



# Association of triglyceride-to-high density lipoprotein cholesterol ratio to cardiorespiratory fitness in men

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## KEYWORDS:

Cardiorespiratory fitness;  
TG/HDL-C ratio

**BACKGROUND:** Both triglyceride-to-high density lipoprotein cholesterol (TG/HDL-C) and cardiorespiratory fitness (CRF) impart risk for all-cause morbidity and mortality independently of conventional risk factors.

**OBJECTIVE:** To determine prevalence and/or incidence of high TG/HDL-C ratio in men with low CRF.

**METHODS:** Clinical characteristics and CRF were used to determine prevalence of a TG/HDL-C ratio  $\geq 3.5$  (high ratio) in 13,954 men of the Cooper Center Longitudinal Study. High-ratio conversion was determined in 10,424 men with normal baseline TG/HDL-C ratio. Hazard ratio (HR) of incident high TG/HDL-C was adjusted for age and waist girth.

**RESULTS:** Men with low CRF had the highest prevalence of a high TG/HDL-C ratio. In the population with normal TG/HDL-C, age-adjusted HR of incident high TG/HDL-C ratio was 2.77 times higher in men with lowest CRF than in those with highest CRF. Incidence of conversion of normal to high ratio was 5.5% per year in low CRF population, compared with 1.7% in high CRF subjects. Incidence HR was independent of waist girth. Men who converted from normal to high TG/HDL-C ratio during the follow-up period had increased number of metabolic risk factors and a higher prevalence of metabolic syndrome. Men who did not convert to a high TG/HDL-C ratio retained a low prevalence of metabolic syndrome risk factors.

**CONCLUSION:** A high TG/HDL-C ratio is common in men with low CRF. Metabolic syndrome also is common among those with a high ratio.

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## Introduction

Moderately elevated levels of plasma triglyceride impart risk for cardiovascular disease beyond the risk expected from high low density lipoprotein (LDL) or low high density lipoprotein (HDL) cholesterol (C) levels.<sup>1,2</sup>

Since a low HDL-C is also predictive, a high ratio of triglyceride-to-high density lipoprotein cholesterol (TG/HDL-C) should be doubly so. Indeed, a high ratio is predictive for all-cause and cardiovascular disease mortality in men, in women with suspected myocardial ischemia, and in patients with type II diabetes mellitus.<sup>3-5</sup> A high ratio further is highly associated with incidence of type II diabetes mellitus.<sup>3</sup> In addition, a high triglyceride and/or low HDL-C is a common lipoprotein phenotype secondary to insulin resistance, and some studies report that a high TG/HDL-C ratio predicts insulin resistance,<sup>6</sup> LDL particle number, presence of small, dense LDL, and the risk of heart disease.<sup>7-9</sup> Thus, it appears that the TG/HDL-C ratio may be clinically useful as an indicator of risk.

Another risk for premature all-cause and cardiovascular disease mortality is low cardiorespiratory fitness (CRF) level.<sup>10-12</sup> CRF is an age- and sex-specific measure of cardiovascular function during maximal exercise performance on a treadmill. Recently, the relation of CRF to metabolic risk was examined in the study population of the Cooper Center Longitudinal Study (CCLS). It was noted that prevalence of metabolic risk factors for cardiovascular disease accounted for a portion of the increased cardiovascular mortality in low-CRF subjects.<sup>13</sup> Farrell et al<sup>14</sup> reported an inverse association of CRF to metabolic syndrome in women. In addition, other studies suggest that high CRF imparts protection from mortality risk due to insulin resistant conditions such as obesity.<sup>15</sup> Because a high ratio of TG/HDL-C is predictive of risk for all-cause and cardiovascular mortality and of insulin resistance, we examined the incidence of the high ratio in relation to CRF.

## Methods

For this report, a secondary data analysis was conducted of subjects who presented to the Cooper Clinic at Dallas, Texas, for a preventive medical visit during 1979 to 2010 and who were enrolled and consented to participate in CCLS. This study is approved by the Institutional Review Board for Investigation in Humans at The Cooper Institute. The CCLS is an ongoing prospective cohort study primarily designed to investigate the effect of CRF on cardiometabolic disease and death. Patients enrolled in the CCLS are mostly non-Hispanic white, about 80% are college graduates, and the subjects are from middle to upper socioeconomic strata. There were a total of 24,074 subjects available for analyses. Women (n = 4623), young (<20 years) or older (>80 years) individuals, subjects with diabetes (glucose  $\geq$  126 mg/dL or had history of diabetes at baseline), and individuals consuming more than 14 alcoholic drinks/week at baseline or/and current smokers at baseline (n = 1944) were excluded. In addition, subjects with a follow-up visit date that was the same as

baseline (n = 25) were excluded. Thus, a total of 13,954 men met inclusion criteria, of these, 10,424 analytic samples had a normal TG/HDL-C ratio (<3.5) at baseline and qualified for analysis of the incidence of a high ratio ( $\geq$ 3.5).

As described previously,<sup>16</sup> the clinical examination followed a 12-hour fast and included a detailed medical history, physical examination, health habits questionnaire, anthropometric measurements, resting and exercise electrocardiograms, blood chemistry analyses, blood pressure measurement, and a standardized maximal exercise test.

## Measures

After a 12-hour fast, serum samples were analyzed for triglyceride, total cholesterol, HDL-C, and estimation of non-HDL-C (total cholesterol minus HDL-C). The assays used were automated in accord with standard operating procedures.<sup>16</sup> A cut point of 3.5 was chosen for the ratio of TG/HDL-C as described previously.<sup>3,8</sup>

Body composition measurements were taken at the clinical visit according to a manual of operations by trained technicians and have been described previously.<sup>16</sup> Briefly, body mass index (kg/m<sup>2</sup>) was computed from measured height and weight. Waist girth (cm) was measured to the nearest 0.1 cm at the level with the umbilicus after a normal exhalation.

Resting blood pressure was auscultated as the first and fifth Korotkoff sounds according to a standard sphygmomanometer protocol.

## Metabolic syndrome

Metabolic syndrome was defined using the Adult Treatment Panel III criteria.<sup>17</sup> Briefly, classification into metabolic syndrome required 3 of the following criteria: waist girth  $\geq$  102 cm, TG  $\geq$  150 mg/dL, HDL-C < 40 mg/dL, and systolic blood pressure  $\geq$  130 mm Hg or diastolic blood pressure  $\geq$  80 mm Hg. Blood glucose cut point was defined for this study based on our previous assessment of high-risk glucose cut point for type II diabetes mellitus.<sup>16</sup> Accordingly, high glucose was defined in the range of 110 mg/dL to 125 mg/dL. Prevalence of each risk factor for metabolic syndrome also was evaluated.

## Physical activity

In the Health Habits Questionnaire, subjects were asked to provide information about their usual patterns of regular exercise, which was used to create physical activity (PA) categories (0 = no reported PA; 1 = participated in sports or exercise activities other than walking or running; 2 = walked or ran less than 10 miles/wk; 3 = walked or ran 11-19 miles per week; 4 = walked or ran 20 or more miles/wk).<sup>18</sup> In this study, physical activity indices (PAIs) are summarized.

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