Analysis of Current Status and Influencing Factors of Elderly Type 2 Diabetes with Mild Cognitive Impairment from a Somatic-Disease Association Perspective: A Sichuan Region Study (Postprint)

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Abstract

Background The high incidence of type 2 diabetes mellitus in older adults has become a severe global public health problem. Diabetes causes substantial damage to cognitive function, and there is currently a lack of simple indicators for its early monitoring and identification, necessitating further exploration and investigation. Based on real-world cross-sectional data analysis, this study examines the disease from a "body-disease correlation" perspective, which holds certain reference value for clinical diagnosis and treatment.

Objective Taking the Sichuan region as an example, to investigate the current status of mild cognitive impairment in elderly patients with type 2 diabetes mellitus and its influencing factors.

Methods From November 2021 to November 2023, elderly patients with type 2 diabetes mellitus aged $ $60 years were selected from multiple communities and 3 nursing homes in 6 cities of Sichuan Province (Chengdu, Deyang, Bazhong, Emeishan, Meishan, and Mianyang) for investigation. Face-to-face surveys were conducted using paper questionnaires, which included basic information, the Changsha version of the Montreal Cognitive Assessment (MoCA), and Traditional Chinese Medicine (TCM) constitution assessment. Univariate analysis combined with multivariate Logistic regression analysis was employed to explore possible independent influencing factors of type 2 diabetes mellitus with mild cognitive impairment.

Results A total of 407 questionnaires were distributed, and 397 valid questionnaires were collected, with an effective recovery rate of 97.54%. The 397 study

subjects included 351 (88.4%) community-dwelling elderly and 46 (11.6%) nursing home elderly; there were 84 patients with mild cognitive impairment, yielding a prevalence rate of type 2 diabetes mellitus with mild cognitive impairment of 21.2%. Based on the presence or absence of mild cognitive impairment, patients were divided into a type 2 diabetes mellitus with mild cognitive impairment group (n=84) and a type 2 diabetes mellitus without mild cognitive impairment group (n=313). Comparisons between the two groups in terms of education level, depression, reading/newspaper reading, Qi deficiency constitution, Yang deficiency constitution, Phlegm-dampness constitution, and Damp-heat constitution showed statistically significant differences (P<0.05). Multivariate Logistic regression analysis results indicated that low education level (junior high school: OR=0.487, 95%CI=0.253~0.939; university and above: OR=0.149, 95%CI=0.034~0.659) and Yang deficiency constitution (OR=2.284, 95%CI=1.220~4.279) were independent influencing factors for mild cognitive impairment in elderly patients with type 2 diabetes mellitus (P<0.05). At the biased constitution level, Yang deficiency constitution scores were negatively correlated with delayed memory cognitive domain scores (r=-0.106, P<0.05).

Conclusion The prevalence of mild cognitive impairment among elderly patients with type 2 diabetes mellitus in Sichuan Province is 21.2%, and low education level and Yang deficiency constitution represent high-risk populations for developing mild cognitive impairment. Based on the TCM theory of "constitution can be classified-body-disease correlation-constitution can be adjusted," early intervention for individuals with Yang deficiency may help reduce the progression to diabetes-related cognitive impairment.

Full Text

Preamble

Study on the Current Status and Influencing Factors of Mild Cognitive Impairment in Elderly Patients with Type 2 Diabetes Mellitus from the Perspective of "Physical Disease-Related Adjustable Constitution": A Case Study in Sichuan Province

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Abstract Background The global rise in the prevalence of type 2 diabetes mellitus (T2DM) among the elderly has emerged as a significant public health concern. T2DM is known to exert detrimental effects on cognitive function.

