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SUMMARY: INTERNATIONAL CLINICAL DIABETIC RETINOPATHY AND DIABETIC MACULAR EDEMA DISEASE SEVERITY SCALES

Need for International Clinical Disease Severity Scale:
There is a need for a unified, international disease severity scale for diabetic retinopathy (DR) and diabetic macular edema (DME) in both the U.S. and all parts of the world. Although the Early Treatment Diabetic Retinopathy Study (ETDRS) staging system is recognized as the gold standard for grading in clinical trials, in everyday clinical practice, it has not proven to be easy or practical to use. There are too many levels, required correlations with standard photographs and additional complicated grading rules for the different stages, and these are difficult to remember. Contemporary studies have documented that the ETDRS grading system is not employed by the vast majority of physicians managing patients with diabetes. It is also useful to have a common disease severity scale for DME, because it is an important cause of visual loss. Thus, a system that can be used globally is needed to facilitate communication between retina subspecialists and general ophthalmologists, and also among general ophthalmologists, retina subspecialists, endocrinologists/diabetologists and primary care physicians.

Intended User Audience:
This system is intended not only for retina subspecialists but also for general ophthalmologists around the world who have a basic understanding of diabetic retinopathy and skills in evaluating the retina. In addition, it is hoped that this system will allow all physicians caring for patients with diabetes to be able to recognize important lesions and combinations of lesions of diabetic retinopathy with direct ophthalmoscopy following dilation. The recognition of the basic lesions associated with diabetic retinopathy (microaneurysms, blot hemorrhages, hard exudates, cotton wool spots, intraretinal microvascular abnormalities (IRMA), venous beading (VB), neovascularization, vitreous/preretinal hemorrhages, fibrosis, and retinal detachments) will result in appropriate staging and serve as a basis for a common terminology for communicating the status of patients between ophthalmologists and endocrinologists, diabetologists and primary care physicians who care for the patients' systemic condition. Although endocrinologists and primary care physicians would be made aware of this system, it is not anticipated that they would use this to classify patients. Nevertheless, the recognition of important lesions and combinations of lesions should dictate the apparent need for referral for further evaluations of the retina by ophthalmologists.

Scientific Rationale:
This system is based on an evidence-based approach, namely the findings of the Early Treatment of Diabetic Retinopathy Study (ETDRS) and the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR). These studies have provided the foundation of the understanding of diabetic retinopathy progression, risk factors, and outcomes of treatment. The findings associated with each stage are correlated with basic previously produced and more extensive evidence of pathology of the retina caused by nonperfusion or ischemia. For example, there is substantial evidence from the ETDRS and WESDR that IRMA and VB are most predictive of the risk of progressing to PDR, and must be included in this scale. There also is solid evidence to support a separate stage for severe NPDR, because early treatment is beneficial for patients with type 2 diabetes and severe NPDR. Factors that determine if macular edema is sight threatening include the location and area of retinal thickening and hard exudates.

Consensus Development Process:
A workshop was held in April 2002 in conjunction with the International Congress of Ophthalmology. The purpose of the workshop was to develop and build broad-based consensus around a clinically relevant and simplified DR disease severity scale. Participants in the invitation-only workshop included

30 of the ophthalmic thought leaders from around the world. Based on the scientific presentations and discussions held at the workshop, a disease severity scale was developed for both DR and DME. A modified Delphi technique was utilized to develop agreement on the scales. Individuals were asked to describe their views on agreement with the proposed scales. The results were explicitly, mathematically aggregated to summarize the group results. To determine agreement and disagreement, the binomial distribution was applied. The final statistical analysis of the group results found that there was strong agreement on the international clinical disease severity scales.

Principles for Development:

The disease severity scales were based on the following principles:

- This should be based on solid scientific evidence, i.e., the ETDRS data. The science should not be compromised.
- This would not replace the ETDRS, but provide a common, user-friendly terminology to describe disease severity and risk of progression categories.
- This should be tied to levels of risk of progression to more severe disease, as described in the ETDRS and other research.
- The number of levels or stages of disease severity should be appropriate for communication, based on scientific evidence and practical for everyday use.

Use of the System:

There are many significant factors that affect an individual's progression to more severe disease, but are outside the scope of these disease severity scales. These factors should be taken into account by the clinician in decision-making, and in informing the patient and primary care physician or diabetologist. Implementation would vary across different regions, because practice patterns and health care delivery systems for patients with diabetes mellitus differ around the world.

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