The Journal of Rheumatology 2021;48:222–7
doi:10.3899/jrheum.191094
First Release November 15 2020

The Journal of Rheumatology

Risk of Renal Failure Within 10 or 20 Years of Systemic Lupus Erythematosus Diagnosis

Michelle Petri[1], Erik Barr[2], and Laurence S. Magder[2]

ABSTRACT. ***Objective.*** The frequency of endstage renal disease (ESRD) from systemic lupus erythematosus (SLE) in the United States has not improved over the last few decades in large population datasets. Understanding the risk factors for renal failure in SLE could lead to earlier detection of lupus nephritis and potentially more effective treatments in those with markers of poor prognosis.

Methods. The Hopkins Lupus Cohort, comprising 2528 patients was used. One hundred fifty-one patients experienced renal failure after SLE diagnosis, defined as dialysis or renal transplant. We estimated the risk of renal failure in subgroups defined by demographics, laboratory tests, and the American College of Rheumatology/Systemic Lupus International Collaborating Clinics (ACR/SLICC) classification criteria satisfied within 1 year of SLE diagnosis.

Results. The overall incidence of renal failure within 20 years of SLE diagnosis was 8.4%. The risk was much higher (20.0%) among those who experienced proteinuria within the first year of diagnosis. Demographic predictors included African American ethnicity [rate ratio (RR) 1.82, $P = 0.0012$] and age ≥ 40 years at SLE diagnosis (RR 0.51 vs those with diagnosis at < 30 yrs of age, $P = 0.019$). Among immunologic markers, low C3 was a strong predictor of renal failure (RR 2.00, $P = 0.0011$).

Conclusion. Proteinuria within the first year of diagnosis of SLE is one of the most important predictors of ESRD. Our data also confirm African American ethnicity, younger age at SLE diagnosis, and low C3 as strong predictors of renal failure.

Key Indexing Terms: cohort studies, kidney failure, lupus nephritis, risk assessment, systemic lupus erythematosus

Models to estimate the risk of endstage renal disease (ESRD) after diagnosis of chronic kidney disease stages 3 to 5 have been developed for the general population[1], but comparable studies have not been performed for patients with systemic lupus erythematosus (SLE). ESRD remains a major challenge in SLE management. Large population datasets have shown no improvement in SLE renal outcomes over the last few decades[2,3]. Groups particularly at risk include African Americans and, to a lesser extent, Hispanic Americans[4]. Patient-specific factors matter as well. Our group previously showed that predictors of poor renal outcomes included nonadherence with clinic visits and uncontrolled hypertension[5].

Advances in the treatment of lupus nephritis (LN) have not yet translated into improvement in long-term renal outcomes. Clinical trials have shown the equivalence (and, in non-Whites, the superiority) of mycophenolate mofetil (MMF) over oral or intravenous cyclophosphamide[6,7] and the superiority[8] or equivalence[9] of MMF over azathioprine. However, on average, only 50% of patients with LN have a complete renal response to MMF at 1 year. The recent phase 1 results of the US National Institutes of Health (NIH) Foundation Amplified Medicines Partnership suggest that nonresponders may have activated other renal pathways (such as interferon-α and fibrotic pathways) that are important[10].

Several demographic and immunologic factors have been shown to predict ESRD in those already diagnosed with LN. The most important demographic factor is ethnicity, with worse outcomes in non-Whites. LN among non-White patients was a predictor of renal failure in the Netherlands[11,12]. African Americans with LN had poorer renal outcomes in the NIH cohort[13]. Both African Americans and Hispanic Americans with LN had worse outcomes in a study in Miami[14]. African American ethnicity increases mortality after LN diagnosis[15].

The important prognostic role of immunologic markers in LN (e.g., better prognosis with early normalization of low complement during treatment) has been identified in both cohort studies and analyses of randomized clinical trials (RCT) of LN[16]. In these studies, low complement, particularly C3, appeared to be an important marker of renal outcomes[13,17,18,19,20]. However, not all lupus nephritis is associated with low complement.

Most previous studies have examined outcomes only after the

The Hopkins Lupus Cohort was funded by grants NIH AR043727 and NIH AR069572.

[1]M. Petri, MD, MPH, Division of Rheumatology, Johns Hopkins University School of Medicine; [2]E. Barr, MPH, L.S. Magder, MPH, PhD, Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, Maryland, USA.

