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Multimodal Retinal Imaging as Biomarker for Cardiovascular Disease in Patients with Diabetes Mellitus

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DESIGN. Bi-center, retrospective, observational case-series.
PURPOSE. To evaluate association between macrovascular systemic comorbidities and multimodal retinal imaging in patients with diabetes mellitus (DM) with different stages of diabetic retinopathy (DR).
METHODS. 516 eyes of 259 DM patients with systemic history and imaging were enrolled in two centers (Milano and Belfast). Ultrawidefield color fundus photos (CFP) were obtained with OPTOS California and OCT/OCT-Angiography (OCT-A) imaging with Heidelberg Spectralis. The presence of predominantly peripheral lesions (PPL) was confirmed by two independent graders as >50% of CFP lesions. OCT-A imaging (3×3 mm) was used to determine perimeter, area and circularity index of the foveal avascular zone (FAZ) and vessel density (VD); perfusion density (PD); fractal dimension (FD) on superficial (SCP), intermediate (ICP) and deep (DCP) plexuses; flow voids (FV) in the choriocapillaris (CC).
RESULTS. 81.5% of patients had DM type 2, with mean age of 67.1 ± 13.7 years. Out of 516 eyes, 108 eyes (20.9%) did not have DR, and 6 eyes were not gradable. The remaining 402 eyes were: 10.3% (53) mild non-proliferative DR (NPDR), 38.2% (197) moderate NPDR, 11.8% (61) severe NPDR, 17.6% (91) proliferative DR (PDR). PPL was present in 35.5%, associated with longer DM duration and worse DR severity ($p < 0.001$). A worse DR stage was associated with a history of stroke ($p = 0.044$). Presence of stroke was associated with: decreased FD on SCP and DCP ($p = 0.011$; $p = 0.048$), decreased VD on SCP and DCP ($p = 0.011$; $p = 0.027$), and decreased PD on SCP ($p = 0.014$). Ischemic cardiopathy was associated with decreased PD and VD on ICP ($p = 0.04$; $p = 0.05$) and increased FV on CC ($p = 0.03$). The multiple regression analysis showed that FAZ circularity and VD in SCP and ICP and PD in ICP accounted for 30% of DR severity variability.
CONCLUSIONS. OCT-A metrics show an association with the cerebrovascular and cardiovascular complications of DM, providing potentially useful biomarkers for estimating systemic vascular risk in DM patients.