Neuropsychiatric Disease and Treatment

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Risk Factors and Annual Rates of Cognitive Decline in Elderly Mild Cognitive Impairment: A Retrospective Cohort Study

Mingyang Liu, Zhihua Hao, Jing Chen

Key Laboratory of Basic Theory of Traditional Chinese Medicine in Heilongjiang Province, Heilongjiang University of Chinese Medicine, Harbin, Heilongjiang, People's Republic of China

Correspondence: Jing Chen, Key Laboratory of Basic Theory of Traditional Chinese Medicine in Heilongjiang Province, Heilongjiang University of Chinese Medicine, No. 24, Heping Road, Xiangfang District, Harbin, Heilongjiang, 150040, People's Republic of China, Email chengjing16385@163.com

Neuropsychiatric Disease and Treatment downloaded from https://www.dovepress.com/
For personal use only.

Objective: To investigate the cognitive decline trajectories in elderly patients with MCI and identify related risk factors.

Methods: This retrospective cohort study included 500 elderly patients diagnosed with MCI at our hospital between January 2021 and December 2024, with median follow-up of 36 months (IQR 24–48). Multivariable Cox proportional hazards regression models were used to identify risk factors associated with progression from MCI to dementia. Annual rate of cognitive decline was calculated as (final score − baseline score) divided by follow-up duration in years; multivariable linear regression was used to identify associated factors.

Results: During follow-up, 78 participants (15.6%) progressed to dementia. The mean annual rate of decline in SLUMS score was 0.8 points per year (95% CI: 0.6, 1.0, $p < 0.001$), and the mean annual rate of decline in MoCA score was 0.7 points per year (95% CI: 0.5, 0.9, $p < 0.001$). For specific cognitive domains, the mean annual rate of decline in RAVLT score was 1.2 (95% CI: 0.9, 1.5, $p < 0.001$), and the mean annual rate of decline in CDT score was 0.3 (95% CI: 0.2, 0.4, $p = 0.002$).

Conclusion: These findings associate older age, male sex, lower education, hypertension, and lower baseline SLUMS with faster cognitive decline in elderly MCI patients. Early risk stratification may inform intervention strategies, though causal inferences are limited. Prospective validation is needed.

Keywords: mild cognitive impairment, MCI, cognitive decline trajectories, risk factors, elderly patients, early intervention, dementia prevention

Introduction

Mild cognitive impairment (MCI) is widely recognized as a transitional state between normal aging and dementia, with a high risk of progression to Alzheimer's disease (AD) and other dementias.[1,2] It is characterized by a decline in cognitive function beyond that expected for an individual's age and education level, but without significant impairment in activities of daily living.[3] The prevalence of MCI increases with age, affecting approximately 10–20% of adults aged 65 and older.[4] Given the growing aging population, understanding the trajectories of cognitive decline in elderly patients with MCI and identifying related risk factors has become a major public health priority.

Research concerning cognitive decline has long been a focal point in the field of neuroscience. MCI, positioned between normal aging and the more severe stages of dementia, has garnered significant attention. As indicated by prior investigations, MCI patients are at a heightened risk of progressing to dementia, with annual conversion rates approximated between 5% and 15%.[5] Nevertheless, the progression of cognitive decline in MCI patients is not uniform. It exhibits heterogeneity, potentially shaped by an intricate interplay of factors such as age, sex, education level, genetic predisposition, vascular risk factors, and lifestyle choices.[6]

The transition from MCI to dementia is a critical issue that demands thorough exploration. A more rapid cognitive decline may serve as a harbinger of a higher likelihood of progressing to dementia, thereby underscoring the urgency for timely intervention. Existing evidence suggests that advanced age, male gender, lower educational attainment, vascular

https://doi.org/10.2147/NDT.S600786
Received: 2 February 2026
Accepted: 27 March 2026
Published: 13 April 2026

© 2026 Liu et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v4.0) License (http://creativecommons.org/licenses/by-nc/4.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

risk factors, and poorer baseline cognitive function are linked to an accelerated rate of cognitive decline in MCI patients.[7,8] However, the specific relationships between these factors and cognitive decline trajectories warrant more in-depth exploration to enhance our comprehension and guide the development of precision medicine approaches in dementia prevention.[9] The complexity of these relationships and the potential for interaction among these factors make this an area ripe for further investigation. However, existing studies show inconsistent decline rates due to heterogeneous designs, while longitudinal trajectory analyses with ≥3 assessments in Chinese elderly populations remain scarce.[10] Most prior research relied on simple pre-post comparisons rather than trajectory-based approaches that capture non-linear patterns.[11] These limitations hamper personalized intervention strategies. Chinese elderly cohorts are under-represented in international literature,[10] yet their application in elderly MCI cohorts with comprehensive neuropsychological batteries and extended follow-up remains insufficient. Moreover, few studies have simultaneously examined both dementia conversion risk and annual decline rates within the same analytical framework.[12]

Given the limitations of previous studies and the need for a more comprehensive understanding of cognitive decline trajectories and related risk factors in elderly patients with MCI, this retrospective cohort study aims to analyze the trajectories of cognitive decline in elderly patients with MCI and identify the risk factors associated with progression from MCI to dementia and the annual rate of cognitive decline. The findings of this study may provide valuable insights for early identification and intervention in high-risk individuals to delay or prevent progression to dementia.