Address correspondence to Dr. M. Petri, Division of Rheumatology, Johns Hopkins University School of Medicine, 1830 E. Monument Street, Suite 7500, Baltimore, MD 21205, USA. Email: mpetri@jhmi.edu.

Accepted for publication April 7, 2020.

onset or identification of LN. Past studies have examined predictors of renal outcomes at 5 years[21] or 10 years[11] but not beyond. This is the first cohort study of predictors of ESRD in an SLE population with both White and African American ethnicity followed for almost 13 years on average, in which detailed information on clinical and immunologic predictors are available since the time of SLE diagnosis. In addition, we have developed a formula to estimate the risk of renal failure within 10 and 20 years of SLE diagnosis.

MATERIALS AND METHODS

Patients. The Hopkins Lupus Cohort is an ongoing longitudinal cohort of patients with SLE presenting from the community and counties surrounding Johns Hopkins University School of Medicine and which was begun in 1986. Patients who met classification criteria for SLE [either the revised American College of Rheumatology (ACR) criteria[22,23] or Systemic Lupus International Collaborating Clinics (SLICC) classification criteria[24]] are enrolled. All patients give written, informed consent. The study has been approved on a yearly basis by the Johns Hopkins University School of Medicine Institutional Review Board (Study number NA_00039294).

At enrollment into the cohort, a detailed patient history of SLE is collected based on patient report and medical records. Subsequently, patients are seen quarterly (or more often if medically necessary). At each visit, disease activity indices [including the physician global assessment as part of the Lupus Activity Index[25] and the Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) revision of the SLE Disease Activity Index[26]] are completed by 1 rheumatologist (MP). Laboratory tests were performed at the Johns Hopkins Clinical Laboratories as well, to complete the indices (complete blood count, serum creatinine, urinalysis, urine protein /creatinine, C3, C4, anti-dsDNA by Crithidia). Renal failure was defined as the need for dialysis or renal transplant.

This analysis is based on the Hopkins Lupus Cohort database as of August 2019. At that time, there were 2577 patients in the cohort who had follow-up since SLE diagnosis. Of these, 13 were excluded because they reported renal failure before the date of SLE diagnosis, and 30 were excluded because the date of renal failure was equivalent to the date of SLE diagnosis. Another 6 were removed due to unknown date of renal failure. The analysis was based on the remaining 2528 patients who were followed for a mean of 12.8 years. Baseline information on patients who were diagnosed with SLE before cohort entry was obtained from the review of all medical record data from onset of SLE. The patient characteristics are shown in Table 1.

Statistical analyses. The survival analyses were based on the time from SLE diagnosis until the end of follow-up or renal failure/transplant for patients in our cohort. For patients diagnosed with SLE before entering our cohort, the date of diagnosis and clinical manifestations at the time of diagnosis were based on the comprehensive review of all medical records and patient history collected at cohort entry.

We estimated the risk of experiencing renal failure over time among all patients and within subgroups of patients using the Kaplan-Meier approach. Cox regression models were used to estimate the joint association between multiple patient characteristics and renal failure. These models were built in a stepwise fashion, including as candidates those variables found significantly associated in univariate models and excluding those which were no longer statistically significant ($P > 0.05$) after adjustment for other variables.

Table 1. Characteristics of patients included in the analysis.

	N (%)
Sex	
Female	2334 (92)
Male	194 (8)
Ethnicity	
White	1335 (53)
African American	992 (39)
Other	201 (8)
Age at diagnosis, yrs	
18–29	1285 (51)
30–39	613 (24)
40–49	378 (15)
50–59	180 (7)
60+	72 (3)
Year of diagnosis	
< 1985	294 (12)
1985–1994	640 (25)
1995–2004	964 (38)
2005+	630 (25)
Follow-up time since diagnosis, yrs	
0–5	638 (25)
5–10	536 (21)
10–15	445 (18)
15–20	349 (14)
> 20	560 (22)
Years of education	
< High school	216 (9)
High school	583 (24)
Some college	670 (28)
College graduate	949 (39)
Family annual income, in 2019 US$	
< 50,000	852 (38)
50,000–99,000	686 (30)
≥ 100,000	726 (32)
SLE manifestations at the time of diagnosis	
Malar rash	867 (35)
Discoid rash	310 (12)
Photosensitivity	931 (37)
Oral ulcers	759 (30)
Musculoskeletal	1259 (51)
Neurologic	113 (4)
Serositis	573 (23)
Hematologic	911 (36)
Proteinuria	468 (19)
Immunologic	1098 (43)
Alopecia	717 (29)
Immunologic markers, ever positive	
Anti-dsDNA	1563 (62)
Low C3	1380 (55)
Low C4	1201 (48)
Anti-Sm	531 (22)
Anticardiolipin	1158 (47)
Lupus anticoagulant	639 (26)
Coombs in the absence of hemolytic anemia	300 (14)

