POSSIBLE ROLE OF ANGIOTENSIN II RECEPTOR BLOCKADE IN THE GLUCOTOXICITY ON HUMAN RETINAL PERICYTES

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INTRODUCTION. Diabetic retinopathy (DR) is characterized by capillary degeneration and pericyte dropout. Angiotensin II (Ang II) regulates several pathologic events, including cellular proliferation/hypertrophy. Elevated Ang II and/or increased sensitivity to Ang II have been etiologically associated with major vascular diseases. Clinical studies have suggested that inhibitors of the angiotensin converting enzyme can slow progression to advanced stages of DR, while antagonists of the angiotensin AT1 receptor resulted in significant regression of DR in type 2 diabetic patients.

PURPOSE. The objective of this study was to verify if the Ang II receptor blocker candesartan can act as an antiapoptotic and protective factor for human retinal pericytes (HRP) in diabetic-like conditions.

METHODS. Pericytes were kept alternatively in high (HG) or normal (NG) glucose at 48-hour intervals for 8 days, with or without 10, 2, 1, or 0.2 µmol/mL candesartan. Control cells were cultured in stable NG or HG. Bax and bcl-2 mRNA expression, as markers of glucose-induced apoptosis, was determined by reverse transcriptase polymerase chain reaction, apoptosis by enzyme-linked immunosorbent assay (ELISA), and cell proliferation by cell counts and BrdU incorporation ELISA. Senescence-associated β-galactosidase activity was also evaluated.

RESULTS. Intermittent, but not stable, high glucose decreased proliferation and increased apoptosis in HRP consistently with our previous findings. Candesartan, 1 and 0.2 µmol/mL, when added to intermittent high glucose, was able to normalize apoptosis (both DNA fragmentation and Bcl-2/Bax expression), while higher concentrations had no significant effects. Even if candesartan does not influence proliferation, it seemed capable of reducing intermittent high glucose-activated senescence.

CONCLUSIONS. Candesartan has a significant antiapoptotic effect on HRP, but further studies are necessary to better understand the mechanisms through which it works, in particular the signaling pathways involved and/or influenced by Ang II.

Purpose

The purpose of the research was to determine the role of mitochondrial ROS on the activation of MMP-2 and the subsequent effects on the extracellular matrix.

Methods

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Conclusions

The data indicate the potential role of mitochondrial-derived ROS in the activation of MMP-2 and the subsequent effects on the extracellular matrix.

FENOFIBRATE EFFECT ON DIABETIC RETINOPATHY

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Introduction

Placebo-controlled study.

Purpose

To estimate the fenofibrate effect on diabetic retinopathy.

Methods

Type 2 diabetic patients (n=60) with nonproliferative diabetic retinopathy were included into the study. Thirty-five patients (70 eyes) were assigned to receive fenofibrate 200 mg/day, and 25 patients (50 eyes) were assigned to a control group. All patients were followed during 1 year. Complete ophthalmic examination including 7-field stereoscopic retinal photography and optical coherence tomography was performed at baseline, month 6, and month 12 visits. In addition, fluorescein angiography was carried out, when needed. At each visit, blood pressure measurement and biochemical blood assay were done.

Results

In the fenofibrate group, retinopathy progressed in 12.8% of cases (9 eyes) over the 12-month period. No neovascularization was registered. Grid photocoagulation for macular edema was necessary in 2.9% of cases (2 eyes). In 7.1% of cases (5 eyes), regression of retinopathy level was detected. In the control group, retinopathy progressed in 28.0% of cases (14 eyes). In 6.0% of cases (3 eyes), proliferative diabetic retinopathy developed. Five eyes (10.0%) required grid photocoagulation for macular edema. Retinopathy regression was revealed in 4.0% of cases (2 eyes). The lipid profile assessment in the fenofibrate group showed significant lowering of total cholesterol, triglycerides, low-density lipoproteins, and very low-density lipoproteins (p=0.001). There was a trend of high-density lipoproteins increase (p=0.11). In the fenofibrate group, no significant changes in mean systolic and diastolic blood pressure were observed. In the control group, significant systolic pressure increase was present (p=0.03), while the diastolic one showed no reliable difference (p=0.92).

Conclusions

Fenofibrate treatment can be effectively applied for lipid profile normalization and prevention of clinically significant retinal changes in patients with type 2 diabetes mellitus. Fenofibrate use significantly lowers the risk of progression of diabetic retinopathy from 28.0% to 12.8% (p=0.04), and the need for laser treatment from 16.0% to 2.9% (p=0.02). The increase of systolic blood pressure, high mean levels of triglycerides, and very low-density lipoproteins were shown to be significant risk factors for progression of diabetic retinopathy and macular edema.

LONG-TERM ASSOCIATIONS BETWEEN SERUM LIPIDS AND PANRETINAL PHOTOCOAUGURATION IN TYPE 1 DIABETES

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Introduction

Cohort study.

Purpose

To examine the predictive value of serum lipids on the need for panretinal photoagulation (PPR) treatment in a long-term follow-up of a cohort of Danish type 1 diabetic patients.

Methods

A total of 243 type 1 diabetic patients were identified from a population-based cohort. Of these, 25 patients (10.3%) already had proliferative diabetic retinopathy (PDR) at baseline and were thus excluded from the study. The remaining 218 patients were followed from January 1993 to November 2006. Serum levels of lipids were collected at baseline. Panretinal photoagulation treatment was considered as indicative of PDR during follow-up. Date of PRR was documented from the Danish National Patients Registry.

Results

At baseline, median age and duration of diabetes was 45.9 years (range 23.9-78.4 years) and 30 years (range 20-72 years), respectively. There was an equal distribution between men (50.5%) and women (49.5%). Serum triglyceride was independently associated with incident PRR. After adjustments for baseline age, duration of diabetes, and gender, each 1 mmol/L increase in serum triglyceride was associated with a hazard ratio of 1.54 (95% confidence interval 1.09-2.18, p=0.02) of PRR. On the other hand, total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol were not associated with a higher risk of incident PRR.

