MINIREVIEWS

Diabetic retinopathy - ocular complications of diabetes mellitus

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Abstract

In industrialized nations diabetic retinopathy is the most frequent microvascular complication of diabetes mellitus and the most common cause of blindness in the working-age population. In the next 15 years, the number of patients suffering from diabetes mellitus is expected to increase significantly. By the year 2030, about 440 million people in the age-group 20-79 years are estimated to be suffering from diabetes mellitus worldwide (prevalence 7.7%), while in 2010 there were 285 million people with diabetes mellitus (prevalence 6.4%). This accounts for an increase in patients with diabetes in industrialized nations by 20% and in developing countries by 69% until the year 2030. Due to the expected rise in diabetic patients, the need for ophthalmic care of patients (*i.e.*, exams and treatments) will also increase and represents a challenge for eye-care providers. Development of optimized screening programs, which respect available resources of the ophthalmic infrastructure, will become even more important. Main reasons for loss of vision in patients with diabetes mellitus are diabetic macular edema and proliferative diabetic retinopathy. Incidence or progression of these potentially blinding complications can be greatly reduced by adequate control of blood glucose and blood pressure levels. Additionally, regular ophthalmic exams are mandatory for detecting ocular complications and initiating treatments such as laser photocoagulation in case of clinical significant diabetic macular edema or early proliferative diabetic retinopathy. In this way, the risk of blindness can considerably be reduced. In advanced stages of diabetic retinopathy, pars-plana vitrectomy is performed to treat vitreous hemorrhage and tractional retinal detachment. In recent years, the advent of intravitreal medication has improved therapeutic options for patients with advanced diabetic macular edema.

Key words: Laser photocoagulation; Diabetic macular edema; Diabetic retinopathy; Intravitreal injection; Prevention

Core tip: Diabetic retinopathy is a potentially blinding complication of diabetes mellitus. In patients with diabetes, regular retinal exams are essential. While laser photocoagulation is effective, if performed in time, advanced stages of diabetic retinopathy need to be treated by vitreo-retinal surgery and have limited visual prognosis. Even though new therapeutic options such as intravitreal medical therapy and sutureless pars-plana vitrectomy have improved ophthalmic care of patients

with diabetes, interdisciplinary care of these patients is essential. Good metabolic and blood pressure control is indispensable for reducing the risk of ophthalmic complications.

INTRODUCTION

Diabetic retinopathy is a potentially blinding complication of diabetes mellitus. Reasons for loss of vision are diabetic maculopathy and complications of proliferative diabetic retinopathy (PDR) such as vitreous hemorrhage, tractional retinal detachment, and neovascular glaucoma. By 2030 developing countries will face an increase by 69% and industrialized countries by 20% of the number of patients with diabetes compared to 2010[1]. For Africa more than 18 million, according to some estimations even 24 million, diabetic patients are predicted for the year 2030[1,2].

Probability of retinal complications increases with increasing duration of disease. In up to 50% of patients with type 1 diabetes and 30% of those with type 2 diabetes potentially vision-threatening retinal changes develop over time, while early retinal changes are not noticed by the patients[3].

Diabetic retinopathy is the most common microvascular complication of diabetes mellitus and affects between 3%-4% of people in Europe, while the relative risk for developing diabetic retinopathy is higher in type 1 diabetes compared to type 2[4-6]. Diabetes mellitus is responsible for about 15% of all cases of legal blindness (best corrected visual acuity less than 0.02) in Germany[7]. It is the main cause of blindness within the working-age population in industrialized nations[4].

While retinal changes are rarely seen in patients with type 1 diabetes before adolescence, about one third of patients have signs of diabetic retinopathy at time of initial diagnosis of diabetes mellitus. The risk of PDR is higher in type 1 diabetes than in type 2, while diabetic macular edema is more commonly found in type 2 diabetes (prevalence after 15 years of disease: type 1 *vs* type 2 = 15% *vs* 25%)[8].

Kramer *et al*[9] reported in a recent study, that in patients with type 1 diabetes progression of diabetic retinopathy and development of nephropathy each increase the risk for incidence of the other. This association was independent of established risk factors for microvascular complications and the authors suggested a shared etiologic basis of these two complications of diabetes mellitus[9]. Another group also found proliferative diabetic retinopathy to be an independent marker of long-term nephropathy in patients with type 1 diabetes[10].

