

Original Articles**Recipient-to-Donor anti-CMV IgG Ratio and CMV Reactivation after Allogeneic Hematopoietic Stem Cell Transplantation: A Pediatric Case-Control Study**

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Abstract. Background: Despite advances in diagnosis and treatment, cytomegalovirus (CMV) reactivation remains a serious complication following allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT). Our objectives were to explore the impact of pre-transplant anti-CMV IgG titers in both donor and recipient on the occurrence of post-transplant CMV reactivation and to determine a threshold titer that would allow for better stratification of the post-transplant reactivation risk.

Methods: We conducted a unicentric retrospective case-control study involving pediatric allo-HSCT recipients. All donors were related (genotypically identical or haploidentical). CMV reactivation was defined by a viral load ≥ 150 IU/ml in plasma. We included 24 cases (patients who had an episode of CMV reactivation in the first 100 days after HSCT) and 48 randomly selected controls (patients without CMV reactivation in the first 100 days after HSCT).

Results: In univariate analysis, factors associated with CMV reactivation were D-/R+ pre-transplant CMV serostatus ($p=0.013$), recipient anti-CMV IgG titer ($p=0.012$), R/D anti-CMV IgG ratio ($p=0.001$), HLA haploidentical related donor ($p=0.0001$), GvHD prophylaxis with combination of cyclosporin A, cyclophosphamide and mycophenolate mofetil ($p=0.0001$), acute GvHD ($p=0.001$) and corticosteroids ($p=0.0001$). Donor anti-CMV IgG titer was a protective factor ($p=0.046$). In an exploratory multivariable analysis, male donor gender (adjusted OR=4.919; 95% CI (1.103 – 21.942); $p=0.037$), D-/R+ pre-transplant CMV serologic status (adjusted OR=6.874; 95% CI (1.372 – 34.444); $p=0.019$), recipient anti-CMV IgG titer (adjusted OR=1.005; 95% CI (1.000 – 1.010); $p=0.033$), HLA haploidentical related donor (adjusted OR=5.472; 95% CI (1.334 – 22.453); $p=0.018$) and acute GvHD (OR=7.116; 95% CI (1.770 – 28.604); $p=0.006$) remained associated with CMV reactivation after allo-HSCT. ROC curve analysis showed that optimal cut-off value to discriminate patients with CMV reactivation was 113.75 AU/ml for the recipient anti-CMV IgG titer (Se=72.2%; Sp= 64.9%; AUC=0.701; $p=0.016$) and 1 for the R/D anti-CMV IgG ratio (Se=77.8%; Sp=78.4%; AUC=0.814; $p<0.001$). The prevalence of CMV reactivation was higher in patients with pre-transplant anti-CMV IgG titer >113.75 AU/mL (50% versus 16%; $p=0.002$) and in those with R/D anti-CMV IgG ratio >1 (64% versus 15%; $p<0.001$).

Conclusion: In summary, we have shown that both pre-transplant anti-CMV IgG titer in recipient and R/D anti-CMV IgG ratio were associated with the risk of CMV reactivation following allo-HSCT. Furthermore, a high pre-transplant anti-CMV IgG titer in the donor was associated with a lower incidence of reactivation. Our findings add to the published experiences that show that pre-HCT CMV serology titer impacts on post-HCT reactivation and warrants validation in larger

Keywords: Cytomegalovirus; Allogeneic Hematopoietic Stem Cell Transplantation; IgG titer; CMV reactivation; Recipient-to-donor anti-CMV IgG ratio.

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Introduction. Cytomegalovirus (CMV) reactivation remains one of the main complications of allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT). Although the preemptive strategy has proven effective in reducing the prevalence of CMV disease after allo-HSCT and its associated mortality, the frequency of CMV reactivation remains high, particularly in countries with high prevalence and where no prophylactic treatment with letermovir is administered.^{1,2} Better knowledge of the risk factors could help with better patient management. Anti-CMV D-/R+ serostatus is the main factor determining this complication.³ Some recent studies suggest that not only qualitative serological status is a risk factor for CMV reactivation, but also the anti-CMV IgG titer.⁴⁻⁷ This quantitative parameter has been investigated in recipients, but to our knowledge not in donors. Our objectives were to explore the impact of pre-transplant anti-CMV IgG titers in both donor and recipient on the occurrence of post-transplant CMV reactivation and to determine a threshold titer that would allow for better stratification of the post-transplant reactivation risk.