Conclusions

In a 13-year follow-up of a population-based cohort of long-term type 1 diabetic patients, serum triglyceride was associated with a 54% increased risk of PRR treatment, which was used as a surrogate endpoint of PDR. These findings expand the knowledge obtained by the FIELD and ACCORD studies that found a beneficial effect of fenofibrate treatment on diabetic retinopathy.

THE PREDICTIVE POWER OF MICROANEURYSM COUNT ON DEVELOPMENT OF SIGHT-THREATENING RETINOPATHY AND THE RESPONSE TO TREATMENT WITH AN ANGIOTENSIN RECEPTOR BLOCKER: RESULTS FROM THE DIRECT PROGRAMME

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Introduction

Multicenter randomized clinical trial.

Purpose

To study the association between baseline retinal microaneurysm (MA) score and development of diabetic maculopathy (CSME) and proliferative retinopathy (PDR), and response to treatment with candesartan in people with diabetes.

Methods

Microaneurysms were scored from yearly retinal photographs according to the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol. Diabetic maculopathy and/or PDR were classified according to the ETDRS definitions. Patients were normoalbuminuric and normotensive with type 1 and type 2 diabetes or had treated hypertension with type 2 diabetes at baseline. They were randomised to treatment with candesartan 32 mg daily or placebo and followed for 4.6 years.

Results

A higher MA score at baseline predicted an increased risk of progression to CSME and/or PDR (hazard ratio [HR] per MA score 1.12, 95% confidence interval [CI] 1.03-1.21, p=0.006 in type 1; HR 1.21, 95% CI 1.07-1.36, p=0.003 in type 2), although the number of events was low (37 events in type 1, and 22 events in type 2 patients). Although fewer progression events were observed in patients treated with candesartan compared to placebo, this difference was not statistically significant (HR for candesartan 0.77, 95% CI 0.40-1.47, p=0.4 in type 1, and HR 0.72, 95% CI 0.30-1.70, p=0.4 in type 2).

Conclusions

Microaneurysm counts are valuable surrogate markers of retinopathy progression, and of particular importance when considering therapies aimed at very early stages of retinopathy.
DETERIORATION OF THE GLOMERULAR FILTRATION RATE AND HIGH VASCULAR ENDOTHELIAL GROWTH FACTOR LEVEL IN THE EYE SEEM TO BE MARKERS OF DIABETIC RETINOPATHY PROGRESSION AFTER CATARACT SURGERY

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INTRODUCTION. Prospective observation study for 12 months in humans. PURPOSE. To estimate the influence of vascular endothelial growth factor (VEGF) in aqueous humor (AH) and glomerular filtration rate (GFR) on diabetic retinopathy (DR) progression after cataract surgery. METHODS. There were 120 patients included in the study. They all had type 1 or 2 diabetes mellitus and underwent cataract surgery with phacoemulsification and intraocular lens implantation. All patients had a full ophthalmologic examination and glycosylation, glycated hemoglobin, and GFR were analyzed before surgery. At the start of the surgery, samples of AH were obtained to establish VEGF value (by enzyme-linked immunosorbent assay). Visual acuity (VA) was tested at the 5th day and at 12 months after surgery and neovascular complications such as neovascular glaucoma (NG) and proliferative DR were established in order to calculate relative risk.

RESULTS. Diabetic retinopathy was found to be more severe in patients with higher VEGF levels in AH. Patients with severe nonproliferative DR (NPDR) and proliferative DR had poor VA after operation than patients with mild NPDR, although before surgery VAs were not different. Patients with high VEGF level in the AH had 9.62-fold increased risk of DR progression (p=0.0004), had NG in 25% of the cases, and had lower VA at 12 months. The incidence of the NG in patients with GFR above 60 mL/min/1.73 m² was 3%; in patients with reduced GFR (below 60 mL/min/1.73 m²) it was 17%. Visual acuity at 12 months was similar in this groups. Reduced GFR was associated with 5.9-fold risk of NG progression after cataract surgery (p=0.009). There was no correlation between GFR and VEGF value in the AH.

CONCLUSIONS. Increased VEGF level in the AH and reduced GFR significantly enhanced the risk of NG development after cataract surgery in patients with diabetes.

RISK FACTORS FOR DIABETIC EYE COMPLICATIONS IN SHORT DURATION (1-10 YEARS) OF TYPE 1 DIABETES IN WARMIA AND MAZURY, POLAND

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INTRODUCTION. Prospective study. PURPOSE. To estimate the risk factors of diabetic eye disease in short duration (1-10 years) of type 1 diabetes mellitus (DM1) in the Warmia and Mazury region of Poland. METHODS. We report on 143 out of the 331 registered patients (69 female and 74 male) with 1-10 years DM1 duration registered in Olsztyn Diabetic Centre. After visual acuity and intraocular pressure were measured, complete detailed ophthalmic examination was carried out with fully dilated pupils in order to establish diabetes-related eye complications. Metabolic control was also determined: HbA1c, body mass index, blood pressure, renal function, and lipids were measured. Statistical analysis was carried out to find the relation between risk factors and eye complications.

RESULTS. Twenty-three patients (42 eyes) with diabetic eye complications were found (13 female and 10 male). The average age was 24 years and average DM1 duration was 6.9 years. The average age at onset of DM1 was 16.8. The following eye complications were observed: diabetic retinopathy (15 patients, 26 eyes), diabetic maculopathy (1 patient), cataract (7 patients, 13 eyes), and glaucoma (2 patients).

We found correlations between diabetic eye complications and DM1 duration as well as between the time of diabetes onset and puberty and eye complications. No relations between diabetic eye complications and metabolic control were observed.