However, there remains a lack of simple and effective indicators for the early detection and monitoring of this condition, highlighting an urgent need for further investigation. The present study utilizes real-world cross-sectional data to explore the disease from the perspective of "physical disease-related adjustable constitution," offering potential clinical value for diagnosis and treatment. **Objective** To investigate the prevalence of T2DM with mild cognitive impairment (MCI) among the elderly in the Sichuan region and to identify factors influencing its occurrence. **Methods** Elderly patients aged 60 years with T2DM were selected for a survey conducted from November 2021 to November 2023. Participants were recruited from various communities and three nursing homes across six cities in Sichuan Province: Chengdu, Deyang, Bazhong, Emeishan, Meishan, and Mianyang. Face-to-face surveys were administered using paper-based questionnaires that collected basic demographic information, the Changsha version of the Montreal Cognitive Assessment (MoCA), and Traditional Chinese Medicine (TCM) constitution assessments. Univariate analysis followed by multivariate logistic regression was performed to identify potential independent factors influencing T2DM with MCI. **Results** A total of 407 questionnaires were distributed, of which 397 were valid (effective response rate: 97.54%). Among the 397 participants, 351 (88.4%) were community-dwelling elderly and 46 (11.6%) were from nursing homes. Eighty-four participants were identified with MCI, yielding a prevalence of 21.2% for T2DM with MCI. Based on cognitive status, participants were divided into two groups: T2DM with MCI (n=84) and T2DM without MCI (n=313). Statistically significant differences between the groups were observed in education level, depression, reading habits, and TCM constitution types including qi deficiency, yang deficiency, phlegm-dampness, and damp-heat ($P < 0.05$). Multivariate logistic regression analysis identified lower educational attainment (junior high school: OR=0.487, 95%CI=0.253-0.939; university and above: OR=0.149, 95%CI=0.034-0.659) and yang deficiency constitution (OR=2.284, 95%CI=1.220-4.279) as independent risk factors for MCI in elderly T2DM patients ($P < 0.05$). Additionally, within the unbalanced TCM constitution subgroup, the yang deficiency constitution score was negatively correlated with the delayed memory domain score ($r = -0.106, P < 0.05$). **Conclusion** The prevalence of MCI among elderly T2DM patients in Sichuan Province is 21.2%. Low educational attainment and yang deficiency constitution represent significant risk factors for MCI development in this population. In line with the TCM theory that "constitution can be differentiated, constitution is disease-related, and constitution can be adjusted," early identification and targeted intervention for yang deficiency constitution may help mitigate the progression of cognitive impairment in diabetic patients.

[**Key words**] Type 2 diabetes mellitus; Mild cognitive impairment; Aged; Root cause analysis; TCM constitutions

Introduction

Type 2 diabetes mellitus (T2DM) is a systemic disease characterized by glucolipid metabolism disorders that affects multiple organs throughout the body[1]. The disease carries an extremely high incidence rate. According to the International Diabetes Federation (IDF), the global prevalence of diabetes has reached 10.5%, with projections indicating that the total number of affected individuals will rise to 783 million by 2045[2]. In China, the diabetic population continues to grow substantially, and the complications affecting various organ systems due to hyperglycemia present an increasingly serious public health challenge. T2DM with concurrent mild cognitive impairment (MCI) is considered an early stage of dementia, clinically manifested by diminished memory, learning ability, and executive function. Research has demonstrated that both elevated glucose levels and prolonged disease duration are risk factors for cognitive impairment[3]. Moreover, the probability of MCI in T2DM patients over 65 years old is 1.4 times higher than in non-diabetic populations, with the former being more susceptible to progression to Alzheimer's disease . These findings underscore that clinical management of T2DM should extend beyond glycemic control to encompass the prevention and management of complications, thereby improving quality of life and reducing societal burden.

Currently, the pathogenic mechanisms underlying the progression from T2DM to cognitive impairment remain incompletely understood from a Western medical perspective, and even fewer studies have elucidated this process using TCM metrics. TCM theory posits that unbalanced constitutions are strongly associated with the development and progression of chronic diseases, and constitution identification facilitates early disease recognition and prevention, making it a widely adopted monitoring approach. Using elderly populations from select regions of Sichuan as an example, this study explores the current status and unbalanced constitution characteristics of T2DM patients with MCI, aiming to identify valuable and easily monitorable indicators for clinical prevention and treatment.

