Correlation of pathologic findings of IgA nephropathy with clinical and laboratory data with regards to the Oxford-MEST-C classification

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Abstract
The Oxford classification system has been found to have significant correlations with clinical and laboratory data in patients with IgA nephropathy. Studies have shown that higher grades of mesangial hypercellularity and endocapillary hypercellularity are associated with younger age, higher blood pressure, and higher levels of proteinuria. Segmental glomerulosclerosis has been found to be associated with more severe proteinuria, lower serum albumin levels, and higher levels of creatinine. Tubular atrophy/interstitial fibrosis has been associated with older age, higher serum creatinine levels, and lower estimated glomerular filtration rates.

Keywords: IgA nephropathy, Oxford-MEST-C classification, Glomerulonephritis

Introduction
IgA nephropathy (IgAN) is the most common primary glomerulonephritis worldwide. It is characterized by the deposition of IgA immune complexes in the glomeruli, leading to glomerular injury, proteinuria, and hematuria (1). Oxford classification, MEST, provides a scoring system to grade and stratify the severity of IgAN based on morphologic findings. This review will discuss the correlation of the pathologic conclusions of IgAN, Oxford classification MEST with clinical and laboratory data (2,3).

Search strategy
For this review, we searched PubMed/Medline, Directory of Open Access Journals, Web of Science, Google Scholar, EBSCO, Scopus, and Embase, using different keywords, including IgA nephropathy, Oxford classification, MEST-C score, glomerulonephritis, Oxford-MEST-C classification, end-stage renal disease and crescents.

Oxford-MEST-C classification for IgA nephropathy
Mesangial hypercellularity (M), endocapillary hypercellularity (E), segmental glomerulosclerosis (S), and tubular atrophy/interstitial fibrosis (T), and crescents (C), are the five elements evaluated in the Oxford classification, MEST-C scoring system. M and E are markers of active glomerular inflammation, whereas S and T reflect chronic and progressive glomerular injury, respectively (4,5). Numerous studies have shown a significant correlation between the Oxford classification MEST-C and clinical and laboratory data of IgAN patients, including the development of progressive renal dysfunction, proteinuria, and hematuria. In particular, S and T lesions on kidney biopsy are associated with a higher risk of progression to end-stage renal disease (ESRD) and a worse clinical outcome. Recent studies have also shown that the degree of tubular atrophy and interstitial fibrosis can provide important prognostic information independent of other pathological lesions (6,7). Furthermore, other factors like hypertension, advanced age, high baseline serum creatinine, and massive proteinuria, in conjunction with MEST lesions on kidney
biopsy, can further predict the risk of renal function decline in IgAN patients (8,9).

Possible limitations of the oxford-MEST classification
This classification system is based solely on morphologic findings and does not incorporate other clinical or laboratory data. The correlation of pathological conclusions like MEST-C lesions on kidney biopsy with clinical and laboratory data provides insight into disease progression, an indication of the type of treatment required, and a predictive guide of the disease's clinical course (10,11). There is a need for further studies that integrate clinical and laboratory data with the Oxford classification MEST-C scoring system to understand the pathogenesis better and develop appropriate management for IgAN patients (12,13). Some recent studies showed that interstitial inflammation, which is not incorporated in the MEST-C, is also associated with disease activity and development and is a neglected factor for prognosis like the other variables (14). The lack of inclusion of clinical data in the Oxford classification MEST scoring system may impact the accuracy of predicting long-term outcomes in IgAN patients. Clinical data, including patient age, comorbidities, and baseline renal function, can influence the progression and overall prognosis of IgAN. Without considering these factors, the MEST-C score may not accurately predict the risk of disease progression and clinical outcomes in individual patients (15,16). Previous studies showed that patients with lower baseline glomerular filtration rates and heavier proteinuria have been associated with worse clinical outcomes and a higher risk of progressing to ESRD. However, the Oxford classification MEST-C scoring system does not account for these patient-specific risk factors, which can limit its accuracy in predicting long-term outcomes (17).

Moreover, a few studies have suggested that incorporating clinical and laboratory data can improve the MEST-C score's accuracy in predicting long-term outcomes in IgAN patients. For instance, adding serum levels of creatinine, proteinuria, and blood pressure measurements to the MEST score can enhance its accuracy in predicting renal outcomes and the progression of IgAN. This suggests the need for a more comprehensive approach to scoring, such as adding clinical data to the Oxford classification MEST-C system to enhance its ability to predict outcomes (18,19) accurately.

Previous investigations have demonstrated the numerous benefits of utilizing the clinical data for the Oxford classification MEST-C scoring system in IgAN patients as follows:

Enhanced accuracy in predicting long-term outcomes
This enables better risk stratification and helps differentiate high-risk patients for whom therapeutic interventions or follow-up regimes should be stepped up (20).

Individualized patient care
Incorporation of clinical data with the MEST score can provide a more personalized approach to disease management. Individualized treatment guidelines can be developed by providing clinicians with a more comprehensive evaluation of the patient's condition, accounting for the particular patient's clinical profile (21).

Reproducibility and consistency
Incorporating clinical data reduces inter-observer variability between pathologists reviewing biopsy specimens, improving the consistency and reproducibility of the MEST-C score (22).

A better understanding of disease progression
Combining clinical and morphological data can help provide a better insight into the pathogenesis of IgAN. This can lead to discovering previously unreported pathways contributing to disease development or help identify patients with uniquely severe or rapidly progressing renal disease, who may have been previously missed based solely on morphological features (23, 24).

Conclusion
Incorporation of clinical data with the MEST-C score can help patients better understand the diagnosis, prognosis, and expected clinical outcomes, allowing informed decision-making and leading to better collaboration and patient engagement in their medical care.

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Conceptualization: Hamid Nasri.
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Supervision: Hamid Nasri.
Validation: Hamid Nasri and Mahoor Abedzadeh.
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