Cytomegalovirus: Strength of Antibody Response and Its Relationship to Risk of Mortality Among Patients With Angiographic Coronary Disease

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Background: IgG seropositivity to cytomegalovirus (CMV) has been shown in a variety of studies to predict future outcome in patients with coronary heart disease (CHD). Seropositivity is usually defined by an arbitrary threshold of antibody response. However, among CHD patients, whether the strength of antibody response to CMV infection is predictive of future outcome is unknown.

Methods: The Registry of the intermountain Heart Collaborative Study provided a cohort of consenting patients (N=2,779) with significant, angiographically-defined atherosclerotic CHD. CMV IgG serology was measured as an immunofluorescence index (IFI) value by ELISA (manufacturer's criterion for seropositivity is IFI=1.1). Patients were followed for up to 7.9 years (mean: 3.3±2.0 years) to determine the incidence of all-cause mortality. The predictive value for mortality of the continuous distribution of IFI levels was evaluated compared to simple seropositivity. Cox regression adjusted for 24 demographics, CHD risk factors, comorbidities, and treatments.

Results: Average age was 66±11 years; 76% were male. A significant linear association with mortality was found for the continuous IFI values (hazard ratio [HR]=1.09/IFI unit, p<0.001). Recursive partitioning confirmed the manufacturer's threshold for seropositivity as an appropriate decision point for CHD risk (seronegative: death=10%; seropositive: death=19%; fully adjusted Cox: p=0.015, HR=1.3, 95% CI=1.1-1.6). However, among seropositive patients it also revealed a second threshold (IFI=3.76) above which the risk of mortality was ameliorated, with death=22% for IFI=1.1-3.76 (n=664, p=0.038 vs. seronegative, HR=1.4, Cox=1.0-1.9) and death=16%, for IFI=3.76 (n=1198, p=0.90 vs. seronegative, HR=1.2, Cox=0.67-1.5).

Conclusions: In this large cohort of patients with coronary disease at baseline, CMV seropositivity was significantly predictive of future mortality. However, the risk was greatest for intermediate antibody levels and was ameliorated at higher levels. This raises new questions about the nature and complexity of the host immunologic response to CMV exposure and how it relates to determination of CHD risk.