Lupus Low Disease Activity State: Predicting Organ Damage Accrual and Cardiovascular Risk in Patients with Systemic Lupus Erythematosus

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Purpose

- Lupus Low Disease Activity State (LLDAS)[1] is a new clinical evaluation tool that assesses low disease activity state in lupus patients.
- Our study examines the statistical relationship between the percentage of time patients spend in LLDAS and whether more time in LLDAS protects against organ damage accrual, cardiovascular events, and death.
- If the evidence supports LLDAS as a valid predictor of low damage, it could provide a new therapeutic target.

Introduction

- Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that affects between 1-3% of the population in the United States, predominantly women.
- SLE is a heterogeneous disease that can cause multisystem inflammation and damage of skin, joints, kidneys, brain, heart and lungs.
- Given that manifestations of SLE vary widely between patients, disease activity is often difficult to quantify.
- We aim to investigate the validity of LLDAS in our patient population and whether it has protective measures against organ damage and cardiovascular risk in lupus patients.

Methods

- We studied a prospective cohort of 245 patients with SLE during a 5-year follow-up period.
- Disease activity was measured using the SELENA SLE Disease Activity Index (SELENA-SLEDAI) and the physician global assessment (PGA).
- Cumulative organ damage was assessed at 1-year, 3-year, and 5-year intervals using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI).
- The determination of LLDAS ≥ 50% of the time (LLDAS-50) was done retrospectively through clinical chart review.
- The longitudinal presence of carotid plaque and intima-media thickness (IMT) was measured at baseline and follow-up three years later.
- Relationships between LLDAS, SDI, IMT, carotid plaque, and PREDICTS profile were determined using multivariate regression analysis. T-tests were used for analysis of continuous variables and chi-squared for parametric variables.

Figures

Figure 1: Progression of SLICC Damage Index Scores

A

	SLICC Baseline (Mean)	SLICC 1 Year (Mean)	SLICC 3 Years (Mean)	SLICC 5 Years (Mean)
LLDAS ≥ 50%	1.43 (N = 127)	1.46 (N = 127)	1.61 (N = 108)	1.95 (N = 101)
LLDAS < 50%	1.53 (N = 121)	1.86 (N = 120)	2.18 (N = 105)	2.59 (N = 102)
p-value	NS	0.11	0.059	0.06

B

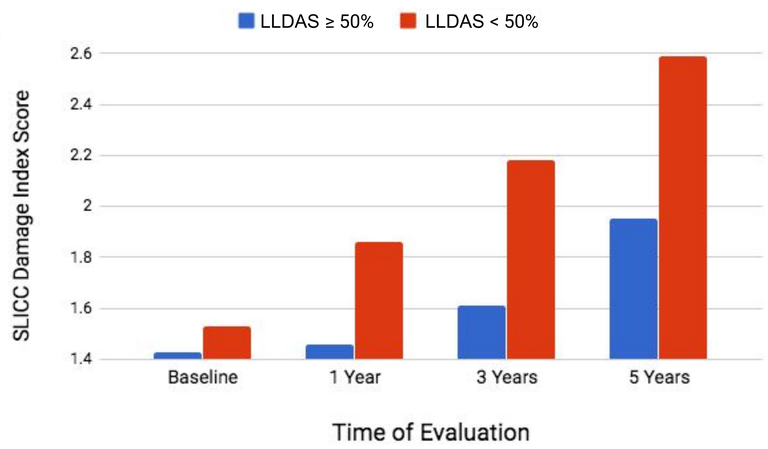

Figure 1: Longitudinal Analysis of Correlation Between LLDAS and SLICC Damage Index Scores. Patients in LLDAS ≥ 50% of the time present with near significantly smaller increases in SLICC Damage Index Score than their non-LLDAS counterparts.

Figure 2: Effects of LLDAS on Cardiovascular Events or Death

	LLDAS ≥ 50%	LLDAS < 50%	Total
Death or CV Events	15	27	42
Total Patients	67	65	132
% Death or CV Events	22.4%	41.5%	31.8%

* χ^2 = 0.018
* CV = cardiovascular (defined as major stroke, myocardial infarction, positive stress test, angioplasty or percutaneous coronary intervention)

Figure 2: Correlation Between LLDAS and Cardiovascular Event or Death. Patients in LLDAS ≥ 50% of the time suffer from significantly fewer cardiovascular events or deaths than their non-LLDAS counterparts.

Results

- Patients in LLDAS-50 or higher during the year after cohort entry had a mean SDI score of 1.5 (± 1.8) at 1 year, a mean SDI of 1.6 (± 1.9) at 3 years, and 1.9 (± 2.1) at 5 years after cohort entry.
- On average, patients who were in LLDAS-50 during the first year after cohort entry had lower SDI scores at 3 years than patients who were not, reaching near significance (p = 0.059). Similar results were found with patients who were in LLDAS-50 at 5 years, who had a near significantly lower mean SDI score than those who were not in LLDAS-50 at 5 years (p = 0.06).
- The average age was 42.8 years for patients in LLDAS-50 and 39.5 years for those not in LLDAS-50 (p = 0.048).
- There was no significant difference in measured IMT or plaque between patients in LLDAS-50 and those not in LLDAS-50 at either baseline or 3-year follow-up.
- Patients in LLDAS-50 were significantly less likely to have major cardiac events (defined as major stroke, myocardial infarction, positive stress test, angioplasty or percutaneous coronary intervention) or death compared with patients who were not in LLDAS-50, 22.4% and 41.5%, respectively (p = 0.018).

Conclusion

- We assessed SLE patients in LLDAS in our cohort of 245 patients.
- With regard to damage progression, there was near significantly less damage among those in LLDAS-50.
- Interestingly, there is no difference between IMT, presence of plaque, or plaque progression at any of the three time points.
- Nonetheless, there was a statistically significant difference in number of deaths or any cardiovascular events in favor of a lower percentage for those in LLDAS-50.

References and Acknowledgements

1. *Franklyn, Kate, et al. "Definition and initial validation of a lupus low disease activity state (LLDAS)." Annals of the rheumatic diseases 75.9 (2016): 1615-1621.*
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