***Supplementary Table 1*. Recommendations for lupus nephritis classification (Cited from Ingeborg M. Bajema, et al. *Kidney Int* 2018 Apr; 93(4):789-796)**

|  |  |  |
| --- | --- | --- |
| **Category** | **Recommendation** | **Comments on ISN/RPS guidelines** |
| Class II | Definition for mesangial hypercellularity adjusted: Four or more nuclei fully surrounded by matrix in the mesangial area not including the hilar region | Cutoff for mesangial hypercellularity unclear |
| Class III and IV | The term endocapillary proliferation is replaced by endocapillary hypercellularity | Definition for endocapillary proliferation unclear; the term proliferation was considered imprecise |
|  | The term crescent is used for a lesion consisting of extracapillary hypercellularity, composed of a variable mixture of cells. Fibrin and fibrous matrix may be present; 10% or more of the circumference of Bowman’s capsule should be involved. | Extracapillary proliferation involving>25% of the circumference of Bowman’s capsule was original cutoff. There were no definitions for fibrous or fibrocellular crescents. |
|  | Cellular crescent: more than 75% cells and fibrin and less than 25% fibrous matrix |  |
|  | Fibrous crescent: more than 75% fibrous matrix and less than 25% cells and fibrin |  |
|  | Fibrocellular crescent: 25%-75% cells and fibrin and the remainder fibrous matrix |  |
|  | Adhesion: an area of isolated continuity of extracellular matrix material between the tuft and capsule even when the underlying segment does not have overt sclerosis | There was no definition for an adhesion |
|  | Fibrinoid necrosis: fibrin associated with glomerular basement membrane disruption and/or lysis of the mesangial matrix; this lesion does not require the presence of karyorrhexis | There was no definition for fibrinoid necrosis |
|  | Elimination of segmental and global subdivions of class IV | Definitions for segmental and global were unclear; interobserver variability was large; clinical significance uncertain |
|  | Modification of the NIH lupus nephritis activity and chronicity scoring system (Table 2) to be used instead of the currently used A, C, and A/C parameters | Designation of activity/chronicity through A, C, and A/C considered too broad and nonspecific; preference for a semiquantitative approach to describe active and chronic lesions |
| Tubulointerstitial lesions | Indicate whether interstitial inflammation occurs in presence or absence of interstitial fibrosis | Lack of cut-off values for reporting the severity of tubulointerstitial lesions |

***Supplementary Table 2*. Proposed modified NIH lupus nephritis activity and chronicity scoring system (Cited from Ingeborg M. Bajema, et al. *Kidney Int* 2018 Apr; 93(4):789-796)**

|  |  |  |
| --- | --- | --- |
| **Modified NIH activity index** | **Definition** | **Score** |
| Endocapillary hypercellularity | Endocapillary hypercellularity in <25% (1+), 25%-50% (2+), or >50% (3+) of glomeruli | 0-3 |
| Neutrophils/karyorrhexis | Neutrophils and/or karyorrhexis in <25% (1+), 25%-50% (2+), or >50% (3+) of glomeruli | 0-3 |
| Fibrinoid necrosis | Fibrinoid necrosis in <25% (1+), 25%-50% (2+), or >50% (3+) of glomeruli | (0-3)×2 |
| Hyaline deposits | Wire loop lesions and/or hyaline thrombi in <25% (1+), 25%-50% (2+), or >50% (3+) of glomeruli | 0-3 |
| Cellular/fibrocellular crescents | Cellular and/or fibrocellular crescents in <25% (1+), 25%-50% (2+), or >50% (3+) of glomeruli | (0-3)×2 |
| Interstitial Inflammation | Interstitial leukocytes in <25% (1+), 25%-50% (2+), or >50% (3+) in the cortex | 0-3 |
| **Total** |  | **0-24** |
| **Modified NIH chronicity index** | **Definition** | **Score** |
| Total glomerulosclerosis score | Global and/or segmental sclerosis in <25% (1+), 25%-50% (2+), or >50% (3+) of glomeruli | 0-3 |
| Fibrous crescents | Fibrous crescents in <25% (1+), 25%-50% (2+), or >50% (3+) of glomeruli | 0-3 |
| Tubular atrophy | Tubular atrophy in <25% (1+), 25%-50% (2+), or >50% (3+) of the cortical tubules | 0-3 |
| Interstitial fibrosis | Interstitial fibrosis in <25% (1+), 25%-50% (2+), or >50% (3+) in the cortex | 0-3 |
| **Total** |  | **0-12** |