Methods

Study Design and Participants

This cross-sectional survey was conducted from November 2021 to November 2023. Elderly T2DM patients aged 60 years were recruited from multiple communities and three nursing homes across six cities in Sichuan Province: Chengdu, Deyang, Bazhong, Emeishan, Meishan, and Mianyang. Sample size was estimated using the formula $n = \mu^2_{\alpha/2}\pi(1-\pi)/\delta^2$ for population proportion estimation , with a test level of $\alpha = 0.05$ ($\mu_{\alpha/2} = 1.96$), allowable error $\delta = 0.05$, yielding a calculated sample size of 340. Considering a 10% attrition rate, the minimum required sample size was determined to be 378; this

study ultimately included 397 participants. The study protocol was approved by the Medical Ethics Committee of Chengdu University of Traditional Chinese Medicine (Ethics No.: 2021KL-055).

Inclusion Criteria Participants were included if they met the diagnostic criteria for diabetes outlined in the *Chinese Guidelines for the Prevention and Treatment of Type 2 Diabetes Mellitus* (2017 edition) , specifically: typical diabetes symptoms (polydipsia, polyuria, polyphagia, and unexplained weight loss) plus random blood glucose $\geq$ 11.1 mmol/L or fasting blood glucose $\geq$ 7.0 mmol/L; age $\geq$ 60 years; residence in Sichuan Province for $\geq$ 10 years; clear consciousness and ability to cooperate; and provision of informed consent.

Exclusion Criteria Patients were excluded if they had severe impairments in speech, vision, or hearing that prevented verbal communication; had been diagnosed with dementia or severe mental disorders; had cognitive impairment due to other identifiable causes; or if they or their legal guardians refused participation.

Survey Methods

Face-to-face surveys were conducted using paper-based questionnaires with one-on-one assistance from trained researchers. The questionnaire comprised three components: basic demographic information, the Changsha version of the Montreal Cognitive Assessment (MoCA), and TCM constitution assessment.

Basic Data Collection Basic data collection encompassed: (1) Sociodemographic characteristics including age, gender, education level, living situation, whether living alone, and number of close friends available for support; (2) Lifestyle factors including alcohol consumption history, smoking history, smartphone usage habits, Pittsburgh Sleep Quality Index (PSQI) scores (comprising 7 items: sleep quality, duration, efficiency, latency, disturbances, medication use, and daytime dysfunction, each scored 0-3 points for a total of 21 points, with 0-5 indicating good sleep, 6-10 fair, and $\geq$ 11 poor), recreational activities, reading habits, and physical exercise; (3) Health status including diabetes duration, diabetes medication use, hearing and vision status, BMI ($<$ 18.5 kg/m^2=underweight; 18.5-23.9 kg/m^2=normal; 24.0-27.9 kg/m^2=overweight; $>$ 28.0 kg/m^2=obese), Barthel Index (BI) scores (comprising 10 items: feeding, grooming, dressing, bathing, bowel and bladder control, toilet use, ambulation, stair climbing, and bed-chair transfer; total score 0-100, with higher scores indicating better daily functioning: 100=no dependence; 75-95=mild dependence; 50-70=moderate dependence; $<$ 45=severe dependence), Instrumental Activities of Daily Living (IADL) scores[1] (comprising 8 items: telephone use, shopping, meal preparation, housekeeping, laundry, transportation, financial management, and medication management; higher scores indicate better functioning: 8=no dependence; 6-7=mild dependence; 3-5=moderate dependence; $<$ 3=severe dependence), Generalized Anxiety Disorder scale (GAD-7)

scores[11] (7 items, total 0-21 points, higher scores indicate greater anxiety: 0-4=no anxiety; 5-9=possible mild anxiety; 10-13=possible moderate anxiety; $\geq$ 14=possible severe anxiety), Patient Health Questionnaire-9 (PHQ-9) depression scores[11] (9 items, total 0-27 points, higher scores indicate greater depression: 0-4=no depression; 5-9=possible mild depression; 10-14=possible moderate depression; $\geq$ 15=possible severe depression), and number of chronic diseases.

