Original Article

Role of TyG, TyG-BMI and METS-IR in osteoporosis risk among older men: a retrospective cohort study

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Background and Objectives: Obese and diabetic individuals tend to have insulin resistance, but are less likely to develop osteoporosis. The association of triglyceride-glucose (TyG) related indices with osteoporosis remains controversial, and longitudinal evidence exploring the male osteoporosis (MOP) is limited. This study aims to examine TyG, TyG-body mass index (TyG-BMI) and the metabolic score for insulin resistance (METS-IR) with osteoporosis risk among older men. **Methods and Study Design:** A cohort study based on 1622 middle-aged and older men in 2015 was conducted, and followed up until 2022. Participants with osteoporosis and admittedly secondary risk factors were excluded. TyG, TyG-BMI, METS-IR and corresponding quantiles were calculated. Cox proportional hazard regression models were used to assess the hazard ratios (HRs) and 95% confidence interval (CI). Receiver operating characteristic (ROC) curve was applied to estimate their performance in osteoporosis screening. **Results:** 72 of 1622 participants were newly developed OP during the 9317 person-years. The adjusted HRs of TyG, TyG-BMI, and METS-IR for MOP were 0.573 (95%CI 0.336-0.976), 0.991 (95%CI 0.984-0.999) and 0.929 (95%CI 0.892-0.968), respectively, and presented at linear dose-response relationships. Subgroup analysis showed that the estimated benefit for MOP incidence was consistent among participants aged more than 70 years and related to BMI and eating mount of milk, fresh fruit and vegetables. No difference was found in the area under ROC curve for screening osteoporosis, ranging from 0.585 to 0.617. **Conclusions:** TyG and relevant indices were associated with the incidence of osteoporosis in the senile men, and the relationship was thought to correlate with BMI and nutritional behaviors.

Key Words: male osteoporosis, TyG, TyG-BMI, cohort study, old people

INTRODUCTION

Osteoporosis (OP) is characterized by the progressive decrease of bone mass and destruction of bone microstructure, and is the leading cause for fragility fractures worldwide.[1] The prevalence of male osteoporosis (MOP) is markedly lower than that of postmenopausal women, but their rate of osteoporotic fractures is comparable in China.[2] Notably, much higher rate of disability and mortality have caused by male osteoporosis fractures.[3,4] Therefore, OP is also an invisible killer of aging health and quality of life in men, which is often overlooked by clinicians.[3] And high-level epidemiological evidence is urgently needed to screen out high-risk groups of MOP for early prevention and treatment.

Obesity is often considered to be an abnormality that impairs health, affecting the risk of diabetes,

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hypertension, and cardiovascular and cerebrovascular diseases.[5] However, the effect of obesity on bone metabolism is widely recognized to be beneficial, and known as an obesity paradox.[6,7] One mechanism that could explain the higher bone mineral density (BMD) in obese people is increased mechanical load and strain.[6] Insulin resistance (IR), as one of the complications of obesity,[8] is also closely associated with OP.[9] Previous studies based on postmenopausal women have demonstrated that the effects of IR on bone mass were still inconsistent, in spite of having T2DM or not.[10,11] Considering the impracticality of gold standard (hyperinsulinemic-euglycemic clamp test) to estimate IR in the daily clinical practice, simple and comparably accurate indicators for IR were frequently applied, including the triglyceride-glucose (TyG), TyG-body mass index (TyG-BMI) and the metabolic score for IR (METS-IR).[12-14]

Previous studies have found that these IR-indicators were independent influence factors for cardiovascular and cerebrovascular diseases, chronic kidney diseases, depression and even mortality.[15-18] However, the conclusion remains controversial about osteoporosis, the same as the relationship between obesity and osteoporosis. Plausible reasons are the difference in indicators of IR, sample size and different multi-variable adjustment. And rare long-term longitudinal studies have been performed to evaluate their associations for the OP risk. Notably, limited evidences cannot reach consensus for men.[19,20] Hence, we aimed to simultaneously examine the associations of TyG, TyG-BMI and METS-IR index for the OP risk among a single-center cohort of Chinese middle-aged and older men.

METHODS

Study design and participants

The cohort study was based on a group of middle-aged and older men, who conducted the routine health examination in our hospital in 2015. A total of 2124 participants were initially recruited. To illuminate the incidence of primary osteoporosis, we excluded those participants who had OP or related fractures at baseline (n=309). Considering the possible effects of recognized risk factors of OP, we additionally excluded 117 participants, who had long-term use of hormones or high dose thyroxine for inhibition therapy, had use of gonadotropin releasing hormone analogues, or had diseases that affected bone metabolism including hyperparathyroidism, chronic liver, hyperthyroidism, prostatic cancer and bone related tumors. Moreover, 76 participants were excluded because of loss to follow-up after baseline, and 1622 participants were continued to follow up until 2022. The median follow-up time was 6.1 and interquartile range (IQR) 5.2-7.0 years. Figure 1 illustrates the flowchart depicting the study inclusion process. The study was approved by the Institution Ethic Committee of Institution Ethic Committee of PLA general hospital (No. S2021-094-01), and informed consent was signed in advance by participants or their legal representatives.