Methods

Study design. A case-control study was performed over a 5-year period (from January 1st, 2018 to December 31st, 2022), involving allo-HSCT recipients from the Immunohematology and Pediatric Transplant Department at the National Bone Marrow Transplant Centre, Tunis. In the Pediatrics Department, a 5-bed transplant unit is dedicated to allo-HSCT for children under the age of 16, with an average of 30 allografts per year. The National Bone Marrow Transplant Centre is the only structure where allo-HSCT is performed in Tunisia.

Case definition. A case was defined as an allo-HSCT recipient who presented at least one episode of CMV reactivation within the first 100 days post-transplant confirmed by quantitative PCR on plasma. This test was performed weekly in all allograft recipients up to 100 days post-transplant, as part of our preemptive strategy.

A CMV reactivation was defined by a viral load ≥ 150 IU/ml on plasma.⁸

No prophylactic anti-CMV treatment was administered. Preemptive treatment with ganciclovir or foscarnet was started if the plasmatic viral load was ≥ 1000 IU/ml, for at least 14 days and until a negative PCR in all cases.

Patients transplanted for a primary immunodeficiency (PID) were not included (their pre-transplant serologies were not interpretable). Patients who received more than one allo-HSCT during the study period were also not included.

Definition and selection of controls. For every case, two controls were selected randomly out of the pool of patients with allo-HSCT who did not have CMV reactivation up to 100 days post-transplant. They received the allograft in the same period as cases did and they had at least a 100-day follow-up after allo-HSCT.

As well as cases, patients transplanted for PID and those who received more than one allo-HSCT during the study period were not included. Patients who presented CMV disease without viremia (negative CMV PCR on plasma) were excluded from the group of controls.

CMV serology for the measurement of anti-CMV IgG. CMV serologies were performed in both donor and recipient prior to transplantation. Determination of anti-CMV IgG titer was performed by electrochemiluminescence (ECLIA) (Cobas e601, Roche®). The limits of quantification for this technique ranged from 1 to 500 AU/ml. Levels above the upper limit of quantification were expressed as > 500 AU/ml. For statistical analysis, an anti-CMV IgG level > 500 AU/mL was considered equal to 500 AU/mL.

For each donor/recipient pair, the recipient-to-donor (R/D) anti-CMV IgG ratio was calculated. When calculating this ratio, values > 500 AU/ml were excluded. When the donor was CMV seronegative, we used the value of 0.15, displayed by the analyzer for a negative serological result, to calculate the R/D anti-CMV IgG ratio.

CMV Viral Load. Detection and quantification of the CMV genome were carried out by automated real-time PCR, COBAS® Ampliprep / COBAS® TaqMan®, with a detection threshold of 60 cp/mL and a quantification range from 150 to 10⁷ cp/ml (1 cp = 0.91 IU).

GvHD prophylaxis. For recipients with HLA haploidentical related donor, combination of cyclosporin A, cyclophosphamide and mycophenolate mofetil was given. For recipients with HLA genoidentical related donor, cyclosporine A, either alone or in combination with methotrexate, was given.

Data collection. The following data was retrospectively collected from medical records: age and sex of both recipient and donor, HLA compatibility between recipient and donor, underlying pathology, pre-transplant CMV serologic status of both recipient and donor, including anti-CMV IgG titer, type of pre-transplant conditioning, Graft versus Host Disease (GvHD) prophylaxis, occurrence of rejection (primary or secondary) and acute GvHD (grades II-IV) (only episodes of acute GVHD occurring prior to CMV reactivation were included in the analysis).

Statistical analysis. Data were presented as percentages for qualitative variables or as means ± standard deviation for quantitative variables. Non-normally distributed quantitative variables were represented by medians and interquartile ranges (IQR). The comparison of clinical features between cases and controls was performed using the Chi-square test or Fisher's exact test (when applicable) for categorical variables or the student t test

for independent samples for continuous variables. The Mann-Whitney U test was used for variables that did not follow a normal distribution. Crude Odds ratios (OR) were calculated using the Mantel-Haenszel method to identify potential risk factors for CMV reactivation. Multivariate analysis was performed using stepwise logistic regression. Variables were introduced into the model if they had a *p* value less than 0.20 in the univariate analysis. A *p* value <0.05 was considered statistically significant. ROC curves were plotted for recipient anti-CMV IgG titer and R/D anti-CMV IgG ratio to determine cut-offs allowing to identify patients at risk of CMV reactivation.