SLE: systemic lupus erythematosus.

RESULTS

A total of 151 patients developed renal failure after the diagnosis of SLE. Figure 1 shows the estimated cumulative incidence of renal failure in our cohort. The risk of renal failure was estimated to be 2.7% (95% CI 2.1–3.5%) within 5 years, 4.8% (95% CI 4.0–5.9%) within 10 years, and 8.4% (95% CI 7.0–10.0%) within 20 years of SLE diagnosis.

The 10- and 20-year risk of renal failure, by patient subgroup,

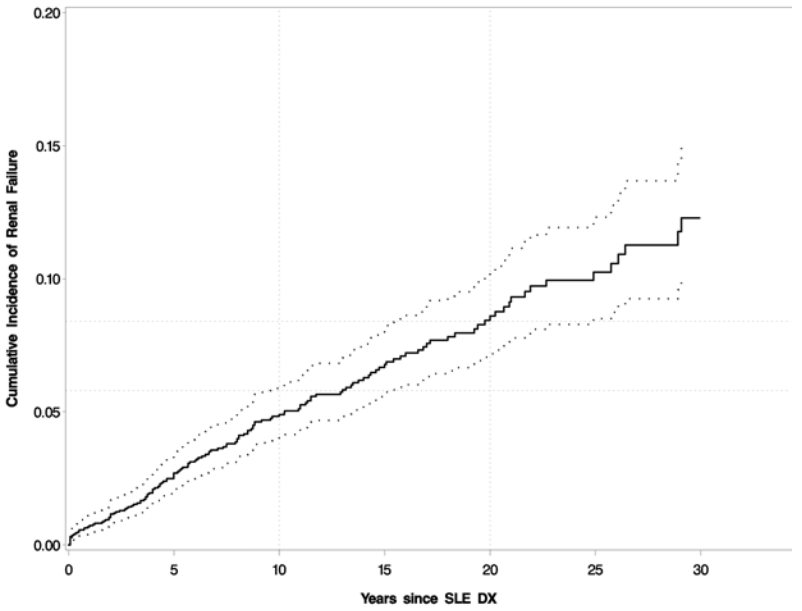

Figure 1. Incidence of renal failure by time since diagnosis based on Kaplan-Meier estimation. The dotted lines constitute 95% CI for the incidence at each timepoint. DX: diagnosis; SLE: systemic lupus erythematosus.

is shown in Table 2. In univariate subgroup analyses, we found a statistically significant elevated risk of renal failure among those who were diagnosed with SLE at a younger age, in African Americans, and those with lower education (high school and below). There was no statistically significant change in risk based on calendar time of diagnosis. Those with proteinuria at the time of SLE diagnosis were at the highest risk. The 10- and 20-year risks of renal failure in patient subgroups defined by the presence of immunologic markers are shown in Table 3. Patients who had low complement, anti-dsDNA, anti-Sm, or lupus anticoagulant (LAC; positive dilute Russell viper venom test) at any time during their disease course were at higher risk of renal failure.

We used multiple Cox regression to derive a formula for risk prediction based on multiple variables. The higher risk of renal failure among African Americans persisted after adjustment for socioeconomic status (as measured by education and income). Education was no longer statistically significantly associated with renal failure after adjustment for race and ethnicity. Although income < US$50,000 was still a statistically significant predictor of higher risk after adjustment for other variables, we did not include it in the final risk formula because (1) it was missing for 10% of the observations, and (2) we chose to confine the risk model to biologic variables. The final multiple regression model is shown in Table 4. Demographic factors that remained in this final model were male sex [rate ratio (RR) 1.69, $P = 0.062$], age ≥ 40 years at SLE diagnosis (RR 0.51 compared to those with age of diagnosis < 30 yrs, $P = 0.019$), and African American ethnicity (RR 1.82, $P = 0.0012$). Those with proteinuria at the time of SLE diagnosis were at significantly increased risk (RR 2.75, $P < 0.0001$). Low C3 was the immunologic marker with the strongest association with renal failure (RR 2.00, $P = 0.0011$). The other immunologic markers were not statistically significantly associated with renal failure after adjustment for low C3. The model had good discrimination (c-statistic = 0.75) and good calibration (Figure 2).