Other studies indicated association of the presence of diabetic retinopathy and increased overall-mortality and cardiovascular events both in type 1 and type 2 diabetes[11].

Therefore an interdisciplinary approach of physicians, endocrinologists, and ophthalmologists is needed for optimal care.

PATHOGENESIS OF DIABETIC RETINOPATHY

Micro-angiopathy due to hyperglycemia in patients with diabetes mellitus results in vascular leakage, which causes diabetic macular edema on one hand, and capillary occlusion on the other hand. Capillary occlusion then again causes retinal ischemia and increased levels of vascular endothelial growth factor (VEGF) which are responsible for the development of neovascularization and the proliferative stage of diabetic retinopathy.

More recently new pathways which may be involved in the pathogenesis of diabetic retinopathy have been identified, such as inflammation, nerve growth factor autophagy and epigenetics. A detailed discussion of all these pathways would go beyond the scope of this mini-review about clinical aspects of diabetic retinopathy, however some aspects should be addressed.

Biochemical alterations such as oxidative stress, activation of protein kinase C and formation of advanced glycation end products have been detected as a response of the retina to hyperglycemia[12]. Also kinin B1 and B2 are thought to increase vascular permeability, infiltration of leukocytes and inflammation. Especially kinin B1, which is almost non-existent in normal tissue, is upregulated in the retina of diabetic patients. These findings may be important for developing new therapeutic strategies aiming at antagonizing kinin receptors or at inhibiting kallikreins[13].

Recent investigations showed that the whole retinal neurovascular system is impaired by diabetes mellitus resulting in loss of neurovascular coupling, neurodegeneration and neuroinflammation, which can be detected even before the advent of vascular damage[14]. Clinically, reduced dark adaption, impaired colour and/or contrast vision and visual field defects are found during functional examinations of diabetic patients[15].

Diabetic retinopathy tends to deteriorate during hormonal changes such as adolescence and pregnancy[16].

CLASSIFICATION AND PATHOPYSIOLOGY OF DIABETIC RETINOPATHY

During fundoscopy, which should be performed after dilation of the pupil (mydriasis) to allow visualization of the entire retina, presence and grade of diabetic retinopathy can be assessed clinically. Typical changes seen in early diabetic retinopathy (non-PDR) are micro-

Figure 1 Non-proliferative diabetic retinopathy. Wide-field fundus photo of a 65-year-old female patient (right eye) showing several retinal hemorrhages.

Figure 2 Non-proliferative diabetic retinopathy. Color fundus photo of a 51-year-old male patient with micro-aneurysms and lipid exudates.

Figure 3 Proliferative diabetic retinopathy with neovascularization at disk.
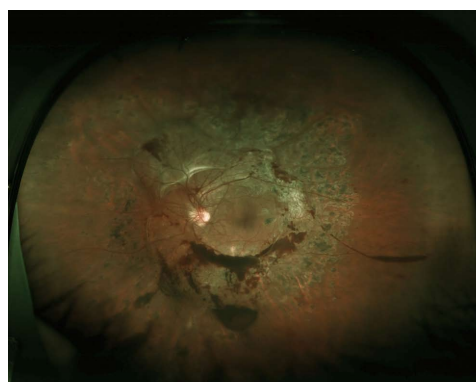

Figure 4 Advanced proliferative diabetic retinopathy with neovascularization and limited vitreous hemorrhage.
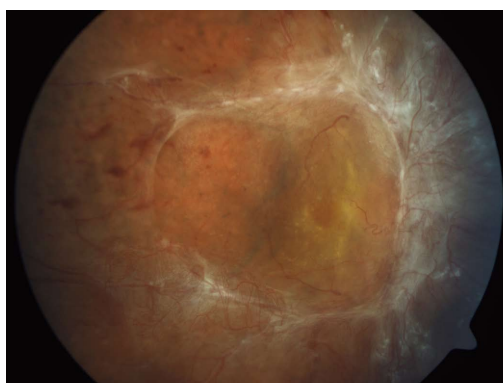

Figure 5 Advanced proliferative diabetic retinopathy with tractional retinal detachment.

aneurysms, retinal hemorrhages, and exudates (Figure 1). In the beginning, these alterations are often found slightly temporal to the central area of the macula (Figure 2). These are caused by deranged vascular integrity and loss of pericytes. In the later course of disease, intra-retinal micro-vascular anomalies may develop, which represent dilated and therefore during fundoscopy visible retinal capillaries, and indicate possible risk of neovascularization and proliferative diabetic retinopathy.