Ethical issues. The study was approved by the Ethics Committee of the National Bone Marrow Transplant Center of Tunis in accordance with the Declaration of Helsinki (approval number: CNGMOEC-1124). Given the retrospective design of the study and the use of anonymized clinical data, the requirement for informed consent was waived by the Ethics Committee. All methods were performed in accordance with the relevant guidelines and regulations.

Results. During the study period, 130 patients received an allo-HSCT in the Pediatrics Department at our center. We identified 24 cases of CMV reactivation (**Figure 1**). The median time until the CMV reactivation was 35 days post-transplant (IQR: 12-54). **Table 1** summarizes demographic and clinical data from our patients and shows univariate comparisons between cases and controls for each studied variable. Out of the 24 cases, 1 recipient had a missing pre-transplant anti-CMV IgG titer (n=23 for cases where recipient serology is

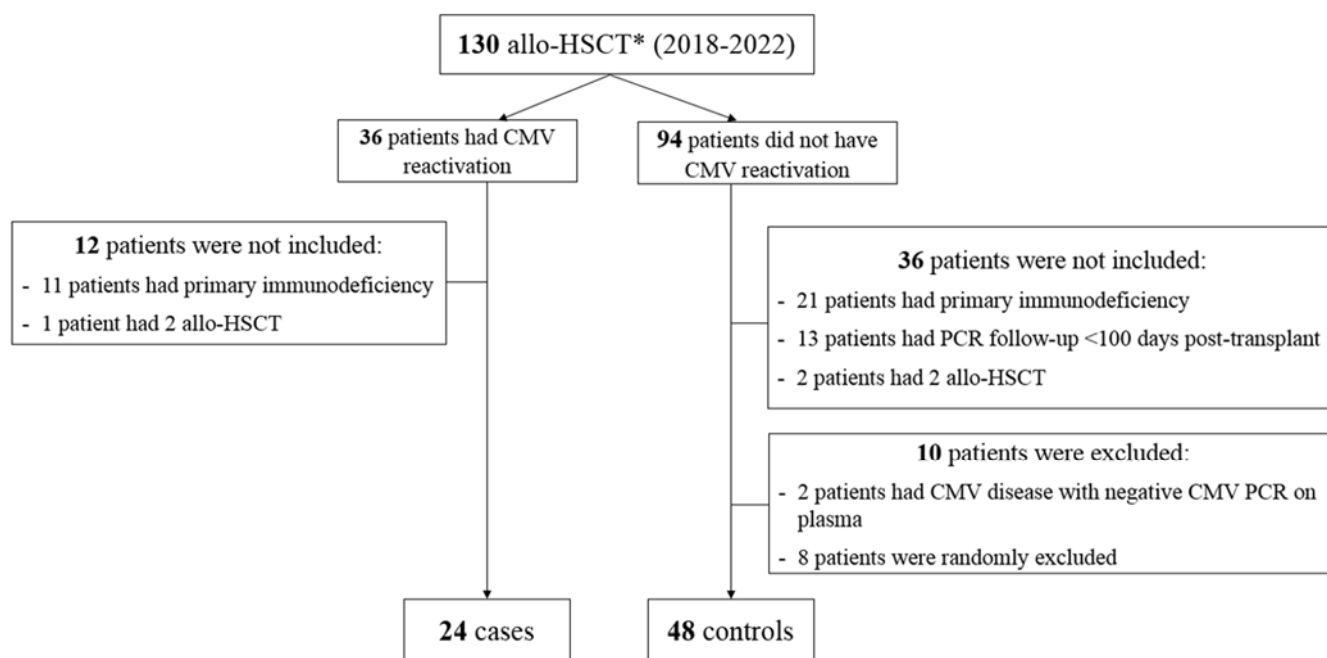


Figure 1. Flow chart of patient recruitment.

Table 1. Univariate analysis of potential risk factors for CMV reactivation in HSCT recipients.

