Identification of leukocyte subpopulations as potential biomarkers of long-term survival with normal allograft function after lung transplantation

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Introduction

Long-term survival after lung transplantation (LT) is limited by the development of chronic lung allograph dysfunction (CLAD). Despite this fact, a small number of lung transplant recipients are long-term survivors with a good allograft function (LTS).

A study of this particular population could be a first step to search for transplant tolerance biomarkers that can lead to the reduction of immunosuppressive drugs in treatment plans and improve personalized medicine. The objective of this study was to identify leukocyte subpopulations as potential biomarkers of LTS after lung transplantation.

Patients & Methods

Sixty-two double lung transplant recipients were included in this multicenter cross-sectional study: 31 patients with CLAD and 31 patients with stable lung allograft function after 10 years from LT (LTS).

Six leukocyte profiling panels computing 4 to 10 markers were used for whole blood leukocyte subset profiling by flow cytometry. The percentages of the different leukocyte subpopulations were compared between both groups.

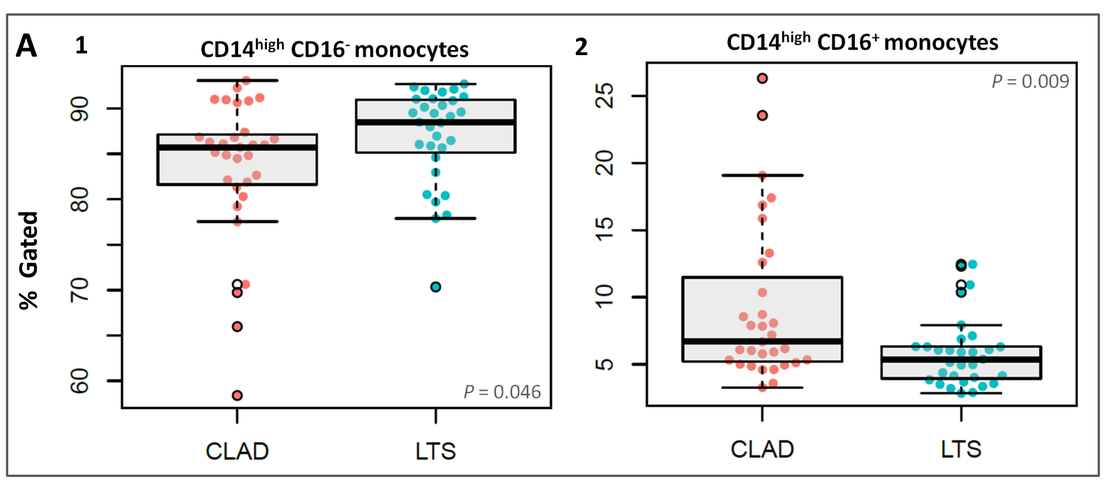
Results

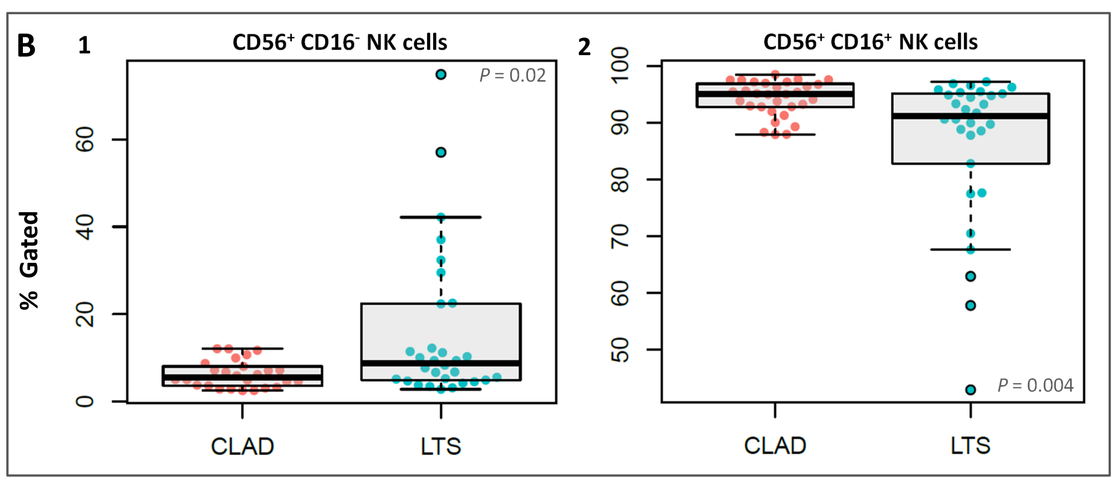
Leukocyte subsets that significantly differ between LTS and CLAD groups are summarized in Table 1.

