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Comparative study of insulin resistance surrogate indices to predict mild cognitive impairment among Chinese non-diabetic adults

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Abstract

Objective The study aims to investigate the associations of triglyceride glucose (TyG), TyG combined with body mass index (TyG-BMI), metabolic score for insulin resistance (METS-IR), the triglyceride to high-density lipoprotein cholesterol ratio (TG/HDL-C), and the risk of mild cognitive impairment (MCI) in individuals without diabetes aged 45 and above.

Methods The most recent data in this study were from a cohort study, which sourced samples from the China Health and Retirement Longitudinal Study, spanning 2011 to 2018. The four indices' associations with MCI risk were analyzed using logistic regression. The predictive capacity was measured using the receiver operating characteristic (ROC) curve.

Results Over a 7-year follow-up, 1,261 individuals (31.34%) of the 4,027 participants developed MCI. Logistic regression analysis revealed significant associations between these surrogate indices and MCI. The findings for the highest quartile compared with the lowest quartile were as follows: TyG: 1.24 (95% *CI*: 1.02, 1.49); TyG-BMI: 1.38 (95% *CI*: 1.13, 1.68); METS-IR: 1.50 (95% *CI*: 1.09, 2.06); TG/HDL-C: 1.34 (95% *CI*: 1.10, 1.64). ROC analysis revealed that TyG, TyG-BMI, TG/HDL-C, and METS-IR demonstrated excellent discriminatory power for MCI, with area under the curve (AUC) values of 0.82 (95% *CI*: 0.80, 0.83), 0.82 (95% *CI*: 0.80, 0.83), 0.83 (95% *CI*: 0.80, 0.84), and 0.83 (95% *CI*: 0.80, 0.84), respectively. The four indices showed stronger ability to predict MCI risk in females compared to males.

Conclusion Elevated levels of four indices are positively correlated with MCI risk. TyG-BMI and METS-IR demonstrate stronger capabilities in identifying MCI across both male and female populations. This suggests that early intervention in patients with elevated IR surrogate indices may help reduce the MCI.

Keywords Mild cognitive impairment, Insulin resistance surrogate indices, Diabetes, China Health and Retirement Longitudinal Study

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Introduction

Dementia is primarily manifested as cognitive impairment, often accompanied by significant decline in social functioning, severely impacting daily life and autonomy [1]. With the accelerating global aging process, dementia prevalence is increasing worldwide, particularly in China [2–4]. According to The Lancet Commission, dementia may develop in middle age, although symptoms may appear at different stages [5]. In China, 608 million people are 45 years or older, comprising 43.44% of its total population [6], indicating a potentially high prevalence of dementia [7]. Given the current lack of effective treatments to significantly slow dementia progression, mild cognitive impairment (MCI) is considered a phase in the transition from normal cognitive functioning to dementia, characterized by subtle yet identifiable cognitive decline [8]. Therefore, timely recognition of individuals at elevated risk for MCI is essential. Early intervention measures, including cognitive therapy, moderate-intensity exercise, and dietary adjustments, can substantially lower dementia risk and conserve healthcare resources [9].

Insulin resistance (IR) is characterized by a reduced biological response to insulin in target organs [10], which may result in elevated blood glucose levels and an increased risk of obesity, cardiovascular disease, metabolic syndrome, and other chronic conditions [11]. In this study, IR levels were assessed using measures independent of insulin. These included triglyceride glucose (TyG), TyG combined with body mass index (TyG-BMI), metabolic score for insulin resistance (METS-IR), and triglyceride to high-density lipoprotein cholesterol ratio (TG/HDL-C) [12–15]. Earlier research has estimated the associations of these IR proxy measures with cognitive decline. For instance, in a large community-based sample study, it has been determined that elevated levels of TyG predict significant cognitive decline in the subsequent five years [16]. Since the TyG-BMI index is a global indicator in IR, it reflects the overall metabolic condition of subjects. TyG-BMI levels have been documented in research to be associated significantly with rapid cognitive decline, particularly in overweight and obese individuals [17]. The METS-IR and TG/HDL-C have demonstrated associations with cognitive decline across diverse populations [18, 19].

Previous research has primarily concentrated on populations with diabetes or the broader populace, which includes diabetics. This focus narrows the applicability of their findings to non-diabetic groups. Additionally, discrepancies in sample composition, the duration of follow-up, and the methods of statistical analysis across these studies diminish their comparability. In response, this study hypothesizes that IR surrogate indices can predict MCI in elderly individuals without diabetes, and that TyG-related indices are better at identifying MCI patients than TyG itself. The innovative aspect of this research lies in its use of the nationally representative China Health and Retirement Longitudinal Study (CHARLS) database to specifically analyze the predictive value of these IR surrogate indices and their clinical significance in non-diabetic populations. This article aims to provide fresh insights for the early detection and intervention of MCI, thereby filling existing research gaps and aiding in the development of strategies to prevent cognitive deterioration in this demographic.