Data collection

The baseline physical examinations were conducted by trained doctors according to the standard process, including basic sociodemographic information, lifestyle, medical history and medication information. Following covariates were involved: smoking (never vs. ever), alcohol drinking (never vs. ever), regular exercise (yes vs. no), milk drinking per day (yes vs. no), eating egg per day (<1 vs. ≥1), mount of eating fresh fruit and vegetables per day (<250 g vs. ≥ 250 g), supplement of calcium or vitamin D (never vs. ever), history of common chronic disease (yes vs. no). Additionally, the medical history and medication information were rechecked from the electronic medical records. Height was measured in meters (no shoes). Weight was measured in kilograms (no heavy clothes). Body mass index (BMI) was then calculated using height and weight. After 10 min of rest, the blood pressure was

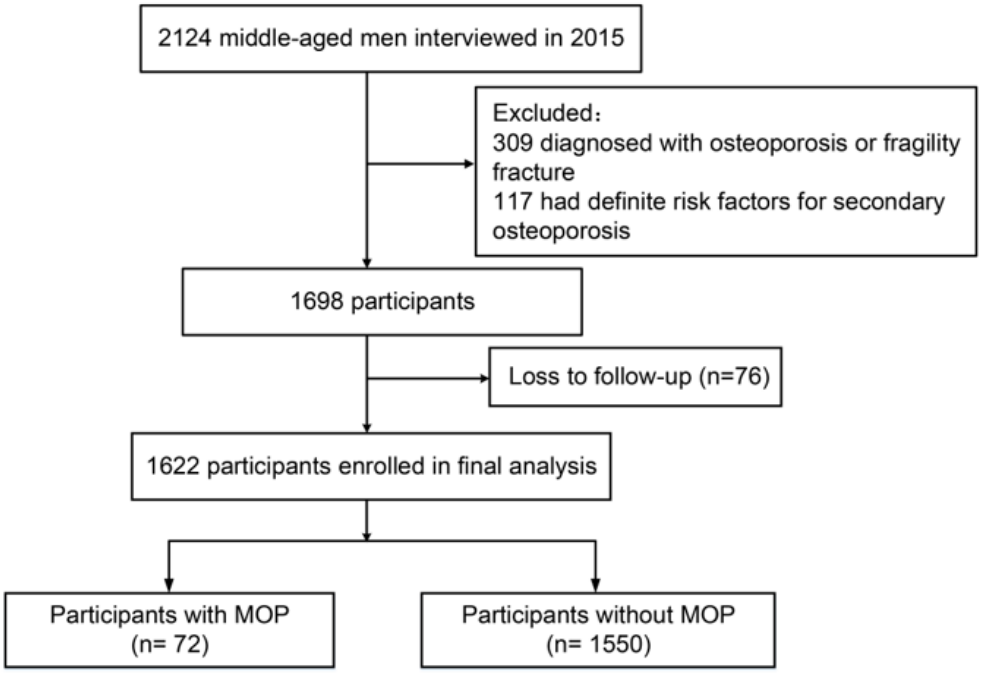

Figure 1. Flow chart of inclusion of participants

taken by mercury sphygmomanometer on the seat. Overnight fasting blood was obtained to test fasting plasma glucose (FPG), total triglyceride (TG), high density lipoprotein cholesterol (HDL-C), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), serum creatinine (Scr), serum uric acid (SUA), alanine aminotransferase (ALT), aspartate aminotransferase (AST), thyroid stimulating hormone (TSH), D dimer (D-D), activated partial thromboplastin time (APTT), albumin, hemoglobin (HGB) and total bilirubin (TBIL) on Beckman automatic biochemical analyzer.

Assessment of TyG and relevant indicators

TyG index,[21] TyG-BMI index[22] and METS-IR[23] were calculated as follows:

TyG index = ln [TG (mg/dL) × FPG (mg/dL)/2].

TyG-BMI index = TyG × BMI.

METS-IR = ln [2×FPG (mg/dL) + TG (mg/dL)] × BMI (kg/m^2) / ln [HDL-C (mg/dL)].

