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The Optimal Cutoff Value of ApolipoproteinB/ApolipoproteinA-I Ratio for the Diagnosis of Metabolic Syndrome and Insulinresistance in the Population of Georgia

Zaza Makaridze[a]*, Ketevan Asatiani[b]

[a]*MD,"Medicore"Ltd,Tbilisi State Medical University Affiliated Clinic,16 Qavtaradze str, Tbilisi 0186, Georgia*
[b]*MD, PhD, National Institute of Endocrinology,Tbilisi State University Affiliated Clinic,2-6 Ljubljana str,Tbilisi 0159,Georgia*
[a]*Email: z.makaridze@medicore.ge*
[b]*Email: asatianiketevan@yahoo.com*

Abstract

Studies have indicated that ApoB/ApoA-I ratio is significantly associated with MetS and IR. This study was designedto assess the optimal cutoff values of ApolipoproteinB/ApolipoproteinA-I (ApoB/ApoA-I) ratio for the diagnosis of metabolic syndrome and insulin resistance (IR) in the population of Georgia. The subjects were 1522 Georgians of Caucasian origin aged 18-80 (653 women and 869 men) without diabetes mellitus. MetS was diagnosed using the updated ATP-III definition of the metabolic syndrome. Receiver operating characteristics (ROC) curve analysis was performed to calculate the cutoff values. ROC analysis showed that areas under the curve (AUCs) of ApoB/ApoA-I ratio for the detection of MetS were 0.786±0.025 (95%CI: 0.737-0.834) in women and 0.815±0.017 (95%CI: 0.782-0.847) in men. AUCs of ApoB/ApoA-I ratio for the diagnosis of IR were 0.887±0.019 (95%CI: 0.850-0.924) in women and 0.816±0.022 (95%CI: 0.773-0.860) in men. After adjustment for age, MetS components and low-density lipoprotein cholesterol, odds ratios according to the determined cutoff values of ApoB/ApoA-I ratio were: for MetS – 1.75 in women and 1.18 in men; for IR – 13.61 in women and 7.75 in men.

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* Corresponding author.
E-mail address: z.makaridze@medicore.ge.

Study showed that in the population of Georgia optimal cutoff values of ApoB/ApoA-I ratio for the detection of MetS were 0.74 in women and 0.82 in men; for the detection of IR these values were 0.82 in women and 0.98 in men.

Keywords: ApoB/ApoA-I ratio; cutoff value; insulin resistance; metabolic syndrome

1. Introduction

The prevalence of metabolic syndrome and insulin resistance (IR) is increasing worldwide [7, 18, 20, 23, 34]. MetS is a condition that promotes atherogenesis and increases the risk of cardiovascular disease and diabetes mellitus (DM) [10, 12, 14, 19, 24] by a grouping of multiple risk factors such as central obesity, arterial hypertension (AH), glucose intolerance, elevated triglycerides and low high-density lipoprotein cholesterol (HDL-C) [2]. These factors are associated with insulin resistance (IR), which is considered to be the underlying shared pathophysiological disturbance [12, 24, 38]. So, determining additional simple markers for the detection of MetS and IR can help better identify patients who are at high risk for cardiovascular disorders and DM. IR can be measured by Homeostasis model assessment of insulin resistance (HOMA-IR), Quantitative Insulin Sensitivity Check Index (QUICKI) and other indices [5, 6, 21, 26-28, 35]. MetS is diagnosed by a combination of various clinical and laboratory criteria, according to different definitions [1-3].Recent studies have indicated that ApoB/ApoA-I ratio is significantly associated with MetS components and IR [9, 22, 29, 30, 33, 37, 39]. Serum concentration of ApolipoproteinA-I (ApoA-I), which is the protein covering the HDL particle, reflects the number of anti-atherogenic particles. Serum concentration of ApoB yields the number of atherogenic particles [11, 32].

