The association between serum triglyceride to high-density lipoprotein cholesterol ratio and sarcopenia in community adults: positive or negative?

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Research

Abstract

Background

The serum triglyceride to high-density lipoprotein cholesterol(TG/HDL) ratio has been identified to be positively correlated with a higher risk of sarcopenia in elderly Korean males in previous study. In this study, we aimed to discover the association between TG/HDL ratio and sarcopenia in Chinese community adults, including males and females.

Methods

Individuals, who participated in medical examinations at the First Affiliated Hospital of Wenzhou Medical University from May 2016 to August 2017 with the age older than 18 years, were enrolled in the study. We applied univariable and multivariable logistic regression analyses to weigh the effects of TG/HDL ratio on the status of sarcopenia. Besides, we further identified the association by subgroup analysis.

Results

The occurrence of sarcopenia significantly decreased with the TG/HDL ratio increased. The odds ratio(OR) of TG/HDL ratio(high vs. low) for sarcopenia was 0.408(95%CI: 0.323−0.516) by univariable analysis and 0.631 by multivariable analysis(95%CI: 0.494−0.806) respectively. Additionally, the effect of TG/HDL ratio on sarcopenia was favorable(HR < 1.0) across a majority of prespecified subgroups, except age ≥ 65 and overweight population.

Conclusions

TG/HDL ratio was negatively correlated with prevalence of sarcopenia in Chinese community adults, especially in individuals with the age < 65 years old and the BMI < 25 kg/m^2.

Introduction

Age-related loss of muscle mass and function, termed "sarcopenia", has aroused a great interest all over the world, including China.[1−5] In 2014, the Asian Working Group for Sarcopenia(AWGS) proposed the definition of the sarcopenia, in which age related loss of muscle mass, plus low muscle strength, and/or low physical performance were essential diagnostic components.[5] In 2019, AWGS defined "possible sarcopenia" as either low muscle strength or low physical performance only. It is increasingly prevalent in the community, with 5.5−25.7% prevalence of sarcopenia.[6−8] Sarcopenia has become a public health problem, along with the accelerated aging of population.

So far the mechanisms underlying the sarcopenia hasn't been elaborated completely,many factors, such as aging, frailty, malnutrition, cachexia, inflammation and hormonal changes, has been regarded as causes of sarcopenia.[9–15]

Serum lipid profiles are simple laboratory parameters that commonly tested clinically, including fasting serum triglyceride(TG) and cholesterol. Tae-Ha *et al.* demonstrated that TG to high-density lipoprotein(HDL) cholesterol ratio(TG/HDL) was positively correlated with an increased prevalence risk of sarcopenia in elderly Korean males.[16] Given this finding, we aimed to discover the association between TG/HDL and occurrence of sarcopenia in Chinese community adults, including males and females, and we found the opposite result.

Methods

Study population

This cross-sectional study included Chinese community adults participating in regular medical examinations at the First Affiliated Hospital of Wenzhou Medical University from May 2016 to August 2017. We included individuals who were 18 years or older and who had bioelectrical impedance analysis(BIA) and serum lipid profiles measures. Exclusion criteria for the study were: (1) individuals younger than 18 years old; (2)individuals with a history of stroke, thyroid disease, chronic kidney disease, chronic liver disease or malignant tumor; (3) individuals taking medicine for dyslipidemia.

A total 2613 subjects were enrolled in the study. All data concerning the demographic and clinical characteristics were reviewed and analyzed in accordance with the Declaration of Helsinki. The study was approved by the institutional review board(IRB) of The First Affiliated Hospital of Wenzhou Medical University and consent was waived by the IRB, given the cross-sectional nature of this study.

Data collection

We collected the data in regard to the health examinations for community adults, included questionnaires containing lifestyle factors and medical histories, and anthropometric, BIA, blood and biochemical measurements.

Lifestyle behaviors were evaluated, including alcohol consumption and smoking. Heavy drinks were defined as alcohol drinking > 140 g/week for males and > 70 g/week for females. Smoking status was stratified as 3 types: never(an individual who has never smoked), past(an individual who smoked in the past and abandoned for 2 years at least) and current smokers(an individual who smokes currently and last for 6 months at least).