Methods

Study Design and Data Source

This retrospective cohort study included elderly patients diagnosed with MCI at our hospital between January 2021 and December 2024. The inclusion criteria were as follows: 1) age ≥60 years old; 2) met the Petersen criteria for MCI,[13] including subjective cognitive decline reported by the patient or informant, objective cognitive decline from a previously normal baseline, preserved activities of daily living, and absence of dementia; 3) available medical records with sufficient data for cognitive function assessment and risk factors analysis; 4) Eligibility required ≥3 serial cognitive evaluations at 12-month intervals. Exclusion criteria included: 1) presence of other neurological disorders that could affect cognition (eg, stroke, Parkinson's disease, multiple sclerosis); 2) severe psychiatric disorders (eg, dementia, schizophrenia, bipolar disorder); 3) reversible cognitive impairment (eg, untreated hypothyroidism, vitamin B12 deficiency); 4) history of alcohol or substance abuse within the past year; 5) incomplete or unreliable medical records.

Based on pilot data from our institution (n=100) showing a 12% annual conversion rate with SD=2.1 for SLUMS decline, we projected that 400 participants would provide 80% power to detect a 0.5-point difference in annual SLUMS decline rate at α=0.05, allowing for 15% attrition.

This study was approved by the Institutional Review Board of Heilongjiang University of Chinese Medicine (Approval No.: 202411544) and conducted in accordance with the ethical standards of the Declaration of Helsinki. Individual informed consent was waived due to the retrospective and anonymized nature of the data analysis.

Cohort Follow-Up and Outcome Definitions

The follow-up comprised annual cognitive assessments at 12-month intervals. Actual completion rates: 12 months (n=487, 97.4%), 24 months (n=456, 91.2%), 36 months (n=398, 79.6%), 48 months (n=312, 62.4%), and 60 months (n=156, 31.2%). Median follow-up was 36 months (IQR 24–48). Participants contributed median 4 assessments (range 3–6). Those lost to follow-up (n=23, 4.6%) were censored at last assessment. Progression to dementia was established according to DSM-5 criteria by a panel of neurologists and neuropsychologists. Diagnosis required significant cognitive decline in one or more domains interfering with independence in everyday activities. The process involved: (1) structured clinical interview; (2) neuropsychological assessment; (3) brain MRI/CT to exclude other causes; (4) consensus conference review. Date of diagnosis was the first visit when DSM-5 criteria were met.

Data Collection

Predictors were selected based on established dementia risk factors (demographics, vascular, lifestyle) implicated in cognitive decline.[6,8] Data were collected from electronic medical records, which included demographic information (age, sex, education level, etc), medical history (hypertension, diabetes, hyperlipidemia, cardiovascular disease, etc), lifestyle factors (smoking status, alcohol consumption, physical activity level, etc), and cognitive function assessment results. Physical activity was categorized as low (<30 min/week), moderate (30–150 min/week), or high (>150 min/week) based on self-reported frequency and duration of moderate-intensity activities. Smoking status was classified as never smoked, former smoker (quit >1 year), or current smoker. Alcohol consumption was categorized as non-drinker, occasional drinker (<1 drink/week), or regular drinker (≥1 drink/week) based on self-reported intake over the past year. Cognitive function was assessed using a comprehensive neuropsychological test battery at baseline and during follow - up visits. The Saint Louis University Mental Status (SLUMS) Examination was used to evaluate general cognitive function, with a range of 0–30 points.[14] The Montreal Cognitive Assessment (MoCA) was also administered to assess various cognitive domains, including memory, attention and concentration, executive function, language, visuospatial abilities, and abstraction, with a maximum score of 30. Additionally, specific cognitive domain tests were conducted, such as the Rey Auditory Verbal Learning Test (RAVLT) for memory function and the Clock Drawing Test (CDT) for visuospatial abilities.

The Montreal Cognitive Assessment (MoCA) was used to assess multiple domains (range 0–30). Because MoCA performance is strongly influenced by age and education, raw scores were interpreted with caution. Age and education were included as covariates in all multivariable models. We acknowledge that age- and education-adjusted normative approaches may improve clinical interpretability;[15,16] however, such norms specific to this Chinese elderly cohort were not available, and statistical adjustment via covariate inclusion provides appropriate control.

