Establishing Viral Load Cut-off for Early Diagnosis of Cytomegalovirus Infection in Renal Transplant Recipients Using International Standardized Real-time PCR Assay
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Abstract

Background: Monitoring quantitative CMV plasma DNA PCR (CMV QNAT) is currently the most accurate method to predict CMV infections and progression to disease in renal transplant (RT) recipients. From April 2015, we adopted a new FDA-approved assay using the WHO international standard namely, COBAS® AmpliPrep/COBAS® TaqMan® CMV Test (CAP/CTM) for measuring CMV QNAT. Clinical viral load (VL) cut-off for the early diagnosis of CMV infection using CAP/CTM assay needs to be established. The aim of this study was to define a standardized CMV VL threshold cut-off using the first FDA-approved/international standardized PCR assay for predicting clinically meaningful CMV viremia.

Methods: All RT recipients at Henry Ford Hospital in Detroit, MI that were tested for plasma CMV VL using CAP/CTM from 4/2015 to 10/2015 were included in this prospective study. Demographic, clinical, CMV serology/microbiology data and outcomes (graft loss and mortality) were reviewed. Patients were followed up for 6 months after inclusion in the study. CMV infection was defined as any positive and rising plasma CMV VL on two consecutive weekly CAP/CTM assay and with clinical symptoms of fever or cytopenia or documented end-organ disease in tissue histology. Receiver-operating characteristic (ROC) plot was used to determine optimal cut-off value of plasma CMV VL in the diagnosis of early and clinically meaningful CMV viremia. Clinically meaningful viremia was defined as any positive plasma CMV VL in two consecutive weekly CAP/CTM assay; in addition assay warranting reduction in immune suppression and/or appropriate antiviral therapy with clearance of viremia.

Results: Ninety-nine RT recipients were included and 19/99 had detectable CMV viremia (>137 IU/ml of plasma). 10 of 19 patients had CMV infection and one patient had CMV colitis without detectable viremia. Using ROC plot, a VL of 500 IU/ml of plasma was established as the optimal cut-off for clinically meaningful CMV viremia with a sensitivity of 81.82%, specificity of 93.18% and negative predictive value of 96.62%.

Conclusion: We have established a plasma CMV VL threshold cut-off using CAP/CTM assay for an uniform early diagnosis of clinically meaningful viremia in renal transplant recipients. This cut-off is being validated further in a larger prospective cohort.

Results: ROC Curve

CMV VL Testing: Management Algorithm

Conclusions

• We have established a plasma CMV VL threshold cut-off using CAP/CTM assay for an uniform early diagnosis of clinically meaningful viremia in renal transplant recipients.

• This CMV VL cut-off is being validated further in a larger prospective cohort of RT recipients.

Methods

• Study Design: A prospective study was performed at Henry Ford Hospital, a large urban medical center in Detroit, MI. All RT recipients that were tested for plasma CMV VL using CAP/CTM assay from 4/2015 to 10/2015 were included for analysis.

• Data abstracted included demographic, clinical, CMV serology/microbiology and outcomes (graft loss and mortality) were reviewed. Patients were followed up for at least 6 months after inclusion in the study.

• Definitions: 1) CMV infection was defined as any positive and rising plasma CMV VL on two consecutive weekly plasma CAP/CTM assay. CMV syndrome was defined as CMV infection with clinical syndrome of fever or cytopenia. CMV disease was defined as documented end-organ disease in tissue histopathology. 2) Clinically meaningful CMV viremia was defined as any positive plasma CMV VL in two consecutive weekly CAP/CTM assay; in addition, the positive assay warranted reduction in immune suppression and/or appropriate antiviral therapy with clearance of plasma CMV viremia over two weeks or longer.

Conclusion

• We have established a plasma CMV VL threshold cut-off using CAP/CTM assay for an uniform early diagnosis of clinically meaningful viremia in renal transplant recipients.

• This CMV VL cut-off is being validated further in a larger prospective cohort of RT recipients.