CONCLUSIONS. We found that 15% of all patients with DM1 had diabetic eye complications. The most common eye complication was diabetic retinopathy. Risk factors for diabetic eye complications were DM1 duration and DM1 onset after puberty (≤13 years).

BLINDNESS AND FREQUENCY OF VITRECTOMY IN YOUNG DANISH TYPE 1 DIABETIC PATIENTS: A 15-YEAR FOLLOW-UP

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INTRODUCTION. Cohort study. PURPOSE. To investigate the prevalence of blindness and frequency of vitrectomy in a nationwide Danish cohort of young type 1 diabetic patients.

METHODS. In 1986-1989, a cohort of 80% of all Danish type 1 diabetic patients below the age of 18 (n=720) was identified. In 1995, 324 patients from the original cohort participated in a clinical examination including retinal photography. In 2010, patients registered as blind by the Danish Society for the Blind were identified. Furthermore, data from the Danish National Patient Registry were used to determine the number of patients who had undergone vitrectomy and the date of their first surgery. Results were correlated to age, gender, diabetes duration, and HbA1c.

RESULTS. Of the 324 patients examined in 1995, 6 have been registered as blind (4 male and 2 female); 5 were between 21 and 29 years of age at registration. They had all had vitrectomy performed and mean HbA1c in 1995 was 10.8%±1.3%. Thirty-seven patients (11%) have undergone vitrectomy. At the time of their first surgery, the mean age of patients was 29.5±4.9 years and the mean duration of DM was 22.7±4.9 years. The rate of male patients were significantly higher among the vitrectomized patients (65%) than among nonvitrectomized patients (53%, p<0.05). There was no difference according to age or duration of diabetes between the 2 groups. For the vitrectomized patients, mean HbA1c in 1995 was 11.1%±1.9% compared to the remaining patients (mean HbA1c 9.9%±6.8%, p<0.05).

CONCLUSIONS. One in 10 patients who had undergone vitrectomy in a 15-year follow-up of a population-based cohort of Danish type 1 diabetic patients. The mean age at the time of surgery was less than 30 years. Our results indicate that high levels of HbA1c in childhood and adolescence, as well as male gender, increase the risk of severe diabetic retinopathy, causing need for vitrectomy and blindness at a very young age.
threatening manifestations—proliferative diabetic retinopathy or diabetic maculopathy—but the background for developing either one or both of these complication types is unknown. The purpose of the present study was to identify clinical and epidemiologic parameters differentiating patients who develop either of the 2 vision-threatening complications.

**METHODS.** All 1430 patients with either type 1 diabetes mellitus (T1D) or type 2 diabetes mellitus (T2D) who had been treated with laser photocoagulation for diabetic maculopathy or proliferative diabetic retinopathy at the Department of Ophthalmology, Aarhus University Hospital, between 1997 and 2009 were included. The Danish National Patient Register was searched for all diagnoses registered at previous admission to hospitals and deaths in the country, and the Death Certificate Register at the Danish National Board of Health was reviewed to collect registered causes of death in these patients.

**RESULTS.** Patients with T2D had a significantly higher age at diagnosis of diabetes mellitus, age at first treatment, age at death, systolic blood pressure, and body mass index than patients with T1D, whereas HbA1c was higher in patients with T1D than in patients with T2D. Significantly more patients with T2D than with T1D had died and been hospitalized with cardiovascular diagnoses, the latter being more frequent in patients who had been treated for maculopathy than for proliferative diabetic retinopathy in T2D, whereas no relation to treatment type was found for T1D patients.

**CONCLUSIONS.** Cardiovascular disease and mortality is higher in T2D patients who develop diabetic maculopathy than in patients who develop proliferative diabetic retinopathy, whereas no relation to treatment type exists for T1D patients. These differences may help in understanding the mechanism of development of either of the 2 vision-threatening complications in diabetic retinopathy.

**SURVIVAL ANALYSIS OF DIABETIC PATIENTS UNDERGOING VITRECTOMY**

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**INTRODUCTION.** Retrospective review.

**PURPOSE.** Proliferative diabetic retinopathy is the most severe form of diabetic eye disease. We aimed to describe survival rates of patients with diabetes who had undergone vitrectomy in the past, to determine what clinical factors might be associated with their survival times and to compare these rates with those of diabetic patients who were being followed conservatively.

**METHODS.** Retrospective review of 87 diabetic patients who had vitrectomy in the past for either nonclearing vitreous hemorrhage or tractional retinal detachment compared to 145 patients with diabetes who did not require any vitrectomy in the past. Clinical factors investigated included hypertension, heart disease, neuropathy, and nephropathy.

**RESULTS.** The 3-year survival rate of patients requiring vitrectomy was 0.69±0.06 years compared to 0.91±0.02 in patients with conservative treatment. The 5-year death rate was 3 times greater in patients who required surgical management (0.51 vs 0.17). Coexistent cardiovascular disease in the same group was found to be associated with significantly lower survival rate (0.51±0.09, p<0.001).

**CONCLUSIONS.** Vitrectomy in patients with diabetes is an indicator of advanced generalized disease and associated with reduced life expectancy. Coexistent cardiovascular disease further decreases survival rates. Such patients require special attention in terms of their general condition.

**RETNAL GLIAL CELLS ACTIVATION IN DIABETIC PATIENTS WITH AND WITHOUT RETINOPATHY: AN IN VIVO STUDY**

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**INTRODUCTION.** Observational case series.

**PURPOSE.** To evaluate if retinal glial cells activation may be detected in vivo in eyes without and with nonproliferative diabetic retinopathy (NPDR).