	Variable		Cases (n=24)	Controls (n=48)	Crude Odds Ratio (95% CI)	p value
Demographics	Recipient gender	<ul style="list-style-type: none"> Male Female 	15 (63%) 9 (37%)	25 (52%) 23 (48%)	1.53 (0.56 – 4.18)	0.402
	Donor gender	<ul style="list-style-type: none"> Male Female 	16 (67%) 8 (33%)	23 (48%) 25 (52%)	2.17 (0.78 – 6.03)	0.132
	Gender mismatch	<ul style="list-style-type: none"> Yes No 	15 (63%) 9 (37%)	26 (54%) 22 (46%)	1.41 (0.52 – 3.84)	0.501
	Recipient age (years)		4.36 ± 3.99	5.80 ± 3.84	NA	0.144
	Donor age (years)		24.21 ± 14.49	18.33 ± 16.79	NA	0.148
Pre-transplant CMV serology	CMV serologic status	<ul style="list-style-type: none"> D+/R+ D+/R- D-/R+ D-/R- 	16 (70%) 0 8 (30%) 0	39 (81%) 2 (4%) 5 (10%) 2 (4%)	NA	0.118
	CMV serologic status	<ul style="list-style-type: none"> D-/R+ Others 	8 (35%) 15 (65%)	5 (10%) 43 (90%)	4.59 (1.30 – 16.21)	0.013
	Recipient anti-CMV IgG titer (AU/ml)		203.34 ± 139.12	115.94 ± 131.20	NA	0.012
	Donor anti-CMV IgG titer (AU/ml)		162.35 ± 175.29	255.47 ± 186.76	NA	0.046
	R/D anti-CMV IgG ratio		1.34 (IQR: 0.85-149.6)	0.52 (IQR: 0.17-0.83)	NA	0.001
Underlying pathology	<ul style="list-style-type: none"> Acute leukemia Aplastic anemia Hemoglobinopathy 		17 (71%) 3 (12%) 4 (17%)	23 (48%) 15 (31%) 10 (21%)	NA	0.142
	<ul style="list-style-type: none"> Acute leukemia Others 		17 (71%) 7 (29%)	23 (48%) 25 (52%)	2.64 (0.93 – 7.52)	0.065
HLA compatibility	<ul style="list-style-type: none"> HLA haploidentical related donor 		13 (54%)	7 (15%)	6.92 (2.23 – 21.53)	0.0001
	<ul style="list-style-type: none"> HLA genoidentical related donor 		11 (46%)	41 (85%)		
Pre-transplant conditioning	<ul style="list-style-type: none"> Myeloablative Not myeloablative 		24 (100%) 0	43 (90%) 5 (10%)	1.56 (1.30 – 1.86)	0.101
GvHD prophylaxis	<ul style="list-style-type: none"> CSA+MMF+CYC Others* 		13 (54%) 11 (46%)	7 (15%) 41 (85%)	6.92 (2.23 – 21.53)	0.0001
Antilymphocyte serum	<ul style="list-style-type: none"> Yes No 		6 (25%) 18 (75%)	16 (33%) 32 (67%)	0.67 (0.22 – 2.01)	0.469
Acute GvHD (grades II-IV)	<ul style="list-style-type: none"> Yes No 		16 (67%) 8 (33%)	12 (25%) 36 (75%)	6.00 (2.06 – 17.51)	0.001
Corticosteroids	<ul style="list-style-type: none"> Yes No 		14 (58%) 10 (42%)	6 (12%) 42 (88%)	9.80 (3.01 – 31.86)	0.0001
Primary rejection	<ul style="list-style-type: none"> Yes No 		1 (4%) 23 (96%)	1 (2%) 47 (98%)	2.04 (0.12 – 34.16)	0.612
Secondary rejection	<ul style="list-style-type: none"> Yes No 		0 24 (100%)	1 (2%) 47 (98%)	0.66 (0.56 – 0.78)	0.476

CMV: Cytomegalovirus; CSA: Cyclosporin A; CYC: Cyclophosphamide D: Donor; GvHD: Graft versus Host Disease; MMF: Mycophenolate Mofetil; NA: Not applicable; R: Recipient. *Others: Cyclosporin A or cyclosporin A with methotrexate.

involved). R/D anti-CMV IgG ratio was calculated in 19 cases and 37 controls (after excluding anti-CMV IgG titers > 500 AU/ml).

