Cohort of Early Systemic Lupus Erythematosus to Inform the Development of New Classification Criteria. *Arthritis & rheumatology (Hoboken, NJ)* 2019;**71**(1):91–98.
4. Tedeschi SK, Johnson SR, Boumpas D, *et al*. Developing and Refining New Candidate Criteria for Systemic Lupus Erythematosus Classification: An International Collaboration. *Arthritis care & research* 2018;**70**(4):571–81.

02 WE NEED A DIFFERENT APPROACH: A MOLECULAR CLASSIFICATION FOR CONNECTIVE TISSUE DISEASES

[1,2]Marta E Alarcón-Riquelme. [1]*Center for Genomics and Oncological Research, Granada, Spain*; [2]*Institute for Environmental Medicine, Karolinska Institute, Stockholm, Sweden*

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Systemic lupus erythematosus (SLE) is a heterogeneous disease with unpredictable patterns of activity measured using mostly SLE disease activity index (SLEDAI). However, patients with similar SLEDAI scores have different molecular abnormalities and prognosis. We reported the longitudinal stratification of SLE into three clusters based on correlation between gene expression and SLEDAI.[1] Each of the clusters showed differences in the molecular pathways involved, the clinical manifestations, and how cell populations evolved with activity. In two clusters, the SLEDAI increase was linked to neutrophil increases, while in the third it was linked to increased lymphocyte counts. The neutrophil-driven clusters showed increased risk to develop proliferative nephritis. This presentation will show how the stratification was estimated and its clinical utility.

For drug analysis we used two cohorts from previous work[1] selecting gene expression data of one visit/patient with active SLE (SLEDAI>5). We compared patient gene signatures with drug derived gene signatures from the CLUE database, giving a connectivity score. The magnitude of the score reflects the potential efficacy of the drug.

Patient stratification based on drug connectivity scores revealed the same cluster structure previously described,[1] implying that differential treatment depends on the cluster to which patients belong. Drugs commonly used in SLE showed different connectivity values for each cluster and this depend on the cell-specific expression of the drug targets, suggesting that expression of target genes may provide insight in the prioritization of compounds. New drugs were also found.

We next constructed a model to classify patients to inform on drug use and predict nephritis applied to three new longitudinal cohorts. A meta-analysis showed a significantly higher incidence of nephritis in patients classified to a neutrophil-driven cluster.

Learning objectives

- Describe the possibility of stratifying patients with lupus using molecular transcriptome data
- Discuss how stratification of lupus can be of clinical use and help identify and prioritize new drugs
- Describe the most recent results on disease stratification
- Explain how unsupervised clustering integrating transcriptome and methylome data can be used to stratify SLE and other systemic autoimmune diseases

REFERENCE

1. Toro-Dominguez D, Martorell-Marugan J, Goldman D, *et al*. Stratification of Systemic Lupus Erythematosus Patients Into Three Groups of Disease Activity Progression According to Longitudinal Gene Expression. *Arthritis & Rheumatology (Hoboken, NJ)* 2018;**70**(12):2025–35.

Plenary I: Lupus Manifestations and Comorbidities: How Have Our Strategies Improved?

01 CARDIOVASCULAR OUTCOMES AND SLE IN 2019

Murray Urowitz. *University of Toronto, Canada*

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The prevalence of atherosclerotic vascular events (AVE) in a systemic lupus erythematosus (SLE) inception cohort in published literature is 10%.[1] However this represents only clinically diagnosed events and gives no indication of the predisposition to such events. Furthermore there has been no study of changing prevalence of AVE over the past decades to the present.

In this presentation the past prevalence AVE in the University of Toronto Lupus Cohort (UTLC) and the SLICC inception cohort will be described.[2] It will then review the approaches for detecting subclinical atherosclerotic changes in SLE patients, which are the possible precursors to clinical events.[3] Then the occurrence of AVE in patients with SLE prior to their diagnosis or in the first 2 years after their SLE diagnosis will be presented.[4 5]

Studies of incidence AVE in the systemic lupus international collaborating clinics (SLICC) cohort are dramatically lower than previously reported. However this cohort includes only inception cohorts seen in the current millennium. The UTLC was then studied for inception patients seen in two eras 1975–1987 and 1999–2011 and then followed for 6 years thus mirroring the SLICC cohort. Similar to the SLICC results the late UTLC revealed a four-fold decrease in AVE compared to its earlier cohort. This will be shown to be due in large part to the more effect management of the classic cardiovascular risk factors in the modern era. This offers significant hope for reducing the impact of this co-morbidity in patients with SLE.

Learning objectives

- Describe the extent of clinical, subclinical and preclinical AVE in patients with SLE.
- Discuss the magnitude of the improvement in the incidence of AVE in patients with SLE in the modern era
- Explain the importance of effectively managing the classic cardiovascular risk factors in patients with SLE to minimize the occurrence of AVE

REFERENCES

1. Sheane BJ.,Urowitz MB, Gladman DD, Atherosclerosis in Systemic Lupus Erythematosus – Epidemiology, Risk Factors, Subclinical Assessment and Future Study. Rheumatology: Current Research 2013;s5(01).
2. Urowitz MB, Su J Gladman DD. Atherosclerotic Vascular Events in Systemic Lupus Erythematosus: An Evolving Story. *The Journal of Rheumatology* 2019, jrheum.180986.
3. Tselios K, Sheane BJ, Gladman DD, Urowitz MB Optimal Monitoring For Coronary Heart Disease Risk in Patients with Systemic Lupus Erythematosus: A Systematic Review. *The Journal of Rheumatology* 2016;**43**(1):54–65.
4. Urowitz MB, Gladman DD, Anderson NM, *et al*. Cardiovascular events prior to or early after diagnosis of systemic lupus erythematosus in the systemic lupus international collaborating clinics cohort. *Lupus Sci Med* 2016;**3**(1):e000143.
5. Tselios K, Gladman DD, Su J, *et al*. Evolution of Risk Factors for Atherosclerotic Cardiovascular Events in Systemic Lupus Erythematosus: A Longterm Prospective Study. *The Journal of Rheumatology* 2017;**44**(12):1841–49.