Association of Peripheral Retinal Vascular Abnormalities Detected on Ultra Wide-Field Fluorescein Angiography With Diabetic Macular Edema and Neovascularization


Purpose: To determine whether peripheral retinal vascular abnormalities are associated with common manifestations of diabetic retinopathy.

Methods: A retrospective review was conducted on 125 consecutive ultrawide-angle angiograms of diabetic patients using the Optomap® 200 fa Dynamic Ultra-widefield Angiography System (Optos plc, Dunfermline, Scotland, UK). Patients were categorized by diagnosis, presence of diffuse or focal macular edema, posterior or peripheral neovascularization, later peripheral vascular staining, and macular or peripheral ischemia.

Results: Using ultra-widefield angiography, peripheral ischemia was significantly associated with peripheral retinal neovascularization.

Conclusions: The use of ultra-widefield angiography to identify peripheral retinal vascular pathology may enhance the sensitivity of detection for treatable conditions in diabetic retinopathy.

Support: Retina Division, JSEI, UCLA

Retinal Blood Flow as a Predictor of Diabetic Retinopathy Progression: A 10-Year Longitudinal Analysis


Purpose: To determine if alteration of retinal blood flow (RBF) in diabetic patients with no to mild diabetic retinopathy (DR) is correlated with long term retinopathy progression.

Methods: RBF was determined from 60 eyes of 32 diabetic patients with no to mild DR using scanning laser ophthalmoscopy fluorescein angiography and dye dilution methodology. Patients with diabetes mellitus (DM) were subsequently followed at the Beetham Eye Institute/Joslin Diabetes Center for an average of 11.2±1.5 years (range 8.4-14.3) with an average of 12 subsequent visits (3-50). Outcomes including best corrected visual acuity, dates of DR progression, time of therapeutic interventions, and onset of systemic co-morbidities were collected by retrospective chart review using standardized forms.

Results: 32 patients (60 eyes) were evaluated with a mean DM duration of 21.2±9.9 years (median 18.4, range 8-55). Mean age was 47.2±11.3 years (median 42.5, range 27-70), with 52% female, 18% Type 2 DM, and HbA1c of 7.2±0.8, N=49) during follow-up (p=0.032).

Conclusions: The use of ultra-widefield angiography to identify peripheral retinal vascular pathology may enhance the sensitivity of detection for treatable conditions in diabetic retinopathy.

Support: None

Retinal Blood Flow in Patients With Diabetes During Euglycemic Eusiinsulinemic Clamps

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Purpose: Retinal blood flow in diabetes has been measured in a variety of studies. The results of these studies are largely contradictory reporting increased, decreased or unaltered blood flow. A number of reasons may account for these discrepancies including methodological aspects, patient selection and glycemic control. The last point is critical, because both insulin and glucose have been shown to induce ocular vasodilatation. Accordingly, we studied retinal blood flow in diabetic patients during euglycemic eusiinsulinemic clamps.

Methods: In the present study 16 patients with insulin dependent diabetes, no or mild non-proliferative diabetic retinopathy, and serum cholesterol levels < 250 mg/dl were included. 16 healthy age- and sex-matched subjects served as controls. In diabetic patients retinal blood flow values were measured in the morning before the insulin morning dose and during euglycemic eusiinsulinemic clamps. During these clamps endogenous insulin production was inhibited with somatostatine. Retinal blood flow was measured by combining temporal venous diameters data obtained with the Retinal Vessel Analyzer and retinal blood velocity data obtained with bi-directional laser Doppler velocimetry. To gain information on total retinal blood flow all veins entering the optic nerve were measured and the data of the individual vessels were added.

Results: Before morning insulin plasma glucose levels were 176 ± 21 mg/dl. This plasma glucose level was normalized during the eusiinsulinemic clamp to 102 ± 4 mg/dl. Retinal blood flow was 51.4 ± 5.3 µl/min before the clamp was started. During the euglycemic eusiinsulinemic clamps retinal blood flow was significantly reduced to 42.1 ± 5.2 µl/min (p < 0.01). As compared to retinal blood flow in the healthy control group (41.2 ± 4.1 µl/min) retinal blood flow in diabetic patients was increased before the euglycemic eusiinsulinemic clamps (p=0.6).

Conclusions: The present study indicates that retinal blood flow is increased in patients with diabetes at high plasma glucose levels but not during euglycemic eusiinsulinemic clamps. These data indicate that in patients with plasma glucose retinal blood flow is fluctuating with fluctuating glucose plasma levels.

Support: None

Effects of Dilation on Visual Acuity Obtained by Electronic-ETDRS Visual Acuity Testing (EVA) in Diabetic Patients

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Purpose: To evaluate the effect of pupillary dilation on electronic-ETDRS visual acuity (EVA) in subjects with diabetes and to assess the suitability of post-dilation EVA as a surrogate for pre-dilation visual acuity (VA).

Methods: Pre-dilation standardized refraction and EVA measurements were performed according to DRCR.net protocol. Subjects underwent pre-dilation assessment of corneal clarity and pupil size. After dilation, pupil measurement, refraction, and EVA were repeated by an independent, masked examiner. Diabetic retinopathy (DR) severity level, extent of cataract, primary cause of visual loss, and post-dilation corneal clarity were evaluated for each eye.