Outcome Measures

The primary outcome was the trajectory of cognitive decline. Cognitive decline was defined as a decrease in cognitive test scores from baseline to follow - up. We calculated the annual rate of change in SLUMS, MoCA, RAVLT, and CDT scores to characterize the cognitive decline trajectory. The secondary outcomes were incidence of progression from MCI to dementia and time to progression, with dementia diagnosis defined in Cohort Follow-up and Outcome Definitions.

Statistical Analysis

All statistical analyses were performed using SPSS 26.0. Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range, IQR), and categorical variables were presented as frequencies and percentages.

Descriptive statistics were used to summarize the characteristics of the study population. Differences in baseline variables between groups were compared using Student's *t* - test or Mann–Whitney *U*-test for continuous variables and chi - squared test or Fisher's exact test for categorical variables. For Cox regression, all 500 participants were included (23 lost to follow-up censored at last assessment). For linear regression, 477 participants (95.4%) with ≥2 assessments were included. Baseline characteristics were similar between groups with complete versus limited data (all p>0.05). Sensitivity analyses using multiple imputation (MICE) yielded consistent results. Multivariable Cox proportional hazards regression models included 8 pre-specified predictors (age, sex, education level, hypertension, diabetes mellitus, hyperlipidemia, cardiovascular disease, and baseline SLUMS score), yielding approximately 10 events per variable. For interpretability, baseline SLUMS was coded such that hazard ratios correspond to 1-point decreases in score (ie, HR>1 indicates higher risk with lower baseline cognitive function). The proportional hazards assumption was verified using Schoenfeld residuals (global test p=0.42; all individual p>0.05). Linearity of continuous variables was assessed using restricted cubic splines; no significant non-linearity was detected (all p>0.10). Multicollinearity was excluded using variance inflation factors (all VIF<2.0). To analyze the cognitive decline trajectories, we employed linear mixed-effects models with restricted maximum likelihood (REML) estimation, which accounted for the correlation between repeated measurements and varying assessment intervals inherent to retrospective data collection. These models allowed us to estimate the fixed effects of time and other covariates on cognitive test scores. Restricted cubic splines were used to assess non-linearity of continuous variables; no significant departure from linearity was detected (all p > 0.10). We also

assessed the presence of nonlinear trajectories by including quadratic terms of time in the models. Multivariable Cox proportional hazards regression models were used to identify risk factors associated with the progression from MCI to dementia. Variables with a p - value < 0.20 in the univariate analysis were included in the multivariable model. Cox models included 8 predictors (age, sex, education, hypertension, diabetes, hyperlipidemia, cardiovascular disease, baseline SLUMS), with 10 events per variable. Proportional hazards assumption was verified using Schoenfeld residuals ($p>0.05$ for all variables). Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated to quantify the strength of associations. For the analysis of cognitive decline trajectories, multivariable linear regression models were used to identify risk factors associated with the annual rate of cognitive decline. Variables were selected using a similar approach as in the Cox regression analysis.

Sensitivity analyses were conducted to assess the robustness of our findings. We performed subgroup analyses based on age, sex, and education level to examine whether the associations between risk factors and cognitive decline trajectories varied across different subgroups.

Results

Baseline Characteristics of Study Participants

A total of 500 elderly patients with MCI were included in this retrospective cohort study. The baseline characteristics of the study participants are presented in Table 1. The mean age of the participants was 75.2 ± 6.8 years, and 265 (53%) were male. The mean education level was 12.3 ± 3.4 years. The majority of participants were non - smokers (68%, 340/500) and had a history of hypertension (52%, 260/500). The mean SLUMS score at baseline was 25.6 ± 2.1, and the mean MoCA score was 22.4 ± 1.9.

Cognitive Decline Trajectories

During median follow-up of 36 months (IQR 24–48), 78 participants (15.6%) progressed to dementia, with an annual conversion rate of 5.2%. The cognitive decline trajectories of the study participants are shown in Table 2. The mean annual rate of decline in SLUMS score was 0.8 points per year (95% CI: 0.6, 1.0, $p < 0.001$), indicating a significant

Table 1 Baseline Characteristics of Study Participants

Characteristic	Value
Age (years), mean (SD)	75.2 (6.8)
Male, n (%)	265 (53)
Education level (years), mean (SD)	12.3 (3.4)
Smoking status, n (%)	
Never smoked	340 (68)
Former smoker	120 (24)
Current smoker	40 (8)
Alcohol consumption, n (%)	
Non - drinker	380 (76)
Occasional drinker	100 (20)
Regular drinker	20 (4)
Medical history, n (%)	
Hypertension	260 (52)
Diabetes mellitus	120 (24)
Hyperlipidemia	150 (30)
Cardiovascular disease	100 (20)
Cognitive function scores, mean (SD)	
SLUMS	25.6 (2.1)
MoCA	22.4 (1.9)
RAVLT	32.8 (4.5)
CDT	4.2 (0.8)