Methods

Study design

The CHARLS database provided the data for this analysis. Employing multi-stage stratified random sampling throughout mainland China, the survey ensured participant consent. The initial survey occurred in 2011, with 17,705 participants undergoing physical examinations and completing questionnaires. Subsequent assessments were conducted biennially, with Waves 2, 3, and 4 occurring in 2013, 2015, and 2018, respectively. The average follow-up period was 6.26 years. Exclusion criteria included: age under 45 years (418 individuals); MCI diagnosis at baseline (1,352 individuals); history of diabetes or lipid-lowering medication use at baseline (507 individuals); missing data on IR surrogate indices (5,077 individuals); absence of cognitive data across all follow-up waves (4,031 individuals); lost to follow-up (1,151 individuals); and missing over 20% of covariate data (1,142 individuals) (Fig. 1).

Definitions of four surrogate indices

This study collected data on fasting plasma glucose (FPG), fasting triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) to calculate the four surrogate indices, as follows: $TyG = \ln[(TG\ (mg/dL) \times FPG\ (mg/dL)/2]$ [20]; $TyG\text{-}BMI = TyG \times BMI$ [21]; $METS\text{-}IR = \ln[(2 \times FPG\ (mg/dL)) + TG\ (mg/dL)] \times BMI / \ln(HDL\text{-}C\ (mg/dL))$ [14]; $TG/HDL\text{-}C = TG\ (mg/dL) / HDL\text{-}C\ (mg/dL)$ [15].

MCI definition

CHARLS designed a questionnaire to assess cognitive function, focusing on Word Recall Test (WRT) and Mental Status Test (MST) [22]. The WRT included immediate and delayed recall tests, each scoring up to 20 points. The immediate recall score was determined by the number of words immediately recalled by the participant, while the delayed recall score depended on the number recalled after completing a depression scale survey, lasting approximately 4 to 10 min. The MST involved the Telephone Interview for Cognitive Status (TICS-10) and a graphic drawing task. Both the serial subtraction and date orientation tasks of the TICS-10 were valued

