Absolute Lymphocyte Count as a Surrogate for Lymphocyte Phenotype Analysis of CD3 count in Monitoring Thymoglobulin Response Post Heart Transplantation

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BACKGROUND

Post-operative anti-thymocyte globulin therapy (ATG) is used for both induction therapy and as a temporary substitute for calcineurin inhibitors (CNIs)[1]. Dosing of ATG is optimally guided by Cluster of Differentiation 3 (CD3) levels[2,3]. At many institutions obtaining a CD3 count requires sending a blood sample to an outside laboratory for testing. Absolute lymphocyte count (ALC) may be used as alternate method to CD3 count to determine appropriate dosing and monitoring the ATG therapy in renal transplant patients when a flow cytometer is not available[4]. However, to our knowledge, there are no known, studies about the use of ALC monitoring when treating heart transplant patients with ATG. The purpose of this study was to establish the validity of using Absolute Lymphocyte Count (ALC) as a substitute for CD3 given its ready availability and low cost.

METHODS

- A retrospective review was conducted of heart transplant recipients from 9/2014 to 2/2019 at our institution who received post-operative ATG and had a CD3 count with corresponding ALC.
- The Pearson correlation coefficient was used to examine the correlation between ALC and CD3.
- A series of validity tests including sensitivity, specificity, positive predictive value (PP), negative predictive value (NPV), and the Youden Index (YI) were performed to identify an appropriate range for an ALC cutoff point that would provide the greatest degree of validity of ALC as an appropriate surrogate for a CD3 cutoff of 100 cells/mm3.
- The logistic regression model also was used to produce complete validity test results at all potential cutoff points and their graphic representation also known as Receiver Operating Characteristics (ROC) curve and the Area Under the Curve (AUC).
- Data were re-analyzed to examine whether gender or age groups made any difference in the ALC and CD3 correlation.

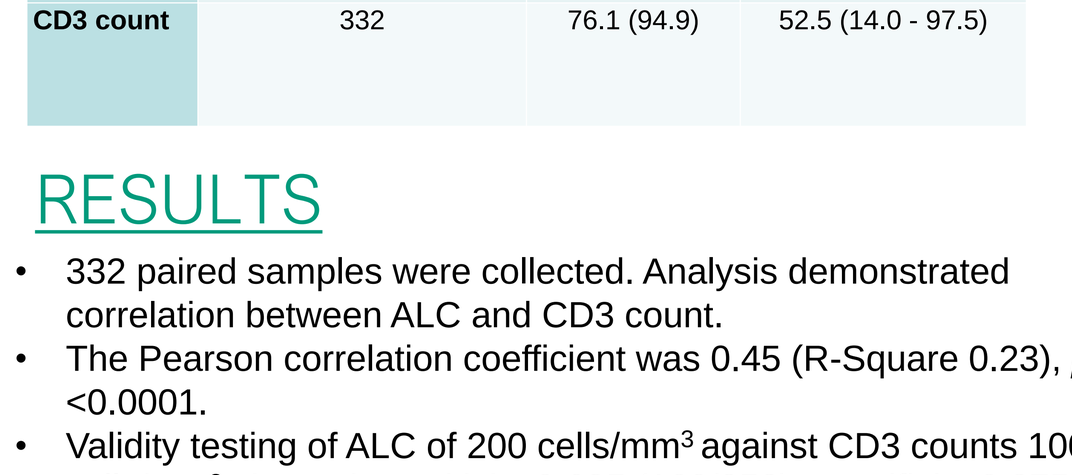
Table 1. Descriptive Statistics of ALC and CD3 Counts

	Number of Observations	Mean (STD)	Median (Q1-Q3)
ALC	332	208.5 (190.7)	160.0 (100.0 - 215.0)
CD3 count	332	76.1 (94.9)	52.5 (14.0 - 97.5)

