Cytomegalovirus (CMV) burden may be used to enhance algorithms to predict future cardiovascular health in renal transplant recipients and healthy controls

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Background: Cytomegalovirus (CMV) has been implicated in accelerated cardiovascular changes and may warrant inclusion in predictive algorithms. This is addressed here in healthy older adults and in renal transplant recipients (RTR) stable on therapy as they retain a high burden of CMV.

Methods: RTR (n=45) stable >2 years after transplantation and 58 age-matched healthy adults were recruited in 2014 and returned in 2017. Venous blood samples and saliva were collected, frozen and stored. Plasma proteins linked with inflammation [soluble interferon a receptor 2 (sIFNaR2), sTNFR1, sCD14, C-reactive protein (CRP)], vasculopathy [p-selectin, intercellular adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1)], and metrics of CMV burden [antibodies reactive with CMV lysate, gB or IE-1 (by ELISA), CMV DNA in saliva (by PCR) and T-cell IFNg responses to CMV antigens (by ELISpot)] were assessed in 2014. In 2017, vascular endpoint measurements included brachial artery flow mediated dilatation (FMD), pulse wave analysis [augmented index corrected to heart rate of 75 beats per minute (Aix@75)] and pulse wave velocity (PWV).

Results: In 2017, RTR had lower FMD % (p<0.001), higher PWV (<0.001) and slightly higher Aix@75 values (p=0.14) compared with healthy adults, indicating inferior vascular health. In a multivariable regression model (adjusted R2=0.42) predicting 2017 FMD in RTR (adjusted for age, sex, BMI, eGFR, sCD14, CMV gB Ab and saliva CMV DNA), each 1AU/mL increase of CMV gB Ab (p=0.03) predicted a 5% increase in FMD – associating with better vascular outcomes, but detectable saliva CMV DNA (p=0.02) associated with a 3% increase in FMD. In healthy adults, however, while predicting 2017 FMD (adjusting for p-selectin, ICAM-1, age, sex, BMI, eGFR; adjusted R2=0.22), a 1 ng/mL increase in p-selectin (p=0.03) predicted a 0.04% increase in FMD, and 1 ng/mL increase in ICAM-1 (p=0.03) associated with 0.03% lower FMD. From the pulse wave analyses of RTR, every 1ng/mL increase of sIFNaR2 (p=0.06) marginally predicted 1.4 unit decrease in Aix@75 (adjusted for CMV IE-1 Ab, sIFNaR2, age, sex, BMI and eGFR; adjusted R2=0.37). However in healthy adults, each 1ng/mL increase of sIFNaR2 levels (p=0.04) associated with 3.5 units worsening of Aix@75 (p=0.04) (adjusted R2 = 0.40). Each 1 AU/mL increase in CMV IE-1 Ab levels associated with 0.08 units decrease in PWV (p=0.02) (adjusting for CMV IE-1 Ab, sCD14, age, sex, BMI and eGFR adjusted R2=0.55).

Conclusions: Overall measures of a high burden of CMV, predicted a low FMD marking poor peripheral vascular health in RTR several years after assessment, with more potency than was achieved with plasma markers of systemic and vascular inflammation, which was observed in healthy controls. CMV antibodies can predict future measures of arterial stiffness such as Aix@75 and PWV in healthy controls, but need further investigation in larger cohorts.