**METHODS.** Eighty-eight subjects were enrolled: 58 subjects had diabetes mellitus and 30 normal subjects served as controls. Proliferative DR, previous laser photocoagulation, intraocular surgery or intravitreal injection, and refractive error >6 diopters were the main exclusion criteria. One eye of each subject was used for statistical analysis. Thirty patients had no DR; 28 patients had nonproliferative DR without macular edema (DR group). Full ophthalmic examination, stereoscopic fundus photography, and spectral domain optical coherence tomography (SD-OCT; RS-3000, Nidek, Japan) were performed in all eyes. After automatic segmentation (layering) of 5 retinal layers by SD-OCT, the thickness of these layers was automatically calculated in the foveal and pericentral area, and values compared among groups. The thickness of selected, more specific layers (inner limiting membrane, inner plexiform and nuclear layers, outer plexiform layer) was also manually quantified. All measurements were performed twice by 2 independent graders.

**RESULTS.** No statistically significant differences were found for age among all groups, and for diabetes duration among diabetic subjects. In the no DR and DR groups, using automatic layering, the mean thickness of inner retina was significantly reduced compared to controls (p<0.001), and no change was detected in the outer retina, both in the fovea and pericentral area. A significant increase of inner limiting membrane, inner plexiform, and nuclear layers was found in DR eyes vs controls (p<0.001), versus a significant decrease of retinal ganglion cell and retinal nerve fiber layers. Intergrader agreement was at least substantial for all measurements.

**CONCLUSIONS.** Increased thickness of retinal layers mainly corresponding to retinal glial cells, even before the appearance of clinically detectable retinopathy, confirms in vivo early glial cells activation in diabetic retina. Glial activation may be detected by SD-OCT using targeted analysis. These data strongly suggest a very early reactive and degenerative process both in neural and glial cells of diabetic retina.

**DIABETIC CHOROIDOPATHY: A SPECTRAL DOMAIN OCT STUDY**

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**INTRODUCTION.** Observational case series.

**PURPOSE.** To investigate if choroidal involvement (diabetic choroidopathy) may be observed in diabetic patients with and without diabetic retinopathy (DR) by spectral domain optical coherence tomography (SD-OCT).

**METHODS.** Eighty-seven subjects were enrolled: 59 diabetic patients (102 eyes) and 28 normal controls. Exclusion criteria were previously treated DR, refractive error higher than ±3 D, and treated or untreated glaucoma. All patients underwent full ophthalmic examination.
stereoscopic color fundus photography, and SD-OCT (RS-3000, Nidek, Japan). Spectral domain OCT was performed in the macula and peripapillary region. Spectral domain OCT examination consisted of linear scans, 6 mm in length, centered onto the fovea, and circle scan positioned around the optic disc (3.46 mm in diameter). Choroidal thickness was measured manually at the fovea, and at 1-, 2-, and 3-mm distance along all scans in the macula. Peripapillary choroidal thickness was measured at 8 points along the circle scan. All measurements were performed independently by 2 masked graders. Results. Mean age was not significantly different between diabetic patients and controls. In the macular area, choroidal thickness was significantly lower in the nasal quadrant vs all other quadrants (p<0.0001), in both groups. In the peripapillary area, choroidal thickness was significantly lower in the inferior quadrant vs all other quadrants (p<0.05), in both groups. Mean macular and peripapillary choroidal thickness progressively and significantly decreased with increasing level of DR (nonproliferative and proliferative DR vs controls, p<0.05). No significant choroidal thickness difference was found between controls and diabetic eyes without detectable DR. Diabetic macular edema did not influence choroidal thickness. Choroidal thickness in the macula and peripapillary area was highly correlated in diabetic patients (R=0.7, p<0.0001). Intergrader agreement was almost perfect for all measurements (k>0.9).

Conclusions. In diabetic patients, DR precedes diabetic choroidopathy. Diabetic choroidopathy starts when DR is already present and parallels development of diabetic maculopathy, exudates within 1 disc diameter of the foveal center, or clinically significant macular edema.

Prevalence of diabetic retinopathy and visual impairment in diabetic patients in sub-Saharan Africa
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Introduction. Cross-sectional study.

Purpose. There are little published data on the prevalence of diabetic retinopathy in sub-Saharan Africa. We report the prevalence of all grades of retinopathy and associations with systemic parameters in patients attending a secondary care diabetes clinic in Blantyre, Malawi.

Methods. Cross-sectional study of all patients attending for diabetes care. Clinical examination and biochemical testing comprised the following: visual acuity (VA), grade of retinopathy (slit-lamp biomicroscopy), microvascular complications, glycemic control, hypertension, HIV status, sight-threatening diabetic retinopathy (STDR): moderate proliferative retinopathy or worse, circinate maculopathy, exudates within 1 disc diameter of the foveal center, or clinically significant macular edema.

Results. In type 2 diabetes (n=249), prevalence (95% confidence interval) of any retinopathy, STDR, and proliferative diabetic retinopathy (PDR) was 32.5% (26.7–38.3), 19.7% (14.7–24.6), and 4.8% (2.2–7.5), respectively. Presence of STDR was associated with albuminuria (odds ratio [OR] 2.61; p=0.02), presence of neuropathy (OR 3.371; p=0.005), and insulin use (OR 5.296; p=0.0004), but not with HIV status. In type 1 diabetes (n= 32), prevalence of any retinopathy, STDR, and PDR was 28.1% (12.5–43.7), 18.8% (5.2–32.2), and 12.5% (1.0–24.0), respectively. A total of 12.1% of the study population had VA worse than 6/18 (20/60).

Conclusions. This study provides baseline information on prevalence of all grades of retinopathy and STDR in an urban/semi-urban diabetic population in sub-Saharan Africa. Prevalence of STDR was high and in type 2 diabetes was associated with albuminuria, neuropathy, and insulin use.

The impact of diabetes on the characteristics of type 2 macular telangiectasia
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Introduction. The Natural History Observation study of Type 2 Macular Telangiectasia (MacTel) has been running for 6 years now. It has been noted that a high proportion of patients with MacTel also have diabetes, but the impact of this on the characteristics of MacTel has not been evaluated before.

