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EDITORIAL COMMENT

Dyslipidemia in Adult Congenital Heart Disease

Highly Prevalent Although Underdiagnosed*

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Over the last decades, advances in pediatric cardiology and cardiothoracic surgery shifted the epidemiology in congenital heart disease (CHD) toward an aging adult population, with a high prevalence of complex congenital and acquired cardiovascular conditions. Aging in adults with congenital heart disease (ACHD) is associated with the development of atherosclerotic cardiovascular disease (ASCVD) risk factors, resulting in a significant impact on cardiovascular morbidity and long-term outcomes.[1] Despite the fact that patients with CHD have a 1.5 to 3 times higher risk for coronary artery disease than non-CHD individuals over time,[2] awareness of ASCVD and management of modifiable ASCVD risk factors is suboptimally addressed in the setting of ACHD. Few studies show a higher prevalence of hypertension, obesity, and diabetes mellitus among ACHD patients compared with age-matched controls.[3]

Dyslipidemia, defined as an increased serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), or triglycerides (TG) concentration or a decreased serum high-density lipoprotein cholesterol (HDL-C) concentration, is a well-established risk factor for cardiovascular disease in the general population.[4] Numerous epidemiological studies and randomized controlled trials have consistently demonstrated a log-linear relationship between the absolute changes in plasma LDL-C and the risk of ASCVD in the general population. The 2019 European Society of Cardiology Guidelines for the management of dyslipidemias suggest even lower targets of LDL-C and non-HDL-C among patients with very-high, high, and intermediate risk for secondary and primary prevention.[4] In contrast, prevalence and management of dyslipidemia in ACHD are less well described, with existing studies presenting conflicting data on the relative frequency of dyslipidemia, probably due in part to the heterogeneity of the ACHD population.[5,6]

In this issue of *JACC: Advances*, Wu et al[7] provide real-world data on the prevalence of dyslipidemia among 186 ACHD patients by conducting a cross-sectional lipid screening study in 4 tertiary centers. Dyslipidemia was defined as TC ≥200 mg/dL, HDL-C <40 mg/dL, or non-HDL ≥130 mg/dL. Wu et al demonstrated high cholesterol values in almost one-half (46%) of the study population, despite only 15% of study participants reporting previous abnormal cholesterol values. Interestingly, different cholesterol values were reported among CHD complexity groups. In detail, dyslipidemia was attributed mainly to high TC levels among adults with simple and moderate CHD lesions and low HDL-C levels among adults with complex CHD. This trend remained significant following adjustment for age, sex, and body mass index (BMI). HDL-C levels positively correlated with higher oxygen saturation (correlation coefficient 0.30; $P < 0.01$), explaining in part why cyanosed patients with complex lesions had lower HDL-C levels. Another explanation could be the presence of

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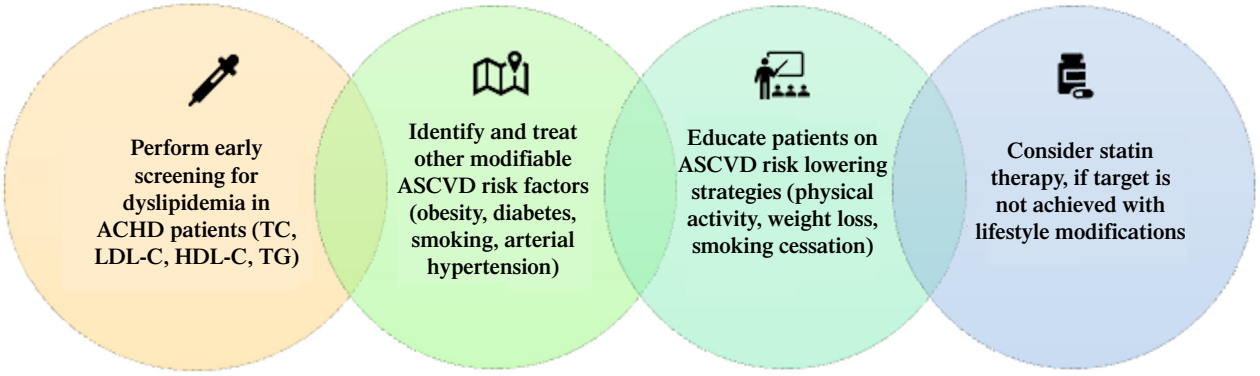
FIGURE 1 Screening for Dyslipidemia and Other Potential Atherosclerotic Cardiovascular Disease Risk Factors Among Adults With Congenital Heart Disease



ACHD = adult congenital heart disease; ASCVD = atherosclerotic cardiovascular disease; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; TC = total cholesterol; TG = triglycerides

chronic inflammation and endothelial dysfunction in patients with a complex defect.[8] Elevated non-HDL-C was also commonly found, with non-HDL-C being approximately 20 mg/dL higher among adults with simple defects compared with complex CHD in age-, sex-, and BMI-adjusted models.[7]

ACHD patients with dyslipidemia were more likely to be obese than those without dyslipidemia in this study.[7] Indeed, there seems to be a steady rise in BMI among patients with CHD between childhood and adolescence, which increases cardiovascular risk early in life.[9] Furthermore, Wu et al[7] demonstrated that patients with a simple defect were more likely to be obese compared with patients with moderate or complex defects, which could explain the different type of dyslipidemia among different CHD complexity group. Finally, modifiable cardiovascular health behaviors were also highly prevalent among ACHD individuals, with nearly 20% of adults with complex and moderate CHD reporting current cigarette smoking, while the majority of study participants reported low regular physical activity.

Overall, in this issue of *JACC: Advances*, Wu et al[7] concluded that: 1) dyslipidemia is highly prevalent among ACHD patients; 2) lipid profile differs by CHD complexity group; and 3) dyslipidemia is associated with the presence of obesity. However, this study was limited, as already acknowledged, by the small number of study participants and its cross-sectional design, which did not enable the investigators to provide follow-up data about: 1) whether measured lipid levels can predict future ASCVD risk; and 2) whether the identification of lipid profile in ACHD patients can lead to lifestyle modification and/or initiation of statin therapy. Future longitudinal studies are needed to answer these questions. In addition, it would be important to investigate whether medical interventions in ACHD population eventually modify ASCVD risk factors and the effect of such interventions on clinical outcomes. Another important issue that should be addressed is the development of an ASCVD risk score, which integrates additional risk factors for patients with CHD, as conventional scores cannot accurately predict cardiovascular risk in this heterogenous population.[10,11] Finally, it would be interesting to measure Lp(a) or apoB, as enhancing cardiovascular risk factors, in future studies on ASCVD risk in ACHD.

In conclusion, ACHD physicians should be highly aware and screen their patients from early adulthood on a regular basis for possible ASCVD risk factors, including dyslipidemia, that could be promptly modified to prevent future cardiovascular events (**Figure 1**). Physical activity and smoking cessation should be strongly encouraged as preventive measures among all CHD patients. Ideally, individualized training programs should be designed to ensure safety of ACHD patients with complex lesions and impaired cardiac function.[12,13]

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