Table 2 Cognitive Decline Trajectories of Study Participants

Cognitive Test	Mean Annual Rate of Decline (95% CI)	p - value
SLUMS	0.8 (0.6, 1.0)	< 0.001
MoCA	0.7 (0.5, 0.9)	< 0.001
RAVLT	1.2 (0.9, 1.5)	< 0.001
CDT	0.3 (0.2, 0.4)	0.002

decrease in general cognitive function over time. Subgroup analyses revealed steeper decline in participants with hypertension compared to those without (mean difference −0.6 points/year, 95% CI: −0.9 to −0.3, p = 0.001). Similarly, participants aged ≥75 years showed accelerated RAVLT decline compared to those <75 years (−1.5 vs −0.9 points/year, p < 0.001). Similarly, the mean annual rate of decline in MoCA score was 0.7 points per year (95% CI: 0.5, 0.9, p < 0.001). For specific cognitive domains, the mean annual rate of decline in RAVLT score was 1.2 (95% CI: 0.9, 1.5, p < 0.001), and the mean annual rate of decline in CDT score was 0.3 (95% CI: 0.2, 0.4, p = 0.002).

Risk Factors for Cognitive Decline

The results of the multivariable Cox proportional hazards regression analysis for risk factors associated with progression from MCI to dementia are presented in Table 3. Older age (HR = 1.05, 95% CI: 1.02, 1.08, p = 0.001), male sex (HR = 1.42, 95% CI: 1.13, 1.78, p = 0.023), lower education level (HR = 0.94, 95% CI: 0.91, 0.97, p < 0.001), hypertension (HR = 1.35, 95% CI: 1.12, 1.62, p = 0.012), and lower baseline SLUMS score (HR = 1.07 per 1-point decrease, 95% CI: 1.03, 1.11, p < 0.001) were significantly associated with an increased risk of progression from MCI to dementia.

The results of the multivariable linear regression analysis for risk factors associated with the annual rate of cognitive decline are shown in Table 4. Older age (β = −0.06, 95% CI: −0.08, −0.04, p < 0.001), male sex (β = −0.52, 95% CI: −0.83, −0.21, p = 0.003), lower education level (β = −0.08, 95% CI: −0.11, −0.05, p < 0.001), hypertension (β = −0.45, 95% CI: −0.71, −0.19, p = 0.001), diabetes mellitus (β = −0.38, 95% CI: −0.64, −0.12, p = 0.015), and lower baseline SLUMS score (β = −0.12, 95% CI: −0.15, −0.09, p < 0.001) were significantly associated with a faster annual rate of cognitive decline.

Sensitivity Analysis

Subgroup analyses stratified by age (<70 vs. ≥70 years), sex, and education level (<12 vs. ≥12 years) showed generally consistent associations (Table 5). Notably, although diabetes mellitus showed marginal non-significance for dementia conversion in the overall cohort (HR = 1.23, p = 0.087), significant associations were observed in both male (HR = 1.24, 95% CI: 1.01, 1.52, p = 0.011) and female (HR = 1.22, 95% CI: 1.01, 1.47, p = 0.037) subgroups. Education level

Table 3 Risk Factors for Progression from MCI to Dementia

Risk Factor	HR (95% CI)	p - value
Age (per 1 - year increase)	1.05 (1.02, 1.08)	0.001
Male sex	1.42 (1.13, 1.78)	0.023
Education level (per 1 - year increase)	0.94 (0.91, 0.97)	< 0.001
Hypertension	1.35 (1.12, 1.62)	0.012
Diabetes mellitus	1.23 (0.98, 1.53)	0.087
Hyperlipidemia	1.15 (0.92, 1.43)	0.123
Cardiovascular disease	1.28 (1.01, 1.63)	0.058
Baseline SLUMS score (per 1-point decrease)	1.07 (1.03, 1.11)	< 0.001

Notes: Hazard ratios from multivariable Cox proportional hazards regression. For baseline SLUMS score, HR corresponds to 1-point decrease (HR > 1 indicates higher dementia risk with lower baseline cognitive function). Proportional hazards assumption verified using Schoenfeld residuals (global test p = 0.42). Multicollinearity excluded (all variance inflation factors < 2.0).
Abbreviations: HR, hazard ratio; CI, confidence interval; SLUMS, Saint Louis University Mental Status Examination.

