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Drs. Kim and Hong reply

To the Editor:

We thank Dr. Zhuo et al[1] for the insightful comments on our article.[2] First, the constitutional symptoms of systemic lupus erythematosus (SLE) are often very complex and difficult to quantify. Because constitutional symptoms are prevalent in patients with SLE, many previous studies have tried to quantify constitutional symptoms, but a clear association with disease activity has been questioned.[3] Fever is one of the constitutional symptoms that we can easily evaluate objectively, unlike other constitutional symptoms such as fatigue, poor mental performance, loss of appetite, and myalgia. For that reason, we mentioned only fever in the constitutional domain section, as with the current SLE diagnostic criteria.[4] Further, a number of other constitutional symptoms, such as myalgia and general weakness, are covered in addition to fever in Table 3,[2] which lists the specific symptoms of each patient who experienced SLE flares in detail. In addition, it is reasonable to point out that HIV, hepatitis virus, organ transplantation, and other factors should be investigated as factors that may influence the disease course. Among the patients included in our study, there were no patients with HIV, hepatitis, organ transplantation, or pregnancy. In terms of malignancy, 4 out of 121 patients (3.3%) had a history of malignancy; 2 had cervical cancer, one had breast cancer, and one had thyroid cancer. All these patients underwent surgery or had complete remission at the start of dialysis.

Second, as Zhuo et al pointed out,[1] the cumulative dose of glucocorticoids (GC) increased significantly over 1 year in the hemodialysis group. We assume that the GC dose increased during the bridging period when the immunosuppressant was discontinued after dialysis was started. Upon the initiation of dialysis, the previously used immunosuppressants were discontinued in many cases because of the reduced SLE activity and risk of infection.[5] For that reason, an increase in steroid dose was observed in some cases. Further studies with larger sample sizes are needed to know the medication use including GCs in patients with chronic kidney disease, particularly before and after the initiation of dialysis.

Third, as our research covered a relatively long time period, there may be some differences in the clinical characteristics, including SLE flares, according to the time period and the advances in SLE management. In this subanalysis, we found that the time from lupus nephritis (LN) onset to endstage renal disease (ESRD) increased as time passed ($P = 0.03$; Table). This suggests that advancing LN treatment could delay the development of ESRD, although the number of patients in each period was not sufficient to draw a conclusion. These results are similar to those of a prior study that included a large number of patients with SLE.[6] However, there were no significant differences in dialysis modality or in the rate of SLE flares across the different time periods.

Finally, Cox proportional regression was used to investigate risk factors associated with SLE flares in the study. Because SLE flares were observed at a median of 17.0 (IQR 8.0-36.0) months after the initiation of dialysis, patients experienced SLE flares at various timepoints after the initiation of dialysis.[2] For a more intuitive and accurate understanding of this issue, we provide

Table. Clinical characteristics of patients with SLE under dialysis over time.

	1995-2000		2000-2010		2010-2020		*P* (Trend Over Time)
	PD	HD	PD	HD	PD	HD	
Patients	2 (40)	3 (60)	11 (28)	27 (71)	12 (15)	66 (84)	0.90
Age, yrs, median (IQR)	37 (32-42)	44 (42-52)	35 (30-37)	34 (31-49)	36 (30-48)	43 (31-53)	0.31
Female sex	2 (100)	3 (100)	9	20	18	51	0.48
BMI, kg/m^2, mean (SD)	17.5 (1.6)	19.3 (1.2)	21.9 (4.7)	20.9 (2.9)	22.0 (3.6)	21.9 (3.8)	0.10
SLE disease duration, months	20 (11-29)	4.8 (4-5.56)	88 (60-101)	72 (40-110)	95 (3-123)	113 (34-188)	**0.01**
Disease duration, LN onset to ESRD, months	19 (10-27)	4.8 (4-5.5)	88 (60-100)	63 (22-98)	70 (2-100)	89 (27-160)	**0.03**
Patients with disease flare during additional follow-up	2 (100)	0 (0)	4 (36)	7 (25)	6 (50)	16 (24)	0.72
Medications[a]							
Hydroxychloroquine	0 (0)	0 (0)	1 (9)	3 (11)	2 (16)	17 (25)	0.63
Corticosteroids	2 (100)	2 (66)	4 (36)	19 (70)	3 (25)	49 (74)	0.12
Mycophenolate mofetil	0 (0)	0 (0)	2 (18)	5 (18)	2 (16)	19 (28)	0.13
Tacrolimus	0 (0)	0 (0)	0 (0)	1 (3)	2 (16)	21 (31)	0.76
Cyclophosphamide	1 (50)	1 (33)	2 (18)	5 (18)	1 (8)	12 (18)	0.22
Azathioprine	1 (50)	0 (0)	1 (9)	3 (11)	0 (0)	4 (6)	0.98
Rituximab	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	3 (4)	0.68

Values are expressed as n (%) unless indicated otherwise. Values in bold are statistically significant. [a] Medications taken 1 year prior to the initiation of dialysis. ESRD: endstage renal disease; HD: hemodialysis; LN: lupus nephritis; PD: peritoneal dialysis; SLE: systemic lupus erythematosus.

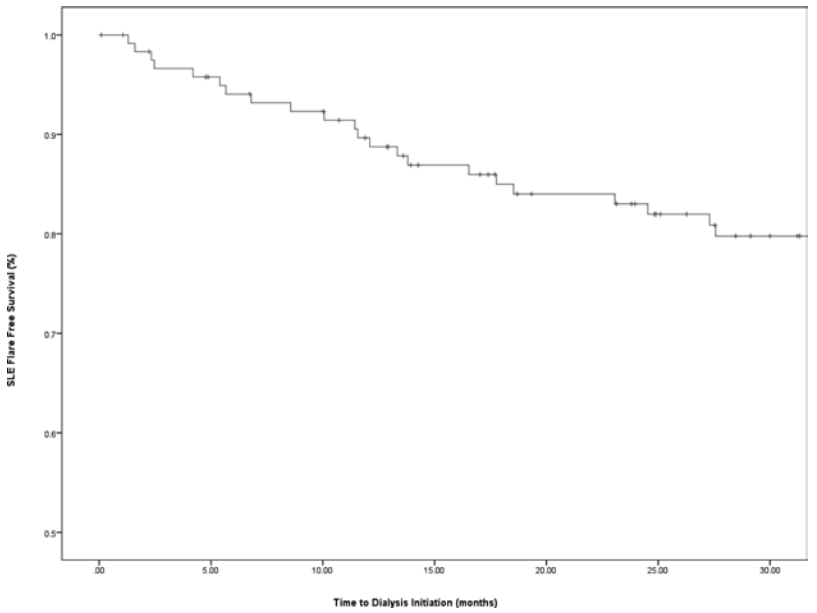

Figure. Kaplan-Meier analysis for time from dialysis initiation to SLE flare. SLE: systemic lupus erythematosus.

a figure generated using Kaplan-Meier analysis (Figure). Thus, it would be more appropriate to use the Cox regression model considering the various time intervals from the start of dialysis to SLE flare onset.

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The authors declare no conflicts of interest relevant to this article.

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