Medical history indicated current or past morbidities, including hypertension, diabetes mellitus, hyperuricemia. Diabetes mellitus(DM) was defined as a self-reported history of the DM, fasting plasma glucose(FPG) above 126 mg/dL(7.0 mmol/L), 2-h plasma glucose(PG) above 200 mg/dL(11.1 mmol/L) or a random PG above 200 mg/dL(11.1 mmol/L).[17] Hypertension(HTN) was defined as a self-reported

history of the HTN, systolic blood pressure(SBP) above 140 mmHg, or diastolic blood pressure(DBP) above 90 mmHg.[18] Hyperuricemia was defined as a self-reported history of the disease, or serum uric acid(UA) above 7.0 mg/dl in males and above 6 mg/dl in females.[19]

After 8-h overnight fasting, the height and weight were measured on the morning. The body mass index(BMI) was calculated as follows: BMI(kg/m^2) = weight(kg) / the square of the height(m^2). Overweight was defined as BMI equal to or more than 25 kg/m^2.

BIA(InBody770; InBody Japan Inc., Tokyo, Japan) was performed in each individual to measure appendicular skeletal muscle mass(ASM; kg). Skeletal muscle mass index(SMI) was computed as follows: SMI(kg/m^2) = ASM(kg) / the square of the height(m^2). And cutoffs for low muscle mass in sarcopenia diagnosis were 7.0 kg/m^2 in males and 5.7 kg/m^2 in females according to AWGS 2019 Consensus.[1]

After at least an 8-h overnight fast, blood samples were collected and measured the blood routine, liver and function, serum lipid profiles. As biochemical and blood parameters, FPG(mg/dL), glycated hemoglobin(HbA1c; %), total cholesterol(TC; mg/dL), low density lipoprotein cholesterol(LDL; mg/dL), high density lipoprotein cholesterol(HDL; mg/dL), triglycerides (TG; mg/dL), UA(µmol/L), albumin(g/dL), leukocyte count(WBC; ×10^9/L), hemoglobin(Hb; g/dL), platelet(PLT; ×10^9/L) were recorded.

Statistical analysis

Continuous variables were presented as medians(ranges), while categorical variables were presented as frequencies(percentages). We applied receiver operating characteristics(ROC) curves to evaluate the accuracies of the TG, HDL and TG/HDL ratio for sarcopenia diagnosis. Based on Youden index and area under curve(AUC), we selected the optimal indicator and grouping according to cutoff of the selected indicator(TG/HDL ratio low and high groups). In order to compare the differences between 2 groups, we performed the χ^2 test for categorical variables, and Mann-Whitney test for continuous variables. To weigh the effects of variables on the prevalence of sarcopenia, we applied univariable and multivariable logistic regression analysis. The variables with p value < 0.1 in univariable logistic regression analysis were brought into the subsequent multivariable analysis. Because frequency of sarcopenia distributed unevenly in different population, we also applied subgroup analyses according to different confounding factors. To further identified the correlation between TG/HDL ratio and prevalence of sarcopenia, individuals were stratified by quartiles(Q1: ≤1.72, Q2: 1.72−2.86, Q3: 2.86−4.85 and Q4: >4.85), and prevalence of sarcopenia were compared by χ^2 test.

All analyses were conducted with R version 3.6.1(https://www.r-project.org/). All statistical tests were 2-sided, and significance level was defined as p value < 0.05.

Results

Population characteristics

A total of 2613 individuals were enrolled in our analysis, with a median age of 48 years (range: 18–91 years), including 1614(61.8) males and 999(38.2) females. The median values of BMI, ASM and SMI were 23.81(15.05–43.02), 20.14(8.9-32.98) and 7.27(4.35–11.50), respectively. In terms of lipid profile, the median values of TC, LDL, HDL and TG were 199.87(85.83-402.84), 119.85(30.54-301.16), 45.23(17.40-108.25) and 127.44(35.40-1896.56), respectively. Other demographic and clinical characteristics were displayed in Table 1. According to AWGS 2019 consensus[17], a total of 362(13.9%) subjects were diagnosed as sarcopenia.