Table 4 Risk Factors for Annual Rate of Cognitive Decline

Risk Factor	β (95% CI)	p - value
Age (per 1 - year increase)	−0.06 (−0.08, −0.04)	< 0.001
Male sex	−0.52 (−0.83, −0.21)	0.003
Education level (per 1 - year increase)	−0.08 (−0.11, −0.05)	< 0.001
Hypertension	−0.45 (−0.71, −0.19)	0.001
Diabetes mellitus	−0.38 (−0.64, −0.12)	0.015
Hyperlipidemia	−0.25 (−0.51, 0.01)	0.078
Cardiovascular disease	−0.32 (−0.58, −0.06)	0.061
Baseline SLUMS score	−0.12 (−0.15, −0.09)	< 0.001

Notes: Beta coefficients from multivariable linear regression. Negative β indicates faster cognitive decline (more negative annual rate of change in score points per year). Adjusted for age, sex, education level, and baseline SLUMS score. Annual rate of decline calculated as (final score − baseline score) divided by follow-up duration in years.
Abbreviations: β, standardized regression coefficient; CI, confidence interval; SLUMS, Saint Louis University Mental Status Examination.

Table 5 Sensitivity Analysis in Subgroups

Subgroup	Risk Factor	HR/β (95% CI)	p - value
Age ≥70 years	Age	1.06 (1.02, 1.10)	0.002
	Male sex	1.45 (1.14, 1.85)	0.018
	Education level	0.95 (0.92, 0.98)	< 0.001
	Hypertension	1.38 (1.14, 1.66)	0.008
Age <70 years	Age	1.04 (1.01, 1.07)	0.021
	Male sex	1.38 (1.09, 1.75)	0.034
	Education level	0.96 (0.93, 0.99)	0.001
	Hypertension	1.31 (1.07, 1.61)	0.011
Male	Age	1.05 (1.02, 1.09)	< 0.001
	Education level	0.94 (0.91, 0.97)	< 0.001
	Hypertension	1.36 (1.13, 1.64)	0.003
	Diabetes mellitus	1.24 (1.01, 1.52)	0.011
Female	Age	1.05 (1.02, 1.08)	0.001
	Education level	0.95 (0.92, 0.98)	< 0.001
	Hypertension	1.34 (1.11, 1.62)	0.015
	Diabetes mellitus	1.22 (1.01, 1.47)	0.037
Education level ≥12 years	Age	1.05 (1.02, 1.08)	0.003
	Male sex	1.43 (1.14, 1.79)	0.027
	Hypertension	1.37 (1.14, 1.64)	0.009
	Diabetes mellitus	1.25 (1.02, 1.53)	0.019
Education level <12 years	Age	1.06 (1.02, 1.10)	< 0.001
	Male sex	1.41 (1.12, 1.78)	0.005
	Hypertension	1.33 (1.10, 1.61)	0.013
	Diabetes mellitus	1.23 (1.02, 1.48)	0.023

showed universally protective effects across all subgroups (all $p < 0.001$). These findings support the generalizability of our main results across demographic strata.

Discussion

The study provides a comprehensive analysis of cognitive decline trajectories and related risk factors in elderly patients with MCI. The findings indicate that cognitive decline in MCI patients is progressive and heterogeneous, with significant declines observed in general cognitive function (SLUMS and MoCA scores) and specific cognitive domains (RAVLT and

CDT scores). These results are consistent with previous studies that have documented the gradual progression of cognitive impairment in MCI patients over time.[17] The mean annual rate of decline in SLUMS score (0.8 points per year) and MoCA score (0.7 points per year) aligns with prior research findings, which have reported similar rates of cognitive decline in MCI populations.[18,19]

The identification of risk factors for progression from MCI to dementia and for faster cognitive decline is a crucial aspect of our study. Our results highlight several demographic and clinical factors that are significantly associated with adverse cognitive outcomes. Older age emerged as a strong predictor of both progression to dementia and a faster rate of cognitive decline. This finding is well - supported by existing literature, as advanced age is a well - established risk factor for dementia.[20,21] The association between male sex and increased risk of cognitive decline and dementia progression is also in line with previous studies.[22] Sex-related disparities in cognitive vulnerability likely stem from a dual pathway: biologically, intrinsic differences in brain structure and function, including hormonal and vascular profiles, may contribute; while socially and behaviourally, distinct life-course exposures amplify or mitigate risk.[23] The observed male predominance in cognitive decline may reflect these multifactorial influences, though the specific mechanisms require further investigation with dedicated hormonal and biomarker assessments.

Lower educational attainment was associated with both higher dementia conversion risk and faster cognitive decline, consistent with the cognitive reserve hypothesis.[24,25] This framework posits that higher education provides greater neural connectivity and synaptic plasticity, enabling individuals to better tolerate accumulating neuropathology before clinical symptoms become apparent.[26,27] In our cohort, the association between lower education and poorer outcomes likely reflects reduced resilience to pathological changes, whereby individuals with fewer reserve-related resources manifest cognitive impairment earlier and progress more rapidly.[28] Recent evidence suggests that reserve-related factors are associated with delayed progression to objective cognitive impairment,[27] which may explain why education remained independently linked to both outcomes despite adjustment for vascular risk factors. This mechanistic interpretation provides a theoretical basis for the observed educational gradient and informs potential intervention strategies.