There are several reports, determining the optimal cutoff value of ApoB/ApoA-I ratio for the detection of MetS and IR [15, 16, 25, 36]. There is no Georgian report available about this subject. So we conducted this study to assess the value of ApoB/ApoA-I ratio for the detection of MetS and IR in the population of Georgia.

2. Materials and Methods

Details about the materials and methods (Subjects, Anthropometric measurements and laboratory data, MetS and IR definition) are described elsewhere [22].

2.1 Subjects

We analyzed 1522 Georgians of Caucasian origin, who had visited the clinics for a related health checkup between 2012 and 2013. Subjects were men and non-pregnant women aged ≥ 18 years, < 80 years (mean age = 45 years, 653 women and 869 men). Informed consent was obtained from every subject.

2.2 Anthropometric measurements and laboratory data

Anthropometric measurements were done using standardized techniques and equipment. Insulin sensitivity index was determined using the updated computer homeostasis model assessment (HOMA2-IR) index. Venous blood samples were drawn after a minimum of 8 h of fasting. ApoB and ApoA-I levels were measured by the immunoturbidimetric assay with Roche Diagnostics kit, using Roche/Hitachi C311 analyzer. Other laboratory measurements were done using HUMAN Diagnostic Kit (GERMANY).

2.3 Metabolic syndrome definition

The updated ATP-III definition of MetS[13] was used when any three or more criteria were present: waist circumference (WC) ≥ 102cm in men and ≥ 88cm in women; impaired fasting glucose - fasting blood glucose (FG) of ≥ 5.6 mmol/l (100mg/dl); systolic blood pressure (SP) ≥ 130mmHg and/or diastolic blood pressure (DP) ≥ 85mmHg or treatment of previously diagnosed hypertension; fasting levels of triglycerides ≥ 1.7 mmol/l (150mg/dl) or treatment for this abnormality; fasting high-density lipoprotein cholesterol (HDL-C) < 1.03 mmol/l (40mg/dl) for men and < 1.30 mmol/l (50mg/dl) for women or treatment for this abnormality

2.4 Statistical analysis

All the analysis were performed using IBM SPSS Statistics for Windows (version 22.0), except for ROC curve analysis, which was done with MedCalc Software bvba (version 11.4.2).

IR was defined as the gender-specific upper quartile ofHOMA2-IR (≥ 2.3 for women and ≥ 2.9 for men) and insulin sensitive (IS) as the remaining three quartiles. We used the Mann-Whitney U test to compare related data between sexes, between subjects with vs. without IR.

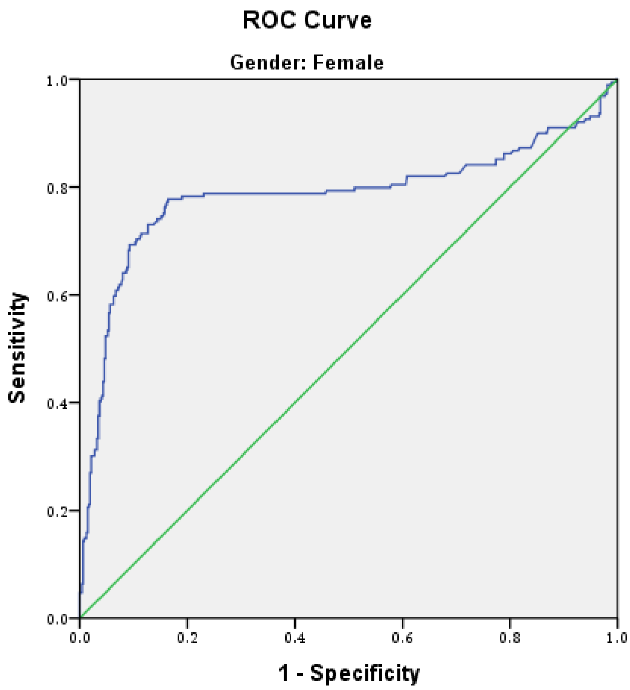

Figure 1: Receiver operating characteristic (ROC) curve of ApoB/ApoA-I ratio for MetS in females.