Outcome measures

Dual-energy X-ray absorptiometry (DEXA) was used to measure lumbar and femur spine BMD (GE-UNAR Company, Boston, MA, USA [coefficient of variation, 1.2%]) by the same technologists. The new onset of OP was defined according to the guidelines of osteoporosis in China[24] as (1) the BMD reduction ≥ 2.5 standard deviation (SD) of the peak bone mass of normal adults of the same sex and race was considered to be osteoporosis; (2) the presence of fragility fracture, resulting from a fall from a standing height or less or occurring in the absence of trauma).

The follow-up time was measured as the interval of physical examination date between 2015 and 2022 wave. For participants who were lost to follow-up or died, the follow-up time was calculated as the half of time between the initial physical examination date and the date of last follow-up or death, which were collected from official death certificates.

Statistical analysis

Statistical analysis was performed using SPSS 26.0 and R 4.0.3. Continuous and normally distributed variables were expressed as mean ± SD used T test, and otherwise were expressed as median (interquartile range, IQR) used Wilcoxon test for comparisons. N (%) and Chi-square test was used for categorical variables. After confirming that the proportional risk assumption was satisfied, multivariable Cox regression model was then conducted to estimate the association of IR and the incidence of OP. The hazard ratio (HR) and 95% confidence interval (CI) was calculated after adjusting for clinically and statistically significant covariates. And the doss-response relationship was explored using restricted cubic regression with three knots located at percentiles (10th, 50th, and 90th) of the TyG and relative indices. A predefined subgroup stratified by age (70 years as cutoff), BMI (24 kg/m^2 as cutoff) and whether or not had diabetes at baseline was conducted. And relative excess risk due to interaction (RERI), proportion attributable to interaction (AP), and multiplication interaction were used to assess the interactive effects.[25] Sensitivity analyses were further performed to verify the robustness of the primary results: (1) excluding participants within half a year of follow-up; (2) using the regression modeling of competing risk to test the association; (3) excluding participants with new occurrence of osteoporotic fracture. A two-sided p value < 0.05 was regarded as statistical significance.

RESULTS

A total of 1622 participants were included in our analysis, with 72 participants newly developed as OP during the 9317 person-years. The total incidence of OP was 4.4% and the corresponding incidence density was 7.7 per 1000 person-years (Supplementary Table 1). Participants aged ≥ 70 years were 7-fold as likely to have the OP as those with aged < 70 years (8.4% vs.1.2%, p < 0.001). Similar results can be seen in different statuses of TyG, TyG-BMI and METS-IR.

Clinical laboratory characteristics of participants

The baseline characteristics presented in Table 1. Compared with non-OP onset, participants with OP were older, and had lower levels of BMI, TG, Alb, HBG, ALT, TyG, TyG-BMI and METS-IR, while had higher levels of HDL-C, SBP, D-D and Scr, and more comorbidity of coronary heart disease (CHD) and cerebrovascular disease (CVD). Additionally, significant difference was found in lifestyles, and more proportions of smoking, drinking, exercise, the eating of milk, egg and fresh fruit and vegetables were in non-OP groups. No significance was observed in calcium and vitamin D supplement.

HRs for osteoporosis incidence in middle-aged and older men

Table 2 showed the HRs and 95% CI of TyG, TyG-BMI and METS-IR for OP incidence. After adjusting for covariates with statistical differences in the univariate analysis or clinical value in the model, the HRs of TyG, TyG-BMI, and METS-IR were 0.573 (95%CI 0.336-0.976, p = 0.040), 0.991(95%CI 0.984-0.999, p = 0.034) and 0.929 (95%CI 0.892-0.968, p < 0.001), respectively. Similar significances were noted regarding further dividing into quantiles, and the estimated benefit for OP incidence was stronger (p < 0.05). Also, dose-response analysis showed that the HR of incident OP gradually decreased and presented a linear correlation (p for non-linear > 0.05) with the increase of TyG, TyG-BMI and METS-IR, especially when at relatively low levels (Figure 2).

Subgroup and sensitive analyses

Subgroup analyses were further conducted to examine the association of TyG, TyG-BMI and METS-IR with osteoporosis risk (Figure 3). The association was relatively robust among participants aged more than 70 years, BMI less than 24 kg/m2 and eating less milk, egg, fruit and vegetables groups at baseline. Interaction was only found in age, milk, and fruit and vegetables groups, and no significant interactions were observed in TyG on osteoporosis risk. Also, sensitivity analyses were conducted to ascertain these associations, and the positive results were similar (Supplementary Table 2).

