Title: Lipoprotein(a) and Oxidized Phospholipids in Cardiac Allograft Vasculopathy

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Background/Synopsis:
Lipoprotein(a) [Lp(a)] is an inherited pro-atherogenic lipoprotein associated with cardiovascular diseases. Lp(a) acts as a carrier of oxidized phospholipids, which activate inflammatory response and promote formation of atherosclerotic plaques. The OxPL-apoB method quantifies the content of oxidized phospholipids on apolipoprotein B-100 containing particles, particularly Lp(a) and LDL-C. Cardiac allograft vasculopathy (CAV) is characterized by progressive coronary intimal thickening in heart allografts. This study aims to investigate the association of Lp(a) and OxPL-apoB with early CAV development in cardiac transplant (HTx) recipients.

Methods:
A single-center, retrospective study analyzed 99 HTx recipients between 2015 to 2025 with measured Lp(a) and at least one post-HTx coronary angiogram with highly sensitive intravascular ultrasound (IVUS). We defined elevated Lp(a) as ≥50 mg/dL and OxPL-apoB levels as ≥3 nmol/L. The primary endpoint was CAV quantified by maximal intimal thickness (MIT) of 0.5, 1, and 1.5mm. Cox proportional hazard models were used to evaluate the association of MIT and Lp(a) ≥50 mg/dL, OxPL-ApoB levels ≥3 nmol/L. Covariates included treated cytomegalovirus infection, AMR rejection, average LDL-C level of two years post-HTx, mTOR inhibitor use, donor ischemic time, BMI, and sex.

Results:
A total of 26 (26.2%) of HTx recipients had an Lp(a) ≥ 50 mg/dL and 21 (21.2%) with OxPL-apoB levels ≥3 nmol/L. The median follow-up after HTx was 2.02 years [1.23, 4.01]. The median Lp(a) level <50 mg/dL was 15 [7, 32.5] and ≥50mg/dL was 101.5 [72.25, 142]. The median OxPL-ApoB level <3 nmol/L was 1.1 [0, 1.8] and ≥3 nmol/L was 4.5 [3.53, 6.8].

In multivariate analysis, higher Lp(a) (>50 mg/dL) and OxPL-apoB (>3 nmol/L) levels were associated with numerically increased hazard of CAV, though these associations did not reach statistical significance. The strongest association for Lp(a) was observed at the MIT 1.5 mm

threshold (HR 1.07; 95% CI, 0.32–3.45; p=0.92), and for OxPL-apoB at MIT 1.0 mm (HR 1.96; 95% CI, 0.85–4.52; p=0.11).

Conclusion:
In our study, elevated level of Lp(a) ≥50 mg/dL and OxPL-apoB ≥3 nmol/L showed a nonsignificant trend towards increased risk for the early development of CAV as determined by IVUS. While these thresholds have been linked to long-term atherosclerotic disease in the general population, their implications in the post-transplant setting remain unclear. Further investigation is warranted to understand how cumulative exposure contributes to CAV development after cardiac transplantation.

Disclosures:
Dr. Tsimikas is a co-inventor and receives royalties from patents owned by UCSD and is a co-founder and has an equity interest in Oxitope and Kleanthi Diagnostics, is a consult to Novartis and has a dual appointment at UCSD and Ionis Pharmaceuticals. The terms of this arrangement have been reviewed and approved by the University of California, San Diego in accordance with its conflict-of-interest policies. No disclosures from other co-authors.