Optimal cutoff of TG/HDL ratio and association between TG/HDL ratio and clinicopathological factors

As pre-processing, ROC curves were utilized to evaluate the performances of TG, HDL, and TG/HDL ratio, and to discover corresponding cut-offs for sarcopenia diagnosis. As Fig. 1 showed, the cutoffs for TG(mg/dl), HDL(mg/dl), and TG/HDL ratio were 138.502 mg/dl(sensitivity: 0.718; specificity: 0.481), 42.719 mg/dl(sensitivity: 0.776; specificity: 0.439) and 2.775(sensitivity: 0.671; specificity: 0.546) respectively.

The AUC for TG(mg/dl), HDL(mg/dl), and TG/HDL ratio were 0.626(p < 0.001), 0.637(p < 0.001), 0.644(p < 0.001), respectively. Based on Youden index and AUC, we selected the TG/HDL ratio as optimal indicator. Individuals were divided into 2 groups: TG/HDL^{low} group(TG/HDL ratio < 2.775) and TG/HDL^{high} group(TG/HDL ratio ≥ 2.775).

There were 1266 subjects with low TG/HDL ratio(< 2.775) and 1347 subjects with high(TG/HDL ratio ≥ 2.775). The association between TG/HDL ratio and clinical variables were summarized in Table 1. Compared with TG/HDL^{low} group, TG/HDL^{high} group showed higher BMI(p < 0.001), ASM(p < 0.001), SMI(p < 0.001), with more elders(p = 0.001) and males(p < 0.001) in this group. In view of blood and biochemical parameters, TG/HDL^{high} group displayed higher values of FPG(p < 0.001), HbA1c(p < 0.001), UA(p < 0.001), TC(p < 0.001), LDL(p < 0.001), TG(p < 0.001), UA(p < 0.001), albumin(p = 0.002), WBC(p < 0.001) and Hb(p < 0.001), and lower values of HDL(p < 0.001). In consideration of clinical parameters, there were more current smokers(p < 0.001), heavy drinkers(p < 0.001), and DM(p < 0.001), HTN(p < 0.001) and hyperuricemia(p < 0.001) patients, existing in TG/HDL^{high} group.

Univariable and multivariable logistic regression analyses

Variables having effects on sarcopenia were identified by the univariable and multivariable logistic regression analyses, and the results were listed in Table 2. In the univariate logistic regression analysis, factors including age[> 65 vs. ≤65, odds ratio(OR): 1.888, 95% confidence interval(95%CI): 1.319–2.703], gender(male vs. female, OR: 1.775, 95%CI: 1.420-2,219), heavy drink(yes vs. no, OR: 0.700, 95%CI: 0.490-1.000), DM(yes vs. no, OR: 0.708, 95%CI: 0.468–1.073), HTN(yes vs. no, OR: 0.757, 95%CI: 0.584–0.983), hyperuricemia(yes vs. no, OR: 0.564, 95%CI: 0.419–0.758), overweight(yes vs. no, OR: 0.031, 95%CI:0.015–0.065) and TG/HDL ratio(high vs. low, OR: 0.408, 95%CI: 0.323–0.516), showed significant association with sarcopenia and were subsequently brought into multivariable analysis. As Table 2

showed, age(> 65 vs. ≤65, OR: 2.100, 95%CI: 1.427−3.089), overweight(yes vs. no, OR: 0.035, 95%CI: 0.016−0.074) and TG/HDL ratio(high vs. low, OR: 0.631, 95%CI: 0.494−0.806) still remained the independent effects on sarcopenia with statistical significance. The C-index for this multivariable analysis model was 0.732.

Subgroup analyses

There were confounding factors existing in this study, including age and overweight, as Table 2 showed. In addition, gender might be a confounding factor, as Chung *et al.* proposed that TG/HDL ratio was associated with sarcopenia in elderly Korean males.[16] Thus, in our study, we chose these 3 factors and conducted further subgroup analyses, which was displayed in Fig. 2.