Cognitive Assessment This study used the Changsha version of the MoCA to evaluate participants' cognitive function. The scale assesses seven cognitive domains: visuospatial/executive function, naming, memory, attention, language, abstract thinking, and delayed memory, with a total score of 30 points[12]. For participants with less than 12 years of education, the final score was increased by 1 point to correct for educational bias. This study used a cutoff score of 22 to identify cognitive impairment, with scores $\geq$ 22 considered normal and $<$ 22 indicating cognitive impairment, of which 18-21 points were classified as MCI[13 1] .

TCM Constitution Assessment According to the *Classification and Determination of TCM Constitution* standards, constitutions are classified into nine types: balanced constitution, qi deficiency constitution, phlegm-dampness constitution, yang deficiency constitution, yin deficiency constitution, damp-heat constitution, blood stasis constitution, and special constitution[1] . This study utilized the *Elderly TCM Constitution Scale*[1] , with each question scored on a 5-point scale. Constitution determination followed the highest score method. A score $\geq$ 11 on the items corresponding to any of the eight unbalanced constitution types was classified as that particular unbalanced constitution, except that a balanced constitution was determined if the balanced constitution score was $>$ 17 and all other eight constitution scores were $\leq$ 10.

Quality Control

All researchers underwent standardized training to ensure they could collect data and administer assessments correctly and understandably. Participants were thoroughly briefed on the survey purpose, precautions, and significance before questionnaire administration. All questionnaires were distributed, completed, and collected on-site. Data were double-entered and cross-checked. Participants with questionnaire data missingness $>$ 10% or those who withdrew mid-survey yielding suboptimal results were excluded.

Statistical Analysis

Data were analyzed using SPSS 26.0 statistical software. Continuous variables with normal or approximately normal distribution were expressed as ($\bar{x} \pm s$) and compared between groups using independent samples t-tests. Categorical variables were expressed as frequencies and percentages, with inter-group comparisons performed using χ^2 tests or Fisher's exact test. Pearson correlation

analysis was used to examine associations between different cognitive domains and yang deficiency constitution. Multivariate binary logistic regression analysis was employed to explore independent influencing factors for T2DM with MCI, with MCI status as the dependent variable (0=no MCI, 1=MCI). Forward conditional method was used for variable selection. Omnibus tests and Hosmer-Lemeshow tests were used for model fit assessment. $P < 0.05$ was considered statistically significant.

Results

Survey Response and Participant Characteristics

A total of 407 questionnaires were distributed, with 10 excluded due to improper completion, yielding 397 valid questionnaires (effective response rate: 97.54%). The 397 participants included 351 (88.4%) community-dwelling elderly and 46 (11.6%) nursing home residents; 154 (38.79%) were male and 243 (61.21%) female, with ages ranging from 60 to 101 years (mean age: 73.4 ± 0.4 years). Eighty-four participants were identified with MCI, resulting in a prevalence of 21.2% for T2DM with MCI. Based on MCI status, participants were divided into two groups: T2DM with MCI (n=84) and T2DM without MCI (n=313). The average MoCA score for all 397 elderly T2DM patients was (21.98 ± 0.26). Specifically, the T2DM without MCI group had an average MoCA score of (22.53 ± 5.77), while the T2DM with MCI group had an average score of (19.96 ± 1.01).

Univariate Analysis of MCI in Elderly T2DM Patients

Statistically significant differences between the two groups were observed in education level, depression, reading habits, qi deficiency constitution, yang deficiency constitution, phlegm-dampness constitution, and damp-heat constitution ($P < 0.05$). No significant differences were found between groups in age, gender, diabetes duration, diabetes medication use, living situation, living alone/cohabitation, social support, smartphone use, vision, hearing, BMI, BI, IADL, PSQI, GAD-7, PHQ-9, smoking, alcohol consumption, number of chronic diseases, recreational activities, physical exercise, yin deficiency constitution, blood stasis constitution, qi stagnation constitution, or special constitution ($P > 0.05$). Detailed results are presented in Table 1 .