The RR in Table 4 can be used to calculate the 20-year risk for a patient with any risk factor profile using the formula:

$$\text{Risk} = 1 - 0.971^{RR}$$

where RR is the RR for that patient relative to a female who was diagnosed with SLE before the age of 30 and who had none of the other risk factors. For example, for a male diagnosed with SLE before the age of 30 with proteinuria in the first year after diagnosis, and no other risk factors, the hazard would be increased by a factor of 1.69 (because the patient is male) and by a factor of 2.75 (because of the proteinuria). Thus, the overall RR for such a patient would be (1.69 * 2.75), which equals 4.65. The 20-year risk is therefore estimated to equal $1 - 0.971^{(4.65)}$, which computes to 12.8%. The 10-year risk can be calculated in the same way after substituting 0.984 for 0.971 in the above formula. Using this approach, we estimated that for females with all other risk factors (low age at diagnosis, African American, proteinuria, low complement, and lupus anticoagulant), the 10-year risk was equal to 21% (95% CI 13–28%) and the 20-year risk was estimated to be 35% (95% CI 23–45%).

DISCUSSION

Based on our cohort, among those without renal failure at the time of SLE diagnosis, the risk of renal failure 5, 10, and 20 years after SLE diagnosis was estimated to be 2.7%, 4.8%, and 8.4%, respectively. Note that this did not include 1.7% of the patients who had renal failure before or at the time of SLE diagnosis, so the percentage of SLE patients with renal failure within 10 or 20 years of SLE diagnosis is somewhat higher than our estimates of

Table 2. 10-year and 20-year risk of renal failure in patient subgroups.

