Plasma Cytomegalovirus Quantitative Polymerase Chain Reaction Testing (CMV qPCR) in Patients with AIDS- An Opportunity for Diagnostic Stewardship

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BACKGROUND

Guidelines recommend against testing for cytomegalovirus (CMV) viremia to diagnose CMV end-organ disease (EOD) in people with HIV/AIDS (PWHA) due to low positive predictive value and because a negative result does not exclude EOD. In this study, we aim to assess the clinical utility of plasma CMV quantitative PCR (qPCR) for the diagnosis of CMV EOD in PWHA and to determine if positive results lead to further testing for EOD or earlier initiation of anti-CMV therapy.

METHODS

- Retrospective identification of PWHA who had a plasma CMV qPCR result or who were diagnosed with CMV EOD between 2014-2021
- Measured plasma CMV qPCR using COBAS® AmpliPrep/COBAS® TAQMAN® CMV Test (Roche Diagnostics)
    - Positive CMV qPCR: >300 IU/mL
    - Negative CMV qPCR: undetectable or lower than the minimum quantifiable value
- EOD confirmed via tissue biopsy, ophthalmology eye exam, or cerebrospinal fluid analysis
- Compared CMV qPCR results for participants with proven EOD and participants without proven EOD
- Statistical significance analysis: two-tailed Mann-Whitney U-test and Fisher's Exact Test
- For PWHA with EOD, we evaluated if positive qPCR result prompted further workup for EOD diagnosis or was a trigger to initiate anti- CMV therapy

RESULTS

• We identified 139 PWHA with a CMV qPCR result and 17 PWHA with a discharge diagnosis of CMV EOD
• 13 of 17 participants with EOD had a qPCR result; the other 4 with EOD did not have a qPCR result
• 28 (20.1%) of 139 qPCR results were positive
• Participants with a positive qPCR were 4.59 (CI 2.65-7.96) times more likely to be diagnosed with EOD than those with a negative qPCR
• 9 (69.2%) of 13 participants with EOD and a qPCR result had a positive qPCR. 7 of them were diagnosed with EOD and started on treatment before the qPCR resulted
• In only 1 case did a positive qPCR result and initiation of therapy precede the diagnosis of EOD

Table 1. Characteristics of 139 Participants with a Plasma CMV qPCR Result

Characteristics	Value
Median age (years) (IQR)	40 (33- 51)
Male sex	100 (71.9%)
Female sex	39 (28.1%)
Median CD4 T-lymphocyte (cells/μL) (IQR)	63 (13- 220)
Taking antiretroviral therapy Yes No	 61 (44.2%) 78 (56.5%)
Proven CMV end-organ-disease Retinitis Colitis Encephalitis Esophagitis	13[a] (9.35%) 8 (5.8%) 2 (1.4%) 2 (1.4%) 2 (1.4%)

IQR, interquartile range.
[a]One participant had CMV colitis and CMV encephalitis.

Table 2. CMV qPCR Results in Participants With and Without Proven EOD

qCMV PCR Level (IU/mL)	Proven EOD (N= 13)	Without Proven EOD (N= 126)	P-value
Mean (SD)	49459 (72865)	6082 (53143)	
Min, max	300, 241508	300, 592876	NS[a]
Median (IQR)	12706 (300- 65441)	300 (300- 300)	
Positive (>300 IU/mL)	9 (69.3%)	19 (15.1%)	0.0001[b]
Negative (≤300 IU/mL)	4 (30.7%)	107 (84.9%)	

EOD, end-organ-disease due to CMV; SD, standard deviation; NS, not significant
[a]Mann-Whitney U test
[b]Fisher's exact test

Table 3. The performance of CMV qPCR for the diagnosis of EOD*

	Result (95% CI)
Sensitivity	69.2% (38.6%- 90.9%)
Specificity	84.9% (77.5%- 90.7%)
Positive predictive value	32.1% (21.5%- 45.1%)
Negative predictive value	96.4% (92.2- 98.4%)

*Using >300 IU/mL as the cutoff for a positive result

CONCLUSIONS

• Contrary to guidelines, plasma CMV qPCR is a commonly ordered test for PWHA
• PWHA who have CMV EOD are more likely to a have a positive qPCR than those without EOD, and a negative test result makes EOD unlikely
• As a diagnostic test for CMV EOD among PWHA, CMV qPCR has a low sensitivity and poor positive predictive value
• Among PWHA with CMV EOD, the CMV qPCR result has very little impact on clinical decision-making