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"Circulating myomiR levels as a clinical indicator of alcohol-induced skeletal muscle dysfunction in PLWH"

There are an estimated 1.15 million people living with HIV (PLWH) in the US. The prevalence ofat-risk alcohol use among PLWH is higher than in the general population. Antiretroviral therapy (ART) has significantly reduced patient mortality, and HIV infection has emerged as a chronic disease with associated comorbidities such as myopathy and insulin resistance. Impaired skeletal muscle (SKM) function and mass is a consistent predictor of mortality and contributes to a decrease in quality of life in PLWH. Chronic alcohol and HIV independently and synergistically contribute to significant SKM derangements such as atrophy, weakness, and dysfunction. Previous studies have shown that chronic alcohol exposure alters the epigenome including muscle specific microRNA (myomiR) expression, correlating with alterations in expression of myogenic genes. MicroRNAs are produced in cells and secreted actively or passively into circulation. Abundance of circulating myomiRs is a function of the regenerative and degenerative capacity of the muscle, the overall muscle mass, and tissue expression levels. Our hypothesis was that circulating myomiRs is decreased in PLWH with at-risk alcohol use, and they would correlate with a decrease in SKM mass and function.

Subjects from the LSUHSC HIV Outpatient Program were stratified into low, mid, and high drinkers based on timeline follow back (TLFB) and corresponding AUDIT scores. Circulating myomiR levels were determined and correlated to measures of AUD severity, hand grip strength, 4-meter walk test, and lean mass.

The muscle-specific miRNAs 206 and 133a expression were significantly increased in individuals with mid- and high-drinking. Copy number calculations of these myomiRs revealed they were positively correlated with TLFB. Sex differentially modulated the relationship, with miR-206 positively correlating with hand grip strength in males.

Contrary to our hypothesis, circulating myomiRs were increased in individuals with at-risk alcohol use. This may be due to alcohol-mediated damage or inflammation in SKM tissue. Confounding variables including high BMI, high fat mass, and low physical activity in low-drinking cohort may have impacted circulating myomiRs and further studies will investigate correcting for these variables and using a composite myomiR score to correlate with SKM function.