Table 1. Clinical characteristics between OP and non-OP groups

	Total (n=1622)	OP (n=72)	Non-OP (n=1550)	p value
Age, mean ± SD (years)	69.9 ± 11.6	81.2 ± 10.0	69.3 ± 11.4	<0.001
BMI, mean ± SD (kg/m^2)	24.8 ± 2.79	23.9 ± 3.01	24.8 ± 2.78	0.004
FPG, mean ± SD (mmol/L)	5.82 ± 1.05	5.87 ± 1.06	5.81 ± 1.05	0.674
TG, mean ± SD (mmol/L)	1.37 ± 0.70	1.14 ± 0.44	1.37 ± 0.71	<0.001
HDL-C, mean ± SD (mmol/L)	1.31 ± 0.33	1.38 ± 0.32	1.30 ± 0.33	0.047
LDL-C, mean ± SD (mmol/L)	2.73 ± 0.77	2.77 ± 0.83	2.72 ± 0.77	0.621
TyG, median (IQR)	8.61 (8.30, 8.94)	8.48 (8.22, 8.70)	8.61 (8.30, 8.95)	0.014
TyG-BMI, median (IQR)	213 (195, 232)	201 (181, 225)	213 (195, 233)	0.001
METS-IR, median (IQR)	36.9 (33.1, 40.9)	34.0 (30.1, 38.5)	36.9 (33.3, 40.9)	0.001
SBP, mean ± SD (mmHg)	127 ± 15	133 ± 17	127 ± 15	<0.001
DBP, mean ± SD (mmHg)	74 ± 9	72 ± 11	74 ± 9	0.105
Alb, mean ± SD (mmol/L)	46.03 ± 2.58	45.3 ± 2.61	46.1 ± 2.57	0.013
HBG, mean ± SD (mmol/L)	148 ± 12.3	143 ± 13.1	148 ± 12.2	<0.001
D-D, mean ± SD (ug/mL)	0.35 (0.27, 0.48)	0.46 (0.34, 0.69)	0.35 (0.27, 0.48)	<0.001
APTT, median (IQR) (s)	35.56 ± 3.46	36.5 ± 4.25	35.5 ± 3.42	0.058
Scr, mean ± SD (μmol/L)	87.1 ± 16.0	92.5 ± 22.7	86.9 ± 15.6	0.042
SUA, mean ± SD (μmol/L)	348 ± 69.9	335 ± 68.6	349 ± 69.9	0.089
ALT, median (IQR) (U/L)	17 (13, 23)	14 (10, 19)	17 (13, 23)	<0.001
TBIL, mean ± SD (μmol/L)	13.3 ± 4.92	12.8 ± 4.53	13.3 ± 4.94	0.406
Current/past smoking, n (%)	702 (43.3)	28 (38.8)	674 (43.5)	0.026
Current/past drinking, n (%)	987 (60.9)	29 (40.3)	958 (61.8)	<0.001
Regular exercise, n (%)	1153 (71.1)	37 (51.4)	1116 (72.0)	<0.001
Milk, n (%)				0.004
No	1003 (61.8)	56 (77.8)	947 (61.1)	
Yes	619 (38.2)	16 (22.2)	603 (38.9)	
Egg, n (%)				0.008
< 1 per day	678 (41.8)	41 (56.9)	637 (41.1)	
≥ 1 per day	944 (58.2)	31 (43.1)	913 (58.9)	
Fruit and vegetables, n (%)				0.001
< 250g per day	969 (59.7)	57 (79.2)	912 (58.8)	
≥ 250g per day	653 (40.3)	15 (20.8)	638 (41.2)	
Calcium supplement, n (%)				0.245
No	1157 (71.3)	47 (65.3)	1110 (71.6)	
Current/past	465 (28.7)	25 (34.7)	440 (28.4)	
Vitamin D supplement, n (%)				0.319
No	1251 (77.1)	59 (81.9)	1192 (76.9)	
Current/past	371 (22.9)	13 (18.1)	358 (23.1)	
CHD, n (%)	487 (30.0)	42 (58.3)	445 (28.7)	<0.001
CVD, n (%)	231 (14.2)	22 (30.6)	209 (13.5)	<0.001
Diabetes, n (%)	452 (27.9)	16 (22.2)	436 (28.1)	0.274

OP, osteoporosis; BMI, body mass index; FPG, fasting plasma glucose; TG, total triglyceride; HDL-C, high density lipoprotein cholesterol; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride-glucose index; TyG-BMI, TyG-body mass index; METS-IR, the metabolic score for insulin resistance; Scr, serum creatinine; SUA, serum uric acid; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TSH, thyroid stimulating hormone; D-D, D dimer; APTT, activated partial thromboplastin time; HGB, hemoglobin; TBIL, total bilirubin; CHD, coronary heart disease; CVD, cerebrovascular disease.

