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The Effect of Cardiorespiratory Fitness on Age-Related Lipids and Lipoproteins

Yong-Moon Mark Park, MD, PhD, MS,* Xuemei Sui, MD, MPH, PhD,† Junxiu Liu, MD,* Haiming Zhou, MS,‡ Peter F. Kokkinos, PhD,†§ Carl J. Lavie, MD,|| James W. Hardin, PhD,* Steven N. Blair, PED*†

ABSTRACT

BACKGROUND Evidence on the effect of cardiorespiratory fitness (CRF) on age-related longitudinal changes of lipids and lipoproteins is scarce.

OBJECTIVES This study sought to assess the longitudinal aging trajectory of lipids and lipoproteins for the life course in adults and to determine whether CRF modifies the age-associated trajectory of lipids and lipoproteins.

METHODS Data came from 11,418 men, 20 to 90 years of age, without known high cholesterol, high triglycerides, cardiovascular disease, and cancer at baseline and during follow-up from the Aerobics Center Longitudinal Study. There were 43,821 observations spanning 2 to 25 health examinations (mean 3.5 examinations) between 1970 and 2006. CRF was quantified by a maximal treadmill exercise test. Marginal models using generalized estimating equations were applied.

RESULTS Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), triglycerides, and non-high-density lipoprotein cholesterol (non-HDL-C) presented similar inverted U-shaped quadratic trajectories with aging: gradual increases were noted until age mid-40s to early 50s, with subsequent declines (all $p < 0.0001$). Compared with men with higher CRF, those with lower CRF developed abnormal values earlier in life: TC (≥200 mg/dl), LDL-C (≥130 mg/dl), non-HDL-C (≥160 mg/dl), and triglycerides/HDL-C ratio (≥3.0). Notably, abnormal values for TC and LDL-C in men with low CRF were observed around 15 years earlier than in those with high CRF. After adjusting for time-varying covariates, a significant interaction was found between age and CRF in each trajectory, indicating that CRF was more strongly associated with the aging trajectories of lipids and lipoproteins in young to middle-age men than in older men.

CONCLUSIONS Our investigation reveals a differential trajectory of lipids and lipoproteins with aging according to CRF in healthy men and suggests that promoting increased CRF levels may help delay the development of dyslipidemia. (J Am Coll Cardiol 2015;65:2091–100) © 2015 by the American College of Cardiology Foundation.

Cardiovascular disease (CVD) is the leading cause of death worldwide (1). Mortality rates from CVD have declined, but its associated burden is persistently high in the United States (2). Dyslipidemia, representing unfavorable blood lipid profiles, plays an important role in the development and progression of coronary heart disease (CHD) (3). Multiple epidemiological studies have demonstrated that high levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and non-high-density lipoprotein cholesterol (non-HDL-C) and lower levels of high-density lipoprotein

From the *Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, South Carolina; †Department of Exercise Science, Arnold School of Public Health, University of South Carolina, Columbia, South Carolina; ‡Department of Statistics, College of Arts and Sciences, University of South Carolina, Columbia, South Carolina; §Cardiology Department, Veterans Affairs Medical Center, and Georgetown University School of Medicine, Washington, DC; and the ||John Ochsner Heart and Vascular Institute, Ochsner Clinical School, University of Queensland School of Medicine, New Orleans, Louisiana. This work was supported by National Institutes of Health grants AG06945, HL62508, and DK088195. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Dr. Blair is a member of the advisory board for Technogym, Santech, and Clarity; has received unrestricted research grants from The Coca-Cola Company, Technogym, and BodyMedia; and has received book royalties from Human Kinetics. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.
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ABBREVIATIONS AND ACRONYMS

BMI = body mass index

CHD = coronary heart disease

CRF = cardiorespiratory fitness

CVD = cardiovascular disease

HDL-C = high-density lipoprotein cholesterol

LDL-C = low-density lipoprotein cholesterol

TC = total cholesterol

TG = triglycerides

WC = waist circumference

cholesterol (HDL-C) are important lipid risk factors for CHD (4-7). Existing evidence also suggests that elevated triglycerides (TG) are an independent risk factor for CHD (8).