**Notes: NIH, National Institutes of Health.**

***Supplementary Table 3.* Distribution of the histopathologic findings**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Variable** |  | **n=101** | **Variable** | |  | **n=101** |
| **Histologic classes, n (%)** | **I**  **II**  **III (III/III+V)**  **IV (IV/IV+V)**  **V**  **VI** | **0 (0)**  **1 (1.0)**  **21 (20.8)**  **58 (57.4)**  **21 (20.8)**  **0 (0)** | **Mesangial hyper-**  **-cellularity score, median (range)** | | **0.76 (0.00-2.40)** | |
| **Global GS, n (%)** | | **Absent** | **71(70.3)** |
| **1%-24% of glomeruli** | **30(29.7)** |
| **25%-50% of glomeruli** | **0 (0)** |
| **>50% of glomeruli** | **0 (0)** |
| **Segmental GS, n (%)** | **Absent**  **1%-24% of glomeruli**  **25%-50% of glomeruli**  **>50% of glomeruli** | **77(76.2)**  **21(20.8)**  **3(3.0)**  **0 (0)** | **Adhesion, n (%)** | | **Absent**  **1%-24% of glomeruli**  **25%-50% of glomeruli**  **>50% of glomeruli** | **59(58.4)**  **41(40.6)**  **1(1.0)**  **0 (0)** |
| **Endocapillary hypercellularity, n (%)** | **Absent**  **1%-24% of glomeruli**  **25%-50% of glomeruli**  **>50% of glomeruli** | **13(12.9)**  **22(21.8)**  **14(13.9)**  **52(51.5)** | **MPGN, n (%)** | | **Absent**  **1%-24% of glomeruli**  **25%-50% of glomeruli**  **>50% of glomeruli** | **55(54.5)**  **32(31.7)**  **10(9.9)**  **4(4.0)** |
| **Fibrinoid necrosis,**  **n (%)** |  | **4(4.0)** | **Neutrophils/karyorr--hexis, n (%)** | | **Absent**  **1%-24% of glomeruli**  **25%-50% of glomeruli**  **>50% of glomeruli** | **34(33.7)**  **51(50.5)**  **14(13.7)**  **2(2.0)** |
| **Hyaline deposits, n (%)** | **Absent**  **1%-24% of glomeruli**  **25%-50% of glomeruli**  **>50% of glomeruli** | **33(32.7)**  **35(34.7)**  **29(28.7)**  **4(4.0)** | **Crescents, n (%)** | | **Absent**  **1%-24% of glomeruli**  **25%-50% of glomeruli**  **>50% of glomeruli** | **29(28.7)**  **42(41.6)**  **18(17.8)**  **12(11.9)** |
| **Interstitial fibrosis,**  **n (%)** | **<25% in the cortex**  **25%-50% in the cortex**  **>50% in the cortex** | **87(86.1)**  **10(9.9)**  **4(4.0)** | **Tubular atrophy,**  **n (%)** | **<25% of the cortical tubules 25%-50% of the cortical tubules**  **>50% of the cortical tubules** | | **82(81.2)**  **15(14.9)**  **4(4.0)** |
| **Interstitial inflammation, n (%)** | **<25% in the cortex**  **25%-50% in the cortex**  **>50% in the cortex** | **81(79.4)**  **16(15.7)**  **4(4.9)** | **Interstitial inflammation distribution, n (%)** | | **scarred areas only**  **scarred and non-scarred areas** | **30(29.7)**  **71(70.3)** |
| **Modified AI, n (%)** | **0-4**  **5-8**  **>8** | **32(31.7)**  **40(39.6)**  **29(28.7)** | **Modified CI, n (%)** | | **0-2**  **3-5**  **>5** | **45(44.6)**  **48(47.5)**  **8(7.9)** |

**Notes: GS, glomerulosclerosis; MPGN, membranoproliferative glomerulonephritis pattern; AI, activity NIH index; CI, chronicity NIH index**

