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LETTER TO THE EDITOR

Cardiovascular risk assessment in lupus nephritis and ANCA-associated vasculitis in real-world nephrology practice

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Observational studies have found that anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis is associated with increased risks of stroke (sub-distribution hazard ratio 1.49 [95% confidence interval (CI) 1.10–2.02] [1], cardiovascular (CV) events [relative risk (RR) 1.65 (95% CI 1.23-2.22)] and ischemic heart disease [RR 1.60 (95% CI 1.39-1.84)] [2], while systemic lupus erythemathosus had greater odds of atherosclerotic CV disease [adjusted odds ratio (OR) 1.46 (95% CI 1.41-1.51)] [3]. Similarly, lupus nephritis and ANCA-associated vasculitis increased the risks of CV-related hospitalization and death among multiethnic Southeast Asians with glomerulonephritis [4]. It is thus timely that the European League Against Rheumatism (EULAR) multidisciplinary task force published recommendations for CV risk prediction and management in lupus and vasculitis, highlighting the need for clinicians to be aware of the increased CV risk and screen for risk factors within 6 months of diagnosis [5].

It is even more imperative that nephrologists caring for patients with kidney involvement, i.e. lupus nephritis and renal vasculitis, proactively screen and manage CV risks; even among the general population with early chronic kidney disease, pooled estimates of hazard ratios for CV disease and mortality ranged from 1.5 to 4.9 compared with normal renal function [6]. Thus 146 adults with lupus nephritis and ANCA-associated vasculitis were identified from our single-center electronic medical records review [4] to evaluate the prevalence of CV risk assessment during routine nephrology clinical practice. Traditional CV risk factors such as comorbidity, blood pressure, kidney function and proteinuria were readily available for all patients. Table 1 shows that CV risk factors such as hypertension and kidney disease were prevalent {42.5% had an estimated glomerular filtration rate <60 mL/min/1.73 m², median urine protein: creatinine ratio 3.2 g/g [interquartile range (IQR) 1.6-5.9]}. Within 6 months after diagnosis, fasting glucose, hemoglobin A1c and fasting lipid were assessed in 89.7%, 30.1% and 67.1%, respectively. The majority (96.6%) received prednisolone at moderatehigh doses [peak dose 50 mg/day (IQR 30-60)], while reninangiotensin system blockers and lipid-lowering medications (mainly statins) were prescribed to 87.0% and 51.4%, respectively. During the follow-up of 37.9 months (IQR 26.8-60.9), 10 patients (6.8%) had hospitalization for CV events (acute myocardial infarction, congestive cardiac failure or cardiac catheterization showing >50% coronary artery stenosis) at 8.1 months (IQR 0.8-32.5) after diagnosis. Hence, more can be done to screen and optimize CV risk in patients with lupus nephritis and vasculitis during routine nephrology practice.

Since atherosclerosis may be driven by endothelial dysfunction in active inflammation, the EULAR guidelines emphasized the benefits of disease remission and low activity to reduce CV risk in lupus and vasculitis [5]. However, remission induction therapy with immunosuppressants such as steroids can exacerbate CV risks such as hyperglycemia, hypertension, obesity and hyperlipidemia [7, 8], thereby propelling interest in steroidsparing and steroid-minimization strategies in recent trials and novel therapies [9, 10]. Further research will be required to as-

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Table 1. CV risk assessment among biopsy-proven lupus nephritis and ANCA-associated vasculitis

Characteristics	All, n = 146
Comorbid conditions	
Age at diagnosis (years)	42.6 (32.8–52.6)
Male, n (%)	32 (21.9)
Diabetes, n (%)	12 (8.2)
Hypertension, n (%)	77 (52.7)
Systolic blood pressure (mmHg)	130 (120–140)
Diastolic blood pressure (mmHg)	76 (70–80)
Hyperlipidemia, n (%)	26 (17.8)
Ischemic heart disease, n (%)	4 (2.7)
Laboratory tests performed	
Hemoglobin A1c, n (%)	
^a Before diagnosis	58 (39.7)
^c After diagnosis	44 (30.1)
Fasting glucose, n (%)	
^a Before diagnosis	118 (80.8)
^c After diagnosis	131 (89.7)
Fasting lipids, n (%)	
^b Before diagnosis	118 (80.8)
^c After diagnosis	98 (67.1)

IQRs are the 25th-75th percentile.

^aPerformed within 6 months before diagnosis.

^bPerformed within 24 months before diagnosis.

 $^{\rm c}{\rm Performed}$ within 6 months after diagnosis.

sess the CV benefits of such strategies in lupus nephritis and vasculitis.

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The study was conducted according to the guidelines of the Declaration of Helsinki and was approved by the SingHealth Institutional Review Board (2015/2882).

CONFLICT OF INTEREST STATEMENT

J.C. has served on steering committees/advisory boards for Novartis, GlaxoSmithKline, Boehringer Ingelheim, Bayer, AstraZeneca and Pfizer. The results presented in this article have not been published previously in whole or part.

REFERENCES

- Massicotte-Azamiouch D, Petrcich W, Walsh M et al. Association of anti-neutrophil cytoplasmic antibody-associated vasculitis and cardiovascular events: a population-based cohort study. Clin Kidney J 2021; https://doi.org/10.1093/ckj/ sfab229
- Houben E, Penne EL, Voskuyl AE et al. Cardiovascular events in anti-neutrophil cytoplasmic antibody-associated vasculitis: a meta-analysis of observational studies. *Rheumatology* (Oxford) 2018; 57: 555–562
- 3. Katz G, Smilowitz NR, Blazer A *et al.* Systemic lupus erythematosus and increased prevalence of atherosclerotic cardiovascular disease in hospitalized patients. *Mayo Clin Proc* 2019; **94**: 1436–1443
- Lim CC, Choo JC, Tan HZ et al. Changes in metabolic parameters and adverse kidney and cardiovascular events during glomerulonephritis and renal vasculitis treatment in patients with and without diabetes mellitus. Kidney Res Clin Pract 2021; 40: 250–262
- Drosos GC, Vedder D, Houben E et al. EULAR recommendations for cardiovascular risk management in rheumatic and musculoskeletal diseases, including systemic lupus erythematosus and antiphospholipid syndrome. Ann Rheum Dis 2022; doi: 10.1136/annrheumdis-2021-221733
- Matsushita K, van der Velde M, Astor BC et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet 2010; 375: 2073–2081
- Rice JB, White AG, Scarpati LM et al. Long-term systemic corticosteroid exposure: a systematic literature review. Clin Ther 2017; 39: 2216–2229
- 8. Lim CC, Gardner D, Ng RZ *et al*. Synergistic impact of prediabetes and immunosuppressants on the risk of diabetes mellitus during treatment of glomerulonephritis and renal vasculitis. *Kidney Res Clin Pract* 2020; **39**: 172
- 9. Oon S, Huq M, Godfrey T et al. Systematic review, and metaanalysis of steroid-sparing effect, of biologic agents in randomized, placebo-controlled phase 3 trials for systemic lupus erythematosus. *Semin Arthritis Rheu* 2018; **48**: 221–239
- Walsh M, Merkel PA, Peh C-A et al. Plasma exchange and glucocorticoids in severe ANCA-associated vasculitis. N Engl J Med 2020; 382: 622–631