	Estimated Percent Risk of Developing Renal Failure Within 10 Years (95% CI)	Within 20 Years (95% CI)	P[a]
All	4.8 (4.0–5.9)	8.4 (7.0–10.0)	
Sex			0.075
Female	4.4 (3.6–5.5)	8.3 (6.9–10.0)	
Male	9.9 (5.9–16.4)	9.9 (5.9–16.4)	
Age of SLE diagnosis, yrs			0.0007
< 30	6.6 (5.2–8.3)	11.0 (8.9–13.5)	
30–39	3.4 (2.1–5.5)	6.4 (4.2–9.5)	
40+	2.0 (1.1–3.7)	4.1 (2.3–7.2)	
Ethnicity			0.0006
White	3.4 (2.5–4.7)	6.1 (4.6–8.2)	
African American	6.8 (5.3–8.9)	11.6 (9.2–14.6)	
Other	4.0 (1.8–8.7)	7.4 (3.3–16.0)	
Year of diagnosis			0.29
< 1985	4.2 (2.4–7.2)	10.3 (7.2–14.7)	
1985–1994	5.4 (3.8–7.7)	8.3 (6.1–11.2)	
1995–2004	4.7 (3.4–6.5)	6.7 (4.8–9.3)	
2004–2015	4.3 (2.5–7.7)	14.3 (6.5–30.2)	
Years of education			0.031
< High school	5.2 (2.7–9.9)	10.9 (6.4–18.4)	
High school	5.9 (4.1–8.5)	10.4 (7.5–14.2)	
Some college	4.6 (3.1–6.9)	8.3 (4.9–11.6)	
College graduate	3.4 (2.3–5.0)	6.2 (4.3–8.9)	
Family annual income (in 2019 US$)			< 0.0001
< 50,000	6.1 (4.6–8.2)	11.7 (9.1–15.0)	
50,000–99,000	3.4 (2.1–5.4)	5.3 (3.5–8.0)	
≥ 100,000	3.0 (1.9–4.8)	5.6 (3.7–8.6)	
SLE manifestations at the time of SLE diagnosis			
Malar rash			0.84
No	4.7 (3.6–6.0)	8.2 (6.1–11.0)	
Yes	4.9 (3.5–6.8)	8.5 (6.8–10.7)	
Discoid rash			0.37
No	4.9 (4.0–6.0)	9.1 (7.5–11.0)	
Yes	4.1 (2.2–7.5)	4.1 (2.2–7.5)	
Photosensitivity			0.0042
No	5.9 (4.7–7.4)	10.3 (8.4–12.7)	
Yes	3.0 (2.0–4.6)	5.6 (3.9–8.0)	
Oral ulcers			0.062
No	5.3 (4.2–5.7)	9.0 (7.3–11.0)	
Yes	3.8 (2.5–5.8)	6.8 (4.6–10.0)	
Musculoskeletal			0.15
No	5.6 (4.3–7.3)	9.4 (7.4–12.0)	
Yes	4.3 (3.1–5.7)	7.3 (5.6–9.5)	
Neurologic			0.13
No	4.8 (3.9–5.8)	8.3 (6.9–9.9)	
Yes	6.2 (2.8–13.3)	12.3 (6.2–2.3)	
Serositis			0.25
No	4.8 (3.8–6.0)	8.7 (7.2–10.6)	
Yes	5.0 (3.3–7.6)	7.3 (4.8–11.1)	
Hematologic			0.90
No	4.8 (3.8–6.1)	8.3 (6.7–10.3)	
Yes	4.9 (3.4–6.9)	8.8 (6.4–12.0)	
Proteinuria			< 0.0001
No	3.3 (2.5–4.3)	5.6 (4.4–7.2)	
Yes	10.8 (8.0–14.6)	20.0 (15.4–25.9)	
Immunologic			0.12
No	5.4 (4.2–6.8)	9.2 (7.4–11.4)	
Yes	4.1 (2.9–5.7)	7.2 (5.2–9.9)	
Alopecia			0.83
No	5.2 (4.2–6.6)	8.4 (6.8–10.3)	
Yes	3.8 (0.2–5.9)	8.4 (5.9–12.0)	

[a] The log-rank test assesses the evidence against the hypothesis that the survival curves are equivalent across the entire range of time. SLE: systemic lupus erythematosus.

incidence after diagnosis. Our 5-year risk estimates are consistent with those of Plantinga, *et al* who reported 5-year risks of 2.5% and 6.4% in White and Black patients, respectively, in Atlanta, Georgia[27]. Our findings are also consistent with the incidence rates reported in Taiwan (2.5% in 6 years)[28], and somewhat below those reported in Okinawa (9.4% in 10 years)[29]. The risk of renal failure did not decline over calendar time.

There are 3 major findings. First, while the 20-year risk of renal failure was 8.4% for the overall cohort, for a patient with a history of proteinuria at the time of SLE diagnosis, the risk of renal failure within 20 years was 20%. This large difference in outcome, not previously appreciated, can allow consideration of more aggressive therapies in this subgroup. Examples include multitarget therapy with MMF and tacrolimus[30], newer calcineurin inhibitors[31], experimental sequential regimens such as rituximab followed by belimumab[32] on a background of MMF, and newer anti-CD20 biologics (ClinicalTrials.gov: NCT02550652).

Second, confirming previous studies, certain demographic factors, including male sex, African American ethnicity, and SLE diagnosis before age 40 years were statistically significant predictors of renal failure. The higher risk among African Americans persisted after adjustment for socioeconomic status as measured by education, although it is possible that socioeconomic status may not be on par with educational attainment in certain ethnic minorities. There was no difference in risk between SLE diagnosis at < 30 years and 30–39 years after adjustment for other predictors.

Third, consistent with the findings of other investigators[13], we found that the immunologic marker that was the strongest predictor of renal failure was low C3. Low C4 and anti-dsDNA (which are highly correlated with low C3) were not statistically significant predictors of renal failure after adjustment for low C3 (although they were significantly associated in univariate analyses).

To our knowledge, this is the first 30-year cohort study to assess demographic, clinical, and immunologic predictors of later renal failure in SLE. It is the largest study to include a balance of White and African American patients, and the only one to have complete data on risk factors (due to the protocolized nature of follow-up).

Table 3. 10- and 20-year risk of renal failure in patient subgroups defined by immunologic markers[a].