Purpose. The aim of this study was to analyze the impact of diabetes on the characteristics of MacTel.

Methods. Of 555 probands enrolled into the study, 188 had diabetes (96% type 2). All had color fundus, fluorescein angiographic, and optical coherence tomography images and these were graded on the Early Treatment Diabetic Retinopathy Study scale for severity of retinopathy and maculopathy. MacTel was graded for disease characteristics. Once grading was finalized, stage of MacTel and corresponding clinical data including visual acuity and diabetes control were analyzed.

Results. Patients with MacTel and diabetes had an average HbA1c of 6.9%±1.4%. Patients with diabetes who have early stages of MacTel had borderline significantly worse starting visual acuity than those without diabetes (stage 1: p=0.101; stage 2: p=0.06; stage 3: 0.114; no difference in stage 4-5 MacTel). After adjustment for duration of MacTel and staging, patients with uncontrolled diabetes had significantly lower visual acuity at baseline compared to probands with no history of diabetes, despite having no difference in the severity of diabetic retinopathy or maculopathy (no diabetes: 70.3±0.7 letters; diabetes controlled: 66.4±1.3 [p=0.008]; diabetes uncontrolled: 65.1±1.6 [p=0.02]). During the up to 5-year follow-up, only one patient developed treatable maculopathy and none developed proliferative diabetic retinopathy.

Conclusions. The relationship between MacTel and diabetes mellitus appears intricate. Diabetes seems to have a clinically meaningful impact on visual acuity and progression of MacTel, especially in early stages of the disease. On the other hand, patients with MacTel and diabetes do not seem to develop treatable diabetic retinopathy or maculopathy at the same rate as the general diabetic population. Further investigations are necessary for developing an optimal management strategy to preserve the vision of these patients.

Filtering normal diabetic retinopathy images through evolutionary computation
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Introduction. In the UK diabetic retinopathy (DR) screening program, about two-thirds of images are normal. On average, graders take about 1.5 times longer to decide an image as normal. An automated system has been developed for filtering normal cases. This system
first permitted understanding of DR images through image samples collected from various sources. The system was then tested on a new set of data, 1680 images from 420 patients, which has a clinical grading, and a grading by Reading Centre at Moorfields Eye Hospital, UK.

**PURPOSE.** To evaluate an automated DR image analysis system as a possible aid to a more productive screening service.

**METHODS.** To address the complicated variability and subtlety in DR images, an integrated approach was developed to combine detection evidence from various processing stages; a contextual environment each time a clinical sign may appear was dynamically captured through a context model. The system first detected the basic clinical signs such as exudates, microaneurysms (MA), hemorrhage, and anatomic structure, e.g., optic disc, macula, and blood vessels, using various image processing techniques followed by a reasoning process. For each above content, multiple classifiers were implemented. For example, for MA alone, there were 180 classifiers. This is to address the variability in DR images. The multiple classifiers were then optimized through genetic algorithms to obtain the best set of classifiers. Statistical modeling method, Hidden Markov Models, were then utilized to recognize contextual relationships among the candidate regions. The Hidden Markov Models were also optimized through evolutionary algorithms to obtain the best representation of the context.

**RESULTS.** The system was tested on 1680 previously unseen images taken from 420 patients. The sensitivity was 95% and the specificity was 98%. Among all the images that the system decided were normal, 99% were true normal according to the double manual grading results. **CONCLUSIONS.** The current automated system seems to be able to filter out the majority of normal images with good accuracy. This result provides a better understanding into the potential of utilizing evolutionary computation to maximize detection accuracy.

**HOW ACCURATE ARE PHOTOGRAPHIC SURROGATE MARKERS USED TO DETECT MACULAR EDEMA IN THE ENGLISH NATIONAL SCREENING PROGRAM?**

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**INTRODUCTION.** Retrospective analysis.

**PURPOSE.** Macular edema is not directly visible on 2-dimensional digital photographs, such that surrogate markers need to be used. In the English national screening program, these are exudate within 1 optic disc diameter (DD) of the fovea, group of exudates within 2 DD of the fovea, and hemorrhages or microaneurysms (HMA) within 1 DD of the fovea with best-corrected visual acuity (VA) worse than 6/9. All patients who present with any of these surrogate markers at screening are referred for an ophthalmologic slit-lamp examination.

**METHODS.** Data were collected from patients attending digital diabetic retinopathy screening. Patients who presented with surrogate markers for macular edema also had an OCT scan. The fast macula scan on the Stratus OCT was used and an ophthalmologist reviewed the scans to determine whether macular edema was present.

**RESULTS.** Maculopathy by exudates: of 155 patients, 45 (29%) showed thickening on the OCT; of these, 12 required laser. Those who also had pre-proliferative retinopathy (n=20) were more likely to have macular edema (75%) than those with background diabetic retinopathy. Maculopathy by HMA and VA worse than 6/9: Of 66 patients, 11 (16.7%) showed thickening on the OCT: 5 (7.6%) of these had macular edema, 5 (7.6%) epiretinal membrane, and 1 (1.5%) age-related macular degeneration. None of these patients required laser.

**CONCLUSIONS.** The likelihood of the presence of macular edema and requiring laser treatment is greater with macular exudation than HMA within 1 DD and reduced VA. Overall, the surrogate markers used show low specificity for macular edema; however, combining OCT with photography identifies those with macular edema who require a true referral for an ophthalmologic slit-lamp examination.

**PROLIFERATIVE DIABETIC RETINOPATHY (R3) REFERRALS FROM THE DIGITAL DIABETIC RETINOPATHY SCREENING PROGRAM: URGENCY OF APPOINTMENT IN THE HOSPITAL EYE SERVICE ACHIEVED AND NEEDED?**

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**INTRODUCTION.** Retrospective analysis.

