

Supplemental materials

Supplementary Table 1: Change in immunosuppressive therapy in the different periods of the study.

Supplementary Table 2: Clinical findings at one year in the 25 patients lost to follow-up and in the 178 who were followed until the end of the study.

Supplementary Table 3: Comparison of correlations with clinical features at renal biopsy of old definitions of “neutrophil infiltration” and “fibrinoid necrosis karyorrhexis”, and the new definitions suggested by the recent revision of histological classification of LN “neutrophil infiltration/karyorrhexis” and “fibrinoid necrosis”.

Supplementary Table 4: Histological predictors of KFI among histological features at renal biopsy in 108 patients with class IV Lupus Nephritis. Univariate and multivariate analysis.

Supplementary Table 1. Change in immunosuppressive therapy in the different periods of the study.

Year of LN diagnosis	N. of patients	Methylpr pulses	CYC	AZA	MMF	CsA	RTX	MTX
Induction immunosuppressive therapy								
1984-2001	94	77.6%	55%	16%	1%	1%	0	2%
2002-2019	109	88%	43%	3.7%	38.5%	2.7%	5.5%	1%
Maintenance immunosuppressive therapy								
1984-2001	94			22%	1%	5.3%		
2002-2019	109			15.6%	64%	4.6%		

Legend: N., number; LN, lupus nephritis; Methylpr., methylprednisolone; CYC, cyclophosphamide; AZA, azathioprine; MMF, mycophenolate mofetil; CsA, cyclosporine A; RTX, rituximab; MTX, methotrexate.

Supplementary Table 2. Clinical findings at one year in the 25 patients lost to follow-up and in the 178 who were followed until the end of the study.

If not otherwise specified, data are expressed as median and interquartile ranges.

	Lost to follow-up	Not lost to follow-up	P
N. of pts (%)	25 (12.3%)	178 (87.7%)	
Serum creatinine, mg/dl	0.8 (0.6-1)	0.7 (0.3-1.1)	0.3
Proteinuria g/24H	0.6 (0-1.2)	0.3 (0-3.4)	0.4
Creatinine Clearance, ml/min	93.5 (58.5-128.5)	90.2 (30.2-120.2)	0.7
C3 g/L	88 (60-116)	83 (75-91)	0.8
C4 g/L	15 (9-21)	11 (3-19)	0.4
Arterial hypertension N. of pts (%)	9 (36%)	93 (54%)	0.08
No response N. of pts (%)	1 (4%)	23 (13%)	0.19

Legend: N., number; pts, patients.

Supplementary Table 3: Comparison of correlations with clinical features at renal biopsy of old definitions of “neutrophil infiltration” and “fibrinoid necrosis karyorrhexis”, and the new definitions suggested by the recent revision of histological classification of LN “neutrophil infiltration/karyorrhexis” and “fibrinoid necrosis”.

