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Impact of Polygenic Risk Scoring on Lipid-Lowering Therapy in Primary Prevention for Coronary Artery Disease

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Background: Polygenic risk scores (PRS) estimate inherited risk for coronary artery disease (CAD) by aggregating multiple genetic variants. Emerging data suggest PRS can enhance traditional risk models, particularly in younger or borderline-risk patients, before clinical risk factors develop. As validation across diverse populations advances, PRS may guide early preventive strategies such as lipid-lowering therapy (LLT).

Methods: A one-year, single-center retrospective study was conducted at a Preventive Cardiology clinic. Patients without known cardiovascular disease who consented to PRS testing (Allelica, Inc.) were included. High genetic risk was defined as PRS $\geq$ 90th percentile. Pre- and post-PRS data were collected on lipid profiles, biomarkers, and LLT (statins, ezetimibe, PCSK9 inhibitors, bempedoic acid, icosapent ethyl).

Results: Among 107 patients (median age 51; 37.2% female; 82.2% White), 20.6% had a high-risk PRS. In this group, 54.5% had a change in LLT—36.4% initiated and 18.2% intensified therapy. Statin prescriptions increased by 18.2% (RR 1.25; 95% CI: 0.94–1.67; $p=0.13$), and non-statin prescriptions by 22.7% (RR 1.63; 95% CI: 0.85–3.12; $p=0.15$). High-risk patients were more likely to be prescribed statins than low-risk patients (RR 1.36; 95% CI: 1.11–1.65; $p<0.01$).

Conclusion: PRS testing identified high genetic risk in one-fifth of patients, with over half of these experiencing changes in LLT. Increased statin and non-statin use among high-risk patients suggests PRS may influence lipid management in primary prevention. Further research is needed to confirm its clinical impact.

Keywords: Polygenic risk score, lipid-lowering therapy, primary prevention

Disclosure Statement: The authors report there are no competing interests to declare.