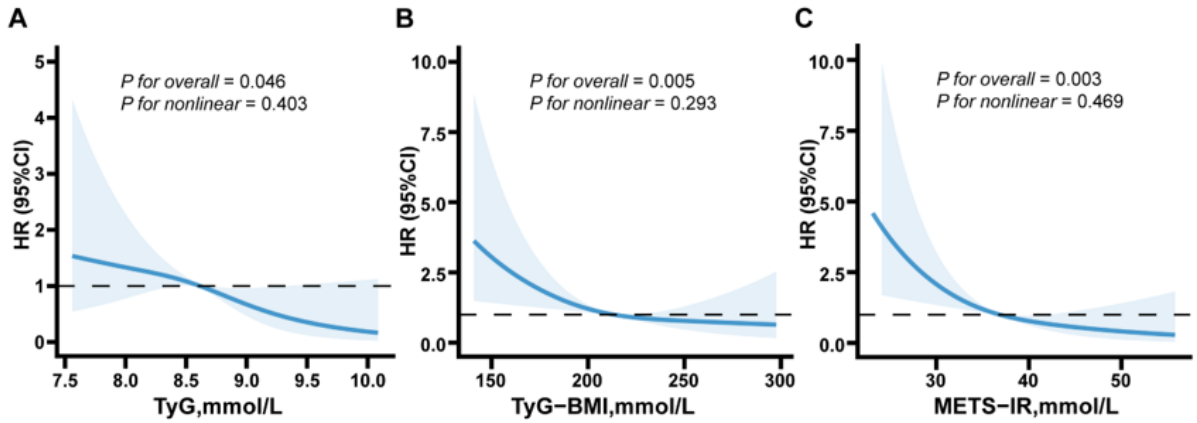

Figure 2. Dose-response analysis using restricted cubic splines. The model was adjusted for age, smoking status, drinking status, regular exercise, diabetes, CHD, CVD, egg, milk, fresh fruit and vegetables, SBP, D-D, APTT, Albumin, Scr, LDL-C, ALT, HBG and BMI (for TyG). The solid line represented the estimations, and the shaded area represented 95% confidence interval.

Table 2. Hazard ratios for the association between TyG, TyG-BMI, METS-IR and OP incidence

	Crude	*p* value	Model 1	*p* value	Model 2	*p* value
	HR (95% CI)		HR (95% CI)		HR (95% CI)	
TyG (continuous)	0.535 (0.321,0.889)	0.016	0.617 (0.369,1.029)	0.064	0.573 (0.336,0.976)	0.040
TyG						
Q1	1 (Ref.)		1 (Ref.)		1 (Ref.)	
Q2	0.545 (0.337,0.882)	0.013	0.639 (0.394,1.037)	0.070	0.587 (0.359,0.957)	0.033
TyG-BMI (continuous)	0.986 (0.978,0.994)	0.001	0.990 (0.982,0.998)	0.014	0.991 (0.984,0.999)	0.034
TyG-BMI						
Q1	1 (Ref.)		1 (Ref.)		1 (Ref.)	
Q2	0.630 (0.392.1.001)	0.056	0.782 (0.485,1.261)	0.314	0.569 (0.349,0.927)	0.023
METS-IR (continuous)	0.934 (0.897,0.972)	0.001	0.950 (0.913,0.988)	0.010	0.929 (0.892,0.968)	<0.001
METS-IR						
Q1	1 (Ref.)		1 (Ref.)		1 (Ref.)	
Q2	0.552 (0.341,0.893)	0.016	0.633 (3.91,1.025)	0.063	0.507 (0.310,0.830)	0.007

OP, osteoporosis; TyG, triglyceride-glucose index; TyG-BMI, TyG-body mass index; METS-IR, the metabolic score for insulin resistance.
Model 1: adjusted age, smoking status, drinking status, regular exercise, diabetes, CHD, CVD
Model 2: adjusted model 1 plus egg, milk, fresh fruit and vegetables, SBP, D-D, APTT, Albumin, Scr, LDL-C, ALT, HBG and BMI (for TyG)

ROC analysis in identifying osteoporosis

The ROC curves were also adapted to evaluate the performance of TyG, TyG-BMI and METS-IR in screening osteoporosis in older men (Figure 3). The area under the curve (AUC) was 0.585 (95%CI 0.524–0.646, $p = 0.014$), 0.615 (95%CI 0.545-0.686, $p = 0.001$) and 0.617 (95%CI 0.547–0.686, $p = 0.001$), but no significant difference was observed ($p = 0.323$).

DISCUSSION

In this longitudinal study based on 1622 Chinese middle-aged and older men, we observed that TyG, TyG-BMI and METS-IR were associated with MOP, especially in older participants with normal weight and with less eating of milk, egg, fruit and vegetables. These potential linearity associations were independent of traditional risk factors, including demographic characteristics, lifestyle, conditions of nutrition and common chronic diseases. Sensitivity analyses revealed the robustness of the findings.