In age < 65 subgroup, more subjects were diagnosed with sarcopenia in TG/HDL^{low} group than in TG/HDL^{high} group[216 of 1161 subjects(18.6%) vs. 100 of 1223(8.2%)]. No matter in male[94 of 564 subjects(16.7%) vs. 86 of 1050(8.2%)] subgroup or in female[149 of 702 subjects(21.2%) vs. 33 of 297(11.1%)], TG/HDL ratio remained the independent effect. In non-overweight population[240 of 1026 subjects(23.4%) vs. 115 of 701(16.4%)], more subjects in TG/HDL^{low} group tend to be diagnosed with sarcopenia. The effect of TG/HDL ratio on status of sarcopenia was favorable (HR < 1.0) across a majority of prespecified subgroups, except age ≥ 65(HR: 0.523, 95%CI: 0.271−1.007) and overweight(HR: 0.492, 95%CI: 0.109−2.216) population.

Correlation between TG/HDL ratio and prevalence of sarcopenia

Individuals were stratified by quartiles into Q1, Q2, Q3 and Q4 groups, respectively. Figure 3 displayed the prevalence of sarcopenia of each group. The prevalence of sarcopenia decreased significantly as TG/HDL ratio increased(p < 0.001): 22.6% of Q1, 15.0% of Q2, 10.3% of Q3 and 7.4% of Q4, respectively.

Discussion

In the study, we discovered that TG/HDL ratio was negatively related with prevalence of sarcopenia in Chinese community adults. In the previous research by Tae-Ha et al, higher TG/HDL ratio was positively associated with a higher risk of sarcopenia in elderly Korean men, which was accompanied by the status of insulin resistance. [16] Compared to the study by Tae-Ha et al, we enrolled a wider group of people, including males and females, with an average age of 48 years(range: 18−91). It might be nationality and gender differences that caused the yield totally different results.

In subgroup analyses, TG/HDL ratio remained the independent association with the risk of sarcopenia in males and females, with the age < 65 years old. But TG/HDL did not show the significantly association with sarcopenia in individuals with the age ≥ 65 years old, which was inconsistent with the previous study by Tae-Ha *et al.* [16] It was speculated that there might be a fluctuant association between TG/HDL

ratio and frequency of sarcopenia with age. In our study, the proportion of subjects over 65 was 8.8%. A further study enrolling more old people is required in the future.

Lipid profile is an easy and economic parameter, which is widely used clinically. As a part of lipid profile, medium-chain TG was verified to be a potential nutrient for sarcopenia in a randomized controlled trial. It was because medium-chain TG could activate the ghrelin to increase muscle function.[20] In addition, plasma TG generated from omega 3 fatty acid attenuate muscle loss, which was reviewed by Stella et al. [21] As an important member of lipid profile, HDL was identified to be negatively associated with muscle strength improving.[22–24] Based on these research findings, the negative correlation between TG/HDL ratio and sarcopenia should be considered. Thus, appropriate supplement of fatty foods might be beneficial to muscle mass and muscle strength, but supplementing to what degree required more further studies.

This study had some limitations. Primarily, because it was a cross-sectional study, a causality could not be developed. Secondly, due to the lack of data, we didn't take new definition of sarcopenia into consideration, which proposed utilizing the existence of low muscle mass and low muscle strength for the diagnosis of sarcopenia[1]. Thirdly, many of the subjects enrolled in our study were younger than 65, and the population was Chinese community adults without any severe diseases. Thus, it might be restrictive to apply to the older and critical patients. Last, cutoff of TG/HDL ratio was defined by ROC curve with a restrictive sensitivity of 0.671 and specificity of 0.546. Therefore, the cutoff of 2.775 was for reference of grouping individuals by TG/HDL ratio only.

In conclusion, our study indicated that low TG/HDL ratio was a promising risk marker for sarcopenia. Further prospective studies, with a larger sample size and more comprehensive data, are required to validated the association between TG/HDL ratio and the frequency of sarcopenia.

