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Editorial

Functional Diabetic Retinopathy: A Switch to Control Diabetes - Related Complications and Vision Loss

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Burden of diabetes

The International Diabetes Federation estimated the global prevalence of DM at 463 million in 2019 [1]. Diabetic retinopathy (DR) is a major complication and a leading cause of visual loss [2]. Among diabetics, global prevalence for DR was 19–25%, 6% for vision-threatening DR (VTDR), and 4% for diabetic macular oedema (DMO) [3]. In 2020, the number of adults worldwide with DR, VTDR, and DMO was estimated to be 103.1 million, 28.5 million, and 18.8 million, respectively [3]. By 2045, it is projected that there will be 700 million people with DM, 160.5 million with DR, 44.8 million with VTDR, and 28.6 million with DMO [1,3].

Functional diabetic retinopathy - diabetic retinal neurodegeneration

Several functional and structural changes precede the emergence of clinical DR: peripapillary retinal nerve fibre layer thinning [4], and reduced combined ganglion cell layer and inner plexiform layer thickness [5]. Functional retinal changes are noted in patients without any signs of DR [6] are due to diabetic retinal neurodegeneration (DRN) preceding microvascular changes [7]. The vascular markers of DR present only after considerable DRN has occurred [8]. Clearly, a state of compromised retinal function prior to classical DR and vascular markers occurs due to suboptimal integrity and compromised function of the retinal neurons, detectable only with functional testings. It may be worthwhile to coin a new term functional diabetic retinopathy (FDR) to highlight early-stage DR.

Perimetry - role in diabetic retinopathy

Subjective automated perimetry (SAP): The structure-function studies have shown that SAP detects visual field defects prior to emergence of clinical DR [9,10], diagnosing functional lesions. This may be helpful is tracking the progression of early-stage DR, basically the FDR.

Multifocal pupillographic objective perimetry (mfPOP), as exemplified by the FDA-approved objective FIELD Analyzer (OFA), is an objective non-contact perimetric method based on pupillometry testing both eyes concurrently. mfPOP identifies early focal lesions of DR in prior to the structural changes, FDR, without any sign of clinical DR [10-12]. Additionally, for mfPOP test, the stimuli are matched to the ETDRS 9 sub-fields corresponding to the EDTRS OCT sub-fields and 8x8 scanning grid [13]. This makes the functional test compatible for point-by-point functional and structural correlation for easy localisation of the lesions and deliver customised therapy.

Current practice in DR management - knowledge gap

In the current practice, vascular markers such as retinal microaneurysms, haemorrhages, exudates, thickened retina or DMO and increased volume are considered the landmarks of clinical DR and are relied upon clinically to diagnose DR corroborated with retinal photographs and optical coherence tomography (OCT) reports. The only functional test performed is the best corrected visual acuity (BCVA), which is the function of the central fovea. With the current approach, we are neglecting the functional integrity of retina except the fovea. There may be a potentially vision-threatening lesion next to the fovea when the BCVA is still normal. This demands a change in approach to the diagnosis and management of DR and DMO by inclusion of functional diagnostics such as multifocal perimetry.

Functional diabetic retinopathy - a switch point

To control diabetes-related visual impairment, blindness, and even other tissue injury, we must focus at the early-stage DR. FDR may be the right switch point – treat functional lesions to prevent the progression to clinical DR and other complications. FDR may also be validated for diagnosing other tissue injury such as peripheral neuropathy and kidney failure. Clinical trials to validate the anti-VEGF in treating FDR, thereby preventing the emergence of DR may be fruitful.

Conclusions

Beyond denial that the neuropathy and functional changes precede vasculopathy and clinical DR, and the functional lesions occur earlier than the clinically detectable signs of DR. FDR can only be detected with functional tests such as perimetry.

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