Proliferative diabetic retinopathy is caused by increased intraocular VEGF-levels due to retinal ischemia because of capillary occlusion of retinal vessels. Proliferation may

grow at the optic disc (neovascularization at the disk) or elsewhere in the retina (neovascularization elsewhere) into the vitreous (Figure 3). These newly formed vessels leak on fluorescein angiography and may cause vitreous hemorrhage and finally tractional retinal detachment (Figures 4 and 5). Tractional retinal detachment results in separation of the neurosensory retina from the retinal pigment epithelium. Detached sections of the retina cause relative visual-field defects (scotoma) and loss of visual acuity in cases with macular involvement.

Further, neovascularization on the iris in the anterior segment of the eye may evolve as anterior segment sequel of ischemia (Figure 6). These new blood vessels grow towards the anterior chamber angle and may obstruct the trabecular meshwork, thus increasing outflow resistance of aqueous humor. This results in increased intraocular pressure followed by optic atrophy (neovascular glaucoma).

CLASSIFICATION AND PATHOPHYSIOLOGY OF DIABETIC MACULOPATHY

Diabetic maculopathy may develop in the non-proliferative and in the proliferative stage of diabetic retinopathy. While complications of untreated proliferative diabetic

Table 1 Types of diabetic maculopathy[19]

|	
Focal	Localized edema
	Lipid exudates
	Intraretinal hemorrhages
	Focal hyperfluorescence in late fluorescein angiography
Clinically significant without foveal thickening (non-center-involving) (sight-threatening)	Edema within 500 μm around the foveola
	Exudates within 500 μm around the foveola accompanied by edema
	Edema ≥ 1 optic-disk diameter within one optic-disk diameter around the foveola
Clinically significant with foveal thickening (center-involving)	Ill-defined edema, which may be cystoid
	Exudates
	Intraretinal hemorrhages
	Origin of leakage often not clearly identifiable by fluorescein angiography
Tractional	Due to vitreous traction to the fovea
	Thickened posterior hyaloid membrane
	OCT visualizes vitreal traction
Ischemic maculopathy (occlusion of the perifoveal capillaries)	Loss of vision without any clearly visible cause on fundoscopy
	Fluorescein angiography needed for diagnosis
	Difficult to diagnose by fundoscopy only
	Edema may be present or absent

OCT: Optical coherence tomography.
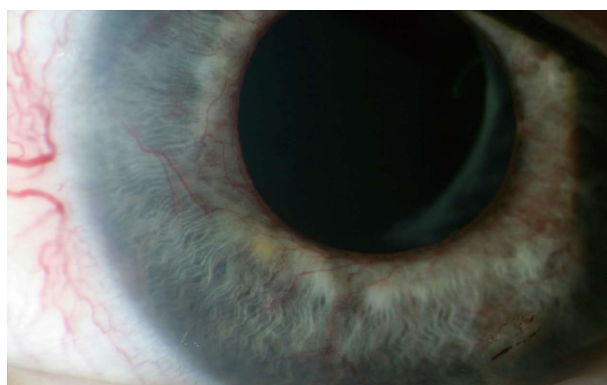
Figure 6 Neovascularization of the iris. These neovascular vessels may block the trabecular meshwork and cause neovascular glaucoma.

retinopathy, such as vitreous hemorrhage and tractional retinal detachment involving the macula may cause the most severe loss of vision in diabetic retinopathy, diabetic maculopathy is the main cause of visual impairment in patients with type 2 diabetes[17].

Diabetic macular edema is caused by a disruption of the inner blood-retinal barrier, formed by the retinal vascular endothelium, due to hyperglycemia, increased levels of growth-factors, inflammation and cytokines. This also causes impairment of pericytes and leads to consecutive exudation of fluid, proteins and lipids by para cellular and trans cellular transport mechanisms[18]. Clinically, areas of thickened retina are often demarcated by surrounding yellowish lipid exudates (Figure 7). Diabetic macular edema may be limited or affect a large retinal area and it may also involve the macula (center-involving) or spare the central area (non-center-involving) (Figure 8).