**PURPOSE.** To assess the clinical characteristics and outcomes of patients identified with proliferative diabetic retinopathy (PDR) referred from the screening program to the hospital eye services (HES).

**METHODS.** This was a retrospective analysis of urgently referred RDR cases to Birmingham Heartlands HES from August 2008 until July 2010.

**RESULTS.** A total of 130 urgent diabetic retinopathy referrals were made and reviewed. A total of 103 (68% male, 80% type 2 diabetes) were referred for PDR with a mean age of 59 years and a mean diabetes duration of 17.8 years. A total of 69% were on insulin treatment at the time of the screening, with mean HbA1c of 10.4% (range 5.7%-16.5%). A total of 65% of the patients were offered appointments at HES within 2 weeks after referral from the screening. A total of 50.5% of the patients were seen in the HES within 2 weeks; 22% and 16% were seen 2-4 and 4-8 weeks after referral, respectively. Six patients never attended ophthalmology examination during the 2 years of review. Of all the attendees, 56% were booked for panretinal photocoagulation (PRP) and 9 (9.3%) for macular laser, respectively, on their first HES visit. A total of 75% of the patients who had newly diagnosed PDR and 26 had previous PRP laser but were lost to follow-up. A total of 63 patients (66%) received either PRP or macular laser treatment (85.7% of which is PRP). A total of 63% of the PRP treatment was performed within a month of first HES attendance. Retinopathy grading discrepancy between the screening program and HES was noted in 20% (21 patients).

**CONCLUSIONS.** These data suggest that the digital screening program is appropriately identifying high-risk patients with PDR with timely PRP laser treatment in the majority of patients but raises concern over patients lost to follow-up (hence fail-safe tracking of appointment attendance), and review of grading discrepancies between the ophthalmology and screening service.

Poster Session

A NEW SYSTEM FOR SCREENING OF DIABETIC RETINOPATHY IN THE INSTITUTE FOR CLINICAL AND EXPERIMENTAL MEDICINE (IKEM)
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INTRODUCTION. Prospective study.
PURPOSE. The constantly increasing number of patients with diabetes attending the Ophthalmologic Outpatient Department of the Institute for Clinical and Experimental Medicine for specialized treatment required that the Center of Diabetology create a sophisticated structure for screening and evaluation of the eye disease of these patients.
METHODS. The system is based on the complex information system called ZLATOKOP (Gold-miner), which contains patients' data and results of performed examinations. It is conceived as a gateway created first for the needs of clinical employees of IKEM—i.e., doctors and nurses. Its basic function is to make accessible as much as possible clinical data accumulated in various information systems in IKEM and facilitating their search in a unified user environment. ZLATOKOP successfully solved the problem of accessing information coming from various hardware platforms and different server databases (Informix, Sybase, Caché, Microsoft SQL, PACS, and DICOM).
RESULTS. A trained nurse photographs the fundus of the eye of the diabetic patient using a non-mydriatic camera and sends the photographs via the software DICOM-PACS. Photographs are automatically adjusted to the highest quality. The evaluating physician obtains the photographs in the computer together with the preconfigured evaluating parameters: type of DM, duration of disease, treatment, level of glycosylated hemoglobin, presence of hypertension, dyslipidemia, nephropathy, neuropathy, diabetic legs, and family occurrence of DM. Certain parameters are automatically copied after opening of the respective window; others which have to be manually imported are accessible after opening the record of the diabetic patient. Windows with the list of performed examinations for automatic transfer to the insurance company are separate. Evaluation of diabetic retinopathy is followed by the possibility to use predefined texts together with the recommendations. The follow-up examination is planned according to the diagnostic conclusion.
CONCLUSIONS. The system is easy, fast, user-friendly, and fulfills all requirements for complex examination of the diabetic patient. It brought considerable speed up of the workload, improving quality and coherency of documentation. In addition, it enables the statistical evaluation of data.

CHANGES IN VASCULAR DIAMETER AFTER LASER TREATMENT IN PATIENTS WITH DIABETIC MACULAR EDEMA
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INTRODUCTION. Retrospective study.
PURPOSE. To examine the change in retinal vessel diameter after photocoagulation treatment for clinically significant macular edema (CSME).

METHODS. Thirty-five diabetic patients with CSME were identified from a photographic screening clinic. Patients had digital retinal photographs (Topcon TRC-NW8S) taken less than 3 months before and 2-8 months after focal/grid retinal photocoagulation treatment. The semi-automatic computer program IVAN was used to identify and measure all vessels within an area of 1/2 to 1 disc diameter from the optic disc. The grader then manually chopped the vessels and distinguished arteries from veins. The program then measured the diameters of the 6 largest arteries and veins and summarized these into the central retinal arteriolar (CRAE) and venular (CRVE) equivalent. Data analysis was performed using paired t test.
RESULTS. Two patients were excluded as not all vessels were identifiable. For the remaining 33 patients (24 male and 9 female), median age was 59.3 years (range 34.3-82.6 years). Overall, for the treated eyes there was no difference in CRAE or CRVE before or after treatment (183.3 µm vs 140.8 µm, and 221.5 µm vs 217.3 µm, respectively). However, in men there was a significant decrease in CRVE after treatment (223.9 µm before vs 218.0µm after, p=0.03), but no change in CRAE. Retinal diameters did not change before and after treatment among women. CONCLUSIONS. Retinal photocoagulation for CSME was associated with venular narrowing among diabetic men but not women. In contrast, the diameters of the retinal arteries were not affected by the treatment. These results expand the knowledge of retinal vessel dynamics as a response to focal/grid laser photocoagulation. For future studies, vascular caliber analysis specific to the macular area should be performed in order to detect if the vascular response of the macular area differs from the rest of the retina.
NO DIFFERENCE IN PREVALENCE OF RETINAL VEIN OCCLUSIONS BETWEEN DIABETIC AND NONDIABETIC PARTICIPANTS IN THE TROMSO EYE STUDY

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INTRODUCTION. Cross-sectional study.

