showed a positive association with MCR ($r = 0.07$, $p < 0.001$) and a negative association with HGS ($r = -0.21$, $p < 0.001$). Notably, HGS and MCR were inversely associated ($r = -0.14$, $p < 0.001$).

Bootstrap analysis revealed the total effect of baseline pain on MCR ($\beta_0 = 1.04 \times 10^{-2}$, p= 0.002). HGS was found to significantly mediate the relationship between pain and MCR, with a mediation effect size of 2.58×10^{-3} ($p < 0.001$). This mediating pathway accounted for 24.87% of the total effect variation. A visual representation of this mediation pathway is provided in Figure 2.

Table 2 Associations of Pain and Handgrip Strength with Motoric Cognitive Risk Syndrome

Variables	No	Unadjusted		Model 1		Model 2		Model 3	
		OR(95% CI)	**p Value**	**OR (95% CI)**	**p Value**	**OR(95% CI)**	**p Value**	**OR (95% CI)**	**p Value**
Number of pain									
0	3340	1(Ref)		1(Ref)		1(Ref)		1(Ref)	
1	236	2.96 (1.67~5.24)	<0.001	2.71(1.51~4.84)	0.001	2.81(1.56~5.06)	0.001	2.76 (1.53~4.99)	0.001
≥2	1215	2.15 (1.51~3.05)	<0.001	2.02(1.40~2.91)	<0.001	2.08(1.42~3.04)	<0.001	1.90 (1.29~2.80)	0.001
Handgrip strength	4795	0.90 (0.88~0.92)	<0.001	0.90(0.88~0.92)	<0.001	0.90(0.88~0.93)	<0.001	0.91 (0.88~0.93)	<0.001

Notes: Model 1: adjusted for age, gender, educational level, marital status, and residence. Model 2: adjusted for model 1 + smoking status, drinking status, and sleep quality. Model 3: adjusted for model 2 + BMI and 14 chronic diseases.
Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval.

Table 3 Subgroup Analysis of the Association Between Handgrip Strength and Motoric Cognitive Risk Syndrome

Subgroup	Total	Event (%)	OR (95% CI)	P.for.Interaction
Age				0.927
<65	1991	31 (1.6)	0.88 (0.83~0.93)	
≧65	2804	116 (4.1)	0.91 (0.88~0.94)	
Sex				0.236
Male	2416	94 (3.9)	0.9 (0.86~0.93)	
Female	2379	53 (2.2)	0.9 (0.87~0.94)	
Residence				0.569
Rural	3009	90 (3)	0.91 (0.88~0.94)	
Urban	1786	57 (3.2)	0.89 (0.85~0.93)	
Marital Status				0.168
Married and living with a spouse	3781	98 (2.6)	0.91 (0.88~0.94)	
Married but living without a spouse	121	2 (1.7)	1.79 (0~Inf)	
Single, divorced, and windowed	893	47 (5.3)	0.87 (0.83~0.92)	
Education Status				0.662
Elementary school or below	3679	124 (3.4)	0.91 (0.88~0.93)	
Middle school or above	1116	23 (2.1)	0.87 (0.81~0.93)	
Smoking Status				0.719
Smoker	2473	77 (3.1)	0.91 (0.88~0.95)	
Non-smoker	2322	70 (3)	0.89 (0.86~0.93)	
Drinking Status				0.427
Non-drinker	3199	115 (3.6)	0.9 (0.87~0.92)	
Drink but less than once a month	377	11 (2.9)	0.96 (0.86~1.06)	
Drink more than once a month	1219	21 (1.7)	0.9 (0.85~0.97)	
Sleep quality, n (%)				0.028
Good	2555	75 (2.9)	0.92 (0.89~0.95)	
Fair	1267	34 (2.7)	0.9 (0.85~0.95)	
Poor	973	38 (3.9)	0.85 (0.79~0.9)	
BMI group				0.636
Normal	344	11 (3.2)	0.93 (0.84~1.03)	
Obesity	2862	69 (2.4)	0.9 (0.87~0.94)	
Overweight	1293	51 (3.9)	0.88 (0.84~0.93)	
Underweight	245	14 (5.7)	0.87 (0.78~0.97)	
Number of chronic conditions				0.376
0	834	12 (1.4)	0.88 (0.8~0.98)	
1	1207	31 (2.6)	0.89 (0.84~0.95)	
≧2	2754	104 (3.8)	0.9 (0.87~0.93)	

Notes: Adjusted for age, gender, educational level, marital status, smoking status, drinking status, sleep quality, BMI, and 14 chronic diseases.
Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval; BMI, body mass index.