Immunologic Marker Ever Present During Study Follow-up	Estimated Percent Risk of Renal Failure Within 10 Years of SLE Diagnosis (95% CI)	Estimated Percent Risk of Renal Failure Within 20 years of SLE Diagnosis (95% CI)	P^b
Anti-dsDNA			0.0002
No	2.7 (1.7–4.2)	5.2 (3.3–7.9)	
Yes	6.0 (4.8–7.4)	10.0 (8.3–12.2)	
Low C3			< 0.0001
No	1.9 (1.1–3.1)	4.7 (9.2–13.4)	
Yes	7.0 (5.7–8.7)	11.1 (9.2–13.4)	
Low C4			0.0015
No	2.9 (2.1–4.2)	6.0 (4.3–8.3)	
Yes	6.7 (5.3–8.4)	10.8 (8.7–13.2)	
Anti-Sm			0.037
No	4.4 (3.4–5.6)	8.0 (6.5–9.9)	
Yes	6.6 (4.6–9.4)	10.1 (7.2–14.2)	
Anticardiolipins			0.29
No	5.2 (3.9–6.8)	8.6 (6.6–11.1)	
Yes	4.5 (3.3–6.0)	8.2 (6.3–10.5)	
Positive dRVVT			0.0089
No	4.5 (3.5–5.7)	6.6 (5.2–8.3)	
Yes	5.5 (3.9–7.9)	12.7 (9.5–16.7)	
Coombs in absence of hemolytic anemia			0.32
No	4.7 (3.8–6.0)	8.0 (6.5–9.8)	
Yes	6.0 (3.6–10.0)	10.5 (6.5–16.8)	

[a] Subgroups defined based on whether a patient ever tested positive for the markers. [b] The log-rank test assesses the evidence against the hypothesis that the survival curves are equivalent across the entire range of time. dRVVT: dilute Russell viper venom test; SLE: systemic lupus erythematosus.

Table 4. Predictors of renal failure based on a multivariable Cox proportional hazards model[a].

	Rate Ratio (95% CI)	*P*
Male (vs female)	1.69 (0.97–2.93)	0.062
History of proteinuria at SLE diagnosis	2.75 (1.94–3.89)	< 0.0001
Age of SLE Diagnosis, yrs		
30–39 (vs < 30)	0.82 (0.53–1.27)	0.37
40+ (vs < 30)	0.51 (0.29–0.90)	0.019
Ethnicity		
African American (vs White)	1.82 (1.27–2.60)	0.0012
Other (vs White)	1.07 (0.52–2.19)	0.86
Low C3 ever (vs never)	2.00 (1.32–3.03)	0.0011
Positive dRVVT test ever (vs never)	1.44 (1.01–2.04)	0.043

[a] The multivariable model was based on only 2351 patients due to missing values for some included variables. dRVVT: dilute Russell viper venom test; SLE: systemic lupus erythematosus.

Our study has several limitations. As this is a single-center study of patients who agreed to participate in the research cohort, drawing inferences about general SLE patients should be done with caution. Like most survival analyses, our estimates are based on the assumption that at any given timepoint, the risk of ESRD among those censored before that timepoint is similar to the risk among those observed at that specific timpoint. To the extent that this assumption is violated, our estimates would be biased. Because we did not have complete information on all deaths in the cohort, we could not account for the competing risk of death in our analysis, resulting in a slight overestimation of the 10- and 20-year cumulative risk. Our multivariable model could also have been biased due to missing covariate information, or unmeasured or residual confounding. Our analyses for immunological markers were based on whether they were ever manifested during cohort follow-up rather than at SLE diagnosis, which could limit their utility for renal outcome prediction early in the disease course. A final limitation is that, even in this large cohort, the number of events was limited to 151, limiting the power to identify subtle associations and the precision of our estimates.