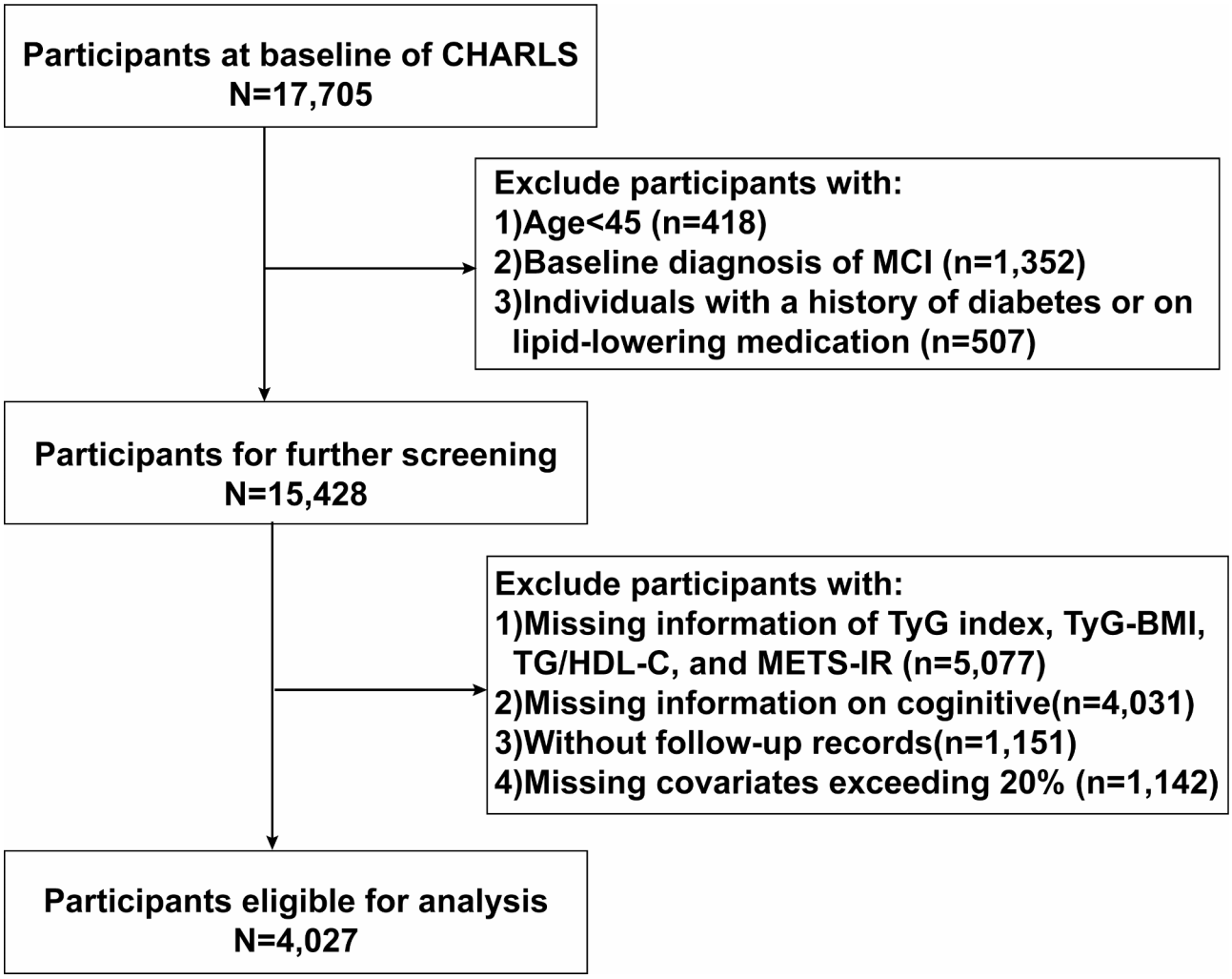

Fig. 1 Research and design flow chart

at 5 points and thus summed to 10 points in total. The graphic drawing task asked for the exact copying of a figure and was valued at 1 point. Thus, the maximum score for cognition would be 31 points and it was summarized from MST and WRT scores [23]. Repeated cognitive assessments at each follow-up used the same methods.

MCI was defined according to the aging-associated cognitive decline (AACD) criteria [24]. Specifically, MCI involves a total score (WRT and MST combined) that falls more than one standard deviation (SD) below the mean for the participant's age group [24]. Participants aged 60 and over were grouped by five-year intervals, and those meeting the AACD criteria were classified as having MCI. See Supplementary Table 1 for detailed classification criteria.

Diagnosis of diabetes

As per Chinese guidelines for type 2 diabetes, the diagnostic criteria include any of the following [25]: (1) Hemoglobin A1c (HbA1c)≥6.5%; (2) FPG≥7.0 mmol/L; (3) a physician's diagnosis of diabetes, or (4) use of diabetes medication or insulin.

Covariates

The covariates included sociodemographic factors, behavioral factors, health status factors, and psychological health factors. Sociodemographic factors encompassed age, gender, educational level, marital status (married/unmarried), and residence (urban/rural). Behavioral factors consisted of social activities, smoking history, and alcohol history. Health status factors included waist circumference, BMI, and various chronic diseases (hypertension, dyslipidemia, cancer, cardiovascular disease, liver disease, chronic lung disease, psychiatric disorders, digestive system diseases, kidney disease, arthritis or rheumatism, and asthma) reported by subjects in response to the question, "Have you ever had any of the following chronic diseases or pain?" Laboratory examination results comprised HbA1c, FPG, TG, HDL, low-density lipoprotein cholesterol (LDL-C), and total

cholesterol (TC). The Center for Epidemiologic Studies Depression Scale (CES-D) was utilized to evaluate psychological health [26].

Statistical analysis

The distribution characteristics of the variables guided the representation of continuous data as either means with SD or medians alongside interquartile ranges (IQR). For comparative analysis between groups, T-tests or rank-sum tests were utilized as deemed necessary. Categorical variables were shown in frequencies (%) and analyzed using the $\chi 2$ test. Associations between four specific indices and the incidence of MCI were explored through a multivariable logistic regression approach. The area under the receiver operating characteristic (ROC) curve (AUC) was applied to measure the predictive ability of the four indices for MCI, with the highest Youden index determining the most effective threshold. Statistical evaluations were conducted utilizing EmpowerStats (version 4.2). The $P<0.05$ exhibited significance.

