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Detection of cytomegalovirus in the lower respiratory tract among patients with critical illness: uncovering enhanced potential benefits

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We were highly interested in reading the clinical research conducted by Kim et al. [1]. This study is a single-center, retrospective clinical cohort investigation with a large sample size, focusing primarily on the significance of lower respiratory tract (LRT) cytomegalovirus (CMV) positivity in the prognosis of critically ill patients. The research departs from the traditional focus on CMV reactivation in blood samples and examines the epidemiological characteristics of critically ill patients with CMV positivity in the LRT. These findings demonstrate CMV positivity in the LRT as a significant risk factor for mortality in patients with critical illness. However, the detection of CMV positivity in the LRT may hold greater significance, and the comprehensiveness of this study could be further enhanced through additional refinements.

First, the direct definition of CMV detection positivity in the LRT as "reactivation" is debatable. Current CMV-related definitions do not explicitly address this issue [2, 3]. Moreover, the prevailing view is that "reactivation" should be defined based on the premise of CMV seropositivity (IgG) and the detection of a certain CMV viral load in blood samples [2–4]. Therefore, the term "CMV detection positivity" is more accurate. Additionally, the CMV viral load may vary among different LRT specimens. Theoretically, the CMV viral load in bronchoalveolar lavage fluid is higher than that in endotracheal aspirates, which may subsequently have different impacts on clinical outcomes. It is necessary to further evaluate the CMV detection positivity and viral load in different LRT specimens and their associations with clinical outcomes.

Second, of particular importance is the observation that CMV detection in the LRT precede its detection in the blood, especially in patients with septic shock [4, 5]. This phenomenon is likely attributed to the high levels of inflammation associated with sepsis. Under conditions of elevated inflammation, latent CMV infection can be reactivated, subsequently leading to CMV-related injury [6]. Notably, clinical studies have demonstrated a close association between CMV reactivation and pulmonary fibrosis in patients with acute respiratory distress syndrome [7], while animal studies have shown that CMV reactivation can induce pulmonary fibroproliferation [8], suggesting that CMV reactivation may trigger lung injury. Therefore, assessing CMV antiviral therapy based on the LRT findings may hold greater value, including both prophylactic and preemptive treatment strategies.

Third, subgroup analyses should be conducted to distinguish patients with different immune statuses, including immunosuppressed and non-immunosuppressed

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individuals, because the incidence of active CMV infection varies across different immune backgrounds, particularly with a higher rate observed in immunosuppressed patients [2–4, 9]. Sepsis patients, who are in an acute state of immunosuppression, merit special attention [10]. In this study, the incidence of sepsis exceeded 70%, and high levels of inflammation were found to be more likely to trigger reactivation of latent CMV infection. The early stages (overwhelming inflammation) and the later stages (refractory inflammation, immunosuppression, and risk of secondary infections) of sepsis are both conducive to CMV reactivation [10–14]. Our research demonstrates that the incidence of CMV reactivation is at least 30% higher among critically ill patients with sepsis compared to those without, and sepsis has been identified as an independent risk factor for CMV reactivation [9, 15].

Fourth, the issue of CMV co-infection with other pathogens should be addressed by employing next-generation sequencing of pathogens to enhance the accuracy of pathogen detection. It is also necessary to distinguish between CMV and colonizing or pathogenic bacteria. In addition, the impact of combined antiviral treatment against CMV and therapy for other pathogens on prognosis needs to be further clarified. Decades of research have shown that CMV infection and reactivation have a negative impact on critically ill patients. Nevertheless, our understanding of the role of CMV positivity in different specimens remains limited. Therefore, we believe that in-depth research into CMV detection in the LRT is of significant importance.

In summary, the study by Kim et al. revealed the adverse clinical outcomes associated with the detection of CMV in the LRT among critically ill patients, thereby contributing to the advancement of the field. A detailed and nuanced exploration of the aforementioned issues is crucial for fully elucidating the complex interplay between LRT CMV positivity and the prognosis of critically ill patients. Future studies should further investigate these complexities to refine our understanding and potentially guide the development of more effective therapeutic strategies.

Abbreviations

CMV	Cytomegalovirus
LRT	Lower Respiratory Tract

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Author contributions

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Availability of data and materials

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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