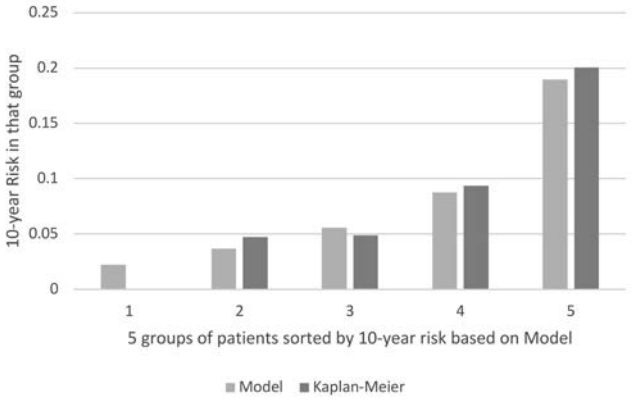

Figure 2. Calibration plots for the estimation of the 20-year risk of endstage renal disease with the Cox models. Dark bars indicate the average 10-year risk in each group based on the model. Gray bars indicate the Kaplan-Meier estimates of the 10-year risk in each group.

We think these predictors of renal failure in SLE will be immediately useful in clinical practice to identify patients who might benefit from more aggressive treatment. In particular, those with LN in the first year after diagnosis have a greatly increased risk of later renal failure that would justify more aggressive induction therapy. These predictors will also be important in either stratifications for RCT or for adjustment in outcome analyses.

REFERENCES

1. Tangri N, Stevens LA, Griffith J, Tighiouart H, Djurdjev O, Naimark D, et al. A predictive model for progression of chronic kidney disease to kidney failure. JAMA 2011;305:1553-9.
2. Costenbader KH, Desai A, Alarcón GS, Hiraki LT, Shaykevich T, Brookhart MA, et al. Trends in the incidence, demographics, and outcomes of end-stage renal disease due to lupus nephritis in the US from 1995 to 2006. Arthritis Rheum 2011;63:1681-8.
3. Tektonidou MG, Dasgupta A, Ward MM. Risk of end-stage renal disease in patients with lupus nephritis, 1971-2015: a systematic review and Bayesian meta-analysis. Arthritis Rheumatol 2016;68:1432-41.
4. Ward MM. Changes in the incidence of endstage renal disease due to lupus nephritis in the United States, 1996-2004. J Rheumatol 2009;36:63-7.