Multivariate Logistic Regression Analysis of MCI Influencing Factors

Multivariate logistic regression analysis was performed with MCI status as the dependent variable (0=no MCI, 1=MCI) and variables showing significant differences in univariate analysis as independent variables. The results identified lower educational attainment and yang deficiency constitution as independent influencing factors for MCI in elderly T2DM patients ($P < 0.05$), suggesting that

lower education levels and yang deficiency constitution may confer higher risk for MCI. Specifically, compared to primary school education or below, junior high school education showed OR=0.487 (95%CI=0.253-0.939) and university education or above showed OR=0.149 (95%CI=0.034-0.659). Yang deficiency constitution demonstrated OR=2.284 (95%CI=1.220-4.279). The Hosmer-Lemeshow test yielded $\chi^2 = 1.142, P = 0.992$, indicating good model fit. Detailed results are presented in Table 2 .

Comparison of Cognitive Domain Scores Between Groups

Significant differences between groups were observed in five cognitive domains: naming, attention, language, abstract thinking, and delayed memory ($P < 0.05$). No significant differences were found in visuospatial/executive function or orientation domains ($P > 0.05$). Detailed results are presented in Table 3 .

Correlation Analysis Between Cognitive Domains and Yang Deficiency Constitution

Correlation analysis between cognitive domain scores and yang deficiency constitution scores revealed that all seven cognitive domains were intercorrelated ($P < 0.05$). Notably, yang deficiency constitution score was negatively correlated with delayed memory domain score ($r = -0.106, P < 0.05$). Detailed results are presented in Table 4 .

Discussion

Diabetes-related cognitive impairment severely affects patients' quality of life, and its pathogenic mechanisms remain incompletely understood. Current evidence suggests that insulin resistance, endoplasmic reticulum stress, neuronal calcium homeostasis imbalance, inflammatory stress responses, and mitochondrial energy imbalance are all implicated in the disease process[1] [1] . As a nation with a large diabetic population facing severe demographic aging, China must proactively address cognitive function in elderly diabetic groups. With no specific cure currently available for cognitive impairment, and given that progression to various degrees of dementia would impose enormous societal burden[2] , early identification and prevention are far more meaningful than treatment.

This study, based on data from multiple regions in Sichuan, determined that the prevalence of T2DM with MCI among elderly residents in parts of Sichuan is 21.2%. This finding aligns closely with a study showing a 21.9% prevalence among elderly communities in Wuhan, Hubei[21], but differs from other reports such as Ma et al.'s finding of 39.3% prevalence among community-dwelling elderly T2DM patients[22] and a 10.28% MCI prevalence among elderly communities in Weifang[23]. These discrepancies may be attributable to differences in study populations, regional factors, and assessment tools.

Multivariate analysis in this study identified education level and yang deficiency constitution as independent risk factors for MCI in T2DM patients. The education finding is consistent with previous research establishing low educational attainment as a risk factor for MCI that is negatively correlated with cognitive status[2] , similar to results reported by Xue et al.[2] . Higher education levels correlate with longer engagement in mentally stimulating activities, better cognitive performance, and enhanced comprehension and thinking abilities. Mental activity strengthens synaptic connections between neurons, thereby slowing the rate of cognitive decline associated with brain aging[2] .

Regarding TCM constitution, this study revealed that elderly T2DM patients with yang deficiency constitution have more than twice the risk of developing MCI compared to those without yang deficiency (OR=2.284, 95%CI=1.220-4.279, $P < 0.05$). This finding differs from Wang et al.'s study , possibly due to variations in age structure and disease duration. We recommend incorporating constitution screening into health monitoring for diabetic populations, with particular emphasis on cognitive assessment for individuals with yang deficiency constitution.