To assess the utility of ApoB/ApoA-I ratio as marker for MetS and IR, we built gender-specific receiver operator characteristic (ROC) curves and calculated the areas under the curve (AUC) and cut-off values of ApoB/ApoA-I ratio for the detection of MetS and IR in both sexes.

A binary logistic regression analysis was carried out to assess the association of determined cutoff values of ApoB/ApoA-I ratio with MetS and IR as definitions (after adjustment for age, MetS components and LDL-C). For all tests performed, a p value of less than 0.05 was considered significant.

3. Results

Main characteristics between sexes and between subjects with vs. without IR are described elsewhere [22].

To assess the predictive value of ApoB/ApoA-I ratio for MetS and IR, we analyzed the ROC curves of ApoB/ApoA-I ratio (Figure 1-4).

ROC analysis results for both sexes are shown in Table 1. AUCs of ApoB/ApoA-I ratio for the detection of MetS were: 0.786 in women and 0.815 in men; AUCs for the detection of IR were: 0.887 in women and 0.816 in men.

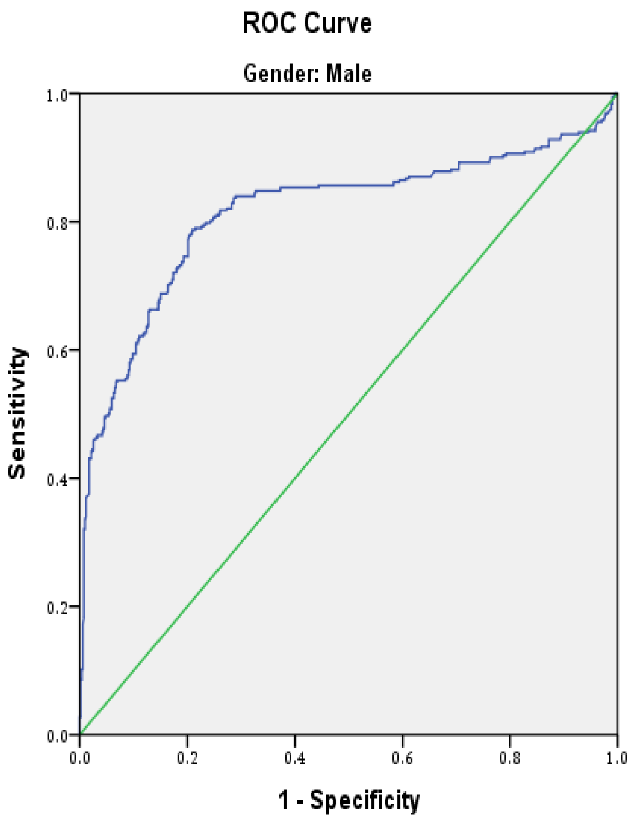

Figure 2: Receiver operating characteristic (ROC) curve of ApoB/ApoA-I ratio for MetS in males.

The optimal cutoff value of ApoB/ApoA-I ratio for the diagnosis of MetS was 0.74 (with sensitivity of 77.8% and specificity of 83.6%) in women and 0.82 (with sensitivity of 78.7% and specificity of 79.1%) in men(Figure

5). The optimal cutoff value of ApoB/ApoA-I ratio for the diagnosis of IR was 0.82 (with sensitivity of 87.7% and specificity of 88.8%) in women and 0.98 (with sensitivity of 74.8% and specificity of 88.3%) in men (Figure 6).