Table 4 Association Among Pain and Handgrip Strength with Motoric Cognitive Risk Syndrome

Variables	Pain	Hand Grip Strength	Motoric Cognitive Risk Syndrome
Pain	1.00		
Handgrip strength	−0.21***	1.00	
Motoric cognitive risk syndrome	0.07 ***	−0.14***	1.00

Notes: *** P-value < 0.001.

Discussion

This study is the first to examine the link between pain, HGS, and MCR in middle-aged and older Chinese using 2015 CHARLS data. The study revealed a positive association between pain and MCR, while HGS exhibited a negative

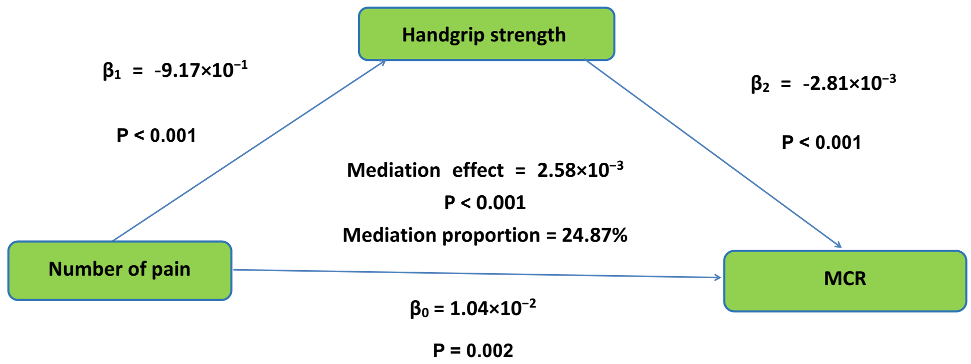

Figure 2 The conceptional framework of the mediation models. β0 was the total effect of number of pain on MCR; β1 represents the effect of number of pain on handgrip strength; β2 represents the effect of handgrip strength on MCR. The mediation effect was computed as the product of "β1" and "β2"(β1 × β2), and the mediation proportion was calculated as the ratio of the mediation effect product to total effects [(β1 × β2)/β0].
Abbreviation: MCR, Motoric cognitive risk syndrome.

association with MCR. Furthermore, HGS was found to mediate the relationship between pain and MCR. Sleep quality also significantly influenced the HGS-MCR relationship, supporting our hypothesis.

MCR is a pre-dementia syndrome marked by subjective cognitive complaints and slow GS, suggesting a higher risk of cognitive decline and dementia. Pain is intricately associated with MCR, and the nature of this association is direct, indirect, or mediated by other risk factors. Controlling for confounders, each unit increase in pain raised the MCR by 1.9 times (OR = 1.90, 95% CI: 1.29–2.80; p = 0.001). Chronic pain, marked by ongoing discomfort, can impair attention, memory, and executive function, leading to cognitive dysfunction.[30] It also slows cognitive processing in middle-aged and older adults, highlighting its impact on cognition.[31] Moreover, the presence of pain can exacerbate other risk factors for MCR, such as depression and sleep disturbances. Depression is a well-documented risk factor for cognitive decline, and its prevalence is higher among individuals experiencing chronic pain. This comorbidity can lead to a more pronounced decline in cognitive functions, as both conditions independently contribute to cognitive impairment.[32,33] Pain can reduce physical activity, essential for cognitive health. Chronic pain often leads to sedentary behavior, a changeable risk factor for cognitive decline and MCR. Promoting exercise and overcoming pain-related obstacles may help lower this risk.[34,35] A prior meta-analysis found that pain was linked to decreased GS in older adults.[36] Pain causes compensatory changes in walking patterns, such as shorter strides and increased support time for both limbs, which can lead to slower GS.