Traction caused by vitreous attachment to the fovea may result in macular thickening, as well. Vitreous traction can excellently be documented by high-resolution optical coherence tomography (OCT, spectral-domain OCT). Vitrectomy is needed in patients with symptomatic tractional macular edema in order to release traction by surgical removal of the vitreous.

Apart from edema, diabetic maculopathy may also present as occlusion of perifoveal capillaries resulting in distinct visual impairment in the absence of edema on fundoscopy. In these cases, fluorescein angiography is needed to confirm the diagnosis by visualizing capillary occlusion in around the fovea.

Table 1 summarizes the different types of diabetic maculopathy (adapted from Nentwich *et al*[19]).

CLINICAL DIAGNOSICS

Dilated fundoscopy is the most important clinical investigation in patients with diabetes during screening examinations by an ophthalmologist. Dilation of the pupil is necessary in order to enable a proper stereoscopic view, which is needed for evaluation of macular edema, and to allow visualization of the peripheral retina.

Fluorescein angiography was introduced by Novotny *et al*[20] in the 1960s into the clinical ophthalmic practice and allows evaluation of the retinal vascular status. Fluorescein, a fluorescent dye, is injected intravenously and distributes throughout the body. In the eye, fluorescence is activated by blue light of 490 nm. During fluorescein angiography vascular leakage, capillary occlusion, ischemic areas of the retina and neovascularization can be seen (Figure 9A and C). It provides information on the area of leakage as well as of the location of non-perfused parts of the retina. In patients with suspected diabetic maculopathy, fluorescein angiography is mandatory for excluding ischemic maculopathy and guiding possible focal laser photocoagulation.

Wide-field fundus photography (2-laser wavelength nonmydriatic 200° ultra-wide-field scanning laser ophthalmoscopy) has been introduced recently. Wide-field images and traditional color fundus photography
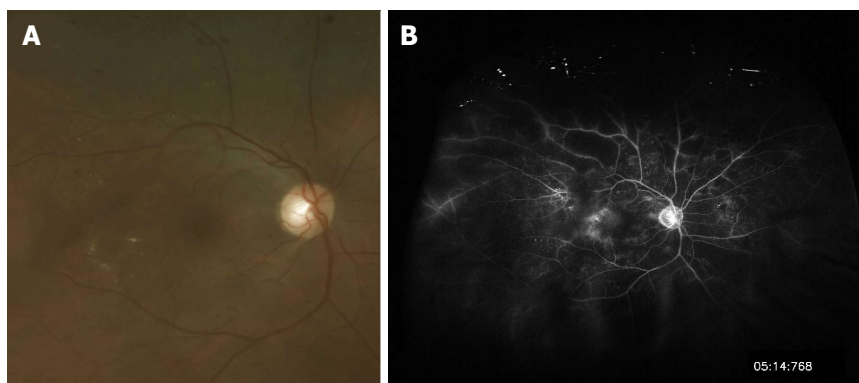
Figure 7 Clinically significant diabetic macular edema without involvement of the fovea. A: Fundus photo; B: Fluorescein angiogram depicting leakage of perifoveal retinal blood vessels.

Figure 8 Center-involving diabetic macular edema with subfoveal edema and numerous lipid exudates.

in mydriasis seem to correlate with regard to the classification of diabetic retinopathy and visualization of diabetic macular edema according to recent studies (Figure 10A)[21-23]. This wide-field imaging technique can be combined with fluorescein angiography and provides information about peripheral retinal ischemia or peripheral neovascularization (Figure 10B)[24].

Probably the most important new imaging technique, which was introduced in ophthalmologic practice, is OCT. Recently, resolution and recording speed have been greatly improved by spectral-domain OCT technique (SD-OCT). OCT provides data on retinal volume and configuration of the macular region. In diabetic macular edema SD-OCT is a very valuable examination technique comparing follow-up visits with baseline data, as modern OCT-devices use eye-tracking for finding the same imaging position during follow-up examinations (Figure 11)[25].