Results

Participants characteristics

The research encompassed 4,027 subjects, of which 1,261 had been recently diagnosed with MCI. The demographic breakdown showed 2,041 males and 1,986 females, averaging 63.69±8.53 years in age.Compared to participants without MCI, those with MCI were generally older, more likely to be female, had lower levels of education, were more frequently unmarried, had a history of alcohol consumption and smoking, participated in fewer social activities, and predominantly resided in rural areas. They also had shorter sleep durations, larger waist circumferences, higher BMIs, and a higher prevalence of chronic diseases. Furthermore, the MCI group had higher CES-D scores, while their Global Cognition Scores, WRT scores, and MST scores were lower. Additionally, distinct differences in laboratory measures, including HbA1c, FPG, LDL-C, HDL-C, and TG, were observed. Levels of the four IR surrogate indices were higher in individuals with MCI than in those without. (Table 1)

Correlation between four IR surrogate indices and MCI risk

During the collinearity screening, substantial collinearity was observed among the exposure variables. To mitigate the impact of multicollinearity on model stability and result interpretability, these variables were excluded from simultaneous inclusion in further regression analyses. Moreover, due to strong correlations between BMI, TC, and HDL-C and these IR indicators, these variables were also omitted from the logistic regression models (Supplementary Table 2). Model 1 showed a positive correlation between the four IR surrogate indices and MCI. Subsequent adjustments for age and gender in Model 2 indicated that the highest quartiles of TyG, TyG-BMI, METS-IR, and TG/HDL-C had a 1.36, 1.70, 1.32, and 1.79-fold increase in MCI risk, respectively, relative to the lowest quartiles. In Model 3, which included comprehensive adjustments, the relationships between these indices and MCI risk persisted as statistically significant ($P<0.05$). (Table 2)

AUC and cut-off points of four IR surrogate indices for predicting MCI

According to Table 3; Figs. 2 and 3, TG/HDL-C and METS-IR demonstrated relatively high AUC values of 0.83, with optimal cut-off values of 2.66 and 33.22, respectively. Subsequently, the AUC values for TyG-BMI and TyG were both 0.82. For both men and women, the AUC values for TyG-BMI and METS-IR exceeded those of the other two indices (Fig. 3A). The best cut-off values for men were 181.20 and 33.36, while for women, they were 198.36 and 33.15 (Fig. 3B).

Discussion

In this longitudinal investigation, the incidence of MCI among non-diabetic individuals aged 45 and older was found to be 31.3%, with occurrence rates of 29.3% in males and 33.3% in females. This study is the first analysis to propose the four IR surrogate indices as potential indicators for MCI within this demographic. Notably, TyG-BMI and METS-IR outperformed the other two indices in identifying MCI across different genders.

IR surrogate indices are closely associated with metabolic disorders [27–29], and these indices have also been used to predict cognitive decline. For instance, Tong et al. found that TyG and TyG-BMI were linked to MCI among those diagnosed with type 2 diabetes [30]. Zhao et al. conducted a study on individuals aged 60 and older and determined that elevated TG/HDL-C levels were significantly linked to decreased cognitive test scores [18]. Importantly, even in the absence of diabetes, IR has been shown to contribute to cognitive decline. Recent studies indicate that METS-IR in non-diabetic individuals is closely related to metabolic disorders [31], which are significantly associated with cognitive decline [32]. Additionally, other studies indicate that IR indices have a significant impact on the ability of prediabetic individuals to restore normal blood glucose levels [33]. These findings corroborate those observed in the non-diabetic population and emphasize the importance of these indices in assessing the risk of MCI.

Research also suggests that IR indices have varying predictive powers depending on the population characteristics. For example, Wang et al., in their study involving a Chinese population, found that elevated TyG levels correlated with a greater likelihood of cognitive decline in males, especially those below 60 years old,

