Metabolic factors and the foveal avascular zone of the retina in diabetes mellitus

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SUMMARY

Aim: To study the foveal avascular zone (FAZ) of the central retina in diabetic patients with retinopathy having undergone metabolic evaluation.

Methods: One hundred and ten digital fluorescein angiograms were chosen from our digital image bank after cross matching diabetic patient lists of the ophthalmology and endocrinology departments of our institution. The patients had undergone day visits with systemic, biological and ophthalmologic evaluation, including digital fluorescein angiography.

Results: Sex ratio was M 62/F 48. Average age was 52.4 years (∂ 13.8) with 44 type 1 diabetics and 66 type 2. Retinopathy was present in all patients (54 background (BDR), 30 pre-proliferative (PPDR), 26 proliferative (PDR)). Age was positively correlated with FAZ grade (47.3 years ∂ 13.2 for normal FAZ, 53.8 years ∂ 13.7 for abnormal FAZ, P = 0.03). Lipid profile showed a protective tendency of the Apo A1 fraction of cholesterol on macular vascularization (1.7 gr./l in normal FAZ patients *vs* 1.43 gr./l in abnormal FAZ patients, P = 0.004). Body mass index was negatively correlated with macular ischemia (28.11 if FAZ not severely altered, 25.97 if FAZ severely altered, P = 0.03).

Conclusions: We found possible relations between BMI and Apo A_1 cholesterol and macular vascularization which may warrant further investigation.

Key-words: Diabetic retinopathy · Foveal avascular zone · Macular ischemia · Body mass index · Apolipoprotein A1.

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RÉSUMÉ

Facteurs métaboliques et zone avasculaire centrale de la rétine dans le diabète sucré

Objectifs : Étudier la zone avasculaire centrale (ZAC) de la rétine chez des patients diabétiques avec une rétinopathie ayant eu une évaluation métabolique.

Méthodes : Cent dix angiographies rétiniennes à la fluorescéine, numérisées, ont été choisies dans notre banque d'images après avoir croisé les listes des patients suivis par les services d'ophtalmologie et d'endocrinologie de notre hôpital. Les patients avaient bénéficié d'un bilan en hôpital de jour avec réalisation d'un examen clinique, biologique et ophtalmologique avec angiographie rétinienne.

Résultats : Le sex ratio était 62 H/48 F. L'âge moyen était de 52,4 ans (∂ 13,8). Il y avait 44 diabétiques de type 1 et 66 diabétiques de type 2. Une rétinopathie diabétique (RD) était présente chez tous les patients (54 RD minimes ou modérées, 30 RD non proliférantes sévères et 26 RD proliférantes). L'âge était corrélé positivement au grade de la ZAC (47,3 ans ∂ 13,2 en cas de ZAC normale, 53,8 ans ∂ 13,7 en cas de ZACa normale, P = 0,03). Le profil lipidique montrait un effet protecteur de la fraction ApoA1 sur la vascularisation maculaire (1,7 g/l en cas de ZAC normale, 1,43 g/l en cas de ZAC anormale, P = 0,004). L'indice de masse corporelle (IMC) était corrélé négativement avec l'ischémie maculaire (IMC = 28,11 en cas de ZAC non ou peu altérée, IMC = 25,97 en cas de ZAC très altérée, P = 0,03).

Conclusion : Des relations possibles entre d'une part la vascularisation maculaire et d'autre part l'indice de masse corporelle et le cholestérol ApoA1 pourraient mériter des explorations plus poussées.

Mots-clés : Rétinopathie diabétique · Zone avasculaire centrale · Ischémie maculaire · Indice de masse corporelle · Apolipoprotéine A1.

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Introduction

It is well known that diabetic retinopathy is related to metabolic control, poorer control being related to higher retinopathy stage, more complications and a greater risk of blindness [1, 2]. The first cause of poor vision in diabetics is diabetic maculopathy [3], which may combine both macular edema and ischemia as well. The importance of macular ischemia in diabetic vision loss is difficult to assess. It is due to macular capillary occlusion in the posterior pole of the eye, and more specifically at the level of the capillary net defining the foveal avascular zone.

The foveal avascular zone or FAZ is an area located in the center of the macula which is physiologically avascular. It is this region that provides highest visual acuity, contrast vision and color vision, with a maximum ratio of photoreceptors (cones) to nerve fibers.

