



Updated Oxford classification of IgA nephropathy: expanding scope of the schema

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With the incorporation of crescents (C) score to all cases of IgAN to indicate the frequency of cellular and/or fibrocellular crescents as C0 (no crescents), C1 (crescents in 1 to 24% glomeruli) or C2 (crescents in $\geq 25\%$ glomeruli), subdivision of the S lesion (podocytopathic or non-podocytopathic in origin) and integration of the clinical data at the time of biopsy with MEST (Oxford classification) classification, the updated Oxford classification aims to further enhance the prognostic power of the classification. As a result, the updated Oxford classification now includes 5 instead of 4 pathological parameters, i.e., MEST-C score.

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IgA nephropathy (IgAN) is the most common glomerulopathy worldwide with divergent incidence and prevalence rates, chiefly reflecting different biopsy practices in different parts of the world. It is a heterogeneous disease with respect to clinical and pathological features and the ultimate outcome. This heterogeneity has defied all the attempts to develop a consensus classification, optimize its management and foretell its prognostication, till recent past (1). A concerted effort over 5-year period by a working group comprising of world-renowned nephrologists (from International IgAN Network) and nephropathologists (from Renal Pathology Society) with special interest in the disease led to the promulgation of the Oxford classification of IgAN in 2009 (2,3). A unique approach was adopted to develop this evidence-based classification. However, the original study cohort that included 265 biopsies was not diverse enough to include all the lesions, which can be seen in IgAN, such as crescents. There were certain other limitations too, such as lack of incorporation of immunofluorescence and electron microscopic data in the development of classification. Ethnic composition was also restricted and comprised of European Caucasians (from North America and Europe) and East Asian (from Japan and China) populations only.

These limitations of the study population were reflected in certain deficiencies in the classification. Some lesions were not studied or analyzed in detail for their prognostic value in the original cohort because of rarity of the lesions or exclusion of such cases from the study cohort (1). The original Oxford classification proposed to focus on four variables in reporting of renal biopsies of patients with IgAN: mesangial hypercellularity (M), endocapillary hypercellularity (E), segmental sclerosis (S), and interstitial fibrosis/tubular atrophy (T). These features were popularly known as MEST scores and Oxford classification is also called the MEST classification.

Due to the above mentioned limitations in the original study cohort, Oxford classification was not meant to be the end classification and the proponents of the classification were cognizant of this fact. The classification was supposed to evolve with time as more data accumulates and more studies are carried out for validation in different parts of the world. In fact, many studies since 2009 have validated the reproducibility and clinical utility of the classification throughout the world (4-15). The classification has also been validated in broader cohorts of patients involving other ethnic groups and the original cohort of the Oxford classification has also been expanded to nearly



5000 patients by continued international collaborative efforts of the Oxford classification Working Group (16-20). The lesions previously not addressed in the original version of the classification have also been studied in these larger cohorts (19-23). The original Working Group is still active, albeit with some change in membership, collaborating with more people from across the world and fully cognizant of the advancements and evidence in this area and is continuously striving to fine tune and enhance the performance of the classification. Working subgroups have been formulated to address problematic areas in the classification (1).

The activity and collaborative efforts of the Working Group have reached fruition recently and an updated version of the classification has been published (1). In this report, there is no change in the adequacy criteria of biopsy. The four key MEST scores also remain unaltered and their clinical utility corroborated. However, some problems in the interobserver variability have been addressed by an online educational material to educate the local pathologists. This has to be complemented. The Working Group is requested to make it freely available to all those interested in it. The main changes recommended in the classification and for which sufficient evidence is available now include: incorporation of crescents (C) score to all cases of IgAN to indicate the frequency of cellular and/or fibrocellular crescents as C0 (no crescents), C1 (crescents in 1 to 24% glomeruli) or C2 (crescents in $\geq 25\%$ glomeruli), subdivision of the S lesion (podocytopathic or non-podocytopathic in origin) and integration of the clinical data at the time of biopsy with MEST classification to further enhance the prognostic power of the classification. As a result, the classification now includes 5 instead of 4 pathological parameters, i.e., MEST-C score (1).

The activity and collaborative efforts of the Working Group have also led to assembly of a large international cohort of IgAN from multiple centers of the world. The objective is to develop a cohort representing the full spectrum of disease severity in IgAN with no limitations on proteinuria or renal function. This cohort will be a powerful substrate for future research studies on IgAN for refining and improving outcome prediction in individual patients and for refining recruitment and outcome criteria in clinical trials (1,24). Another area of future research focus is the identification of a biomarker or a panel of markers for the non-invasive diagnosis, therapy selection, therapeutic monitoring and prognostication of IgAN. However, efforts in this area have not reached fruition. With rapid advances in the field of "omics" technologies, this dream may be realized in near future. Variable collection and storage of biological samples for biomarker studies represents one important confounding factor in this area. It is anticipated that recommendations will be agreed on and published, based on the large international IgAN cohort, that cover the collection, storage, and transport of biological specimens for biomarker analysis (1,24).

In summary, Oxford classification of IgAN represents a significant and novel development in the pathological classification of renal diseases, and it continues to evolve as new data and evidence emerges. Continuing efforts of IgAN classification group will pave way for advancements in understanding the pathogenesis, pathology, treatment and outcome of IgAN patients.

Author's contribution

MM is the single author of the paper.

Conflicts of interest

The author declares no conflict of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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