***Supplementary Table 4*. Intraobserver reproducibility and interobserver reproducibility between observers of different institutes**

|  |  |  |
| --- | --- | --- |
|  | **ICC/κ-score** | |
| **Intraobserver reproducibility** | **Interobserver reproducibility of different institutes** |
| **Number of patients** | **101** | **20** |
| **Global and/or segmental GS** | **0.858** | **0.446** |
| **Endocapillary hypercellularity** | **0.980** | **0.645** |
| **Fibrinoid necrosis** | **0.990** | **0.722** |
| **Neutrophils/karyorrhexis** | **0.706** | **0.560** |
| **Hyaline deposits** | **0.916** | **0.419** |
| **Cellular+fibrocellular crescents** | **0.993** | **0.604** |
| **Fibrous crescents** | **0.608** | **0.402** |
| **Interstitial fibrosis** | **0.821** | **0.529** |
| **Tubular atrophy** | **0.821** | **0.476** |
| **Interstitial inflammation** | **0.677** | **0.476** |
| **Modified AI** | **0.958** | **0.625** |
| **Modified CI** | **0.892** | **0.400** |
| **Histologic classes** | **0.769** | **0.500** |

**Notes: GS, glomerulosclerosis; MPGN, membranoproliferative glomerulonephritis pattern; AI, activity NIH index; CI, chronicity NIH index; ICC, intraclass correlation coefficients.**

**.**

***Supplementary Table 5.* Correlations between pathologic variables**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **End1** | **End2** | **GlobGS** | **SegGS** | **Adh** | **MPGN** | **Neu** | **Hya** | **Necr** | **Extr1** | **Extr2** | **Extr3** | **Extr4** | **Extr5** | **IntFib** | **TubAt** | **Intlnfl1** | **Intlnfl2** |
| **End1** | **­—** | **0.607** |  |  |  |  | **0.404** | **0.523** |  | **0.375** | **0.396** | **0.360** |  |  |  |  |  |  |
| **End2** |  | **—** |  |  |  | **0.660** | **0.709** | **0.781** |  | **0.596** | **0.622** | **0.607** |  |  |  |  |  | **0.481** |
| **GlobGS** |  |  | **—** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **SegGS** |  |  |  | **—** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Adh** |  |  |  |  | **—** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **MPGN** |  |  |  |  |  | **—** | **0.621** | **0.577** |  | **0.565** | **0.588** | **0.594** |  |  |  |  |  | **0.414** |
| **Neu** |  |  |  |  |  |  | **—** | **0.679** |  | **0.605** | **0.664** | **0.658** |  |  |  |  |  | **0.526** |
| **Hya** |  |  |  |  |  |  |  | **—** |  | **0.567** | **0.549** | **0.528** |  |  |  |  |  | **0.409** |
| **Necr** |  |  |  |  |  |  |  |  | **—** |  |  |  |  |  |  |  |  |  |
| **Extr1** |  |  |  |  |  |  |  |  |  | **—** | **0.822** | **0.809** |  |  |  |  |  | **0.399** |
| **Extr2** |  |  |  |  |  |  |  |  |  |  | **—** | **0.989** |  |  |  |  |  | **0.560** |
| **Extr3** |  |  |  |  |  |  |  |  |  |  |  | **—** |  |  |  |  |  | **0.552** |
| **Extr4** |  |  |  |  |  |  |  |  |  |  |  |  | **—** | **0.998** |  |  |  |  |
| **Extr5** |  |  |  |  |  |  |  |  |  |  |  |  |  | **—** |  |  |  |  |
| **IntFib** |  |  |  |  |  |  |  |  |  |  |  |  |  |  | **—** | **0.848** | **0.825** |  |
| **TubAt** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | **—** | **0.971** |  |
| **Intlnfl1** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | **—** |  |
| **Intlnfl2** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | **—** |

**Notes: End, endocapillary; GlobGS, global glomerulosclerosis; SegGS, segmental glomerulosclerosis; Adh, adhesion; MPGN, membranoproliferative glomerulonephritis pattern; Neu, Neutrophils/karyorrhexis; Hya, Hyaline deposits; Necr, necrosis; Extr, extracapillary; IntFib, interstitial fibrosis; TubAt, tubular atrophy; Intlnfl, interstitial inflammation.**

**Correlations between pathology variables were carried out using the Spearman test. Statistically significant correlations were determined using the Holm-Bonferroni method to minimize the probability of making a Type 1 statistical error. Only statistically significant R values (correlation coefficients ) are shown（P<0.01）.**