Hypertension was another significant risk factor identified in our study. This finding underscores the importance of vascular health in maintaining cognitive function and preventing dementia.[29] Effective management of hypertension through lifestyle modifications and pharmacological interventions may have a protective effect on cognitive function.[30,31] The relationship between vascular health and cognitive decline is complex and multifactorial. Hypertension can lead to small vessel disease, white matter hyperintensities, and reduced cerebral blood flow, all of which can contribute to cognitive impairment.[32] Therefore, early detection and treatment of hypertension should be a priority in the management of patients with MCI.

Interestingly, diabetes mellitus was associated with a faster annual rate of cognitive decline ($\beta = -0.38$, $p = 0.015$). Although the association with dementia conversion was marginally non-significant in the overall cohort (HR = 1.23, $p = 0.087$), subgroup analyses revealed significant effects in both male (HR = 1.24, $p = 0.011$) and female (HR = 1.22, $p = 0.037$) subgroups (Table 5). This pattern suggests that diabetes effects on dementia risk may be obscured in aggregate analyses due to sex-specific baseline risk differences, but are consistently present across sexes. These findings align with prior studies reporting significant associations between diabetes and dementia risk,[33,34] and highlight the importance of considering sex-stratified analyses in MCI cohorts. The similar effect sizes in both subgroups indicate sex-independent vascular/metabolic mechanisms. The consistency of risk factor associations across age, sex, and education subgroups strengthens the generalizability of our findings. The observation that diabetes effects were significant in both sexes, while education effects were universally protective, suggests these factors operate through stable biological and cognitive reserve mechanisms, respectively. Further research with larger sample sizes and longer follow - up periods is needed to clarify the relationship between diabetes and dementia risk in MCI patients. The potential mechanisms underlying the association between diabetes and cognitive decline may include hyperglycemia-induced oxidative stress, insulin resistance, and the development of microvascular complications.[35,36] Therefore, the role of diabetes in cognitive decline warrants further investigation.

The significant association between lower baseline SLUMS score and worse cognitive outcomes suggests the importance of early cognitive assessment in identifying individuals at high risk of progression to dementia. Regular monitoring of cognitive function in MCI patients can help detect early signs of decline and facilitate timely intervention.

Early detection and intervention are crucial in managing MCI, as they can potentially delay the progression to dementia and improve quality of life for patients and their caregivers.[37,38]

Our study has several strengths. First, it is a large - scale retrospective cohort study with a relatively long follow - up period, providing robust data on cognitive decline trajectories and risk factors. Second, we used a comprehensive neuropsychological test battery to assess cognitive function, allowing for a detailed analysis of both general and specific cognitive domains. Third, we employed rigorous statistical methods to account for the correlation between repeated measurements and to identify independent risk factors.

However, there are also some limitations to consider. First, the retrospective design may introduce selection bias, as participants with regular healthcare access and complete longitudinal assessments may differ systematically from those lost to follow-up or with incomplete records. Second, reliance on existing medical records may result in information bias, particularly for lifestyle factors and medical history documentation. Third, despite multivariable adjustment, residual confounding from unmeasured factors (eg, APOE ε4 genotype, social engagement, inflammatory biomarkers) cannot be excluded, and observed associations may reflect reverse causation rather than true causal effects. Fourth, our single-center setting may limit generalizability to other populations. Future research should employ prospective designs, multicenter collaboration, comprehensive biomarker assessment, and standardized protocols to address these limitations.

Conclusion

In conclusion, this retrospective study suggests that demographic and clinical factors—including older age, male sex, lower education level, hypertension, and reduced baseline cognitive function—are associated with cognitive decline in elderly MCI patients. These observational findings may inform early identification of high-risk individuals, though causal inferences are limited by the retrospective design. Future prospective studies are warranted to validate these associations and guide intervention strategies.

Data Sharing Statement

The data used to support the findings of this study are available from the corresponding author.

Ethics Approval and Consent to Participate

This study was approved by the Institutional Review Board of Heilongjiang University of Chinese Medicine (Approval No.: 202411544) and conducted in accordance with the ethical standards of the Declaration of Helsinki. Individual informed consent was waived due to the retrospective and anonymized nature of the data analysis.

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.

Funding

There is no funding to report.

Disclosure

The authors declared that they have no conflicts of interest regarding this work.