TCM classics have long documented that yang qi nourishes the spirit: "When yang qi is abundant, it nourishes the spirit; when gentle, it nourishes the sinews" (*Suwen* · *Shengqi Tongtian Lun* [Basic Questions · On the Generation of Qi and Communication with Heaven]) and "Exhaustion of yang qi causes forgetfulness" (*Suwen* · *Sishi Ci Ni Cong Lun* [Basic Questions · On the Four Seasons and Contrary Treatment]). These classical statements provide theoretical foundations for yang qi nourishing the spirit. Elderly individuals experience deficiency of the five viscera and yin-yang imbalance, with yang deficiency constitution being particularly common[2] . Unbalanced constitutions contribute to the development of numerous chronic diseases[3] . In diabetic patients, constitutional insufficiency and improper diet lead to early-stage yin deficiency with heat excess, which over time damages yang qi, resulting in mixed cold-heat patterns. As Huang Yuanyu explained in *Si Sheng Xin Yuan* [Four-Sheng Heart Source] regarding the pathogenesis of diabetes: "Drinking one dou [unit] and urinating one dou indicates upper injury by dryness-heat and lower disease by damp-cold; dryness-heat resides in the liver and lung channels, while damp-cold resides in the spleen and kidney organs." Sichuan's basin geography exposes viscera to chronic dampness; dampness is a yin pathogen that readily damages yang qi, thereby fostering yang deficiency constitution. The brain governs the marrow, which is generated from essence and blood. In yang deficiency individuals, insufficient generation of qi, blood, and fluids leads to two consequences: first, clear yang fails to ascend, inadequately filling the brain marrow; second, yang deficiency cannot transform dampness, allowing damp evils to obstruct the clear orifices and block the spirit mechanism, manifesting as MCI. If yang deficiency progresses further, cold-dampness accumulates and generates phlegm, leading to intermingling of phlegm-turbidity, blood stasis, and toxic evils that ultimately cause dementia[31]. Therefore, early intervention for unbalanced constitutions holds long-term value.

Liu Wansu stated in *San Xiao Lun* [Treatise on the Three Xiao]: "For diabetes patients with extreme spleen-stomach deficiency, warming and supplementation are appropriate; administering cold medicinals will damage spleen-stomach yang qi, making the condition difficult to treat due to underlying qi deficiency." This advocates warming the spleen as a therapeutic approach. Chen Rui proposed that T2DM treatment should balance cold and heat, eliminate turbidity, and support yang[32], with discriminating use of qi-benefiting and yang-warming medicinals such as cinnamon twig, dried ginger, and astragalus[33]. Additionally, studies by Wang et al.[3] and Zhu et al.[3] demonstrated significant efficacy of moxibustion on the Governor Vessel in treating MCI, underscoring the importance of protecting yang qi in cognitive preservation. These findings suggest that applying TCM's disease prevention concepts—"constitution can be differentiated, constitution is disease-related, and constitution can be adjusted"—may improve clinical recognition of MCI development in T2DM and enable earlier preventive interventions.

This study found that patients with MCI showed higher impairment rates than those without MCI in naming, attention, language, abstract thinking, and delayed memory domains, with delayed memory being most significantly affected—results consistent with previous research[2] [2]. This suggests that T2DM-related cognitive impairment may initially damage these five cognitive domains. Our results also demonstrated a close association between delayed memory and yang deficiency constitution, indicating that while T2DM-related cognitive impairment is widespread, yang deficiency constitution may primarily affect delayed memory, thereby reducing overall cognitive level. Clinically, assessing delayed memory decline may enable early disease interception.

In summary, this study demonstrates that low educational attainment and yang deficiency constitution are closely associated with MCI in elderly T2DM patients. For elderly T2DM patients, comprehensive geriatric assessment including cognitive function should be emphasized during regular follow-up to improve quality of life. TCM constitution theory holds important value for monitoring and managing chronic diseases, and introducing constitution indicators may open new avenues for TCM prevention and treatment of this condition. However, this study had a relatively small sample size, necessitating future research with larger cohorts for deeper exploration.

Conclusion

The prevalence of MCI among elderly T2DM patients in Sichuan Province is 21.2%. Low educational attainment and yang deficiency constitution are high-risk factors for MCI development. Based on the TCM theory of "constitution can be differentiated—constitution is disease-related—constitution can be adjusted," early intervention targeting yang deficiency constitution may help reduce the conversion to diabetic cognitive impairment.

Author Contributions

MA Yuping conceptualized the primary research objectives, designed the study, and wrote the manuscript. QIAO Mengyuan and HE Yanyun collected and organized data and performed statistical analysis. XU Manru and CHEN Chongli revised the manuscript. WU Wenbin was responsible for quality control and review, overall article supervision, and project management.

Conflict of Interest

The authors declare no conflict of interest.

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Note: Figure translations are in progress. See original paper for figures.