***Supplementary Table 6*. Associations between pathological indices and clinical features at the time of renal biopsy**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **SLEDAI** | | **P-value** | **Scr**  **(umol/L)** | **P-value** | | **Proteinuria**  **(g/day)** | **P-value** | **C3**  **(g/L)** | **P-value** | **ds-DNA** | **P-value** |
| **Mes (≤0.76)** | **16±6** | | **0.014** | **68.1(36.8-544.3)** | **<0.001** | **3.8(0.2-12.9)** | | **0.128** | **0.47(0.15-1.53)** | **0.008** | **39.1%** | **0.057** |
| **Mes (>0.76)** | **19±6** | |  | **113.0(48.0-520.0)** |  | **4.1(0.7-14.1)** | |  | **0.38(0.14-0.73)** |  | **58.2%** |  |
| **End2 (≤50%)** | **15±6** | | **0.001** | **66.0(36.8-544.3)** | **<0.001** | | **2.7(0.2-12.9)** | **0.002** | **0.51(0.14-1.53)** | **<0.001** | **42.9%** | **0.023** |
| **End2 (>50%)** | **19±6** | | **110.0(48.0-520.0)** | **4.8(1.1-14.1)** | **0.38(0.14-1.10)** | **65.4%** |
| **No GlobGS** | **17±6** | **0.422** | | **82.0(36.8-544.3)** | **0.769** | | **4.0(0.2-14.1)** | **0.832** | **0.40(0.14-1.53)** | **0.043** | **53.5%** | **0.772** |
| **Any GlobGS** | **18±6** | **83.0(42.8-273.7)** | **3.9(0.5-12.9)** | **0.47(0.20-1.19)** | **56.7%** |
| **No SegGS** | **17±6** | **0.592** | | **81.0(36.8-544.3)** | **0.508** | | **3.9(0.2-11.8)** | **0.050** | **0.42(0.14-1.53)** | **0.555** | **53.2%** | **0.662** |
| **Any SegGS** | **18±7** | **90.3(42.8-371.0)** | **4.5(0.5-14.1)** | **0.38(0.15-1.08)** | **58.3%** |
| **No Neu** | **13±4** | | **<0.001** | **60.0(36.8-466.4)** | **<0.001** | | **3.5(0.5-11.1)** | **0.134** | **0.55(0.20-1.53)** | **<0.001** | **35.3%** | **0.006** |
| **Any Neu** | **20±6** | | **102.0(45.0-544.3)** | **4.0(0.2-14.1)** | **0.38(0.14-1.10)** | **64.2%** |
| **No Hya** | **13±5** | | **<0.001** | **63.0(36.8-544.3)** | **<0.001** | | **3.2(0.2-12.9)** | **0.117** | **0.53(0.24-1.53)** | **<0.001** | **33.3%** | **0.003** |
| **Any Hya** | **20±6** | | **93.8(45.0-520.0)** | **4.1(0.6-14.1)** | **0.38(0.14-1.10)** | **64.7%** |  |
| **Extr2** |  | |  |  |  | |  |  |  |  |  |  |
| **None (0%)** | **14±5\*†** | | **0.001** | **64.0(36.8-544.3)\*†** | **<0.001** | | **3.0(0.2-10.0)†** | **0.007** | **0.51(0.14-1.53) \*** | **0.005** | **36.7%** | **0.063** |
| **1-24%** | **18±7\*** | | **85.0(42.8-520.0) \*** | **3.9(0.5-12.9)§** | **0.35(0.15-1.19) \*** | **60.5%** |
| **≥25%** | **19±5†** | | **122.6(57.0-371.0)†** | **5.4(1.7-14.1)†§** | **0.40(0.14-1.10)** | **64.3%** |
| **No Extr4** | **17±6** | **0.411** | | **82.0(36.8-544.3)** | **0.825** | | **4.0(0.2-14.1)** | **0.986** | **0.41(0.14-1.53)** | **0.300** | **53.1%** | **0.578** |
| **Any Extr4** | **18±8** | **89.0(42.8-270.0)** | **4.3(0.5-10.3)** | **0.46(0.18-1.19)** | **60.0%** |
| **IF/TA** |  |  | |  |  | |  |  |  |  |  |  |
| **<25%** | **17±6** | **0.913** | | **77.0(36.8-544.3)\*†** | **<0.001** | | **3.9(0.2-14.1)** | **0.166** | **0.41(0.14-1.53)** | **0.373** | **54.0%** | **0.681** |
| **25-50%** | **17±6** | **150.6(68.1-466.4) \*** | **5.4(0.5-12.9)** | **0.50(0.20-1.19)** | **50.0%** |
| **>50%** | **18±7** | **214.5(114.0-270.0)†** | **7.4(1.1-7.9)** | **0.41(0.14-0.53)** | **75.0%** |
| **Intlnfl** |  |  | |  |  | |  |  |  |  |  |  |
| **0** | **16±7** | **0.158** | | **61.5(40.0-176.0)** | **<0.001** | | **3.7(0.5-10.0)** | **0.154** | **0.46(0.14-1.53)** | **0.021** | **46.7%** | **0.307** |
| **1** | **18±6** | **105.0(36.8-544.3)** | **4.0(0.2-14.1)** | **0.40(0.14-1.19)** | **57.7%** |
| **Lym** |  |  | |  |  | |  |  |  |  |  |  |
| **no aggregates** | **16±6** | **0.049** | | **70.0(36.8-544.30)** | **0.009** | | **3.9(0.2-11.0)** | **0.129** | **0.42(0.15-1.53)** | **0.358** | **56.3%** | **0.730** |
| **aggregates** | **19±6** |  | | **90.6(45.0-520.0)** |  | | **4.8(0.5-14.1)** |  | **0.40(0.14-1.19)** |  | **52.8%** |  |