Table 1 Baseline characteristics of the study population

Variables	Total *N* = 4027	Without MCI *N* = 2766	With MCI *N* = 1261	*P* value
Age(years)	63.69(8.53)	62.18(7.75)	66.99(9.18)	< 0.001
Gender(%)				< 0.001
Male	2041(50.68)	1442(52.13)	599(47.50)	
Female	1986(49.32)	1324(47.87)	662(52.50)	
Marital status(%)				< 0.001
Married	3692(91.68)	2597(93.89)	1095(86.84)	
Unmarried	335(8.32)	169(6.11)	166(13.16)	
Educational Level(%)				< 0.001
Primary school	821(20.39)	206(7.45)	615(48.77)	
Middle school	1755(43.58)	1239(44.79)	516(40.92)	
High school and above	1451(36.03)	1321(47.76)	130(10.31)	
Alcohol history(%)				< 0.001
Yes	1925(47.80)	1038(37.53)	887(70.34)	
No	2102(52.20)	1728(62.47)	374(29.66)	
Smoking history(%)				0.009
Yes	1939(48.15)	1145(41.40)	794(62.97)	
No	2088(51.85)	1621(58.60)	467(37.03)	
Social Activities(%)				< 0.001
Yes	2095(52.02)	1494 (54.01)	601 (47.66)	
No	1612(47.98)	1272 (45.99)	660 (52.34)	
Location(%)				< 0.001
Urban	267(6.63)	229(8.28)	38(3.01)	
Rural	3760(93.37)	2537(91.72)	1223(96.99)	
Sleep time(h)	7.00(1.94)	7.10(1.86)	6.78(2.09)	< 0.001
Waist Circumference (cm)	82.97(77.00,90.00)	81.80(75.80,89.00)	83.60(77.20,90.00)	< 0.001
CES-D(score)	6.00(3.00,11.00)	6.00 (3.00,10.00)	7.00 (4.00,12.00)	< 0.001
BMI(kg/m2)	23.13(3.50)	22.86(3.74)	23.26(3.38)	< 0.001
Chronic Disease(%)				0.948
Yes	2226(55.28)	1528(55.24)	698(55.35)	
No	1801(44.72)	1238(44.76)	563(44.65)	
HbA1c(%)	5.10(4.90,5.30)	5.10(0.39)	5.11(0.39)	0.246
FPG(mg/dl)	99.54(92.88,106.74)	99.54 (93.06,106.74)	99.72(92.34,106.56)	0.641
TC(mg/dl)	191.87(36.84)	191.34(36.94)	193.03(36.63)	0.125
TG(mg/dl)	97.35(69.92,138.50)	96.46(69.03,133.63)	97.35(70.80,141.38)	0.044
HDL-C(mg/dl)	52.58(15.15)	53.83(15.24)	52.01(15.08)	< 0.001
LDL-C(mg/dl)	113.49(92.34,134.78)	111.78(92.69,136.47)	116.89(91.56,138.84)	< 0.001
TYG	8.52(0.55)	8.49(0.54)	8.53(0.55)	0.047
TYG-BMI	197.52(36.12)	191.00(33.82)	200.50(36.75)	< 0.001
TG-HDL-C	2.65(2.81)	2.50(2.67)	2.72(2.87)	0.005
METS-IR	34.19(7.26)	32.87(6.72)	34.78(7.42)	< 0.001
Global Cognition Score	14.70(6.52)	17.37(4.06)	8.83(7.03)	< 0.001
WRT	6.98(4.05)	8.53(3.24)	3.58(3.56)	< 0.001
MST	7.72(3.31)	8.84(2.32)	5.24(3.79)	< 0.001

CES-D, Center for Epidemiologic Studies Depression Scale; BMI, Body Mass Index; **HbA1c**,Hemoglobin A1c; FPG, Fasting Plasma Glucose; TC, Total Cholesterol; TG, Triglycerides; HDL-C, High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol; TYG, Triglyceride-Glucose Index; TYG-BMI, Triglyceride-Glucose Body Mass Index; TG-HDL-C, Triglyceride to High-Density Lipoprotein Cholesterol Ratio; METS-IR, Metabolic Score for Insulin Resistance; WRT Score, Word Recognition Test Score; MST Score, Mental Status Test Score.

while no association could be seen in females [34]. On the other hand, the current study suggested that IR surrogate indices performed better in females than in males from the perspective of predictive performance. Several issues related to the design of this study can explain this disagreement. The pioneering work by Wang et al. was carried out on elderly subjects within the wider population, but this study specifically was targeted on non-diabetic subjects in order to avoid interference with the correlation between IR and cognitive function due to

Table 2 Association of Baseline IR Surrogate Indices with Incident MCI

Variables	Model1	*P*	Model2	*P*	Model3	*P*
TyG						
Q2	1.15(0.95, 1.39)	0.1470	1.10(0.75, 1.61)	0.6389	1.14(0.96, 1.37)	0.1838
Q3	1.21(0.95, 1.53)	0.1173	1.29(0.98, 1.71)	0.0730	1.19(0.75, 1.88)	0.4558
Q4	1.25(1.03, 1.51)	0.0228	1.36(1.12, 1.67)	0.0025	1.24(1.02, 1.49)	0.0296
P for trend	0.0139		0.0184		0.0195	
TyG-BMI						
Q2	1.18(0.98, 1.42)	0.0727	1.11(0.91, 1.35)	0.2949	1.01(0.81, 1.27)	0.9146
Q3	1.54(1.28, 1.86)	< 00001	1.38(1.13, 1.68)	0.0016	1.26(0.97, 1.64)	0.0799
Q4	1.81(1.50, 2.20)	< 0.0001	1.70(1.39, 2.09)	< 0.0001	1.38(1.13, 1.68)	0.0016
P for trend	< 0.0001		< 0.0001		0.0313	
TG/HDL-C						
Q2	1.13(0.94, 1.36)	0.1900	1.13(0.93, 1.38)	0.2157	1.15(0.94, 1.40)	0.1726
Q3	1.23(1.02, 1.48)	0.0301	1.26(1.03, 1.53)	0.0237	1.26(1.03, 1.54)	0.0215
Q4	1.35(1.12, 1.63)	0.0018	1.32(1.08, 1.61)	0.0058	1.34(1.10, 1.64)	0.0040
P for trend	0.0198		0.0213		0.0383	
METS-IR						
Q2	1.26(1.05, 1.51)	0.0132	1.12(0.92, 1.36)	0.2493	1.04(0.59, 1.86)	0.8833
Q3	1.77(1.47, 2.13)	< 0.0001	1.55(1.27, 1.89)	< 0.0001	1.47(1.14, 1.90)	0.0031
Q4	2.03(1.68, 2.46)	< 0.0001	1.79(1.46, 2.19)	< 0.0001	1.50(1.09, 2.06)	0.0122
P for trend	< 0.0001		< 0.0001		< 0.0001	