In univariate analysis, factors associated with CMV reactivation were D-/R+ pre-transplant CMV serostatus ($p=0.013$), recipient anti-CMV IgG titer ($p=0.012$), R/D anti-CMV IgG ratio ($p=0.001$), HLA haploidentical related donor ($p=0.0001$), GvHD prophylaxis with combination of cyclosporin A, cyclophosphamide and mycophenolate mofetil ($p=0.0001$), acute GvHD ($p=0.001$) and corticosteroids ($p=0.0001$). Donor anti-CMV IgG titer was a protective factor ($p=0.046$) (**Table 1**).

In multivariate analysis, male donor gender (adjusted OR=4.919; 95% CI (1.103 – 21.942); $p=0.037$), D-/R+ pre-transplant CMV serologic status (adjusted OR=6.874; 95% CI (1.372 – 34.444); $p=0.019$), recipient anti-CMV IgG titer (adjusted OR=1.005; 95% CI (1.000 – 1.010); $p=0.033$), HLA haploidentical related donor (adjusted OR=5.472; 95% CI (1.334 – 22.453); $p=0.018$) and acute GvHD (OR=7.116; 95% CI (1.770 – 28.604); $p=0.006$) remained associated with CMV reactivation after allo-HSCT (**Table 2**).

We calculated, from ROC curve analysis (**Figure 2**), sensitivity and specificity for the optimal cut-off value for the recipient anti-CMV IgG titer (23 cases vs 48 controls) and the R/D anti-CMV IgG ratio (19 cases vs

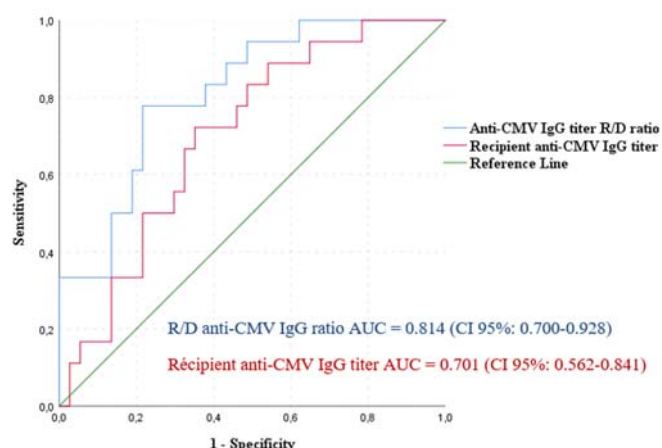
Table 2. Multivariate analysis of potential risk factors for CMV reactivation in HSCT recipients.

Variable			Cases (n=24)	Controls (n=48)	Adjusted Odds Ratio (95% CI)	p value
Donor gender	• Male		16 (67%)	23 (48%)	4.919 (1.103 – 21.942)	0.037
	• Female		8 (33%)	25 (52%)		
Pre-transplant CMV serology	CMV serologic status	• D-/R+ • Others	8 (35%) 15 (65%)	5 (10%) 43 (90%)	6.874 (1.372 – 34.444)	0.019
	Recipient anti-CMV IgG titer		203.34 ± 139.12	115.94 ± 131.20	1.005 (1.000 – 1.010)	0.033
HLA compatibility	• HLA haploidentical related donor		13 (54%)	7 (15%)	5.472 (1.334 – 22.453)	0.018
	• HLA genoidentical related donor		11 (46%)	41 (85%)		
Acute GvHD	• Yes		16 (67%)	12 (25%)	7.116 (1.770 – 28.604)	0.006
	• No		8 (33%)	36 (75%)		

CMV: Cytomegalovirus; D: Donor; GvHD: Graft versus Host Disease; R: Recipient.

Table 3. Area under the ROC curves and Cut-off values of recipient anti-CMV IgG titer and recipient-to-donor (R/D) anti-CMV IgG ratio.