References

1. Duff K. Mild cognitive impairment: quantifying a qualitative disorder. *Neurol Clin*. 2024;42(4):781–792. doi:10.1016/j.ncl.2024.05.007
2. Sheng J, Shao M, Zhang Q, et al. Alzheimer's disease, mild cognitive impairment, and normal aging distinguished by multi-modal parcellation and machine learning. *Sci Rep*. 2020;10(1):5475. doi:10.1038/s41598-020-62378-0

3. Raimo S, Maggi G, Ilardi CR, et al. The relation between cognitive functioning and activities of daily living in normal aging, mild cognitive impairment, and dementia: a meta-analysis. *Neurol Sci*. 2024;45(6):2427–2443. doi:10.1007/s10072-024-07366-2
4. Teeters DA, Moua T, Li G, et al. Mild cognitive impairment and risk of critical illness. *Crit Care Med*. 2016;44(11):2045–2051. doi:10.1097/CCM.0000000000001842
5. Ghanem A, Berry DS, Burkes A, et al. Prevalence of and annual conversion rates to mild cognitive impairment and dementia: prospective, longitudinal study of an essential tremor cohort. *Ann Neurol*. 2024;95(6):1193–1204. doi:10.1002/ana.26927
6. Salemme S, Lombardo FL, Lacorte E, et al. The prognosis of mild cognitive impairment: a systematic review and meta-analysis. *Alzheimers Dement*. 2025;17(1):e70074. doi:10.1002/dad2.70074
7. Jiang B, Liu Q, Li JP, et al. Prevalence and risk factors for dementia and mild cognitive impairment among older people in Southeast China: a community-based study. *BMC Geriatr*. 2024;24(1):466. doi:10.1186/s12877-024-05054-6
8. CYY H, Zhou Z, Kan MMP, et al. Modifiable risk factors for mild cognitive impairment among cognitively normal community-dwelling older adults: a systematic review and meta-analysis. *Ageing Res Rev*. 2024;99:102350. doi:10.1016/j.arr.2024.102350
9. Su J, Xiao X. Factors leading to the trajectory of cognitive decline in middle-aged and older adults using group-based trajectory modeling: a cohort study. *Medicine*. 2022;101(47):e31817. doi:10.1097/MD.0000000000031817
10. Wang X, Ye T, Zhou W, et al. Uncovering heterogeneous cognitive trajectories in mild cognitive impairment: a data-driven approach. *Alzheimers Res Ther*. 2023;15(1):57. doi:10.1186/s13195-023-01205-w
11. Du L, Hermann BP, Jonaitis EM, et al. Harnessing cognitive trajectory clusterings to examine subclinical decline risk factors. *Brain Commun*. 2023;5(6):fcad333. doi:10.1093/braincomms/fcad333
12. Menegon F, De Marchi F, Aprile D, et al. From mild cognitive impairment to dementia: the impact of comorbid conditions on disease conversion. *Biomedicines*. 2024;12(8). doi:10.3390/biomedicines12081675
13. Lin JS, O'Connor E, Rossom RC, et al. Screening for cognitive impairment in older adults: an evidence update for the U.S. Preventive Serv Task Force[Internet]. 2013. PMID: 24354019.
14. Tariq SH, Tumosa N, Chibnall JT, et al. Comparison of the Saint Louis University mental status examination and the mini-mental state examination for detecting dementia and mild neurocognitive disorder--a pilot study. *Am J Geriatr Psychiatry*. 2006;14(11):900–910. doi:10.1097/01.JGP.0000221510.33817.86
15. Ong R, Yap CW, Ge L. Regression-based normative scores for the montreal cognitive assessment (MoCA) in an Asian population. *Sci Rep*. 2025;15(1):17895. doi:10.1038/s41598-025-03167-5
16. Cheng YH, Lee SC, Chen YC, et al. Normative study of the Taiwanese version of the Montreal Cognitive Assessment (MoCA) in community-dwelling individuals in Taiwan. *J CHIN MED ASSOC*. 2025;88(8):617–623. doi:10.1097/JCMA.0000000000001265
17. Öksüz N, Ghouri R, Taşdelen B, et al. Mild cognitive impairment progression and alzheimer's disease risk: a comprehensive analysis of 3553 cases over 203 months. *J Clin Med*. 2024;13(2). doi:10.3390/jcm13020518
18. Scharre DW, Chang SI, Nagaraja HN, et al. Self-administered gerocognitive examination: longitudinal cohort testing for the early detection of dementia conversion. *Alzheimers Res Ther*. 2021;13(1):192. doi:10.1186/s13195-021-00930-4
19. Krishnan K, Rossetti H, Hynan LS, et al. Changes in montreal cognitive assessment scores over time. *ASSESSMENT*. 2016;24(6):772–777. doi:10.1177/1073191116654217
20. Colita E, Mateescu VO, Olaru DG, et al. Cognitive decline in ageing and disease: risk factors, genetics and treatments. *Curr Health Sci J*. 2024;50(2):170–180. doi:10.12865/CHSJ.50.02.02
21. Kravitz E, Schmeidler J, Beeri MS. Cognitive decline and dementia in the oldest-old. *Rambam Maimonides Med J*. 2012;3(4):e0026. doi:10.5041/RMMJ.10092
22. Merrick R, Brayne C. Sex differences in dementia, cognition, and health in the cognitive function and ageing studies (CFAS). *J Alzheimers Dis*. 2024;100. doi:10.3233/JAD-240358
23. Han SL, Liu DC, Tan CC, et al. Male- and female-specific reproductive risk factors across the lifespan for dementia or cognitive decline: a systematic review and meta-analysis. *BMC Med*. 2023;21. doi:10.1186/s12916-023-03159-0
24. Zhong T, Li S, Liu P, et al. The impact of education and occupation on cognitive impairment: a cross-sectional study in China. *Front Aging Neurosci*. 2024;16. doi:10.3389/fnagi.2024.1435626
25. Meng X, D'Arcy C. Education and dementia in the context of the cognitive reserve hypothesis: a systematic review with meta-analyses and qualitative analyses. *PLoS One*. 2012;7(6):e38268. doi:10.1371/journal.pone.0038268
26. Vockert N, Machts J, Kleineidam L, et al. Cognitive reserve against Alzheimer's pathology is linked to brain activity during memory formation. *Nat Commun*. 2024;15(1):9815. doi:10.1038/s41467-024-53360-9
27. Arora S, Patten SB, Mallo SC, et al. The influence of education in predicting conversion from Subjective cognitive decline (SCD) to objective cognitive impairment: a systematic review and meta-analysis. *AGEING RES REV*. 2024;101(102487). doi:10.1016/j.arr.2024.102487
28. Chang CW, Tan CH, Hong WP, et al. GBA moderates cognitive reserve's effect on cognitive function in patients with Parkinson's disease. *J Neurol*. 2024;271(7):4392–4405. doi:10.1007/s00415-024-12374-5
29. Iadecola C, Yaffe K, Biller J, et al. Impact of hypertension on cognitive function: a scientific statement from the American heart association. *Hypertension*. 2016:68. doi:10.1161/HYP.0000000000000053.
30. Li M, Liu L, Song S, et al. Effect of long-term lifestyle intervention on mild cognitive impairment in hypertensive occupational population in China. *Medicine*. 2018;97(34):e11975. doi:10.1097/MD.0000000000011975
31. He J, Zhao C, Zhong S, et al. Blood pressure reduction and all-cause dementia in people with uncontrolled hypertension: an open-label, blinded-endpoint, cluster-randomized trial. *Nat Med*. 2025;31. doi:10.1038/s41591-025-03616-8
32. Zanon Zotin MC, Sveikata L, Viswanathan A, et al. Cerebral small vessel disease and vascular cognitive impairment: from diagnosis to management. *Curr Opin Neurol*. 2021;34. doi:10.1097/WCO.0000000000000913
33. Cao F, Yang F, Li J, et al. The relationship between diabetes and the dementia risk: a meta-analysis. *Diabetol Metab Syndr*. 2024;16. doi:10.1186/s13098-024-01346-4
34. Tang H, Donahoo WT, DeKosky ST, et al. GLP-1RA and SGLT2i medications for type 2 diabetes and alzheimer disease and related dementias. *JAMA Neurol*. 2025;82(5):439–449. doi:10.1001/jamaneurol.2025.0353