RESULTS

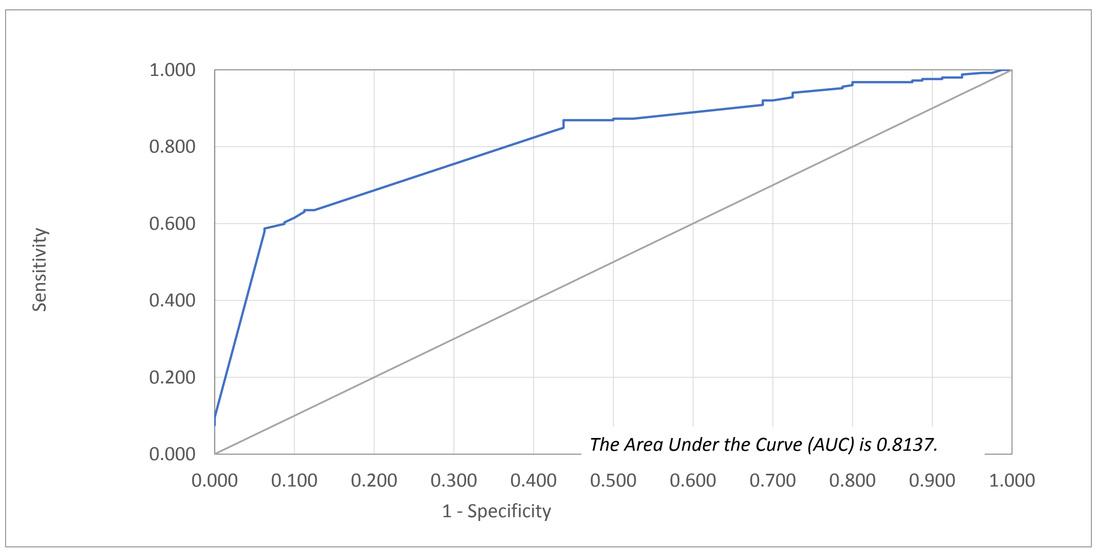
- 332 paired samples were collected. Analysis demonstrated correlation between ALC and CD3 count.
- The Pearson correlation coefficient was 0.45 (R-Square 0.23), p <0.0001.
- Validity testing of ALC of 200 cells/mm^3 against CD3 counts 100 cells/mm^3 showed sensitivity 0.635 (160/252), specificity 0.875 (70/80), positive predictive value (PV) 0.941 (160/170), and negative PV 0.432 (70/162).
- Based on the YI, the zone for the optimal cutoff points ranged from 100 to 200 cells (Figure 1).
- AUC for the ROC analysis was 0.81 (Figure 2).
- Gender and age did not affect the validity analysis of ALC as a surrogate estimate for CD3 in this group of transplant patients.

Figure 1. Correlation Between ALC and CD3



RESULTS

Figure 2. Receiving Operating Characteristic Curve

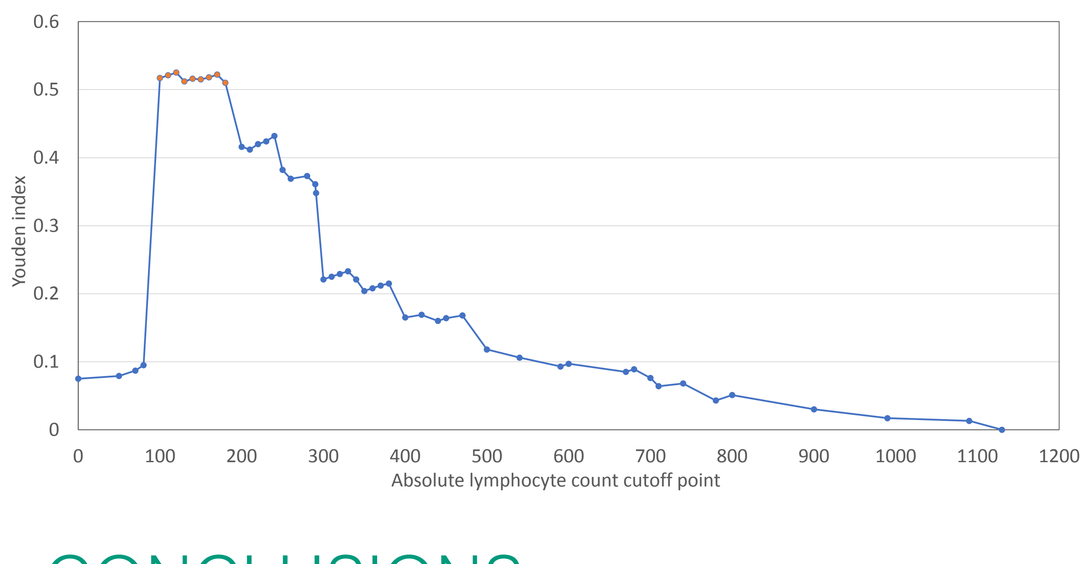


Cutoff points based on the data and associated validity tests

Cut point	True positive	True negative	False positive	False negative	Sensitivity	Specificity	PPV	NPV	YI	Prob
100	146	75	5	106	0.579	0.938	0.967	0.414	0.517	0.852
110	147	75	5	105	0.583	0.938	0.967	0.417	0.521	0.846
120	148	75	5	104	0.587	0.938	0.967	0.419	0.525	0.839
130	151	73	7	101	0.599	0.913	0.956	0.420	0.512	0.833
140	152	73	7	100	0.603	0.913	0.956	0.422	0.516	0.826
150	155	72	8	97	0.615	0.900	0.951	0.426	0.515	0.820
160	159	71	9	93	0.631	0.888	0.946	0.433	0.518	0.813
170	160	71	9	92	0.635	0.888	0.947	0.436	0.522	0.805
180[a]	160	70	10	92	0.635	0.875	0.941	0.432	0.510	0.798
200[b]	212	46	34	40	0.841	0.575	0.862	0.535	0.416	0.782

(a) Same as less than 200 cells/mm3 (b) Same as equal to or less than 200 cells/mm3

Figure 3. Youden Index at Various ALC Cutoff Points



CONCLUSIONS

- This study suggests that ALC may have validity as a selective substitute for CD3 monitoring in patients receiving ATG.
- Further studies of this novel approach are warranted.

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DISCLOSURE

The authors have not used any off label or unapproved product. The authors have no financial or professional affiliations to disclose related or derived from the information in this research.