Model 1: Unadjusted.

Model 2: Adjusted for age and gender.

Model 3: Adjusted for age, gender, marital status, educational level, alcohol consumption history, smoking history, social activity, residence, sleep duration, waist circumference, CES-D score, chronic diseases, HbA1c, FPG, TG and LDL-C.

Table 3 AUC and cutoff values of four IR surrogate indices for MCI Risk Prediction

Variables	AUC(95%CI)	Cut-off	Specificity	Sensitivity
Total				
TyG	0.82(0.80,0.83)	8.85	0.65	0.82
TyG-BMI	0.82(0.80,0.83)	185.29	0.64	0.83
TG/HDL-C	0.83(0.80,0.84)	2.66	0.67	0.79
METS-IR	0.83(0.80,0.84)	33.22	0.62	0.85
Males				
TyG	0.77(0.75,0.80)	8.84	0.82	0.60
TyG-BMI	0.79(0.75,0.80)	181.20	0.78	0.64
TG/HDL-C	0.78(0.75,0.81)	2.44	0.81	0.62
METS-IR	0.79(0.75,0.81)	33.36	0.78	0.63
Female				
TyG	0.84(0.82,0.86)	8.48	0.74	0.82
TyG-BMI	0.88(0.83,0.89)	198.36	0.74	0.83
TG/HDL-C	0.84(0.82,0.86)	1.15	0.73	0.82
METS-IR	0.88(0.83,0.89)	33.15	0.75	0.83

TYG, Triglyceride-Glucose Index; TYG-BMI, Triglyceride-Glucose Body Mass Index; TG-HDL-C, Triglyceride to High-Density Lipoprotein Cholesterol Ratio; METS-IR, Metabolic Score for Insulin Resistance.

diabetes. However, this has given a more valid estimate of predictive capability regarding those IR surrogate indices in a non-diabetic setting. This research followed participants from 2011 to 2018, and this duration was longer than the four-year follow-up conducted by Wang et al. from 2011 to 2015. In effect, long-term changes in cognitive function could be captured with great detail alongside the associated pattern with IR indices. Afilalo et al. also reported the same findings, as the increased risk for IR was directly proportional to the increase in the chances of MCI, especially in female patients. Women are more susceptible to the ill effects of IR due to socioeconomic factors like lifestyle, hormonal changes, and fat distribution that increase susceptibility to cognitive decline [35]. Moreover, Chen et al. found that females are more vulnerable to IR-induced cognitive decline compared with males [36]. These findings suggest the importance of wider application of surrogate indices of IR in predicting MCI among female populations. These differences need more explanation based on extensive studies across different genders. Additionally, it is imperative that future research expand its focus to include a variety of age groups, ethnicities, and backgrounds to enhance understanding of the IR surrogate indices' utility and efficacy across diverse populations.

Subsequent ROC analyses revealed that TyG-BMI and METS-IR exhibit excellent forecasting power for MCI compared to other indices among both genders. Existing literature supports that TyG-BMI, by incorporating BMI, offers a more precise estimation of an individual's fat accumulation [37]. Specifically, obesity impacts insulin sensitivity through multiple pathways, including adipocytes' secretion of pro-inflammatory agents and insulin antagonists, substantially elevating IR risk. METS-IR integrates various non-insulin lab indices and