IMPORTANCE OF PREVENTION

In early diabetic retinopathy, laser photocoagulation can be used effectively for preventing loss of vision[26]. However, early diabetic retinopathy is not noticed by patients because of the absence of visual loss in early diabetic retinopathy. Thus, regular retinal exams with dilation of the pupil are necessary in patients with diabetes mellitus in order to detect sight-threatening changes timely and enable ophthalmologists to perform treatment.

Patients with type 1 diabetes should undergo retinal exams starting at the age 11 and/or after 5 years of diagnosis on a yearly basis. In case of retinal changes, shorter follow-up intervals are recommended.

In type 2 diabetes, the first retinal exam should be performed immediately after first diagnosis of diabetes, because the previous duration of the disease is unknown. Annual follow-up examinations are recommended in the absence of retinal changes, otherwise shorter intervals are recommended.

Pregnancy bears an increased risk of worsening of diabetic retinopathy due to hormonal changes. During pregnancy diabetic retinopathy may start in about 10% of cases and may worsen in an even higher percentage in case of preexisting diabetic retinopathy at time of conception[27]. In case of proliferative diabetic retinopathy before or shortly after conception, pan-retinal laser photocoagulation should be performed as retinal changes may worsen in one out of two women in this population. This risk can be reduced by half by thorough retinal laser photocoagulation. Therefore all females with diabetes, who are planning to get pregnant, should undergo fundoscopy prior to conception and then every three months during pregnancy to enable early intervention, if needed. Additionally good metabolic control should be achieved before conception[28].

On the other hand, the presence of diabetic retinopathy is no indication for cesarean section per se, as no study has indicated so far, that Valsalva-maneuvers during vaginal delivery bear an increased risk of vitreous hemorrhages[29].

The German Diabetes Society recommends scheduling of follow-up examinations depending on the grade of diabetic retinopathy as summarized in Table 2 (Adapted from[30]).

These recommended examination intervals will result in an increased work-load for ophthalmologists due to the rising number of diabetic patients. Studies examined the effect of an extension of follow-up intervals and found no increased risk of progression to sight-
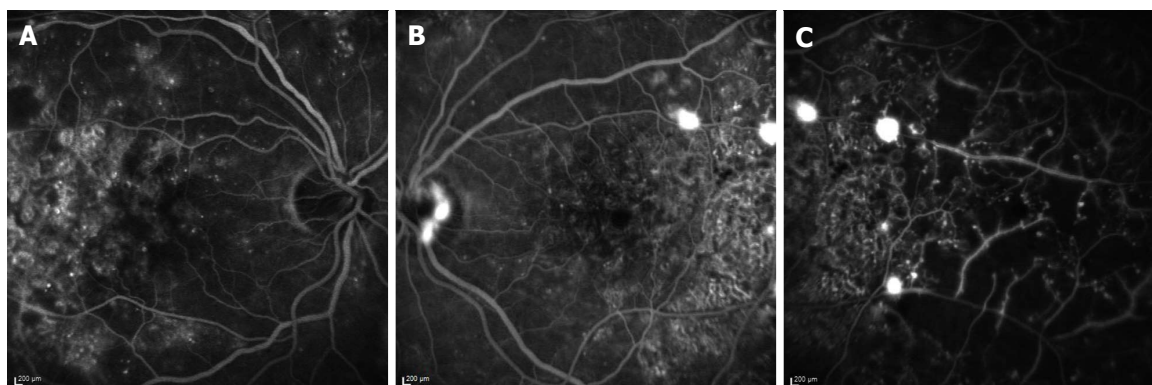
Figure 9 Fluorescein angiogram of a 49-year-old female patient. A: Fluorescein angiogram of the right eye 50 s after intravenous injection of fluorescein dye. Here, leaking micro-aneurysms in the macula can be seen; B: Fluorescein angiogram of the left eye 25 s after intravenous injection of fluorescein dye. Leakage from neovascular blood vessels causes spots of increased fluorescence at the optic disk and temporal to the fovea; C: Fluorescein angiogram of the temporal part of the left eye 30 s after intravenous injection of fluorescein dye. Areas of retinal non-perfusion can be seen as reason for neovascularization.
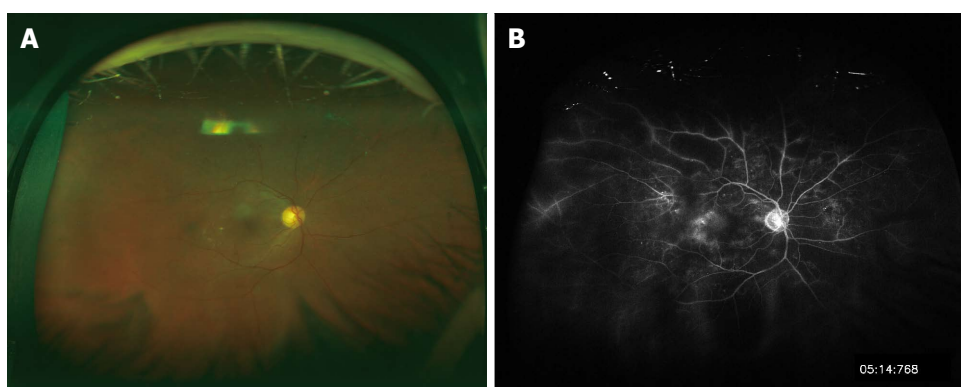

