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**Comparison of Renal Outcomes after induction treatment between Segmental and Global Subclasses of Class IV Lupus Nephritis; CMC GN registry**

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**Objectives:** Renal involvement in systemic lupus erythematosus is highly variable, as reflected by the broad spectrum of histologic abnormalities found at renal biopsy. International Society of Nephrology and Renal Pathology Society (ISN/RPS) subdivided diffuse proliferative lupus nephritis (LN class IV) into the segmental (IV-S) and the global (IV-G) subclasses. However, whether renal outcomes differ between IV-S and IV-G is unclear. Here, we compared the renal outcomes between IV-S and IV-G subclasses of diffuse proliferative lupus nephritis.

**Methods:** All adult patients with a renal biopsy-confirmed diagnosis of LN class IV in the Nephrology and Rheumatology Division between April 2015 and November 2020 were enrolled. Biopsies were classified according to ISN/RPS 2003 classification and were examined by light microscopy and direct immunofluorescence. Induction treatment was performed in all the enrolled patients. Renal outcomes were estimated by treatment responses classified as complete remission, partial remission and treatment failure after induction treatment. Median follow-up period after induction treatment was 6 months.

**Results:** This multicenter retrospective study included 51 patients with LN class IV (14 and 37 patients were diagnosed as IV-S subclass and IV-G subclasses, respectively). The renal function of patients with IV-G subclasses at baseline were significantly decreased compared to those with IV-S subclass (IV-G  $112.6 \pm 40.1$  vs IV-S  $73.3 \pm 40.0$ ,  $p=0.003$ ). Induction treatment was performed in IV-S and IV-G patients (MMF induction: 85.7% vs 67.6%, respectively, CYC induction: 14.3% vs 16.2 %, respectively,  $p = 0.431$ ). There was no difference of treatment response after induction treatment between IV-S and IV-G subclasses ( $p = 0.265$ ).

**Conclusions:** There are definite clinical differences in renal function at baseline between class IV-S and IV-G lesions. However, our data showed no significant difference in treatment response between Subclasses IV-S and IV-G. Long-term follow-up analysis may needed to the determine the clinical significance of Subclasses IV-S and IV-G.

Comparison of clinical data between lupus nephritis patients with subclass IV-S and IV-G

Table 1 Comparison of clinical data between lupus nephritis patients with subclass IV-S and IV-G

Patient characteristics	IV-S (n=14)	IV-G (N=37)	p value
Age (years; mean±SD)	31.7 ± 10.8	42.1±11.9	0.006
Female n (%)	12 (85.7)	34 (91.9)	0.421
BMI (kg/m <sup>2</sup> )	22.4 ± 3.7	24.1 ± 5.4	0.294
Creatinine baseline (mg/dL; mean±SD)	0.7 ± 0.3	1.1 ± 0.6	0.003
MDRD baseline (ml/min/1.73m <sup>2</sup> ; mean±SD)	112.6 ± 40.1	73.3 ± 40.0	0.003
MDRD at 6-month (ml/min/1.73m <sup>2</sup> ; mean±SD)	112.8 ± 16.3	81.1 ± 38.7	0.001
Albumin (mg/dL; mean±SD)	2.8 ± 0.7	2.8 ± 0.6	0.862
Urine protein-creatinine ratio baseline (g/g; median-IQR)	4.0 (1.3-6.7)	2.4 (1.3-5.7)	0.342
Urine protein-creatinine ratio at 6-month (g/g; median-IQR)	0.9 (0.2-1.1)	0.4 (0.1-1.3)	0.513
Anti-dsDNA (IU/mL; median-IQR)	100.0 (32.6-410.2)	100.0 (39.7-346.7)	0.960
C3 (mg/dL; mean±SD)	48.1 ± 19.1	50.3 ± 27.5	0.787
C4 (mg/dL; median-IQR)	9.2 (3.5-15.8)	6.4 (3.1-13.9)	0.729

MDRD: Modification of Diet in Renal Disease Study; C3: complement component 3; C4: complement component 4; SD: standard deviation; IQR: interquartile range.

Comparison of treatment data between lupus nephritis patients with subclass IV-S and IV-G

Table 2 Comparison of treatment data between lupus nephritis patients with subclass IV-S and IV-G

	IV-S (n=14)	IV-G (N=37)
Induction		
CYC	2 (14.3%)	6 (16.2%)
MMF	12 (85.7%)	25 (67.6%)
Steroid only	0 (0.0%)	4 (10.8%)
Missed	0 (0.0%)	2 (5.4%)
Response to treatment		
Complete remission	4 (28.6%)	18 (48.6%)
Partial remission	8 (57.1%)	12 (32.4%)
Treatment failure	2 (14.3%)	7 (18.9%)

CYC: cyclophosphamide pulses; MMF: mycophenolate mofetil

No significant differences between the groups.