PURPOSE. To determine the prevalence of retinal vein occlusions in a general population and evaluate the association between retinal vein occlusions and diabetes.

METHODS. The Tromso Study is a repeated multipurpose population-based study conducted in the municipality of Tromso, Norway. The Tromso Eye Study is a substudy of the Tromso Study and from October 2007 to December 2008 retinal photography was performed on 6542 participants aged 38-87. All photographs were graded for central and branch retinal vein occlusions (BRVO/CRVO) by one single grader and masked for all other variables except for visual acuity, self-reported cataract, glaucoma, and age-related macular degeneration.

RESULTS. A total of 6426 participants with at least one gradable eye were included in the analysis. Signs of CRVO were found in a total of 85 participants. The prevalence of BRVO was 1.3% (95% confidence interval [CI] 1.0-1.6) in participants without diabetes and 1.7% (95% CI 0.7-3.5) in participants with diabetes. This difference was not statistically significant with a risk ratio of 1.31 (95% CI 0.64-2.68) between diabetic and nondiabetic patients. Signs of CRVO were found in a total of 9 participants and none of them had diabetes.

CONCLUSIONS. We found no difference in the prevalence of BRVO in participants with and without diabetes.

BRITISH OPHTHALMIC SURVEILLANCE UNIT STUDY OF PROGRESSION TO SIGHT-THREATENING RETINOPATHY IN PREGNANCY

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INTRODUCTION. British Ophthalmic Surveillance Unit (BOSU) is a facility to enable ophthalmologists to participate in the nationwide surveillance of uncommon ophthalmologic conditions. It relies upon a monthly response from consultant and associate specialist ophthalmologists in the United Kingdom about new cases of the particular condition under investigation. Reporting cards are forwarded to the investigators. Follow-up is via questionnaires to assess demographics and baseline findings, and with a subsequent questionnaire to assess clinical outcomes.

PURPOSE. To determine the number of cases occurring per year in the United Kingdom of progression to sight-threatening retinopathy (STDR) in pregnancy and the postpartum period and to describe associated clinical features and outcomes.

METHODS. Cases of proliferative retinopathy and/or clinically significant macular edema occurring in pregnancy and postpartum were identified over a 2-year period using the BOSU reporting system.

RESULTS. Pregnancy has previously been associated with progression to STDR. Ninety-seven cases were identified. The mean age was 29 years. Initial and follow-up questionnaires were received for 49 cases. A total of 34 were bilateral and 15 were unilateral. A total of 58 eyes had proliferative retinopathy only, 9 had CSMO only, and 16 had both. A total of 47 eyes underwent PRP in pregnancy, 17 macular laser, and 7 underwent vitrectomy. A total of 45% of patients were reported to have experienced a loss of vision. In 10% of eyes vision of 2 lines or more was lost. Vision loss was not significantly associated with parity, duration of diabetes, smoking, hypertension, or pre-eclampsia. As a group, there was a significant reduction in Hba1c between pre-pregnancy levels and first-trimester levels. Causes of vision loss included macular pathology, vitreous hemorrhage, and tractional retinal detachment.

CONCLUSIONS. Progression to sight-threatening DR in pregnancy is an uncommon condition but may be associated with loss of vision. Affected women show a significant reduction in Hba1c in the first trimester.
CONCLUSIONS. Annual diabetic retinopathy screening provides opportunistic identification of asymptomatic cholesterol emboli and provides an opportunity for review of medical management in the high-risk patient group with appropriate identification and referral for carotid stenosis surgery. A total of 11 patients were identified with suboptimal cardiovascular risk management: e.g., statin use.

DO LONG CHAIN POLYUNSATURATED FATTY ACIDS PROTECT AGAINST DIABETIC RETINOPATHY?
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INTRODUCTION. Case history and epidemiologic study.
PURPOSE. To elucidate whether long chain polyunsaturated fatty acids (PUFA) protect against diabetic retinopathy.
METHODS. Fifty-six patients with insulin-dependent diabetes mellitus (IDDM) and 432 patients with non-insulin-dependent diabetes mellitus (NIDDM) were monitored regularly in ophthalmologic practice on the Norwegian west coast. In the IDDM group, the median duration was 11 years (range 1-42), and median age was 45. Hemoglobin A1C levels were known by the patients in 92%. One-third took antihypertensive medication and statins and 50% omega-3 supply on a regular basis. They had on average 2 warm fish dinners and 2.5 lunch meals with fish per week. In the NIDDM group, the median duration was 7 years (range 1-50), and median age was 65. Seventy-seven percent knew their Hba1C level. Two-thirds took antihypertensive medication and statins and 55% omega-3 supply on a regular basis. They had on average 1.9 warm and 2.7 cold fish meals per week.
RESULTS. A 64-year-old man, after 12 years with NIDDM, showed intraretinal microvascular abnormalities (IRMA) in his left retina. After starting with 500 mg omega-3 a day for 6 months, IRMA disappeared for at least 3 years, verified with fluorescein angiography. Forty-one percent had diabetic retinopathy (DR) in the IDDM group: 10.7% of these had proliferative retinopathy (PDR) and 12.5% diabetic macular edema (DME) and were laser treated. All had visual acuity (VA) at or better than 0.5 in the best eye. In the NIDDM group, 19.7% had DR, 3% PDR, and 4.4% DME. Four patients (1.4%) had VA below 0.3, none of them due to DR. Ninety-eight percent had VA at or above 0.5 in the best eye.
CONCLUSIONS. Daily normal level intake of PUFAs does not accelerate the development of diabetic microangiopathy. Recent animal model investigations and the epidemicologic findings of low prevalence of DR and diabetic blindness in the present patients with a high daily intake of fish and fish oils compared to other reported cohorts supports the theory that PUFAs may protect against the progression of diabetic microangiopathy including retinopathy.