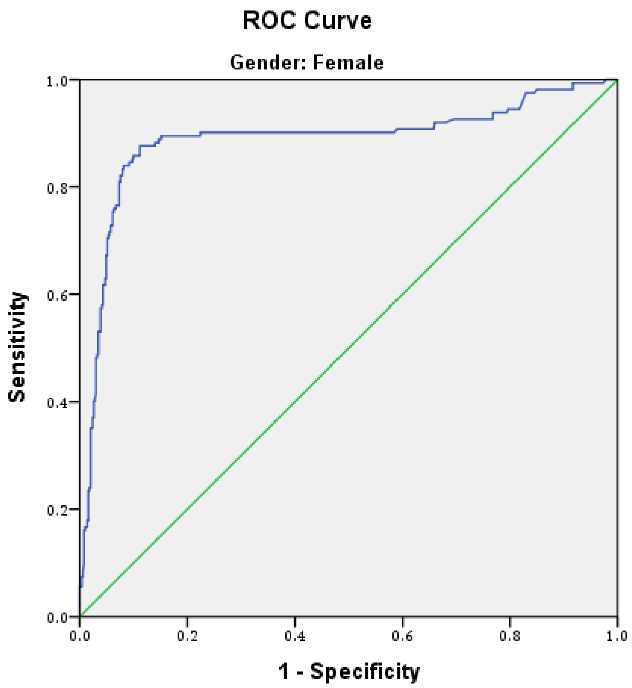

Figure 3: Receiver operating characteristic (ROC) curve of ApoB/ApoA-I ratio for IR in females.

Logistic regression models demonstrated that after adjustment for age, MetS components and LDL-C, determined cutoff values of ApoB/ApoA-I ratio were associated significantly with MetS: OR = 1.75 in women and 1.18 in men and with IR: OR = 13.61 in women and 7.75 in men (all $p < .05$) (Table 2).

4. Discussion

The prevalence of IR and MetS is increasing worldwide [7, 8, 18, 20, 34]. Many studies have indicated that ApoB/ApoA-I ratio is significantly associated with MetS components and IR [4, 9, 22, 29-31, 33, 37, 39]. But fewer studies (predominantly in Asian ethnicities) have focused on the optimal cutoff values of ApoB/ApoA-I ratio for the diagnosis of MetS and IR. The authors in [25] in the ATTICA study investigated the ApoA-I, ApoB and ApoB/ApoA-I ratio in relation to the MetS. Using the ROC curve analysis, they found that ApoB/ApoA-I ratio was the best diagnostic marker of MetS and the optimal discriminating cutoff value of this ratio was 0.72 (with sensitivity – 74% and specificity – 67%). The authors in [36] investigated 160 Chinese adolescent women with polycystic ovary syndrome. They concluded that ApoB/ApoA-I ratio was a good predictive marker of MetS and pre-MetS with a threshold value of ApoB/ApoA-I ratio of 0.63 for MetS (with sensitivity – 86.2% and specificity – 79.4%) and 0.58 for pre-MetS.

The authors in [16] investigated 10.940 Korean subjects who participated in a routine health screening examination. They found that the optimal ApoB/ApoA-I ratio cutoff value for the detection of MetS was 0.65 (with sensitivity – 63.5% and specificity – 61.3%) in men, and 0.62 (with sensitivity – 67.9% and specificity – 61.9%) in women.

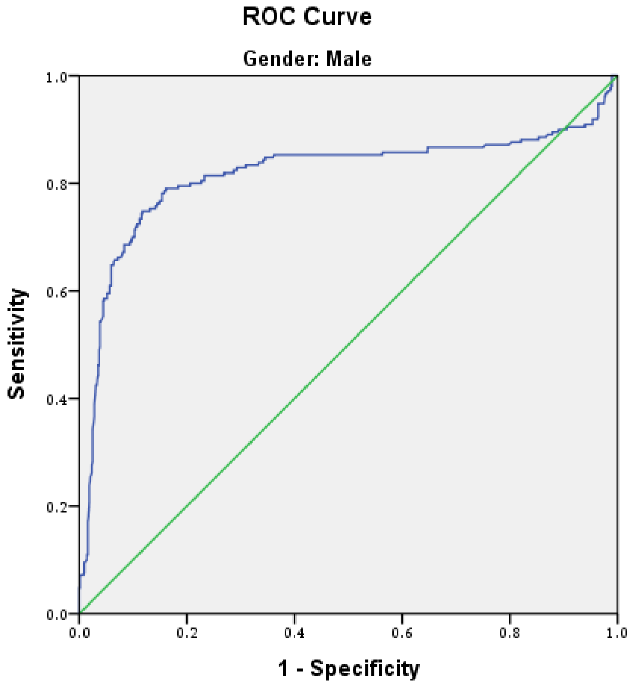

Figure 4: Receiver operating characteristic (ROC) curve of ApoB/ApoA-I ratio for IR in males