The relationship between pain and HGS in middle-aged and older individuals is a multifaceted issue that can be influenced by various physiological and psychological factors. Studies have shown that chronic pain in the older people can lead to muscle disuse and atrophy, which in turn reduces muscle strength, including HGS.[14] Inflammation is another potential mechanism linking pain and HGS, which negatively affects muscle function. Inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) are associated with muscle weakness and reduced HGS in the older population.[14,15] Furthermore, chronic pain can induce changes in neuromuscular function, resulting in diminished motor control and coordination, which subsequently reduces muscle efficiency and HGS.[37] Psychological factors like depression and anxiety, often seen in chronic pain patients, can impact HGS. Depression is linked to decreased physical activity and muscle strength, including HGS, in older adults. This connection might be two-way, as lower HGS can also increase the risk of depression.[38,39]

Mediation analyses revealed that HGS partially mediated the association between pain and MCR. Following comprehensive adjustment for covariates, each 1-unit elevation in HGS corresponded to a 9% decline in MCR (OR=0.91, 95% CI: 0.88–0.93; p < 0.001), underscoring an inverse relationship between HGS and MCR. Extensive empirical evidence suggests that HGS may serve as a robust predictor of MCR. Muscle weakness as indicated by reduced HGS may lead to decreased physical activity and exacerbate cognitive decline through decreased cerebral blood flow and neuroplasticity.[40] In addition, lower HGS is linked to higher cardiovascular risk markers like hypertension and inflammation, which can reduce cerebral perfusion and increase the risk of cerebrovascular events, potentially leading to cognitive decline and MCR.[41] Furthermore, HGS is linked to brain structure and function, with stronger HGS correlating to more grey matter in cognitive areas like the temporal cortices. This may indicate better neural health and cognitive reserve, possibly guarding against MCR.[22]

Our study has several strengths. Firstly, the analysis leverages a prospective, nationally representative cohort dataset from China, strengthening the validity and broader applicability of the findings. Secondly, this investigation represents the inaugural effort to systematically examine the relationships between pain, HGS, and MCR within middle-aged and older populations. Finally, the potential mediator HGS was evaluated, which further supports the mechanistic framework and provides a strong rationale for preventing and improving MCR. Concurrently, this study acknowledges several limitations. Firstly, the study's focus on middle-aged and older adults within the cultural and demographic setting of China constrains the extrapolation of results to younger demographics or other ethnicities/cultural contexts. Secondly, the cross-sectional survey design inherently restricts causal inference, as temporal sequencing between exposures (eg, pain, HGS) and MCR outcomes cannot be established, leaving mechanistic pathways unresolved. The association between pain, HGS, and MCR remains contentious, and it is not feasible to ascertain whether a bidirectional relationship exists among these variables. Thirdly, unmeasured confounders (eg, dementia, chronic inflammation, and physical activity) may have biased the association and influenced the magnitude of the mediating proportion. Lastly, the dependence on self-reported questionnaires for MCR (cognitive complaints) introduces the potential for information bias in our results. The operationalization of subjective cognitive complaints was based on a single-item question, which cannot distinguish between stable low memory perception and genuine subjective cognitive decline reflecting progressive deterioration. It may misclassify individuals with lifelong lower memory confidence as having memory impairment.

Conclusion

The study revealed a significant positive association between pain and MCR and a significant negative association between HGS and MCR. Mediation analysis identified HGS as a partial mediator in the pathway linking pain and MCR. These findings hold critical implications for healthcare policy and public health interventions targeting the enhancement of well-being among aging populations vulnerable to MCR and dementia.

Data Sharing Statement

This study analyzed publicly available datasets found at http://charls.pku.edu.cn/en.

Ethics Approval and Consent to Participate

The Ethics committee of Bengbu Medical University follows the Declaration of Helsinki and the international ethical standards for human health research, and performs the responsibility of independent ethical assessment. This study used publicly accessible data that were legally obtained and met the criteria for exemption from review outlined in the Ethical Review Protocol for Life Science and Medical Research Involving Human Subjects.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have declared that they have no conflicts of interest.

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