Figure 10 Wide-field picture of the right eye of a 65-year-old female patient. A: On scanning-laser-ophthalmoscope-Imaging some micro-aneurysms and lipid exudates can be seen; B: Fluorescein angiogram shows leakage from micro-aneurysms and extensive areas of retinal non-perfusion.
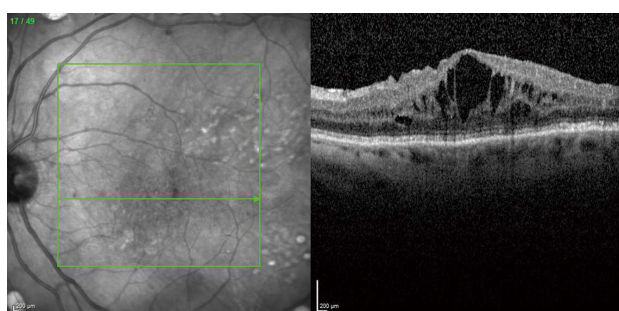

Figure 11 Spectral-domain optical coherence tomography of a female patient with center-involving diabetic macular edema. On the left side of the picture, an infra-red image shows the exact location of the OCT-scan on the right. The OCT-scan visualizes intraretinal edema with thickening of the fovea. OCT: Optical coherence tomography.

threatening diabetic retinopathy in patients with good metabolic control (HbA1c < 8%) and no known diabetic retinopathy[31-35]. By adequate selection of patients, the number of necessary screening examinations could be reduced by 40% according to one study and even by 59% in case a special mathematical algorism is used[31,33]. However, feasibility of these strategies remains to be proven in routine clinical practice and until then ophthalmic screening intervals as indicated above are recommended.

GENERAL MEDICAL THERAPY AND INTERVENTIONS

Blood glucose and blood pressure control

Good metabolic and blood-pressure control are essential for successful ophthalmic care of patients with diabetes.

In type 2 diabetes, a reduction of HbA1c from 7.9% to 7.0% resulted in a decline in the frequency of laser treatments needed[36]. In type 1 patients, improved blood glucose control with a reduction of HbA1c values from 9.1% to 7.1% reduced the risk of developing diabetic retinopathy within 6.5 years by 76%, the risk of progression of diabetic retinopathy by 54%, and the risk of developing proliferative diabetic retinopathy by 47%[37]. Therefore an HbA1c level of about 7% should be aimed for from the ophthalmologist's point of view[19], for the individual patient a bespoke treatment regime may be needed.

Rapid improvement of metabolic control may result in temporary worsening of diabetic retinopathy ("early-worsening") in patients with long-lasting disease and

Table 2 Recommended timing of retinal examinations in patients with type 2 diabetes[6]

Patient characteristics	Timing of retinal examination
Initial diagnosis of type 2 diabetes	Soon
No diabetic retinopathy	Once a year
Presence of symptoms such as	During the next few days
Loss of vision	
New difficulties during reading	
Altered color perception	
New, moving dark spots in the eye	
Presence of diabetic retinopathy	Depending on the severity of retinopathy, *e.g.*, every 3-6 mo

high HbA1c levels. Thus, retinal exams should be performed every three months during the first year after initiation of an improved anti-diabetic treatment[5,38]. However, in the long-term, positive effects of good metabolic control outweigh these initial problems[37,39]. Also a slow decrease of blood sugar levels, which would be a therapeutic challenge, does not have any advantages in the long term and is not recommended from the ophthalmologist's point of view[19].