Osteoporosis is highly prevalent worldwide, most of which are among postmenopausal women.[26] Given the characteristic of slow onset and lack of attention on MOP, the incidence of osteoporosis in men has not been well reported. In this six-year follow-up study, the total incidence of MOP was 4.4% and 7.7 per 1000 person-years during 9317 person-years. The incidence was lower than that of a 2-year longitudinal follow-up study based on physical examination population.[20] Specially, the incidence was varied by age, and those aged above 70 years were at 7-fold greater risk of osteoporosis. Results for age subgroups were consistent with the recommended screening age of MOP in guidelines.[3,4] Again, the necessity of screening osteoporosis in this age group is reiterated to reduce the potentially heavy burden of disease.[4]

However, the relationship between IR and osteoporosis is still unclear.[9] IR is a notoriously important cause in the pathological mechanism of metabolic diseases, especially in T2DM.[18,27] More and more indicators are being developed to represent IR, including HOMA-IR, TyG, TyG-BMI and METS-IR, given the impracticability of HECT in clinical practice.[28] A 2-year longitudinal follow-up study based on 8,770 physical examination population showed that TyG indicated IR has a negative association with OP in both sexes, but covariate adjustment of this study did not take into account the effect of diabetes.[20] On the contrary, a cross-sectional study including 210 diabetic postmenopausal women presented that METS-IR was a protective factor for OP, no significance was showed in TyG and HOMA-IR.[28] TyG-BMI may contribute to low bone turnover in participants with T2DM.[22] And another cross-sectional study about adults aged ≥ 20 years from NHANES datasets showed that HOMA-IR were related with elevated BMD at the hip,[29] while the findings were opposite in the Korean population study.[30] More complicated, however, is the different degree of IR might have effect on the association. That is to say, the association might be nonlinear and have a threshold effect. A previous study used HOMA-IR to explore this association and found that HOMA-β ≥ 100 was associated with a lower risk of osteoporosis when HOMA-IR < 2 and no significant when HOMA-IR ≥ 2.11 And higher degree of HOMA-IR (CP) (> 4.00) was found to increase the risk of osteoporosis among postmenopausal women with T2DM. For men, the OR and 95%CI was 0.80 (0.46-1.38), and could not draw conclusions with limited sample size.[19]

In our cohort study, we applied IR-related indicators TyG, TyG-BMI and METS-IR, and reached an inverse and linear association with MOP, especially when at relatively low levels. These finding suggested that, unlike the effects of insulin resistance on cardiovascular blood