	Recipient anti-CMV IgG titer	R/D anti-CMV IgG ratio
Area under the ROC curve	0.701	0.814
95% Confidence Interval	(0.562 – 0.841)	(0.700 – 0.928)
p value	0.016	0.0001
Cut-off value	113.75	1
Sensitivity	72.2%	77.8%
Specificity	64.9%	78.4%

**Figure 2.** ROC curves for recipient anti-CMV IgG titer and recipient-to-donor anti-CMV IgG ratio.

37 controls) to discriminate patients with CMV reactivation after allo-HSCT. The optimal cut-off value for the recipient anti-CMV IgG titer was 113.75 AU/ml, with a sensitivity of 72.2% and a specificity of 64.9% (**Table 3**). The optimal cut-off value for the R/D anti-CMV IgG ratio was 1, with a sensitivity of 77.8% and a specificity of 78.4% (**Table 3**). The prevalence of CMV reactivation was higher in patients with pre-transplant anti-CMV IgG titer >113.75 AU/mL (50% versus 16%; $p=0.002$) and in those with R/D anti-CMV IgG ratio >1 (64% versus 15%; $p<0.001$).

Discussion. CMV reactivation remains one of the most frequent viral infections after allo-HSCT. Before the

advent of letermovir (a molecule not yet available in Tunisia and in many other countries), preemptive treatment was the method of choice for CMV disease prevention in the majority of HSCT centers around the world, including our center.^{2,9} This approach has gained in effectiveness with the introduction of PCR, which has proved reliable for CMV detection.¹⁰ Weekly monitoring between D7 and D100 post-transplant is currently recommended using quantitative PCR (on whole blood or plasma).¹¹ All patients included in our study, both cases and controls, had weekly PCR monitoring on plasma until D100 post-transplant or beyond. The viral load threshold of ≥ 150 IU/mL was used for defining CMV reactivation. It reflects our local institutional standard practice using plasma quantitative PCR. Because viral load thresholds and biological specimens (plasma vs. whole blood) vary across international guidelines and centers, this specific threshold may limit the direct external generalizability of our findings to institutions using different assay platforms or clinical thresholds.

Pre-transplant CMV serologic status remains the most important determinant of CMV reactivation after allo-HSCT in the era of preemptive therapy.¹² In our multivariate analysis, a D-/R+ status remained associated with CMV reactivation. It's known in the literature that CMV reactivation was more frequent in recipients with previous contact with CMV (R+) prior to transplantation, especially if the donor was seronegative (D-).^{3,13} On the other hand, a donor with previous contact with CMV

(D+) seemed to protect the recipient. Indeed, the graft from the seropositive donor (D+) provides mature T lymphocytes specific to the virus, thus enabling the host's immunity to be restored.^{14,15} The prognosis of patients who underwent HSCT depends significantly on the CMV serostatus of their donors. If the donors are CMV-positive, immune recovery in recipients after transplantation is faster, with a higher number of CD4+CD25 high T lymphocytes specific to CMV being recorded, compared with transplants from seronegative donors.¹⁶

Our study shows that not only qualitative anti-CMV serostatus is a risk factor, but also that anti-CMV IgG titer is associated with CMV reactivation: the higher the IgG anti-CMV titer in the recipient, the higher the risk of reactivation, and conversely, the higher the IgG anti-CMV titer in the donor, the lower the risk. Similar results regarding recipient anti-CMV IgG titer have been reported in some recent studies.⁴⁻⁷ But, to our knowledge, this study is the first study on CMV serology in allogeneic HCT performed exclusively in paediatric patients. Cellular immunity, particularly CMV-specific CD4+ and CD8+ T cells, certainly plays the predominant role in controlling CMV reactivation, and donor memory T-cell transfer is key to post-transplant immune reconstitution. The recipient anti-CMV IgG titer reflects cumulative past antigen exposure and repeated subclinical reactivations rather than direct humoral protective immunity.^{7,17,18} In immunocompetent hosts, attempts at reactivation are suppressed by the adaptive immune response. Following allo-HSCT, the process of immune reconstitution compromises this ability, particularly in patients with high pre-transplant anti-CMV IgG titers.¹⁷ Thus, a high level of anti-CMV IgG in the recipient likely serves as a surrogate biomarker indicating a higher latent viral load or frequent episodes of reactivation prior to transplantation, rather than constituting a direct causal factor.

