NON-INVASIVE SURVEILLANCE OF THE PRESENCE OF LUPUS NEPHRITIS AND ITS RESPONSE TO THERAPY USING THE RAIL URINE BIOMARKERS IN THE GLADEL COHORT

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Background

Effective, non-invasive surveillance for the presence and course of active kidney inflammation (or lupus nephritis, LN) of patients with systemic lupus erythematosus (SLE), remains a clinical challenge. Kidney biopsies are recommended for SLE patients with otherwise unexplained new proteinuria of >0.5 gram and are also considered for LN patients with persistent proteinuria to discriminate LN activity from LN damage. The Renal Activity Index for Lupus (RAIL) measures the degree of kidney inflammation. The RAIL-score is calculated from the creatinine-adjusted RAIL biomarkers (NGAL, KIM-1, MCP-1, adiponectin, hemopexin, ceruloplasmin) and higher scores indicate higher kidney inflammation.

Objectives

The objectives of this study were
1) evaluate the role of RAIL to screen for the presence of active LN in patients with and without proteinuria;
2) evaluate the role of RAIL in predicting inactive LN over time.

Methods

152 SLE adult patients (pts) were enrolled and studied longitudinally at enrollment into the GLADEL cohort (T0), at 6 months (T1) and 12 months (T2). Absolute and changes in RAIL-scores over time were measured using LUMINEX multiplex technology. Active LN was defined as a renal SLE Disease Activity (renal-SLEDAI) score of ≥4 by statistical (GEE, logistic) models, adjusted for: age at diagnosis, sex, and diagnosis of LN and renal-SLEDAI score at T0. Model accuracy was assessed by area under the ROC curve (AUC).

Results

A total of 403 visits from SLE pts (86% female, 32/33/47/40 pts w/o LN history, with inactive, active and incidental LN) were included in the study with pts characteristics and disease courses shown in Table 1. Irrespective of proteinuria or a prior diagnosis of LN, higher RAIL-scores (X2 = 5.9 – 6.79; p = 0.016- 0.021) increases of RAIL scores between T0-T1 visit (X2 = 3.86 – 3.93; p = 0.039-0.050) significantly predict active LN at T2. RAIL scores alone had 72% (95% CI, 0.61 ~ 0.84) accuracy to predict the absence of LN 12 months later; in adjusted models the RAIL-scores had over 88% (0.82, 0.95) AUC to anticipate the course of LN (Figure 1). Subgroup analyses in patients with known LN, RAIL-score and lack of RAIL increase between T0-T1 predicted presence of inactive LN 12 months later (T2) with 68% (0.53, 0.82) AUC, and adjusted model had AUC of 76.5% (0.63, 0.90).

Conclusion

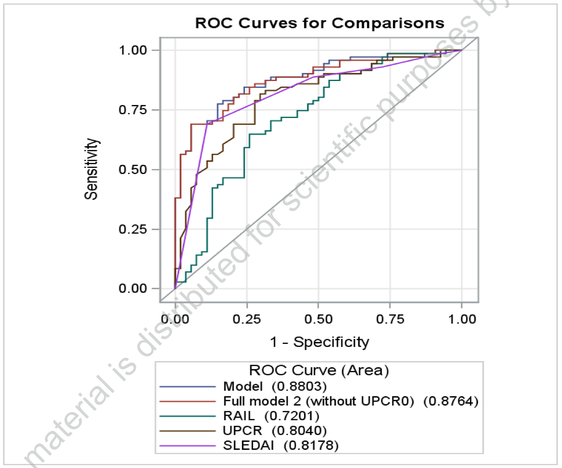
RAIL scores over time anticipate the presence of inactive LN 12 months later in the GLADEL cohort. This supports that the RAIL could be useful for the surveillance of later onset LN and predicting the achievement of inactive LN.

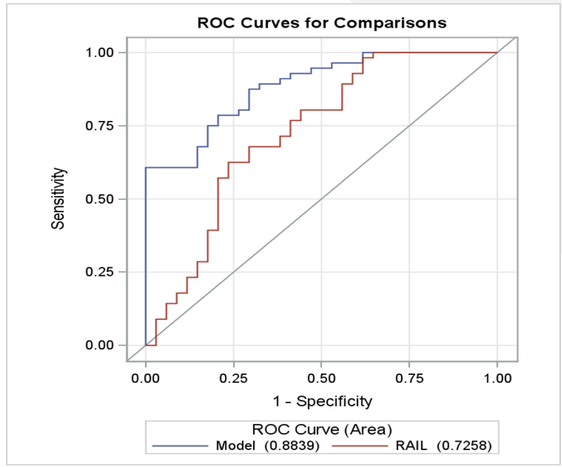
TABLE 1.
Patient characteristics & RAIL-scores over time*

VARIABLE	T0 (n=152)	T1 (n=137)	T2 (n=114)
Demographics			
Sex – female, n (%)	139 (91.4)		
Age diagnosis in years	26 (21, 35.5)		
Age at enrollment in years	35 (25, 44)		
Age at first kidney biopsy in years	28 (22, 37)		
Kidney involvement			
Renal SLEDAI score	4 (0, 8)	0 (0, 4)	0 (0, 4)
Proteinuria > 0.5 gram/day, n (%)	56 (36)	81 (59)	70 (61)
Hematuria > 5 cells/ HPF, n (%)	37 (24)	18 (13)	14 (12)
Pyuria > 5 cells/ HPF, n (%)	27 (18)	14 (10)	6 (5.3)
Cellular casts, n (%)	21 (14)	6 (4)	4 (3.5)
Renal SLEDAI = 0 , n (%)	37 (54)	51 (88)	55 (93)
SDI Renal Value	4 (0, 8)	0 (0, 4)	0 (0, 4)
Urine protein:creatinine ratio	0.78 (0.19, 2.6)	0.34 (0.12, 1.01)	0.3 (0.1, 0.8)
Kidney biopsy performed, n (%)	107 (70.4)	4 (2.9)	-
Class I or II	6 (3.9)	-	-
Class III or IV	84 (55)	3 (2.2)	-
Class V	16 (11)	1 (0.7)	-
Class VI	1 (0.7)	-	-
RAIL score	**3.74 (2.72, 4.88)**	**3.47 (2.47, 4.12)**	**3.46 (2.43, 4.62)**

*Values are medians (Q1, Q3) unless stated otherwise; % values reflect the subset of patients with available results

FIGURE 1.
Predictive Performance of RAIL Scores and Clinical Variables for 12-Month Lupus Nephritis Outcomes





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