Declarations

Acknowledgement

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Tables

Table 1 Clinical characteristics of the study population according to TG to HDL cholesterol ratio.

Variables	Total(N=2613)	TG/HDL ratio		P value
		Low(N=1266)	High(N=1347)	
Age(years)	48(18-91)	47(18-91)	49(21-83)	0.001
Gender(%)				
Male	1614(61.8)	564(44.5)	1050(78.0)	<0.001
Female	999(38.2)	702(55.5)	297(22.0)	
BMI(kg/m2)	23.81(15.05-43.02)	22.41(15.05-32.63)	24.92(16.44-43.02)	<0.001
Overweight(%)	886(33.9)	240(19.0)	646(48.0)	<0.001
ASM(kg)	20.14(8.9-32.98)	17.69(8.9-28.73)	21.56(11.67-32.98)	<0.001
SMI(kg/m^2)	7.27(4.35-11.50)	6.70(4.35-9.38)	7.64(4.99-11.50)	<0.001
Systolic blood pressure(mmHg)	124(77-196)	121(77-194)	126(86-196)	<0.001
Diastolic blood pressure(mmHg)	74(40-119)	71(40-111)	76(41-119)	<0.001
Blood and biochemical parameters				
Fasting plasma glucose(mg/dL)	86.4(54.0-327.6)	84.6(54.0-246.6)	88.2(55.8-327.6)	<0.001
Glycated hemoglobin(%)	5.4(3.3-16.7)	5.3(3.9-11.9)	5.5(3.3-16.7)	<0.001
Total cholesterol(mg/dL)	199.87(85.83-402.84)	194.07(85.83-400.52)	206.44(103.22-402.84)	<0.001
LDL cholesterol(mg/dL)	119.85(30.54-301.16)	115.01(30.54-301.16)	124.49(42.53-272.94)	<0.001
HDL cholesterol(mg/dL)	45.23(17.40-108.25)	53.74(25.90-108.25)	39.43(17.40-74.23)	<0.001
Triglycerides (mg/dL)	127.44(35.40-1896.56)	88.50(35.40-247.80)	192.93(82.31-1896.56)	<0.001
Uric acid(μmol/L)	5.76(1.73-12.89)	5.09(1.73-11.51)	6.375(2.81-12.89)	<0.001
Albumin(g/dL)	4.44(2.97-5.60)	4.43(3.32-5.60)	4.45(2.97-5.48)	0.002
Leukocyte count(×10^9/L)	5.88(1.74-14.72)	5.44(1.74-14.33)	6.25(2.90-14.72)	<0.001
Hemoglobin(g/dL)	146(42-191)	139(42-181)	151(77-191)	<0.001
Platelet(×10^9/L)	229(31-638)	230(31-638)	227(90-489)	0.194

