

WHY HAVE OUTCOMES OF LUPUS NEPHRITIS BEEN IMPROVING OVER THE LAST 40 YEARS? A MONOCENTRIC EXPERIENCE.

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BACKGROUND

Outcomes of patients with lupus nephritis (LN) have been improving due to a variety of reasons and relative contributions are difficult to assess.

METHODS

We included all patients with biopsy-proven LN followed-up at our center and analysed evolution of epidemiological, clinical, histological features and therapeutic immunosuppressive protocols over the last 4 decades.

RESULTS

We enrolled 130 patients stratified by diagnosis over the following periods: ≤ 1980 , n = 43; $>1980 \leq 1990$, n = 34; $>1990 \leq 2000$, n = 33; >2000 , n = 20. Age at diagnosis decreased from 30 to 26 years old and the interval between diagnosis of Lupus and that of LN has extended from 1 to 3 years.

The mortality rate fell from 41.8 % to 0%, paralleling decrease in complications.

The proliferative classes remained the most represented (59.2 %); the need for dialysis has been dramatically reduced (from 23% to 0%). The most significant therapeutic changes in induction therapy between the first and fourth decade were the increasing use of pulse steroid (ST) (from 0% to 65 %) and the association of cyclophosphamide (CYCLO) (from 25% to 65 %).

Cumulative load of oral drugs was sharply reduced: ST decreased from 533 to 269 mg/Kg and CYCLO from 505 to 180 mg/Kg over the first 5 years. Multivariate analysis showed that survival improvement is mainly associated with the youngest age at diagnosis and on more recent historical periods (Table I).

The renal prognosis was worse in male, age >30 years, renal failure, proliferative classes with indexes of chronicity, while it appeared to improve with induction therapy other than only oral ST and with high activity index (TAB II).

Table I. - Results of multivariate Cox proportional hazard analysis of the effects of several covariates on patient survival in all patients with SLE nephritis

COVARIATES	HR	95% CI	P
PERIOD OF DIAGNOSIS:			
<1980	1		
1980-1995	0.372	0.114-1.215	0.101
>1995	0.197	0.041-0.952	0.043
AGE AT DIAGNOSIS CONTINUOUS VARIABLE	1.048	1.017-1.079	0.002
AGE AT DIAGNOSIS:			
<20 YEARS	1		
>20<30 YEARS	2.841	0.685-11.780	0.150
>30 YEARS	4.899	1.401-17.127	0.012
SEX (M)	1.426	0.467-4.357	0.533
PROLIFERATIVE CLASSES	1.320	0.493-3.533	0.580
INDUCTION THERAPY DIFFERENT FROM STEROID ALONE	0.851	0.283-2.564	0.774

Table II. - Results of multivariate Cox proportional hazard analysis of the effects of several covariates on cumulative renal survival in overall patients with sle nephritis .

COVARIATES	HR	95% CI	P
PERIOD OF DIAGNOSIS:			
<1980	1		
1980-1995	0.397	0.093-1.696	0.2126
>1995	0.058	0.004-0.859	0.0384
AGE AT DIAGNOSIS:			
<20 YEARS	1		
>20<30 YEARS	2.037	0.598-6.936	0.255
>30 YEARS	4.086	1.336-12.499	0.013
SEX (M)	1.123	0.409-3.082	0.050
PROLIFERATIVE CLASSES	13.550	1.743-105.325	0.012
CHRONICITY INDEX CONTINUOUS VARIABLE	2.986	1.151-7.743	0.024
ACTIVITY INDEX			
≤ 4	1		
>4	0.24	0.084-0.681	0.007
SERUM CREATININE AT BIOPSY	2.233	1.009-4.942	0.047
PROTEINURIA	0.870	0.362-2.089	0.754
RENAL FLARE UP	4.238	0.887-20.447	0.072
INDUCTION THERAPY DIFFERENT FROM ORAL STEROID ALONE	0.072	0.006-0.913	0.042

CONCLUSIONS

The most important factors which determined improved outcomes of LN over the last 4 decades were a progressively earlier diagnosis (from 30-31 to 26-29 years old) and qualitative/quantitative modifications in therapeutic strategies.

Adoption of sequential schedules of aggressive induction and fast tapering of immunosuppression have been crucial to achieve better control of the acute phase and reduced toxicity long-term.

