Histological Classification of IgA nephropathy; Comparison between the Oxford classification and the Japanese Grade Classification

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Abstract.

The task of histological classification is to provide easily digestible information concerning prognosis and to offer guidance in making therapeutic decisions. It does this taking individual cases with their inherent individual variability, and using characteristic feature to subclass them into groups within a classification. The challenging aspect of this work is accurately ascertaining the parameters that will optimally sub-classify patients.

Two evidence based histological classifications, the Oxford Classification (Oxford) and Japanese grade classification (JGC), have been recently developed. However, they differ on a number of points in the methodological approach to developing the classification schemes, classification system (split or lumped), and in the predictive pathological parameters. As these two classification systems co-exist in Japan, there has been a great deal of motivation to compare the two in order to try and determine which approach may produce the most informative information for the sake of clinicians and ultimately for the benefit of the patients. Oxford was developed in a truly evidenced-based manner and includes four independent histologic parameters such as M (mesangial hypercellularity), E (endocapillary hypercellularity), S (segmental sclerosis), and T (tubular atrophy/interstitial fibrosis) using split system of dichotomous scoring. Within Japan, an alternate classification system, JGC has been developed. Four histological grades (HGs), such as HG 1, HG 2, HG 3 and HG 4, were established corresponding to <25%, 25-49%, 50-74% and ≥75% of glomeruli exhibiting the active lesions (cellular or fibrocellular crescents), or chronic lesions (global sclerosis, segmental sclerosis, or fibrous crescents).

These two classification systems were compared using the 411 Japanese cohort of earlier stage of IgAN. In multivariate Cox regression analysis, hazard ratio (HR) of MEST in Oxford for 1.5 time's increase of serum creatinine (sCr) was not significant,

whereas HG3 and HG4 in JGC were significant even after adjustment by steroid, RAS blockade, initial proteinuria, initial eGFR, and initial mean arterial pressure (MAP). When comparing HG score, M, E, S and T, HG score was the only independent predictor in isolation or in comparison to varied combinations of MEST parameters. In multivariate Cox regression analysis for proteinuric remission, the HR for an endpoint of proteinuria as 0.3 g/day was not significant in MEST, whereas HG3, initial MAP and steroid were independent predictors. Therefore, the HG score in JGC system was more effective than MEST of Oxford in predicting both renal functional decline and proteinuric remission in the Japanese cohort.

The inherent flexibility in a lumped approach of JGC as opposed to a split system of Oxford may make the HG score more robust when being applied to diverse cohorts with different follow up period, different stage of the disease and different therapy allowing a wider application of this grading score. Even though JGC was not produced with the same rigor as Oxford, its utility can be evaluated by the clinical information that it provides. Oxford may reduce the complexity and diversity of the histology observed in the biopsy into a series of dichotomous values (present/absent) thus potentially losing valuable information on the pathology within the lesion. The limitation of such a purely evidence based method may be its ability to be generalized to a wide range of cohorts whose clinical parameters do not match those used to develop the method. Hence, in addressing the aim to overcome the task of histological classification, lumped system that has been validated in a number of studies and been empirically developed may not be inferior to purely evidence-based Oxford classification.