Lower platelet count early after the heart transplantation is associated with lower rates of cellular-mediated rejection within 24 months after heart transplantation

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Background: Decrease in platelet count following the induction with polyclonal anti-thymocyte globulin (ATG) is deemed as an adverse event, while decrease in lymphocyte count represents a therapeutic goal[1]. Still, the effect on platelets may represent an important part of ATG anti-rejection mechanisms.

Patients and Methods: This was a retrospective single-center study of consecutive HTx (heart transplantation) patients (pts) from February 2010 to February 2018 in University Hospital Centre Zagreb. All pts received rATG (Thymoglobulin®) 1.5 mg/kg daily during the first 5 days. Complete blood count with differential was assessed on days 0, 7 and 14 after HTx. The incidence of cellular-mediated rejection (ACR) was monitored for two years after HTx. ACR was classified according to ISHLT classification from 1990 and expressed as ACR of grade 1B or higher (≥1B).

TABLE 1. Univariate Analysis of Acute Cellular Rejection (ACR of grade ≥1B) in the first 2 years after heart transplantation.

Variable	HR	95% CI	p value
Recipient age, years	**0.961**	**0.939-0.984**	**0.001**
Recipient gender Male	0.625	0.281-1.392	0.25
Positive pre-transplant recipient CMV IgG	**0.319**	**0.133-0.766**	**0.011**
Donor/recipient CMV mismatch	2.646	0.778-8.994	0.119
Donor age, years	0.971	0.943-1.001	0.059
Donor gender Male	1.594	0.643-3.949	0.314
Pre-transplant mechanical circulatory support	1.677	0.573-4.908	0.345
Ischemia time, min	1.001	0.995-1.007	0.678
Absolute lymphocyte count on day 7, x 10^3/μL	1.000	0.999-1.002	0.446
Absolute lymphocyte count on day 14, x 10^3/μL	1.001	1.000-1.001	0.074
Platelet count on day 7, x 10^3/μL	**1.007**	**1.002-1.013**	**0.006**
Platelet count on day 14, x 10^3/μL	1.004	1.000-1.008	0.074
Positive post-transplant CMV PCR	0.501	0.118-2.127	0.349
Calcineurin inhibitor, No. (%) Tacrolimus vs Cyclosporine	0.840	0.393-1.796	0.653

CMV = Cytomegalovirus; PCR = polymerase chain reaction.

Results: A total of 159 pts were transplanted. Median age was 55 years (IQR, 47-62 years), 76% were male. A total of 27 pts (17 %) experienced ACR ≥1B during 24 months. Pts with ACR of grade ≥1B had higher platelet count on day 7 (145 vs 104 x 10^3/μL, p<0.001). They also had higher the absolute lymphocyte count (ALC) on the same day, but this did not reach statistical significance (162 vs 130 x 10^3/μL, p=0.19) and there was no correlation between ALC and platelet counts on day 7 (Pearson's correlation coefficient was 0.064, p=0.459). Conversely, more rejection was observed in pts with higher ALC on day 14 (326 vs 190 x 10^3/μL, p=0.035), with a trend towards statistical significance in the relationship with higher platelet count (210 vs 199 x 10^3/μL, P=0.076). In the univariate analysis, higher platelet count on day 7, younger recipient age and negative pre-transplant Cytomegalovirus (CMV) IgG serology were found as predictors of the ACR ≥1B in the first 2 years after HTx (**Table 1**). In multivariable model, platelet count on day 7 and pre-transplant CMV serostatus were independent predictors of rejection. ROC analysis of the aforementioned model showed a satisfying AUC of 0.75.

Conclusion: Decrease in platelet count following the induction with rATG is strongly related to less graft rejection that is independent from the lymphodepleting effect. This indicates the importance of platelet involvement in anti-rejection mechanisms of ATG induction, and consequently a possible rationale for targeting platelets in future immunosuppressive regimens.

LITERATURE

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