**Notes: Scr, serum creatinine; Mes, mesangial hypercellularity score; End, endocapillary, GlobGS, global glomerulosclerosis; SegGS, segmental glomerulosclerosis; Neu, Neutrophils/karyorrhexis; Hya, Hyaline deposits; Extr, extracapillary; IF/TA, interstitial fibrosis and tubular atrophy; Intlnfl, interstitial inflammation, scarred only 0, scarred and non-scarred 1. Lym, lymphocyte distribution;** **no aggregates including no interstitial inflammation and diffuse lymphocytic infiltration.**

**Normally distributed variables were expressed as mean ± s.d. and compared using Student’s t-test, univariate analysis of variance, or the Bonferroni (multiple comparisons). Non-parametric variables were expressed as median(range) and compared using either Mann-Whitney, Kruskal-Wallis, or all pairwise (multiple comparisons). Categorical variables were expressed in percentages and compared using Chi-square. \*, †,§indicates *P<0.05.***

***Supplementary Table 7.* Correlations between lymphoid aggregates and composite outcomes in lupus nephritis**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Combined Event (Cox regression)** | | | | |
|  | **Univariate hazard ratio(95%CI)** | **P-value** | **Multivariate hazard ratio(95%CI)** | **P-value** |
| **Lymphoid distribution** |  | **0.012** |  | **0.044** |
| **no aggregates** | **1** |  | **1** |  |
| **aggregates** | **3.208 (1.295-7.950)** |  | **2.571 (1.024-6.455)** |  |
| **Age(years)** | **1.033 (1.005-1.062)** | **0.021** | **1.038 (1.008-1.069)** | **0.013** |
| **Gender** |  | **0.275** |  | **0.191** |
| **female** | **1** |  | **1** |  |
| **male** | **0.447 (0.105-1.897)** |  | **0.353 (0.074-1.679)** |  |
| **Scr (lg transformed)** | **2.277 (0.462-11.232)** | **0.312** | **4.981 (0.772-32.142)** | **0.091** |
| **Proteinuria (g/day)** |  | **0.506** |  | **0.176** |
| **<3.5** | **1** |  | **1** |  |
| **≥3.5** | **0.774 (0.363-1.650)** |  | **0.576 (0.259-1.281)** |  |

**Note: CI, confidence interval; no aggregates including no interstitial inflammation and diffuse lymphocytic infiltration; Scr, serum creatinine.**

***Supplementary Table 8.* Correlations between histologic class and composite outcomes in lupus nephritis**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Combined Event (Cox regression)** | | | | |
|  | **Univariate hazard ratio(95%CI)** | **P-value** | **Multivariate hazard ratio(95%CI)** | **P-value** |
| **Histologic class** |  | **0.036** |  | **0.029** |
| **II, V** | **1** | | **1** | |
| **III, IV** | **3.697 (1.088-12.560)** | | **4.318 (1.158-16.108)** | |
| **Age(years)** | **1.033 (1.005-1.062)** | **0.021** | **1.047 (1.018-1.078)** | **0.002** |
| **Gender** |  | **0.275** |  | **0.206** |
| **female** | **1** |  | **1** |  |
| **male** | **0.447 (0.105-1.897)** |  | **0.372 (0.081-1.723)** |  |
| **Scr (lg transformed)** | **2.277 (0.462-11.232)** | **0.312** | **2.418 (0.375-15.578)** | **0.353** |
| **Proteinuria (g/day)** |  | **0.506** |  | **0.205** |
| **<3.5** | **1** |  | **1** |  |
| **≥3.5** | **0.774 (0.363-1.650)** |  | **0.595 (0.266-1.329)** |  |

**Note: CI, confidence interval; Scr, serum creatinine.**