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Reduced level of circulating cell-free nuclear and mitochondrial DNA fragments among Persons who Inject Drugs with HIV

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Background

After cellular death, circulating cell-free mitochondrial (ccf-mtDNA) and genomic (ccf-gDNA) DNA fragments are released into circulation. The level of ccf-gDNA fragments can reflect cell turnover, and ccf-mtDNA fragments can be used to distinguish the mode of cell death (apoptotic vs. necrotic) based on their size (short vs. long fragments, respectively). Previous literature showed inconsistent results in level of serum ccf-DNA comparing people with and without HIV.

Methods

Using ultrasensitive digital PCR, ccf-gDNA and ccf-mtDNA were quantified in serum among HIV-infected and uninfected participants in the AIDS Linked to the IntraVenous Experience (ALIVE) cohort of current and former persons who inject drugs (PWID). Linear regression models with generalized estimating equations (GEE) were used to compare differences in log-transformed circulating cell-free DNA fragments by HIV markers after adjusting for covariates (demographics, BMI, drug/alcohol abuse, and white blood cell [WBC]).

Results

Of 1007 participants followed for 2810 (median: 3.5) person-years, median age was 48 years, 46% HIV+ (50% of them virally suppressed), 64% male, 88% black, 52% overweight or obese at index visit. Compared to people without HIV, People with HIV (PWH) with undetectable and detectable viral load had lower levels of ccf-gDNA (Figure, predicted mean: 4025 vs. 3703, 3263 copies/mL, respectively, $p<0.01$) and short (apoptotic) ccf-mtDNA fragments (predicted mean: 7089 vs. 6566, 5731 copies/mL, respectively, $p<0.01$) after controlling for covariates (all $p<0.01$).

Conclusion

Our data suggested circulating cell-free DNA fragments reduced significantly among PWH, especially PWH with detectable viral load. Further research needs to investigate the role of circulating DNA fragments in aging and HIV progression among PWH.