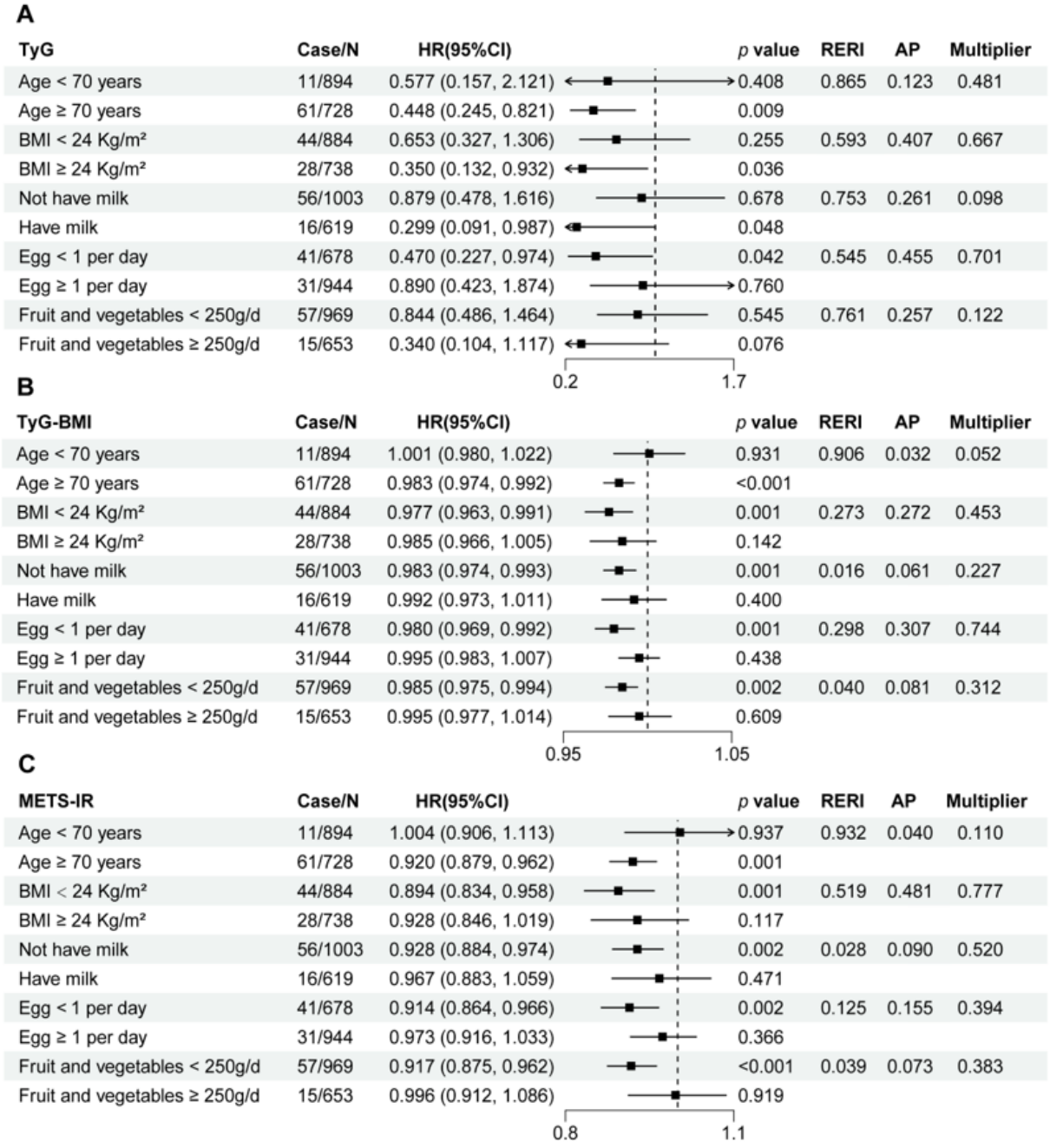

Figure 3. HRs for osteoporosis among sub-populations. Adjusted age, BMI, smoking status, drinking status, regular exercise, diabetes, CHD, CVD, egg, milk, fresh fruit and vegetables, SBP, D-D, APTT, Albumin, Scr, LDL-C, ALT and HBG. Grouping variables are not adjusted for the corresponding subgroup

vessels, moderate levels of insulin resistance may not be harmful to bone. The same phenomenon exists in the relationship between obesity and osteoporosis.[31] Previous evidences present that participants with low body weight (BMI <18.5 kg/m^2) have a significantly increased risk of osteoporosis,[1,32] while overweight or obesity have an increased risk of IR.[33] Our research also confirmed this phenomenon and found the inverse associations between TyG, TyG-BMI and METS-IR and MOP were more clearly established in the population with normal BMI. In our study, participants were divided into two groups using BMI 24 kg/m^2 as cutoff, given the small proportion of low body weight without new occurrence of osteoporosis. In other words, the positive association between IR and osteoporosis in men could not be interfered with low body weight. And more large-scale studies are required to explore these associations in older men with overweight or obese.

Moreover, eating eggs, milk, fresh fruits and vegetables in daily life are recognized as good nutritional behaviors for human health.[34] Our study also found their benefit for bone health and reduced the incidence of osteoporosis in men.[35] Especially, interaction between nutritional behaviors and TyG-BMI, METS-IR was observed, and it did underscore the importance of considering these nutritional factors in osteoporosis risk assessment.

The mechanism behind the controversial findings is also complex and unclear.[9,36] The potentially protective effect of IR on OP may attribute to the anabolic effects of hyperinsulinemia. As we known, IR is an impairment of

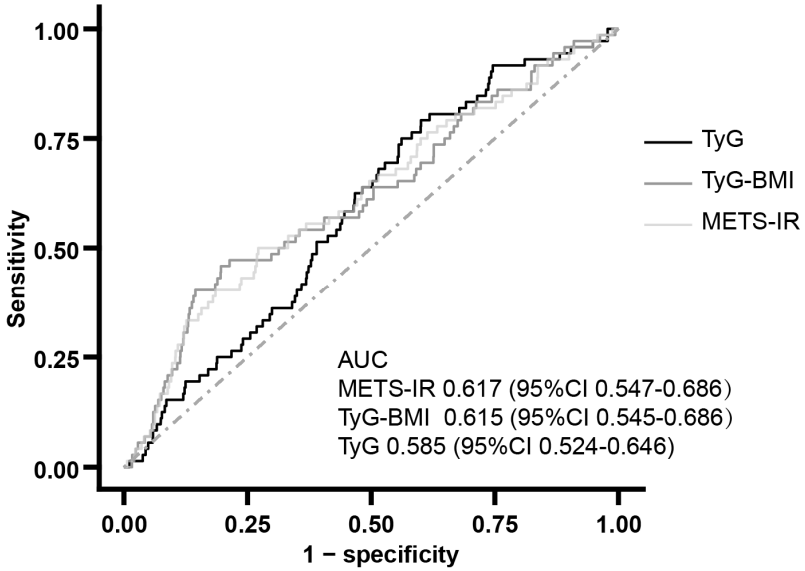

Figure 4. Comparison of area under the curve for the older men without OP.