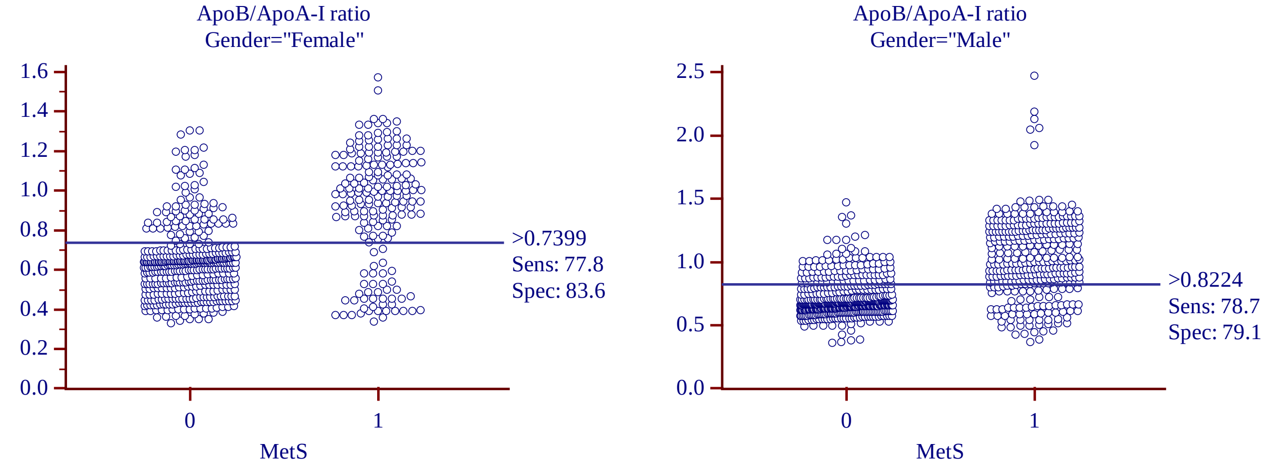

Figure 5: Dot diagram for cut-off values of ApoB/ApoA-I ratio for the detection of MetS in women and men

Table 1: Receiver operating characteristic (ROC) curve analysis of ApoB/ApoA-I ratio for MetS (a) and IR (b) in both sexes.

(a)

				Asymptotic 95% Confidence Interval	
Gender	AUC	Std. Error	Asymptotic Sig.	Lower Bound	Upper Bound
Female	.786	.025	.000	.737	.834
Male	.815	.017	.000	.782	.847

(b)

				Asymptotic 95% Confidence Interval	
Gender	AUC	Std. Error	Asymptotic Sig.	Lower Bound	Upper Bound
Female	.887	.019	.000	.850	.924
Male	.816	.022	.000	.773	.860

