

New Paradigms in Rejection Monitoring: Lymphocyte Subsets as Non-Invasive Graft Markers in Vascularized Composite Allotransplantation

Sachin R. Chinta BS¹, Alay R. Shah MD¹, David L. Tran MD¹, Wen-Yu Lee MS², Massimo Mangiola PhD³, Bruce E. Gelb MD⁴, Daniel J. Ceradini MD¹, Eduardo D. Rodriguez MD DDS¹

¹Hansjörg Wyss Department of Plastic Surgery, NYU Langone Health, New York, NY, ²Division of Biostatistics, NYU Langone Health, New York, NY, ³Department of Pathology, NYU Langone Health, New York, NY, ⁴Department of Surgery, NYU Langone Health, New York, NY.



INTRODUCTION

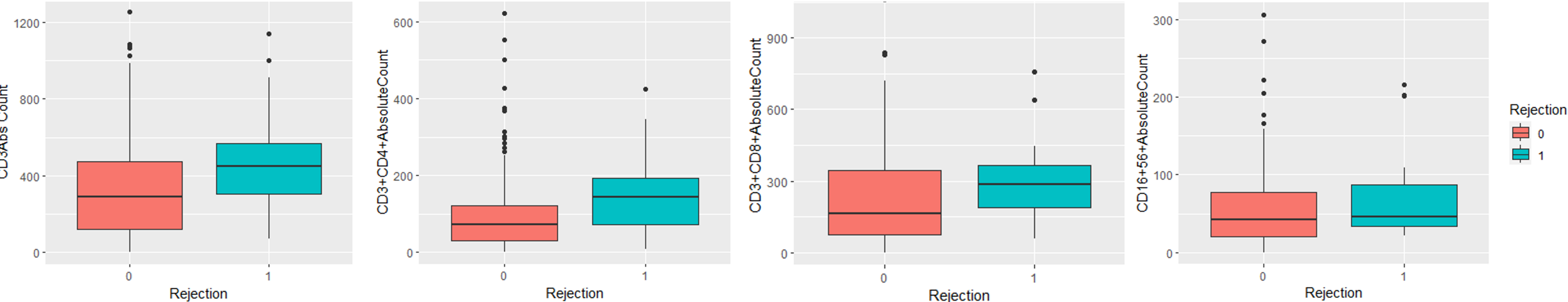
- Vascularized composite allografts (VCAs) are comprised of multiple tissue types each with a unique physiological profile.
- Inclusion of immunogenic tissues, like skin, predispose patients to graft rejection.
- The current gold standard for graft monitoring is currently biopsy, however this can be overly invasive for many recipients.
- Elucidating possible trends of blood borne markers in relation to acute rejection episodes can provide clinical decision support to VCA providers by providing a readily available and cost-effective metric for graft monitoring.
- **This purpose of this study is to determine if there is a relationship between a state of acute rejection and a patient’s concurrent lymphocytic subset distribution at the time of presentation.**

METHODS

- Retrospective review was conducted of three patients who underwent a total of three facial VCAs and two hand VCAs at NYU Langone Health
- **Data Collected:** Patient demographics, lymphocytic subsets (CD3+, CD3+CD4+, CD3+CD8+, CD19+, and CD16+56+ absolute counts; CD3%, CD3+CD4+%, CD3+8+%, CD19+%, and CD16+56+%; CD4+/8+ ratio), immunosuppressive regimen, current medications, Banff grading of available skin biopsies, and presence of clinically suspected or confirmed infection were collected. Rejection was defined as Banff Grade > 2 + clinical signs of rejection
- **Statistical Analysis:** Linear mixed effect models were used fit data, give non-independent nature of sample results.

RESULTS				
A total of three patients who received three face transplants and one bilateral hand transplant were included in this study. All patients were male and Caucasian with patient age ranging from 21 to 45 years old. Mechanism of initial injury was thermal burn in two patients, and ballistic trauma in one. Follow up was an average of 50.85 months.				
Table1. Linear mixed effect model with inclusion of tacrolimus as a fixed effect				
Subset	Estimate	Std. Error	t-value	p-value
CD3+ Abs Count *	163.22	64.40	2.53	0.0113*
CD3+CD4+ Abs Count *	66.14	23.96	2.76	0.0058*
CD3+CD8+ Abs Count *	88.15	44.77	1.97	0.0490*
CD19+ Abs Count	55.44	31.11	1.77	0.0769
CD16+56+ Abs Count *	36.24	11.65	3.11	0.0019*
CD3%	0.42	5.15	0.08	0.9351
CD3+CD8+%	1.24	4.56	0.27	0.7861
CD3+CD4+%	-1.02	2.30	-0.44	0.6591
CD19+%	2.86	4.17	0.69	0.4928
CD16+56+%	0.92	2.25	0.41	0.6825
CD4/CD8 Ratio	-0.09	0.10	-0.95	0.3398
Abs, Absolute.; *, p<.05				

Figure 1. Significant lymphocyte subsets stratified by clinical rejection status



DISCUSSION

- Issues surrounding specificity, cost efficacy, and access currently limit the clinical applicability of molecular markers.
- CD3+ T-lymphocytes, CD4+ T-helper cells, CD8+ cytotoxic T-cells, and CD16+56+ natural killer cells were all identified as being significantly upregulated during acute rejection, in our patient cohort.
- All of the aforementioned cell lineages have been previously documented as significant mediators of VCA rejection, on histological analysis.
- Histological and clinical outcomes do not necessarily correlate, but the findings of our study suggest that these cells are not only locally upregulated in graft tissue but are also upregulated on a systemic level.

CONCLUSIONS

- Lymphocyte subsets can be a useful adjunct for providers in the diagnosis of acute VCA rejection.
- These markers can help optimize management, reduce biopsy burden, and decrease longitudinal risk incurred upon VCA recipients.
- Further research is required to delineate the exact role these immune cells play in the rejection cascade and how they fluctuate during and after treatment.

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