Ischemia of the foveal region secondary to diabetes has aroused less research interest than macular oedema, perhaps because to this day, no physical or pharmacological treatment such as laser photocoagulation [4] or corticosteroid injections [5] (both used to treat diabetic macular edema) exists to specifically manage macular ischemia. This paper deals with the study of the metabolic parameters that may be correlated with macular vascularization.

Patients and methods

One hundred and ten high quality digital fluorescein angiograms (1024x1024 pixels) of 110 patients were retrospectively chosen from our digital image bank after cross matching diabetic patient lists of the ophthalmology and endocrinology departments of our institution. The patients had undergone day visits with ophthalmologic, systemic and biological evaluation.

Ophthalmologic evaluation included visual acuity, refraction, slit lamp examination, intra-ocular pressure measurement, dilated fundus examination (with evaluation of retinopathy level) and a digital fluorescein angiogram (5 ml of 10% sodium fluorescein were injected rapidly into the antecubital vein) with early, mid and late phase pictures. Angiograms were chosen on the basis that the FAZ must be sufficiently visible to allow quantitative and qualitative evaluation: the chosen study eye was the eye for which the FAZ was best visible on the digital fluorescein angiogram. Diabetic retinopathy (DR) was classified by fundus examination as background (BDR, ETDRS levels 20 to 47), preproliferative (PPDR, ETDRS levels 53) or proliferative (PDR, ETDRS levels 61 and above). The FAZ was evaluated qualitatively and quantitatively as described elsewhere [6]. Briefly, a single layer capillary ring surrounds the center of the fovea. Capillary dropout may be estimated by evaluating the amount of this ring that has been interrupted by capillary closure, with a qualitative grade ranging from 0 to 4 being assigned to each FAZ *(Fig. 1)*. Quantitative FAZ evaluation was performed using the Image J freeware to outline the FAZ *(Fig 2)* and subsequently determine surface area in mm^2.

Systemic evaluation included age, date of onset of diabetes, type of diabetes, height, weight, body mass index, presence or absence of arterial hypertension, presence or absence of peripheral neuropathy, nephropathy, and macroangiopathy (assessed by presence or absence of coronary ischemia and/or carotid stenosis).

Biological evaluation included glycated hemoglobin (HbA_{1c}) levels, which had been measured by HPLC on the VARIANT II® machine (Bio-Rad, Hercules, California, USA). ApoA1 and ApoB cholesterol had been dosed by immunonephelemetry (BN II®, Dade-Behring, Liederbach, Germany).

Statistical analysis

Correlations of systemic and biological factors to both retinopathy and macular ischemia were sought out, as well as the relations between retinopathy and macular ischemia, by statistical analyses using the SPSS 10 software package. Non-parametric tests were preferred as the population of subgroups was rarely above 30 (ANOVA requiring a normal distribution in subgroups). Quantitative variables were compared using the U test of Mann-Whitney or

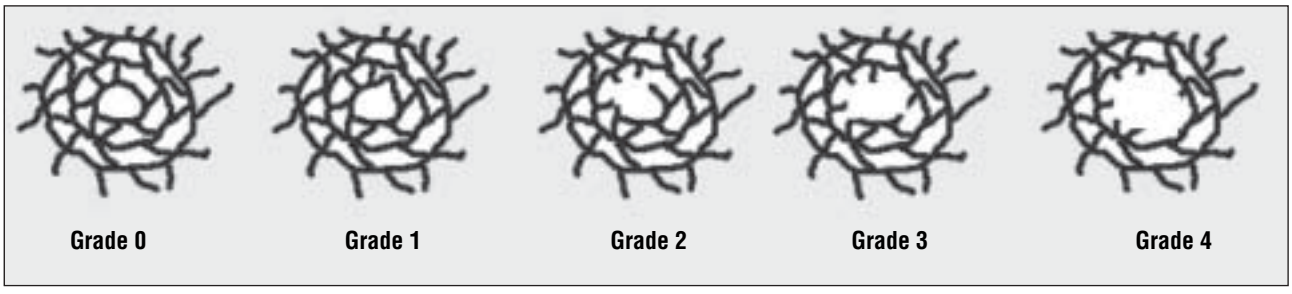

Figure 1
Schematic representation of the different grades of the foveal avascular zone in diabetic retinopathy. Grade 0 is a normal contour, grade 1 questionnable, grade 2 has less than half of the circumference destroyed, grade 3 more than half of the circumference destroyed but some remnants remain and grade 4 has the whole original circumference destroyed.