	Neutrophils Infiltration		P	Neutrophils. Infiltration/ karyorrhexis		P	Fibrinoid necrosis/ karyorrhexis		P	Fibrinoid necrosis		P
	0	>0 (75.4%)		0	>0 (74.9%)		≤1	>1 (35%)		≤1	>1 (22.2%)	
Serum creatinine, mg/dl	1 (±1.1)	1.3 (±1)	NS	1 (±0.5)	1.4 (±1)	NS	1.2 (±1)	1.3 (±1)	NS	1.5 (±1.1)	1.2 (±0.9)	0.05
Proteinuria, g/24h	3.3 (±2.5)	4.2 (±3.5)	Ns	3.3 (±2.5)	4.3 (±3.5)	0.029	4.3 (±3.7)	3.5 (±2.3)	Ns	4.3 (±3.6)	3.1 (±1.6)	Ns
Urinary eryth. number/HPF	10.6 (±25)	28.4 (±30)	<0.001	10.6 (±25)	28.5 (±30)	<0.001	20.2 (±28)	31 (±32)	<0.001	22.4 (±28)	30.3 (±34)	Ns
Serum albumin, mg/dl	3.1 (±0.8)	2.9 (±0.7)	Ns	3.1 (±0.8)	2.9 (±0.7)	Ns	2.9 (±0.8)	3 (±0.7)	Ns	2.9 (±0.7)	3.1 (±0.7)	Ns
C3, mg/dl	77.4 (±27)	56.3 (±23)	<0.001	76.9 (±30)	56.4 (±23)	<0.001	65.3 (±28)	54.9 (±21)	0.005	62.1 (±28)	60 ±20)	0.023
C4, mg/dl	16.9 (±12)	10.8 (±8.8)	0.004	16.7 (±12)	10.8 (±8.8)	0.005	14 (±11)	9.4 (±8)	<0.001	13.1 (±11)	9.7 (±7.5)	Ns
Hematocrit, %	36.7 (±5.8)	32.4 (±5.7)	<0.001	36.7 (±5.7)	32.4 (±5.7)	<0.001	34.3 (±6.2)	32.1 (±5.3)	0.001	33.1 (±6.1)	33 (±5.6)	Ns
Class III, n° (%)	4 (8)	41 (26.8)	<0.001	5 (9.8)	40 (26.3)	<0.001	27 (20.4)	18 (25.4)	<0.001	33 (20.9)	12 (26.7)	<0.001
Class IV, n° (%)	6 (12)	102 (66.7)		6 (11.8)	102 (67.1)		56 (42.4)	52 (73.2)		76 (48.1)	32 (71.1)	
Class V, n° (%)	38 (76)	10 (6.5)		38 (74.5)	10 (6.6)		47 (35.6)	1 (1.4)		47 (29.7)	1 (2.2)	

Supplementary Table 4: Histological predictors of KFI among histological features at renal biopsy in 108 patients with class IV Lupus Nephritis. Univariate and multivariate analysis. Similarly, to what observed in the entire group, at multivariate analysis glomerular sclerosis, fibrous crescent and interstitial fibrosis were the independent predictor of KFI.

	Univariate analysis			Multivariate analysis		
	OR	CI	P	OR	CI	P
Activity index \$	0.922	0.817-1.042	0.195			
Endocapillary hypercellularity*	0.251	0.091-0.693	0.008			
Neutrophils infiltration*	0.180	0.053-0.616	0.006			
Hyaline deposits/wire loops*	0.855	0.569-1.284	0.453			
Cellular/fibrocellular crescent* *	2.255	0.901-5.641	0.084			
Fibrinoid necrosis/ karyorrhexis**	0.448	0.177-1.129	0.090			
Interstitial inflammation*	2.187	0.914-5.121	0.080			
Interstitial Inflamm pure >0	0.543	0.204-1.443	0.223			
Interstitial Inflamm in presence of chronic T-I lesions >0	3,785	1.715-8.353	0.001			
Neutrophils infiltration/ karyorrhexis*	0.181	0.053-0.616	0.006			
Fibrinoid necrosis* *	0.245	0.058-1.038	0.057			
Chronicity index \$	1.608	1.372-1.883	0.0000001			
Glomerular sclerosis**	4.661	1.905-11.405	0.0008	4.092	1.553-10.780	0.005
Fibrous crescents**	6.710	2.781-16.186	0.00001	4.273	1.518-12.027	0.006
Tubular atrophy**	5.038	2.915-8.708	0.00001			
Interstitial fibrosis**	2.573	1.701-3.894	0.00001	3.227	1.151-9.049	0.027
Extraglomerular deposits***	2.133	0.894-5.094	0.089			
Tubular deposits***	1.330	0.606-2.921	0.479			
Interstitial capillary wall deposits***	0.501	0.117-2.138	0.353			
Vascular deposits ***	2.150	1.143-5.198	0.022			

Legend: OR: Odd ratio, CI: confidential interval; Inflamm: inflammation, T-I: tubulo-interstitial

\$: for any unit increase in activity and in chronicity index;

*These variables were categorized as: 0 vs 1+2+3, **These variables were categorized as: 0+1 vs 2+3 being: 0 if absent; 1+ if mild (in less than 25% of glomeruli and/or in tubulointerstitial area; 2+ if moderate (in between 25% and less than 50% of glomeruli and/or in tubulointerstitial area), and , 3+ if severe (in more than 50% of glomeruli and/or in tubulointerstitial area).

*** these variables were categorized as present absent.