In univariate analysis, a high pre-transplant anti-CMV IgG titer in the donor was a protective factor against CMV reactivation. Although immune control of CMV infection is primarily cellular, some studies suggest that humoral immunity contributes to the control of viremia during CMV reactivation.^{19,20} Hypotheses that may explain the protective activity of anti-CMV antibodies include early neutralization of the virus in its extracellular phase and improved phagocytosis of CMV-infected cells for more effective opsonization.²⁰ In fact, intravenous injections of human immunoglobulins containing high titers of anti-CMV neutralizing antibodies can be used as an adjuvant treatment for CMV reactivation after HSCT.²¹

Based on ROC curves analysis, threshold values were identified for both the recipient pre-transplant anti-CMV IgG titer (113.75) and the R/D anti-CMV IgG ratio (1), with good sensitivity and specificity values. A

comparable threshold of recipient anti-CMV IgG titer of around 100 AU/mL was reported by Arcuri et al, with a significantly higher CMV reactivation incidence in recipients with titers above the threshold.⁵ CMV diseases were observed exclusively in the group of patients with a pre-transplant anti-CMV IgG titer above the threshold.⁴ Since CMV reactivation depends on the anti-CMV IgG titer in both recipient and donor, the sensitivity and specificity values were better for the ratio threshold value than for the recipient anti-CMV IgG titer. In our study, the ratio cut-off was 1, which means that the lower the recipient's titer compared to the donor's, the lower the risk of reactivation. The biological rationale for the R/D IgG ratio lies in its capacity to integrate two distinct clinical and immunological vectors into a single quantitative parameter: the recipient's latent viral burden/prior antigen exposure (represented by the recipient IgG titer) and the potential strength of donor-transferred immunity/prior viral exposure (reflected by the donor IgG titer). Thus, the ratio reflects a biological equilibrium between the host's reactivation risk and the graft's capacity to contain viral replication. These results would be useful for better risk stratification of CMV reactivation and adaptation of surveillance strategies. Even in centers where letermovir prophylaxis is routinely available, post-transplant CMV management remains challenging due to the risk of late-onset CMV reactivation following prophylaxis discontinuation or breakthrough infections. High-risk stratification based on pre-transplant recipient IgG titers and R/D ratios could guide clinicians in identifying patients who may benefit from extended prophylaxis, secondary prophylaxis, or intensified viral PCR monitoring after stopping letermovir.⁷

Our study has some limitations to mention. The exact value of IgG anti-CMV titers >500 was not determined (no routine dilution performed), so we could not explore the performance of higher cut-offs and their potential relationship with the risk of CMV reactivation. For seronegative donors, the minimum analytical threshold of the assay (0.15 AU/mL) was used as the denominator, which inherently yielded very high ratio values in D-/R+ pairs. Another potential limitation is that we reported serological results in AU/mL (other manufacturers may use different units of measurement). This compromises comparability between different studies. Indeed, there is currently no common standard for comparison. Furthermore, the retrospective nature of this study resulted in missing data and the small sample size reduces the performance of statistical analyses. Our multivariable model includes five variables relative to 24 reactivation events; therefore, these multivariable findings should be considered exploratory rather than definitive independent predictors and require validation in larger cohorts. Several important determinants of CMV reactivation (donor type beyond HLA matching,

ATG dose, lymphocyte recovery, neutrophil engraftment, CD34 dose, T-cell depletion, CMV-specific immune monitoring...) were not consistently documented for all patients and could not be included in the analysis. Additional studies, particularly prospective multicenter studies, would be necessary to refine our findings. We recommend diluting sera with an anti-CMV IgG titer above the upper limit of quantification.

Conclusions. CMV serology remains the only test available prior to transplantation to assess the risk of CMV occurrence post-transplantation. So far, the determination of CMV serostatus in transplant recipients has been used as a qualitative parameter. In this study,

we have shown that both pre-transplant anti-CMV IgG titer in recipient and R/D anti-CMV IgG ratio were associated with the risk of CMV reactivation following allo-HSCT. Furthermore, a high pre-transplant anti-CMV IgG titer in the donor would be a protective factor. More studies are needed to explore how these findings can be incorporated into the CMV reactivation risk algorithm.

Author Contributions Statement. Siwar Frigui wrote the main manuscript text. Salma Daly and Samia Rekaia collected data. Hedia Bellali performed statistical analysis. All authors reviewed the manuscript.

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