5. Petri M, Perez-Gutthann S, Spence D, Hochberg MC. Risk factors for coronary artery disease in patients with systemic lupus erythematosus. Am J Med 1992;93:513-9.
6. Ginzler EM, Dooley MA, Aranow C, Kim MY, Buyon J, Merrill JT, et al. Mycophenolate mofetil or intravenous cyclophosphamide for lupus nephritis. N Engl J Med 2005;353:2219-28.
7. Chan TM, Li FK, Tang CS, Wong RW, Fang GX, Ji YL, et al. Efficacy of mycophenolate mofetil in patients with diffuse proliferative lupus nephritis. Hong Kong-Guangzhou Nephrology Study Group. N Engl J Med 2000;343:1156-62.
8. Dooley MA, Jayne D, Ginzler EM, Isenberg D, Olsen NJ, Wofsy D, et al. Mycophenolate versus azathioprine as maintenance therapy for lupus nephritis. N Engl J Med 2011;365:1886-95.
9. Tamirou F, D'Cruz D, Sangle S, Remy P, Vasconcelos C, Fiehn C, et al. Long-term follow-up of the MAINTAIN Nephritis Trial, comparing azathioprine and mycophenolate mofetil as maintenance therapy of lupus nephritis. Ann Rheum Dis 2016;75:526-31.
10. Der E, Suryawanshi H, Morozov P, Kustagi M, Goilav B, Ranabathou S, et al. Tubular cell and keratinocyte single-cell transcriptomics applied to lupus nephritis reveal type I IFN and fibrosis relevant pathways. Nat Immunol 2019;20:915-27.
11. Rijnink EC, Teng YKO, Wilhelmus S, Almekinders M, Wolterbeek R, Cransberg K, et al. Clinical and histopathologic characteristics associated with renal outcomes in lupus nephritis. Clin J Am Soc Nephrol 2017;12:734-43.
12. Korbet SM, Schwartz MM, Evans J, Lewis EJ; Collaborative Study Group. Severe lupus nephritis: racial differences in presentation and outcome. J Am Soc Nephrol 2007;18:244-54.
13. Austin HA, Boumpas DT, Vaughan EM, Balow JE. Predicting renal outcomes in severe lupus nephritis: contributions of clinical and histologic data. Kidney Int 1994;45:544-50.
14. Contreras G, Lenz O, Pardo V, Borja E, Cely C, Iqbal K, et al. Outcomes in African Americans and Hispanics with lupus nephritis. Kidney Int 2006;69:1846-51.
15. Nee R, Martinez-Osorio J, Yuan CM, Little DJ, Watson MA, Agodoa L, et al. Survival disparity of African American versus non-African American patients with ESRD due to SLE. Am J Kidney Dis 2015;66:630-7.
16. Dall'Era M, Cisternas MG, Smilek DE, Straub L, Houssiau FA, Cervera R, et al. Predictors of long-term renal outcome in lupus nephritis trials: lessons learned from the Euro-Lupus Nephritis cohort. Arthritis Rheumatol 2015;67:1305-13.
17. Esdaile JM, Levinton C, Federgreen W, Hayslett JP, Kashgarian M. The clinical and renal biopsy predictors of long-term outcome in lupus nephritis: a study of 87 patients and review of the literature. Q J Med 1989;72:779-833.
18. Esdaile JM, Abrahamowicz M, MacKenzie T, Hayslett JP, Kashgarian M. The time-dependence of long-term prediction in lupus nephritis. Arthritis Rheum 1994;37:359-68.
19. Austin HA 3rd, Boumpas DT, Vaughan EM, Balow JE. High-risk features of lupus nephritis: importance of race and clinical and histological factors in 166 patients. Nephrol Dial Transplant 1995;10:1620-8.
20. Cortes-Hernandez J, Ordi-Ros J, Labrador M, Segarra A, Tovar JL, Balada E, et al. Predictors of poor renal outcome in patients with lupus nephritis treated with combined pulses of cyclophosphamide and methylprednisolone. Lupus 2003;12:287-96.
21. Hanly JG, Su L, Urowitz MB, Romero-Diaz J, Gordon C, Bae SC, et al. A longitudinal analysis of outcomes of lupus nephritis in an international inception cohort using a multistate model approach. Arthritis Rheumatol 2016;68:1932-44.
22. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271-7.
23. Hochberg MC. Updating the American College of Rheumatology Revised criteria for the classification of Systemic Lupus Erythematosus. Arthritis Rheum 1997;40:1725.
24. Petri M, Orbai AM, Alarcón GS, Gordon C, Merrill JT, Fortin PR, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum 2012;64:2677-86.
25. Petri M, Hellmann D, Hochberg M. Validity and reliability of lupus activity measures in the routine clinic setting. J Rheumatol 1992;19:53-9.
26. Petri M, Kim MY, Kalunian KC, Grossman J, Hahn BH, Sammaritano LR, et al. Combined oral contraceptives in women with systemic lupus erythematosus. N Engl J Med 2005;353:2550-8.
27. Plantinga L, Lim SS, Patzer R, McClellan W, Kramer M, Klein M, et al. Incidence of end-stage renal disease among newly diagnosed systemic lupus erythematosus patients: the Georgia Lupus Registry. Arthritis Care Res 2016;68:357-65.
28. Lin WH, Guo CY, Wang WM, Yang DC, Kuo TH, Liu MF, et al. Incidence of progression from newly diagnosed systemic lupus erythematosus to end stage renal disease and all-cause mortality: a nationwide cohort study in Taiwan. Int J Rheum Dis 2013;16:747-53.
29. Iseki K, Miyasato F, Oura T, Uehara H, Nishime K, Fukiyama K. An epidemiologic analysis of end-stage lupus nephritis. Am J Kidney Dis 1994;23:547-54.
30. Liu Z, Zhang H, Liu Z, Xing C, Fu P, Ni Z, et al. Multitarget therapy for induction treatment of lupus nephritis: a randomized trial. Ann Intern Med 2015;162:18-26.
31. Rovin BH, Solomons N, Pendergraft WF 3rd, Dooley MA, Tumlin J, Romero-Diaz J, et al. A randomized, controlled double-blind study comparing the efficacy and safety of dose-ranging voclosporin with placebo in achieving remission in patients with active lupus nephritis. Kidney Int 2019;95:219-31.
32. Kraaij T, Kamerling SWA, de Rooij ENM, van Daele PLA, Bredewold OW, Bakker JA, et al. The NET-effect of combining rituximab with belimumab in severe systemic lupus erythematosus. J Autoimmun 2018;91:45-54.