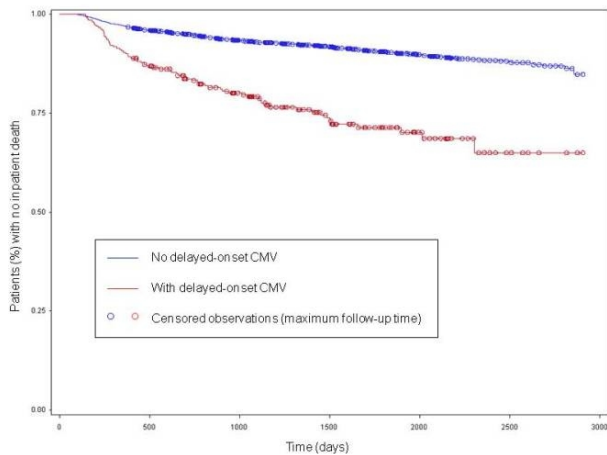


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**Objectives:** Widespread use of prophylactic anti-cytomegalovirus (CMV) therapy for at least 3 months after liver transplantation in the United States can result in delayed-onset CMV. Delayed-onset CMV has not been well-studied since many patients transition care away from transplant centres, limiting prolonged follow-up. We assembled a large retrospective cohort of liver transplant recipients using inpatient billing data from four longitudinal Healthcare Cost and Utilization Project State Inpatient Databases sponsored by the Agency for Healthcare Research and Quality, to study the epidemiology of delayed-onset CMV coded during hospital readmission.

**Methods:** We identified 7,229 persons  $\geq 18$  years of age who had a liver transplant (ICD-9-CM code 50.59) from 2004 to 2010 using California, Florida, New York and North Carolina State Inpatient Databases. Exclusion criteria included residence in a state other than the state where the transplant was performed, transplantation at a pediatric hospital, another solid-organ transplant during the same hospitalization, and persons coded for CMV within 1 year before or during the liver transplant hospitalization. Demographics, comorbidities, CMV (ICD-9-CM code 078.5) and clinical sepsis coded during hospital readmission (995.91, 995.92) and inpatient death were identified. CMV was categorized as early-onset ( $\leq 100$  days post-transplant) or delayed-onset ( $> 100$  days post-transplant). Multivariate Cox proportional hazards models were used to determine risk factors for delayed-onset CMV, and examine associations between previous CMV and clinical sepsis occurring  $> 100$  days post-transplant, and delayed-onset CMV and death  $> 100$  days post-transplant.

**Results:** Delayed-onset CMV occurred in 4.3% (n=309) and early-onset CMV occurred in 2% (n=142) of the liver transplant cohort. In multivariable analysis, delayed-onset CMV was associated with previous transplant failure or rejection (aHR 1.4, 95% CI 1.1-1.7). Clinical sepsis  $> 100$  days post-transplant was associated with previous CMV (aHR 1.3, 95% CI 1.0-1.7), along with previous transplant failure or rejection (aHR 2.1, 95% CI 1.8-2.4), female sex (aHR 1.3, 95% CI 1.1-1.5), Medicare health insurance (aHR 1.2, 95% CI 1.0-1.5), hepatitis C cirrhosis (aHR 1.2, 95% CI 1.1-1.4), prior solid-organ transplant (aHR 2.1, 95% CI 1.4-3.0) and several comorbidities. Death  $> 100$  days post-transplant was associated with delayed-onset CMV (aHR 1.5, 95% CI 1.1-1.9), clinical sepsis  $> 100$  days post-transplant (aHR 6.4, 95% CI 5.3-7.7), new-onset dialysis post-transplant (aHR 2.2, 95% CI 1.8-2.6), transplant failure or rejection (aHR 2.9, 95% CI 2.3-3.7), increasing age (by decade: aHR 1.1, 95% CI 1.0-1.2), Medicare health insurance (aHR 1.2, 95% CI 1.0-1.5), hepatocellular carcinoma (aHR 1.4, 95% CI 1.2-1.7), and some comorbidities.



**Figure 1.** Time (days) to inpatient death  $> 100$  days post-transplant in a cohort of adult liver transplant recipients, stratified according to presence or absence of delayed-onset CMV coded during readmission.

**Conclusions:** Delayed-onset CMV is more common than early-onset CMV among liver transplant recipients. Previous CMV may be a risk factor for clinical sepsis  $> 100$  days post-transplant, and delayed-onset CMV may be a risk factor for death  $> 100$  days post-transplant.