Age-related changes in lipid and lipoprotein concentrations are overall unfavorable. For example, TC, LDL-C, and TG increase up to middle age, then decrease (9-14), whereas the change in HDL-C with aging is not consistent (11-16). Most previous studies had substantial limitations, including cross-sectional study design (9,11), restricted age range (14-16), relatively small sample size (10,12,14,16), nonfasting samples (13), and a lack of analysis assessing time-varying covariates (12,15).

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Strong evidence suggests that physical activity is a major modifiable lifestyle factor for preventing dyslipidemia (17-20). Meta-analyses and systematic reviews support that aerobic physical activity reduces LDL-C and non-HDL-C, with no consistent effect observed on TG and HDL-C (17). However, an increasing effect on HDL-C with specific amounts of exercise and decreasing effects on TG has been reported in healthy, middle-age men and in the overweight/obese population (20,21). Previous studies have shown that improved cardiorespiratory fitness (CRF), an objective indicator of habitual physical activity, resulted in a more favorable lipoprotein-lipid profile, with different effects across age groups (18,19). However, there is little evidence on the effect of CRF on age-related changes in lipids and lipoproteins. Because age-related changes in the lipid profile are mostly unfavorable, the aim of the current study is to identify the age-related trajectory for lipids and lipoproteins and, due to its important public health and clinical implications, to explore factors that might modify the trajectory.

More specifically, using data from the ACLS (Aerobics Center Longitudinal Study), we assessed the longitudinal aging trajectory for TC, LDL-C, TG, HDL-C and non-HDL-C and determined whether CRF modifies these trajectories in healthy men.

METHODS

STUDY POPULATION. The ACLS is a prospective study of adults who received extensive preventive medical examinations at the Cooper Clinic in Dallas, Texas. The study participants are mainly non-Hispanic whites (>95%) and college graduates from middle to upper socioeconomic strata. Our analyses included male participants who received at least 2 medical examinations (2 to 25 visits; mean number of visits = 3.5) between 1970 and 2006. All study participants had complete data on TC, HDL-C, and TG at baseline, had normal resting and exercising electrocardiograms, had a body mass index (BMI) ≥18.5 kg/m^2, and were able to reach 85% of age-predicted maximal heart rate during the treadmill tests at each visit. We excluded participants who had a history of myocardial infarction, stroke, and cancer at baseline and during the follow-up. In addition, participants with self-reported high cholesterol or high triglycerides during any visit were excluded to remove potential treatment effects on lipid and lipoprotein levels. Finally, a total of 11,418 individuals with 43,821 observations were analyzed (**Figure 1**). The study protocol was approved annually by the Cooper Institute Institutional Review Board, and all participants gave their informed consent for the baseline examination and follow-up study.

ASSESSMENT OF CRF. CRF was measured using a modified Balke protocol (22), and details of the measurements are described elsewhere (23). Exercise treadmill duration on this protocol is highly correlated with measured peak oxygen uptake in men (24). Treadmill time, expressed in metabolic equivalents, corresponds to maximal aerobic power and is considered an objective laboratory measure of CRF. In a previous study using ACLS data, CRF was demonstrated to decline at a nonlinear rate with aging (23). Thus, CRF was standardized for age, and the study subjects were further categorized into low (lower than 33.3th percentile), middle (those within 33.3th to 66.7th percentile), and high (higher than 66.7th percentile) CRF groups according to the distribution of age-standardized CRF at baseline.

ASSESSMENT OF CLINICAL AND LIFE-STYLE RELATED VARIABLES. Details of the clinical examination in ACLS are described elsewhere (23,25,26). Examinations were conducted after an overnight fast of at least 12 h. Serum TC, TG, HDL-C, and fasting plasma glucose (FPG) were analyzed by automated laboratory techniques in the Cooper Clinic in accordance with quality control standards of the Centers for Disease Control and Prevention Lipid Standardization Program. Blood pressure (BP) was measured with mercury manometers after at least 5 min of quiet sitting. BMI was calculated from measured weight and height in accordance with standard procedures. Waist circumference (WC) was measured at the level of the umbilicus. Underwater weighing, sum of skin fold-thickness, or both were used to estimate percent body fat (% BF). When available, hydrostatically-estimated % BF was chosen (26,27). A standardized