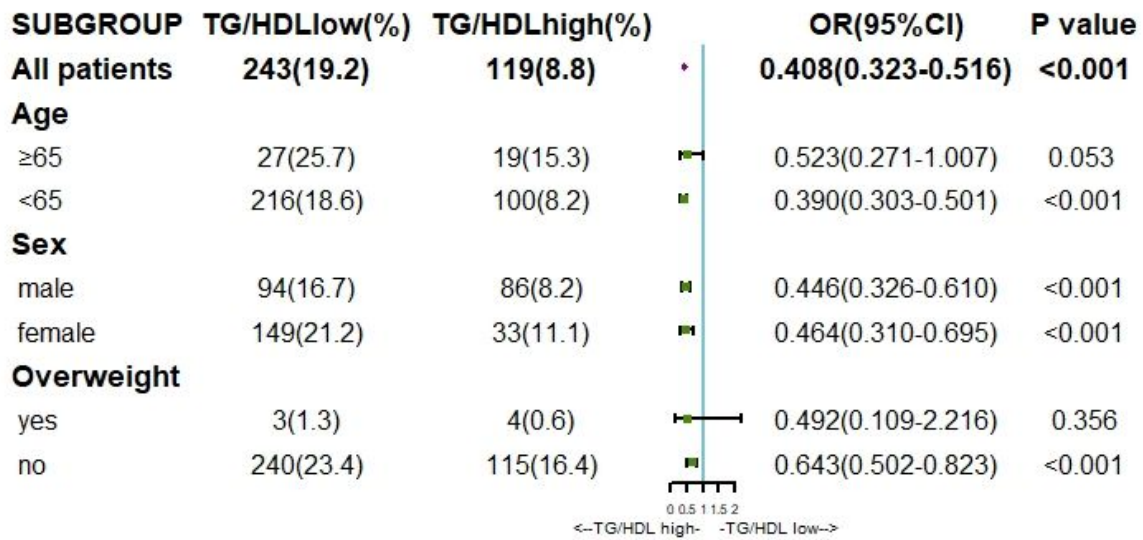|				
Clinical parameters				
Smoking(%)				
Never	1922(73.6)	1052(83.1)	870(64.6)	<0.001
Past	60(2.3)	21(1.7)	39(2.9)	0.037
Current	631(24.1)	193(15.2)	438(32.5)	<0.001
Heavy drink(%)	361(13.8)	121(9.6)	240(17.8)	<0.001
Diabetes mellitus (%)	257(9.8)	61(4.8)	196(14.6)	<0.001
Hypertension(%)	726(27.8)	292(23.1)	434(32.2)	<0.001
Hyperuricemia	628(24.0)	152(12.0)	476(35.3)	<0.001
BMI, body mass index; ASM, appendicular skeletal muscle mass; SMI, skeletal muscle mass index.				

Table 2. Univariable and multivariable analysis of clinical characteristics for sarcopenia				
	Univariate analysis		Multivariate analysis	
Variables	Crode OR(95% CI)	P value	Adjust OR(95% CI)	P value
Age, >65 vs. ≤65	1.888(1.319-2.703)	<0.001	2.100(1.427-3.089)	<0.001
Gender, male vs. female	1.775(1.420-2,219)	<0.001	1.158(0.898-1.494)	0.258
Smoking(%)				
past vs. never	0.784(0.353-1.743)	0.551		
current vs. never	0.838(0.640-1.096)	0.197		
Heavy drink, yes vs. no	0.700(0.490-1.000)	0.050	0.950(0.639-1.413)	0.800
Diabetes mellitus, yes vs. no	0.708(0.468-1.073)	0.103		
Hypertension, yes vs. no	0.757(0.584-0.983)	0.037	0.985(0.737-1.317)	0.918
Hyperuricemia, yes vs. no	0.564(0.419-0.758)	<0.001	0.970(0.698-1.349)	0.858
Overweight, yes vs. no	0.031(0.015-0.065)	<0.001	0.035(0.016-0.074)	<0.001
TG/HDL ratio high vs. low	0.408(0.323-0.516)	<0.001	0.631(0.494-0.806)	<0.001