AUC – Area under the curve; MetS – metabolic syndrome; IR – insulin resistance

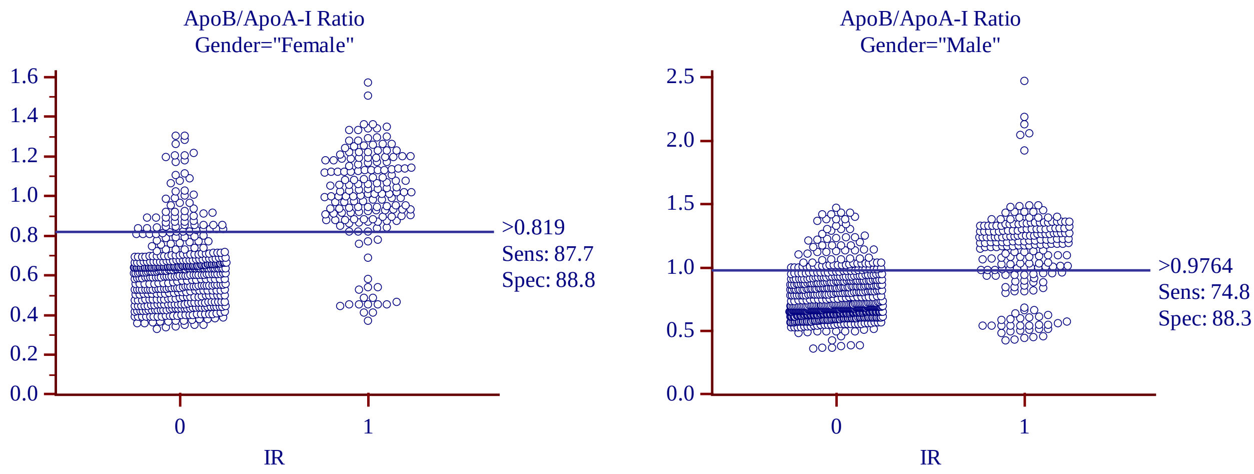

Figure 6: Dot diagram for cut-off values of ApoB/ApoA-I ratio for the detection of IR in women and men

The authors in [17] performed a retrospective study of 41.821 Korean adults who participated in a routine health screening examination. They found that the optimal cutoff value of ApoB/ApoA-I ratio for the detection of MetS was 0.64 (with sensitivity – 74.1% and specificity – 67.4%) in women and 0.72 (with sensitivity – 64.3% and specificity – 59%) in men. AUCs of ApoB/ApoA-I ratio for IR was 0.58 in men and 0.62 in women.

In this study AUCs of ApoB/ApoA-I ratio for MetS and IR were significantly higher in women than in men, indicating that the predictive value of ApoB/ApoA-I ratio for the detection of MetS and IR was higher in women than in men. In our study this tendency was found only for IR (AUCs: 0.89 in women and 0.816 in men). The authors in [15] investigated 8.120 subjects from the China Health Nutrition Survey in 2009. They found that ApoB/ApoA-I ratio higher than 0.85 in men and 0.80 in women may be a promising and convenient marker for MetS.

Our study showed that AUCs of ApoB/ApoA-I ratio for IR were significantly higher than these for MetS, indicating that the predictive value of ApoB/ApoA-I ratio for the detection of IR was higher than that for MetS in both sexes ($p < .0001$).

Further studies in other ethnicities are needed to confirm these findings providing ethnic cutoff differences of ApoB/ApoA-I ratio for the prediction of MetS and IR.

5. Study Limitations

This study has several limitations. The subjects were not a general population but visitors to the clinic. IR was diagnosed using surrogate marker (HOMA2-IR) of IR and not the “gold standard” (euglycemic clamp), although they correlate well.

Table 2: Odds ratios for MetS and IR (as definitions) according to the determined cutoff values of ApoB/ApoA-I ratio after adjustment for age, MetS components and LDL-C in both sexes

	Women			Men		
	OR	95% CI	P value	OR	95% CI	p
MetS as difinition	1.75	.78 - 3.90	.026	1.18	.58 – 2.40	.047
IR as definition	13.61	6.49 – 28.54	< .0001	7.75	4.30 - 13.97	< .0001

OR odds ratio, *CI* confidence interval, *MetS* Metabolic syndrome, *IR* Insulin resistant, defined as the gender-specific upper quartile ofHOMA2-IR ≥ 2.3 for women and ≥ 2.9 for men, *LDL-C* low-density lipoprotein cholesterol, *NS* nonsignificant

6. Conclusion

In the population of Georgia the optimal cutoff values of ApoB/ApoA-I ratio for the detection of MetS were 0.74 in women and 0.82 in men; for the detection of IR these values were 0.82 in women and 0.98 in men.

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