insulin action on the regulation of glucose metabolism in targeted tissues, involving muscle, liver and fat.[28] And when in the IR status, the capacity of insulin secretory by pancreatic β-cells would increase and then develop hyperinsulinemia.[9] The role of insulin secretion can physiologically promote proliferation of osteoblast, inhibit activity of osteoclast, and lead to an increase in bone mass.[28] Moreover, excessive insulin has the synergistic effect with other hormones, liking insulin-like growth factor and parathyroid hormone, to further boost the bone mass.[37] Additionally, some studies have pointed out that IR positively affected the level of periostin, which was a matricellular protein from osteoblast and osteocytes,[38] and strongly associated with chronic inflammation.[39] And IR was also related to slerostin, a noted inhibitor of osteoblast differentiation.[40,41] However, the real role of bone-specific insulin resistance in human body and the difference between sex still remain to be established.[9,42]

This was a cohort study focusing on osteoporosis from nonoccurrence to occurrence in a wide age range of men, which were easily overlooked by the public. And we hoped to provide more ideas for the future researches of MOP, through this relatively high-level epidemiological evidence. However, there were several limitations in this study. First, the complicatedly causal relationship between osteoporosis and insulin metabolism could not be verified in an observational design. Second, compared with the onset cycle of disease, longer follow-up is still required. And sufficient cases can better clarify the age and BMI specific-effects. Third, this study was from a single center, and more large-scale and multi-center studies are needed. Finally, we have adjusted many covariables and considered the potential effects of vegetables and fruits, but still cannot distinguish their respective roles, and detailed information on falls, social support, and health care medications were not involved, which might have impact on the incidence of OP. And the changes of TyG and relative indices and common chronic diseases over time may also affect this risk.

Conclusion

This cohort study showed that TyG, TyG-BMI and METS-IR were associated with reduced incidence of MOP, and the relationship was thought to correlate with BMI and nutritional behaviors among senile adults. Future large-scale and multi-center prospective studies and mechanism researches are still essential.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURES

The authors declare no conflict of interest.

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Supplementary Tables

Supplementary Table 1. Incidence of OP among the older men

	OP (Number)	Incidence (%)	Total person-years	Incidence density (per 1000 person-years)
Total	72/1622	4.4	9317.0	7.7
Age <70 years	11/894	1.2	5527.6	2.0
Age ≥ 70 years	61/728	8.4*	3789.4	16.1*
TyG Q1	46/807	5.7	4593.2	1.0
TyG Q2	26/815	3.2*	4723.8	0.6*
TyG-BMI Q1	44/811	5.4	4646.7	0.9
TyG-BMI Q2	28/811	3.5	4670.3	0.6*
METS-IR Q1	46/810	5.7	4610.9	1.0
METS-IR Q2	26/812	3.2*	4706.1	0.6*

*Comparison between groups $p<0.05$

Supplementary Table 2. Sensitivity analysis of HRs for the OP incidence

	Crude HR (95%)	*p* value	Adjusted HR (95%)	*p* value
Excluding participants within a year of follow-up (n = 27)				
TyG	0.522 (0.306,0.889)	0.017	0.566 (0.324,0.989)	0.045
TyG-BMI	0.987 (0.979,0.995)	0.001	0.985 (0.976,0.993)	0.001
METS-IR	0.935 (0.897,0.976)	0.002	0.929 (0.890,0.970)	0.001
Excluding participants with new occurrence of fragility fracture (n = 25)				
TyG	0.513 (0.273,0.965)	0.038	0.422 (0.210,0.848)	0.015
TyG-BMI	0.982 (0.973,0.992)	<0.001	0.980 (0.970,0.990)	<0.001
METS-IR	0.912 (0.869,0.957)	<0.001	0.909 (0.864,0.957)	<0.001
Used the regression modeling of competing risk				
TyG	0.536 (0.336,0.854)	0.009	0.512 (0.280,0.935)	0.029
TyG-BMI	0.986 (0.978,0.995)	0.002	0.988 (0.980,0.997)	0.006
METS-IR	0.934 (0.896,0.975)	0.002	0.938 (0.900,0.977)	0.002

Adjusted age, smoking status, drinking status, regular exercise, diabetes, CHD, CVD, egg, milk, fresh fruit and vegetables, SBP, D-D, APTT, Albumin, Scr, LDL-C, ALT, HBG and BMI (for TyG).