Figures
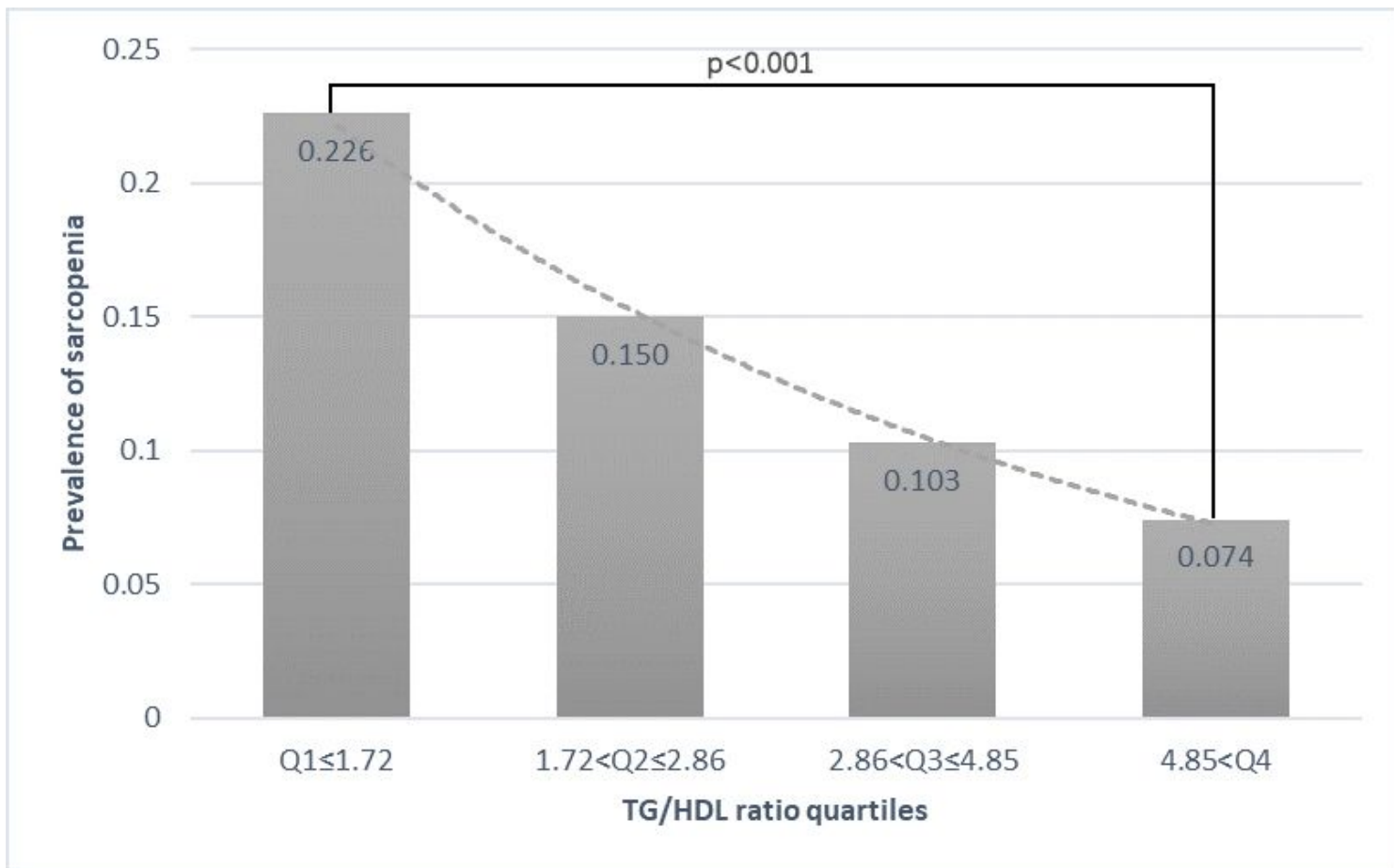
Figure 1

Receiver operating characteristic(ROC) curve analyses of the TG, HDL and TG/HDL ratio in sarcopenia status.

SUBGROUP	TG/HDLlow(%)	TG/HDLhigh(%)		OR(95%CI)	P value
All patients	243(19.2)	119(8.8)		0.408(0.323-0.516)	<0.001
Age					
≥65	27(25.7)	19(15.3)		0.523(0.271-1.007)	0.053
<65	216(18.6)	100(8.2)		0.390(0.303-0.501)	<0.001
Sex					
male	94(16.7)	86(8.2)		0.446(0.326-0.610)	<0.001
female	149(21.2)	33(11.1)		0.464(0.310-0.695)	<0.001
Overweight					
yes	3(1.3)	4(0.6)		0.492(0.109-2.216)	0.356
no	240(23.4)	115(16.4)		0.643(0.502-0.823)	<0.001

0 0.5 1 1.5 2

<--TG/HDL high-   -TG/HDL low-->

Figure 2

Subgroup analysis of TG/HDL ratio in sarcopenia status. Note: The second column lists numbers(%) of individuals with sarcopenia in TG/HDLlow group. The third column lists numbers(%) of individuals with sarcopenia in TG/HDLhigh group.