A 7-year longitudinal association of total cholesterol with premature structural and functional cardiac damage progression in youth: the ALSPAC birth cohort study

A.O. Agbaje¹

¹University of Eastern Finland, Institute of Public Health and Clinical Nutrition, School of Medicine, Faculty of Health Sciences, Kuopio, Finland

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Background: Recent evidence suggests that childhood total cholesterol was associated with midlife cardiovascular mortality. Cumulative total cholesterol has been associated with subclinical atherosclerosis during growth from mid-adolescence through young adulthood. It remains unexamined whether total cholesterol independently associates with signs of premature cardiac damage in apparently healthy youth due to the paucity of repeated measures of cardiac structure and function.

Purpose: To investigate the longitudinal association of changes in total cholesterol with structural and functional cardiac damage progression during growth from adolescence through young adulthood.

Methods: From the Avon Longitudinal Study of Parents and Children (ALSPAC), UK birth cohort, 1595 adolescents aged 17 years who had fasting plasma total cholesterol measured at 17- and 24-year clinic visits were included. Repeated echocardiography measured LVM indexed for height2.7 (LVMi2.7), relative wall thickness (RWT), LV diastolic function from mitral E/A ratio (LVDF), and LV filling pressure from E/e’ ratio (LVFP) were available at baseline and follow-up. LVMi2.7 ≥51g/m2.7, RWT ≥0.44, LVDF <1.5, and LVFP ≥8 were categorised as LV hypertrophy, high RWT, LVD dysfunction, and high LVFP, respectively. Multivariable adjusted associations were examined using generalized linear mixed-effect models and generalized logit mixed-effect models and adjusted for sex, and time-varying covariates measured at both baseline and follow-up such as age, insulin, high-sensitivity C-reactive protein, heart rate, systolic blood pressure, glucose, fat mass, lean mass, smoking status, family history of hypertension/diabetes/high cholesterol/vascular disease, socioeconomic status, sedentary time, light physical activity, and moderate to vigorous physical activity.

Results: Among 1595 adolescents (mean [SD] age at baseline, 17.74 [0.38] years; 955 [59.8%] females) mean total cholesterol values increased in males from 3.55 mmol/L to 4.25 mmol/L and in females from 3.97 mmol/L to 4.46 mmol/L, over 7 years. The prevalence of LV hypertrophy increased in males from 3.6% to 11.9% and in females from 1.6% to 4% over 7 years. The prevalence of LV dysfunction increased in males from 7.8% to 16.6% and in females from 10.3% to 15.4%. In a fully adjusted model, each 1 mmol increase in total cholesterol was significantly associated with higher odds of LV hypertrophy progression (odds ratio 1.18; [95% CI, 1.09 – 1.27], p<0.0001), high RWT (1.11; [1.02 – 1.21], p=0.015), and high LVFP (1.12; [1.05 – 1.20], p=0.001) but not LVD dysfunction (1.03 [0.95 – 1.13], p=0.461), over 7 years.

Conclusion: Increased total cholesterol was independently associated with progressive structural and functional cardiac damage in asymptomatic youth during growth from adolescence through young adulthood.