**Association of histopathological variants with outcomes in IgA Nephropathy**

**Introduction**

IgA nephropathy is the most prevalent cause of glomerular disease worldwide. The OXFORD MEST criteria gave a consensus criterion for the pathological classification of IgA nephropathy that would enable accurate prediction of disease progression and individual prognostication. The IgA Nephropathy Classification Working Group now recommends adding crescents (C) to the MEST scoring criteria. Ongoing evaluation of the predictive utility of these scoring systems is recommended for early effective treatment intervention.

**Objectives**

To investigate the association of baseline clinical data and histological variants upon renal outcomes in our cohort of patients with IgA nephropathy over a long-term follow-up.

**Methods**

All available patients with biopsy-proven IgA nephropathy in our centre between January 2001 and December 2013 were recruited to this longitudinal retrospective observational study. Baseline data at the time of biopsy included demographics, laboratory and histopathological variants. Follow up data on renal function and mortality data were collected until the study end points which included death, loss to follow-up, end-stage renal disease (ESRD) and an arbitrary end date 31/7/2017. Cox regression analysis was used to assess the association of baseline characteristics and histopathological variants with renal outcomes: doubling of serum creatinine or reaching ESRD.

**Results**

A total of 115 patients were recorded over this 13-year period. The median age of our cohort at baseline was 41 years. Men represented 71% of the cohort. At baseline 84% were hypertensive and 11% diabetic. 77% were on a renin-angiotensin blocker, with 53% being on a statin. The median number of glomeruli on the renal biopsy samples was 19. Over a median follow up of 13 years, 59% had stable renal functions. 47 (41%) had a doubling of creatinine of which 18 (38%) reached ESRD requiring renal replacement therapy. 14 (12%) died during this follow-up period. The distribution of the histological variants is illustrated in Table 1. Univariate Cox regression model showed age, hypertension, high baseline creatinine and histological variants including global sclerosis (G), segmental sclerosis (S), mesangial hypercellularity (M), IFTA, and presence of inflammation (I) as having a strong association with renal outcomes (p<0.001). Among these, high baseline creatinine, segmental sclerosis, and IFTA showed further independent associations in a multivariate model adjusted for all factors significant in the univariate model. (Table-2)

**Conclusion**

In-addition to other histological variants, we observed the presence of global sclerosis (G1) and inflammation (I1) showing association with renal outcomes which has not been previously reported. The presence of crescents in biopsy was not found to be associated with adverse outcome in our cohort. Further studies are warranted to strengthen these associations.

**Table 1: Renal Biopsy-Histopathological variants:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variables** | **Total patients**  **115** | **Stable Creatinine**  **68 (59%)** | **Doubling of creatinine/ESRD**  **47 (41%)** | **p- Value** |
| **Mesangial Hypercellularity (M0/M1)** | 33 (29%) | 8 (12%) | 25 (53%) | **0.000** |
| **Endocapillary Hypercellularity (E0/E1)** | 7 (6%) | 5 (7.4%) | 2 (4.25%) | 0.495 |
| **Global Sclerosis**  **(G0/G1)** | 73 (64%) | 36 (53%) | 37 (78.72%) | **0.005** |
| **Segmental Sclerosis (S0/S1)** | 26 (23%) | 3 (4.4%) | 23 (49.93%) | **0.000** |
| **IFTA (Y/N)** | 69 (60%) | 25 (36.8%) | 44 (93.6%) | **0.000** |
| **Inflammation (I0/I1)** | 47 (41%) | 17 (25%) | 30 (63.8%) | **0.000** |
| **Crescents (C0/C1)** | 21 (18%) | 9 (13.3%) | 12 (25.53%) | 0.093 |

**Table 2: Multivariate Cox-regression model:**

|  |  |  |
| --- | --- | --- |
| **Factor** | HR (95% CI) | P Value |
| **Baseline Creatinine** | 1.01 (1.01-1.01) | 0.020 |
| **Segmental Sclerosis (S0/S1)** | 2.85 (1.50-5.43) | 0.001 |
| **IFTA (Y/N)** | 11.5 (3.02-44.09) | 0.000 |