CLINICAL VIGNETTE

Lp(a) as CVD Risk Factor in South Asians

Happy Thakkar, MD and Ravi Dave, MD

Case Report

A 36-year-old male with a history of dyslipidemia and pre-diabetes presented to the emergency department with two days of chest pain. The patient initially dismissed the symptoms as related to his recent upper body workouts. However, he presented to the emergency department (ED) after the symptoms persisted and seemed to be worsening. He described the chest pain as constant, worse with exertion, left sided, non-radiating, and associated with nausea. He had no dyspnea, vomiting, or diaphoresis. He denied a history of substance use. His family history was notable for early onset coronary artery disease in his father, who had died of a myocardial infarct (MI) in his early 50s. The patient was of South Asian ancestry, had a vegetarian diet, and was of normal weight.

In the ED, his vital signs were normal and his physical exam was unremarkable, including normal heart sounds and no chest tenderness with palpation. The patient's chest pain significantly improved with sublingual nitroglycerin. His EKG showed normal sinus rhythm with a heart rate of 99 beats per minute, early repolarization, and right axis deviation. Initial labs showed a positive high sensitivity troponin, which trended up on repeat measurements. Echocardiography showed a preserved left ventricular ejection fraction of 60-65% and mild concentric left ventricular hypertrophy.

The patient was hospitalized for non-ST elevation myocardial infarction (NSTEMI) and started on dual antiplatelet therapy as well as heparin drip. The next morning, he underwent invasive coronary angiography, which showed one vessel obstructive coronary artery disease with a 99% mid right coronary artery (RCA) stenosis. The patient underwent optical coherence tomography (OCT) guided percutaneous coronary intervention (PCI) of the culprit lesion with two overlapping drug-eluting stents (Xience Skypoint, 2.75x38 mm and 2.75x18 mm, post-dilated to 3.0 mm). This intervention was complicated by ventricular fibrillation (VF) with cardiac arrest. The patient was successfully resuscitated after three VF shocks, and subsequently admitted to the intensive care unit for monitoring. He remained hemodynamically stable thereafter, and subsequently had an unremarkable hospital course. Labs prior to discharge showed a total cholesterol of 225 mg/dL (N<200mg/dl), LDL of 137 mg/dL (N<130mg/dl), HDL of 47 mg/dL (N<40mg/dl), triglycerides of 203 mg/dL (N<150mg/dl), and a hemoglobin A1c of 5.9% (N<5.7%). His lipoprotein(a) [Lp(a)] was 161 mg/dL, over five times the upper limit of normal of 30 mg/dL.

Discussion

Coronary artery disease (CAD) in young individuals with minimal traditional risk factors presents a unique clinical challenge that underscores the importance of considering non-traditional risk factors and genetic predisposition. Lp(a) has emerged as a significant risk factor for early onset CAD, notably in South Asian patients. Lp(a) is a pro-atherogenic, pro-thrombotic, LDL-related lipoprotein whose levels are largely genetically determined. It is a strong risk factor for lifetime development of coronary artery disease and stroke, with higher levels correlated to higher risk. Importantly, the association between high Lp(a) concentrations (>50 mg/dL) and cardiovascular risk appears to be independent of established risk factors, including diabetes mellitus, smoking, high blood pressure, and apolipoprotein B and A ratio.[1]

The population-attributable risk of high Lp(a) for MI varies across ethnic groups, with South Asians showing one of the highest burdens at 9.5%.[2] Indeed, South Asians have been observed to have higher median Lp(a) levels compared to other ethnic groups.[3] South Asian individuals face approximately double the risk of atherosclerotic cardiovascular disease (ASCVD) events compared to those of European ancestry, a disparity not accurately captured by current prediction tools like the Pooled Cohort Equation. This elevated risk persists even after accounting for higher rates of traditional risk factors in South Asians, suggesting potential influences from social determinants of health, genetic factors, or other unidentified causes.[4] The genetic predisposition to elevated Lp(a) levels suggests that it may play a particularly crucial role in the development of CAD in South Asian patients.[2] This underscores the importance of considering Lp(a) as an independent risk factor, especially in younger South Asian patients who may not exhibit other conventional risk factors.

For clinicians managing young South Asian patients, this case emphasizes the importance of including Lp(a) measurement in cardiovascular risk assessments, particularly for those under 50 years of age. While current treatment options for lowering Lp(a) are limited, early screening and risk stratification using Lp(a) levels could be valuable in identifying individuals at increased risk. This approach of identifying high-risk individuals based on elevated Lp(a) levels could inform decisions regarding the intensity of lifestyle interventions and the use of other lipid-lowering therapies. Furthermore, as new therapeutic agents targeting Lp(a) are being developed and evaluated, young South Asian patients with elevated Lp(a) may represent

a key population for future interventional studies aimed at reducing cardiovascular risk.

REFERENCES

1. **Farzam K, Zubair M, Senthilkumaran S**. Lipoprotein A. 2024 Feb 27. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 34033383.
2. **Bilen O, Kamal A, Virani SS**. Lipoprotein abnormalities in South Asians and its association with cardiovascular disease: Current state and future directions. *World J Cardiol*. 2016 Mar 26;8(3):247-57. doi: 10.4330/wjc.v8.i3.247. PMID: 27022456; PMCID: PMC4807313.
3. **Joshi P, Islam S, Pais P, Reddy S, Dorairaj P, Kazmi K, Pandey MR, Haque S, Mendis S, Rangarajan S, Yusuf S**. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. *JAMA*. 2007 Jan 17;297(3):286-94. doi: 10.1001/jama.297.3.286. PMID: 17227980.
4. **Patel AP, Wang M, Kartoun U, Ng K, Khera AV**. Quantifying and Understanding the Higher Risk of Atherosclerotic Cardiovascular Disease Among South Asian Individuals: Results From the UK Biobank Prospective Cohort Study. *Circulation*. 2021 Aug 10;144(6):410-422. doi: 10.1161/CIRCULATIONAHA.120.052430. Epub 2021 Jul 12. PMID: 34247495; PMCID: PMC8355171.