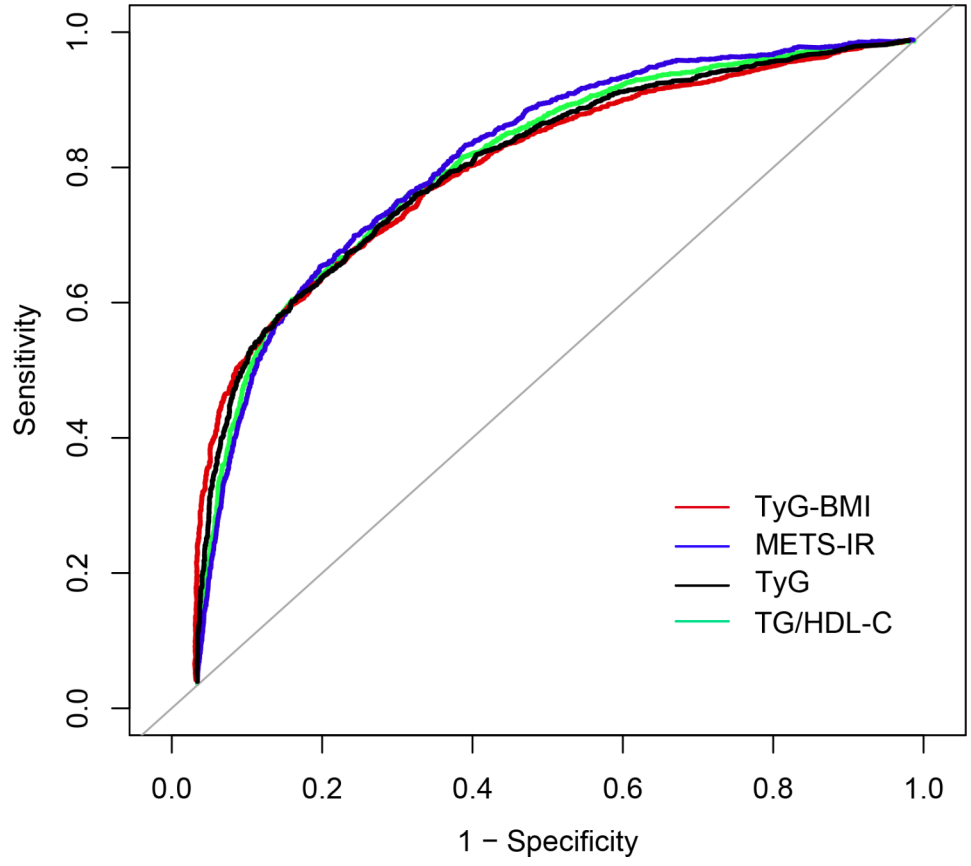

Fig. 2 ROC for different IR surrogate indices to predict MCI

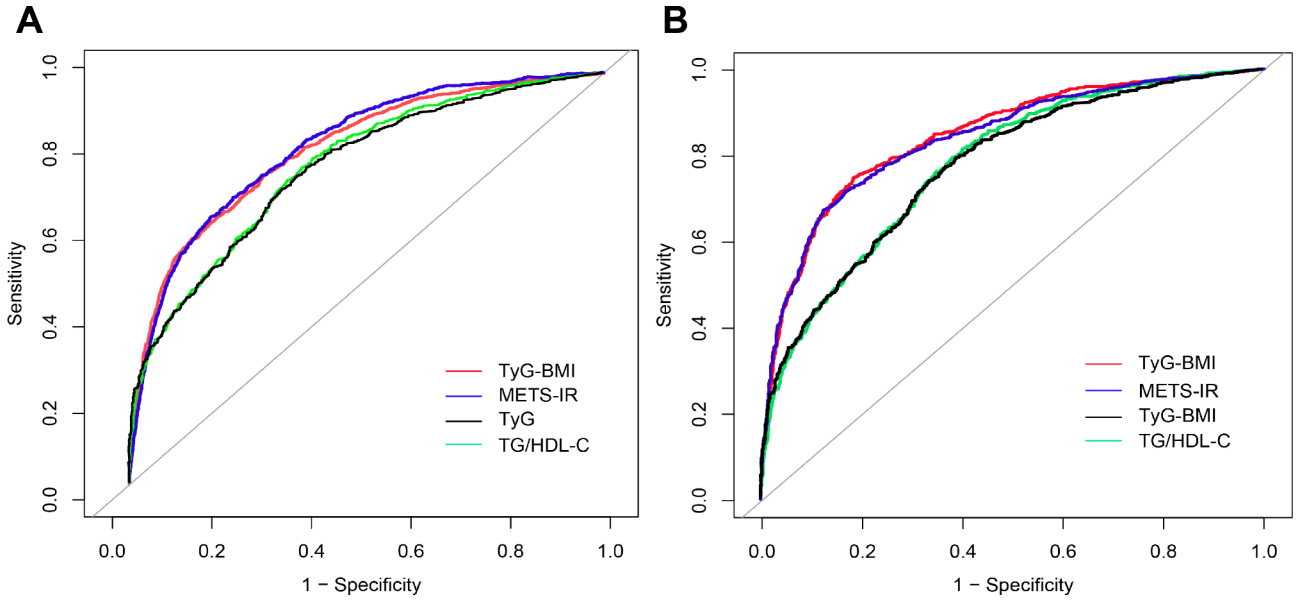

Fig. 3 ROC curves of different IR surrogate indices for predicting MCI across genders. (**A**) Males (**B**) Females.