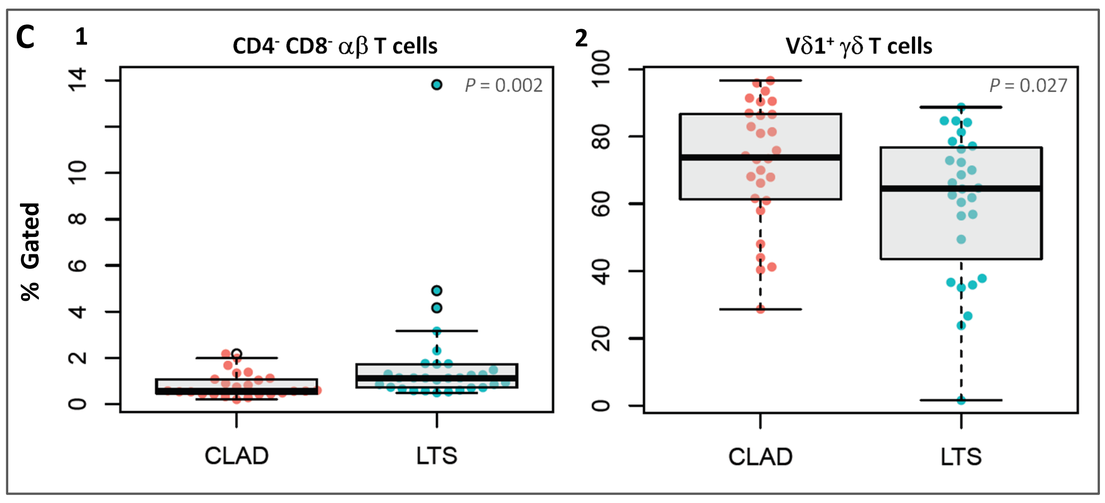
	Leukocyte Subsets (%)		p value
	LTS vs.	CLAD	
Monocytes	$CD14^{high}CD16^{-}$	86.9	83.5	0.046
	$CD14^{high}CD16^{+}$	5.8	9.3	0.009
NK cells	$CD56^{+}CD16^{-}$	15.6	6.2	0.02
	$CD56^{+}CD16^{+}$	86.3	94.2	0.004
T cells	$CD4^{-}CD8^{-}\alpha\beta$	1.8	0.8	0.002
	$V\delta1^{+}\gamma\delta$	59.9	71.9	0.027
Granulocytes	$CD62L^{+}$	99.8	98.8	0.007

Table 1. Leukocyte subpopulations with significant differences between LTS (cases) and CLAD (controls) groups.

LTS: Long-term survivors;
CLAD: Chronic lung allograph dysfunction;
NK: Natural killer.







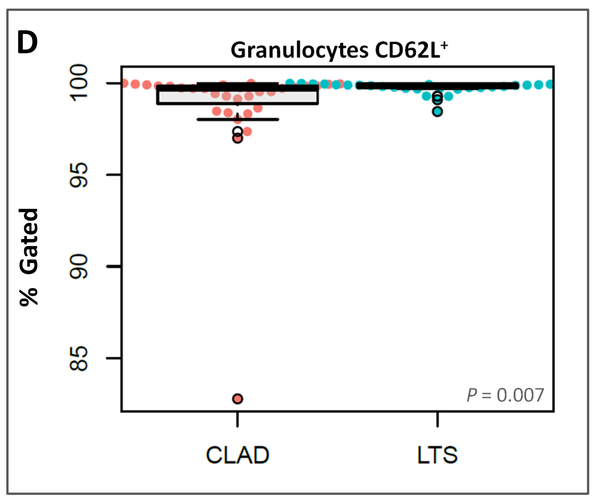


Figure 1. **Quantitative differences of leukocyte subpopulations between LTS and CLAD groups. (A) Monocytes**, expressed as the percent of $CD14^{h}$ $CD16^{-}$ (1) and $CD14^{h}$ $CD16^{+}$ (2) of the total monocytes. **(B) Natural killer cells**, expressed as the percent of $CD56^{+}$ $CD16^{-}$ (1) and $CD56^{+}$ $CD16^{+}$ (2) of the total NK cells. **(C) $CD4^{-}$ $CD8^{-}$ αβ T cells** (1) shown as the percent of the total αβ T cells and **$V\delta1^{+}$ T cells** (2) shown as the percent of the total γδ T cells. (D) **Granulocytes $CD62L^{+}$** expressed as the percent of the total granulocytes. Boxes depict median and IQR; whiskers denote 1.5 x IQR. Two-sided *P* values for Mann-Whitney *U* test comparisons between groups are shown (P<0.05).

Conclusions

These results suggest that **$CD14^{high}$ $CD16^{-/+}$ monocytes**, **$CD56^{+}$ $CD16^{-/+}$ NK cells**, **$CD4^{-}$ $CD8^{-}$ αβ** and **$V\delta1^{+}$ γδ T cell subpopulations** could be potential biomarkers of long term allograft survival in lung transplant patients.

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No relationships to disclosure