DIABETIC RETINOPATHY PREVALENCE IN PATIENTS WITH SHORT DURATION (1-10 YEARS) OF TYPE 1 DIABETES IN WARMA AND MAZURY, POLAND
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INTRODUCTION. Prospective study.
PURPOSE. To estimate diabetic retinopathy (DR) prevalence in patients with short duration (1-10 years) of type 1 diabetes mellitus (DM1) and to check the clinical usefulness of color fundus photography as a method applied in DR screening in our clinic. The main outcome was presence and severity of DR.
METHODS. There are 331 patients with DM1 (155 female and 176 male) on the register in our region. Of these, 143 patients (69 female and 74 male) had short duration of DM1 (1-10 years). Out of this cohort, 125 had DR screening photographs taken during the last 6 months. At their clinic visit, they had HbA1c, body mass index, blood pressure, renal function, and lipids measured first. Then, they all had complete eye examination with fully dilated pupils following visual acuity and intraocular pressure measurements. Finally, 2-field color fundus images of both eyes (one centered on the optic disc and one of the macula) were taken.
RESULTS. Of the 125 patients with color eye fundus photographs, there were 13 patients with DR. On clinical examination, 15 patients were found to have DR. There was an additional patient who had DR (0.7%). We also found that imaging was not possible in small children and these patients needed to be seen in the eye clinic without photography. A further 7 patients had cataracts (4.9%) and 2 patients were found to have glaucoma (1.4%).
CONCLUSIONS. Overall, 15% of this cohort of DM1 patients had diabetic eye complications. Colour fundus photography proved to be a useful, simple, and inexpensive method for DR screening when used by a trained professional. In some cases, however, clinical examination in addition to or instead of photography is essential.

EVALUATION OF THE EFFECTIVENESS OF SURGICAL TREATMENT OF IDIOPATHIC MACULAR HOLES USING OPTICAL COHERENCE TOMOGRAPHY
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INTRODUCTION. Retrospective study.
PURPOSE. To evaluate the effectiveness of surgical treatment of idiopathic macular holes rated as morphologic closure in optical coherence tomography.
METHODS. We studied 25 eyes of 25 patients in whom surgical therapy, involving removal of the internal limiting membrane (ILM) with air tamponade of the retina, was applied to treat idiopathic macular hole. Efficacy was evaluated by comparing the retina morphology in the macula in optical coherence tomography before surgery, and then 2 weeks, 1 month, and 3 months after surgery. Retinal morphology was related to the best-corrected visual acuity before and after surgery. RESULTS. In 9 eyes, there was morphologic closure of idiopathic macular hole after surgery, which was confirmed by optical coherence tomography examination. In 17 eyes, there was average improvement of 2.3 Snellen lines in best-corrected visual acuity for distance.
CONCLUSIONS. Removal of the ILM with air tamponade of the retina is an effective treatment for idiopathic macular holes.

POSTERIOR VITRECTOMY IN THE OPHTHALMOLOGY UNIT OF GENERAL DISTRICT HOSPITAL IN OLSZTYN, POLAND
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INTRODUCTION. Retrospective study.
PURPOSE. To estimate the indications and number of procedures of posterior vitrectomy in our unit.
METHODS. Posterior vitrectomy via pars plana was performed using the
newly acquired Accurus (Alcon) vitrectomy apparatus and 20-G, 23-
G, and 25-G probes. For endotamponade we applied SF6 and silicone oil (1000 cs and 5000 cs).

RESULTS. In the time period from January 28, 2010, to December 31, 2010, 57 procedures were performed. The indications for vitrectomy were as follows: retinal detachment (36 cases), complications of cataract surgery (7 cases), severe eye globe trauma (4 cases), diabetic eye complications (3 cases), and vitreoretinal traction syndrome (1 case). Early postoperative complications such as prolonged inflammations (3 cases), hemorrhage into the vitreal cavity (3 cases), and secondary glaucoma (2 cases) were observed. Late postoperative complications occurred in 10 cases, these were recurrent retina detachments due to severe proliferative vitreoretinopathy.

CONCLUSIONS. Vitrectomy is a complicated and expensive procedure, but it offers a chance to save vision in very severe cases. In spite of early and late complications, this procedure is worth trying.

PREVALENCE AND INCIDENCE OF DIABETIC MACULAR EDEMA IN THE PEDIATRIC POPULATION
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INTRODUCTION. Retrospective pooled analysis.

PURPOSE. Currently, there are limited data regarding the prevalence and incidence of diabetic macular edema (DME) in the pediatric population. The present study was undertaken to develop estimates of these parameters based on the best available evidence.

METHODS. A literature search was performed using the Medline database (PubMed) with the key words DME, prevalence, incidence, population-based, cross-sectional studies, and epidemiology. The incidence and prevalence of DME in a general pediatric population (≤18 years old) was not available. There were, however, very limited data on the incidence and prevalence of DME in pediatric diabetic populations. An estimate of the incidence of diabetes in general pediatric populations was calculated using information from the Wisconsin Epidemiologic Study of Diabetic Retinopathy and the Iceland (International Diabetes Federation) population.

RESULTS. To estimate the incidence, the most current incidence of diabetes for Caucasians younger than 20 years in the United States (26.1 per 100,000 persons per year) and the most current incidence of type 1 diabetes for individuals younger than 15 years in Iceland (14.7 per 100,000 persons per year) were multiplied by the respective incidence of DME in young adult populations in Wisconsin and Iceland. The estimated incidence of DME in general pediatric populations is 0.30 per 100,000 persons per year in Wisconsin and 0.13 per 100,000 persons per year in Iceland.

CONCLUSIONS. The incidence of DME in a general pediatric population may vary depending on ethnic background and geographic locations. The incidence of DME in a pediatric population is likely less than 1 per 100,000 persons per year. In view of this, DME seems to occur almost exclusively in adult populations.