anthropometric data, such as FG, TG, and HDL-C, which collectively reflect an individual's metabolic health status [38]. Metabolic disorders are closely linked to the risk of MCI, and METS-IR effectively identifies these disorders, thereby assessing the risk of MCI. Additionally, IR is associated with chronic inflammation and oxidative stress, which have been proven to negatively impact brain health [39]. Consequently, METS-IR, as an IR surrogate,

indirectly indicates levels of inflammation and oxidative stress, thereby predicting cognitive function alterations [40].

Study strengths and limitations

First, the study data were derived from CHARLS, a comprehensive nationwide survey with significant representativeness. This source provides valuable supplementary data on non-diabetic individuals aged 45 and above, particularly within the Chinese population in Asia. Second, the study employed a cohort design, enabling the establishment of causal links between the four IR surrogate indices as independent risk factors and MCI. Additionally, these four IR surrogate indices are readily obtainable and simple to calculate, offering low screening costs, which supports their large-scale application. These indices are instrumental in research and serve as effective tools for the early detection and intervention of MCI in clinical practice, thereby improving the motivation for early diagnosis and treatment among individuals and healthcare providers.

However, this research acknowledges several limitations. First, constraints of the CHARLS database restricted the adjustments for certain confounding factors, such as dietary habits, medication use, and detailed information on MCI complications. Second, the diagnosis of MCI is self-reported, which can present subjective bias because participants' memory and comprehension abilities may affect the accuracy of the information provided. Moreover, the population mainly originated from the older generations of Chinese individuals and requires further verification among external groups in order to generalize the findings to other regions and countries. IR surrogate indices, on the other hand, though valuable in assessing IR and the risk of its related diseases, are far less sensitive in measuring the physiological mechanisms that pertain to IR compared to techniques such as the hyperinsulinemic-euglycemic clamp and the quantitative insulin sensitivity index. The results thus have to be approached with caution and much reservation.

Conclusion

This study demonstrates that four surrogate indices of IR have significant clinical value in predicting MCI in non-diabetic elderly populations. Notably, TyG-BMI and METS-IR show the best predictive performance regardless of gender. These findings suggest that high values of these IR indices might necessitate regular follow-ups of cognitive performance as a means to apply early interventions with the purpose of decelerating cognitive decline. Given the accessibility and low cost of these indices, they could potentially be integrated into community and primary healthcare systems to enhance large-scale screening and early diagnosis of MCI, thus providing better overall patient care and health management.

Abbreviations

TyG	Triglyceride glucose
TyG-BMI	Triglyceride glucose combined with body mass index
METS-IR	Metabolic score for insulin resistance
TG/HDL-C	Triglyceride to high-density lipoprotein cholesterol ratio.
MCI	Mild cognitive impairment
CHARLS	China health and retirement longitudinal study
ROC	Receiver operating characteristic
AUC	Area under the curve
IR	Insulin resistance
FPG	Fasting plasma glucose
TG	Triglycerides
HDL-C	High-density lipoprotein cholesterol
WRT	Word recall test
MST	Mental status test
TICS-10	Telephone interview for cognitive status-10
HbA1c	Hemoglobin A1c
BMI	Body mass index
LDL-C	Low-density lipoprotein cholesterol
TC	Total cholesterol
CES-D	Center for epidemiologic studies depression scale
SD	Standard deviation
AACD	Aging-Associated Cognitive Decline
IQR	Interquartile range

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-024-02353-0.

Supplementary Material 1

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Author contributions

YC., designed the study. Z.X., Z.C., Y.G., and W.P. handled data collection and analysis. Y.C., Z.X., and Z.C. drafted the manuscript, while X.Z., Y.G., and P.W. provided critical revisions. All authors contributed to and approval of the final manuscript.

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Data availability

This study's analysis used publicly available datasets, accessible at http://charls.pku.edu.cn.

Declarations

Ethics approval and consent to participate

This cohort study was approved by the Ethics Review Committee of Peking University (IRB00001052–11015) and follows the ethical guidelines outlined in the Declaration of Helsinki.

Consent for publication

All authors have reviewed and approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

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