Results: 129 eyes of 66 subjects with diabetes were examined. The median [lower, upper quartiles] pre-dilation EVA score was 69 [54, 86], Snellen equivalent 20/80 [20/80, 20/20], ranging from 0 to 95 [<20/800 to 20/12.5]. Pre-dilation VA was 20/40 or better in 42 eyes (48%), worse than 20/40 but better than 20/80 in 34 eyes (26%), and worse than 20/80 in 33 eyes (26%). Overall median post-dilation change in VA was -3 [0, 7] letters. A VA decline of ≥ 15 letters occurred in 9% of subjects overall. Although pre- and post-dilation VA were correlated, the VA change ranged from +12 to -25 letters. This effect was partially dependent on baseline VA. Of eyes with baseline VA ≥ 20/40 and 20/40 > VA ≥ 20/80, a ≥ 15 letter change was observed in 5% and 15% and a ≥ 5 letter change occurred in 35% and 53%, respectively. No substantial relationship was identified between change in VA and gender, race, lens status, phakic refractive error, educational level, DR severity level, or primary cause of vision loss.

Conclusions: In an optimized clinical trial setting using experienced examiners, there is a general decline in best corrected visual acuity after pupillary dilation. Although pre- and post-dilation VA are correlated, the wide range and large magnitude of VA change after dilation preclude the use of post-dilation EVA testing as a surrogate for undilated VA.

Support: Diabetic Retinopathy Clinical Research Network
4528 - 4:00PM
Increased Shedding of Endothelial Microparticles Following Anti-VEGF Therapy of Human Proliferative Diabetic Retinopathy
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Purpose: Development of retinal neovascularization in proliferative diabetic retinopathy (PDR) is correlated to vitreous VEGF levels. Intravitreal administration of Bevacizumab, a humanized recombinant antibody that binds all isoforms of VEGF, causes at least short-term inhibition of retinal neovascularization. We hypothesized that endothelial microparticles (MP), which are submicron membrane vesicles released following endothelial cell activation or apoptosis, accumulate in vitreous fluid from patients with PDR following anti-VEGF therapy.

Methods: Undiluted vitreous fluid samples were collected at the start of standard surgery for the treatment of retinal disease in diabetic (D, n=14, 61±5 yrs, 7.5±0.2% HbA1c) and non-diabetic (ND, n=15, 65±4 yrs) patients. Five patients with PDR received intravitreal injection of Bevacizumab 0.6 mg/µl one week before surgery. Levels of MP in vitreous fluid were analysed by flow cytometry, using markers for platelet (CD41), endothelial (CD144), microglial (Bandeiraea Simplicifolia Lectin; ILB4) and photoreceptor (Arachis hypogaea Lectin; PNA) cells.

Results: Vitreous levels of endothelial and platelet MP were markedly increased in PDR when compared to ND patients (139±53 vs 231±57 CD41+MP/µl p=0.02; 238±36 vs 62±12 CD144+MP/µl p=0.004; respectively). Levels of MP of microglial or photoreceptor origin did not differ significantly in D and ND vitreous samples (89±51 vs 77±6 F4/80+MP/µl p=0.3; 47±25 vs 20±13 ILB4+MP/µl p=0.32; respectively). Intravitreal injection of anti-VEGF antibody led to an eight fold increase in endothelial Mps shedding (1980±602 CD144+MP/µl) and a complete disappearance of platelet-derived CD41+MPs in PDR vitreous samples. Anti-VEGF treatment also reduced microglial ILB4+MP (3±3 MP/µl; p=0.16) levels.

Conclusions: Microparticle identification in vitreous samples indicates that local anti-VEGF therapy induces massive vascular endothelial cell apoptosis. In addition, augmented platelet MP levels in diabetic vitreous samples suggests that PDR is associated with an increased endothelial permeability, which is restored to basal level by anti-VEGF therapy.

CR: M. Benzerroug, None; S. Chahed, None; A. Leroyer, None; S. Picaud, None; A. Gaudric, None; G. Brasseur, None; A. Tegdui, None; C. Boulanger, None; P. Massin, None.
Support: None

4530 - 4:30PM
Three-Dimensional Optical Coherence Tomography Guided Vitrectomy for Proliferative Diabetic Retinopathy
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Purpose: To evaluate the three-dimensional structures of proliferative membrane in proliferative diabetic retinopathy using three-dimensional optical coherence tomography (OCT). To detect the locations and the extents of the epicenters in proliferative diabetic membranes using three-dimensional OCT data sets, and evaluate the usefulness for membrane resection in vitrectomy.

Methods: We prospectively examined 10 eyes of 5 patients with proliferative diabetic retinopathy. Three-dimensional OCT data sets were obtained using a commercial spectral-domain OCT (Topcon 3D-HR, center wavelength 840 nm, 18000 Ascan/sec). Using the three-dimensional OCT data sets, the epicenters in proliferative membranes were detected. The extents and the locations of the epicenters were registered in the color fundus photograph images, and were compared with the findings during vitrectomy.

Results: In all eyes, three-dimensional structures of proliferative membranes could be visualized, and the epicenters could be clearly detected. The extents and the locations of epicenters corresponded well with the findings during vitrectomy, and these information were useful for safe and secure surgical procedures in membrane resection.

Conclusions: Three-dimensional OCT is an effective tool to understand the three-dimensional structure of proliferative membrane in proliferative diabetic retinopathy. Detection of the epicenters is useful for planning the surgical procedure in vitrectomy, and for the education and the training of the vitrectomist.

CR: C. Matsushima, None; M. Miura, None; T. Iwasaki, None.
Support: None