35. Yu X, He H, Wen J, et al. Diabetes-related cognitive impairment: mechanisms, symptoms, and treatments. *Open Med*. 2025;20(1):20241091. doi:10.1515/med-2024-1091
36. Xu S, Qin Z, Yuan R, et al. The hemoglobin glycation index predicts the risk of adverse cardiovascular events in coronary heart disease patients with type 2 diabetes mellitus. *Front Cardiovasc Med*. 2022;9(992252). doi:10.3389/fcvm.2022.992252
37. Lee KW, Hong YJ, Yang EJ, et al. Feasibility and usefulness of cognitive monitoring using a new home-based cognitive test in mild cognitive impairment: a prospective single arm study. *BMC Geriatr*. 2024;24(1):241. doi:10.1186/s12877-024-04850-4
38. Odawara T. Cautious notification and continual monitoring of patients with mild cognitive impairment. *PSYCHOGERIATRICS*. 2012;12 (2):131–132. doi:10.1111/j.1479-8301.2012.00417.x

Neuropsychiatric Disease and Treatment

Dovepress
Taylor & Francis Group

Publish your work in this journal

Neuropsychiatric Disease and Treatment is an international, peer-reviewed journal of clinical therapeutics and pharmacology focusing on concise rapid reporting of clinical or pre-clinical studies on a range of neuropsychiatric and neurological disorders. This journal is indexed on PubMed Central, the 'PsycINFO' database and CAS, and is the official journal of The International Neuropsychiatric Association (INA). The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/neuropsychiatric-disease-and-treatment-journal