Additionally, optimizing blood pressure helps to reduce the necessity of laser photocoagulation and the risk of loss of vision[40]. While some studies suggested a protective effect of ACE inhibitors, according to the results of studies available to date, reduction of blood pressure itself seems to be more important than the type of blood pressure lowering medication[41-43]. Levels of about 140/80 mmHg should be aimed for.

Acetylsalicylic acid and smoking

Acetylsalicylic acid has neither been shown to have any positive effect on diabetic retinopathy or diabetic macular edema, nor to be harmful for patients with diabetic retinopathy Therefore acetylsalicylic acid should be recommended for cardiovascular reasons in patients with early non-proliferative diabetic retinopathy, in case there are no contraindications[44].

Data on the effect of smoking on diabetic retinopathy is heterogeneous. While some studies did not find an association of smoking with diabetic retinal changes, others identified smoking in a multiple regression analysis as risk factor for any grade of diabetic retinopathy[45-47]. However, results of a recent experimental study suggest that nicotine expedites diabetes-induced retinal changes[48]. Additionally, patient characteristics such as selective mortality among smokers and patients with proliferative diabetic retinopathy at baseline may provide some explanation for the apparently absent association, reported in some studies[47]. Cessation of smoking should therefore be recommended from the ophthalmologist's point of view.

OPHTHALMIC THERAPEUTIC OPTIONS

Diabetic macular edema

Until the advent of anti-VEGF medication, focal and grid laser photocoagulation was the standard of care

Figure 12 Color fundus photo of a 53-year-old male patient several months after focal laser photocoagulation because of clinical significant diabetic macular edema. While the laser scars and some remaining dot-hemorrhages are visible, lipid exudates and retinal edema have disappeared.

for clinical significant diabetic macular edema (CSME) as well as for diffuse diabetic macular edema.

In patients with focal CSME without involvement of the fovea, focal laser photocoagulation of micro-aneurisms and localized areas of leakage reduces the relative risk of moderate loss of vision by 50% (from 24% to 12%) as demonstrated by the ETDRS Group (Figure 12)[49]. In case of persisting areas of leakage two to three months after initial focal laser photocoagulation, repeated laser treatment should be considered[26].

Apart from the direct effect by coagulating micro-aneurisms, focal laser photocoagulation is thought to increase oxygenation of the retina by improving diffusion of oxygen from choroidal vessels and to reestablish the blood-retinal barrier by thermal stimulation of the retinal pigment epithelium and of endothelial cells of retinal capillaries[50].

Grid laser photocoagulation of diffuse diabetic macular edema with involvement of the fovea ("center-involving") has a limited functional prognosis[49]. Therefore, grid laser photocoagulation has been replaced by intravitreal anti-VEGF therapy, which provides superior functional results[51].

VEGF is associated with a breakdown of blood-retinal barrier causing leakage and retinal edema[52]. Intravitreal application of anti-VEGF medication enables high local concentrations in the vitreous and a low systemic exposure. However, repeated intravitreal injections of anti-VEGF medications are necessary in patients with center-involving diabetic macular edema. The average number of injections is around 7 in the first year of treatment and 4 in the second year as indicated by recent studies[53,54]. Intravitreal anti-VEGF therapy is generally safe with regard to side-effects of medication, although the incidence of systemic thromboembolic events varies among trials[55]. As the intravitreal application of medication is a surgical procedure, it is associated with the possible risk of postoperative infection, which is called endophthalmitis in case of severe infection of the inner eye and its internal structures. For this reason several recommendations of ophthalmologic societies

Figure 13 Wide-field picture of the right eye of a 48-year-old male patient after pan-retinal laser photocoagulation because of proliferative diabetic retinopathy. The peripheral laser scars can be seen in the picture, while neovascularization have regressed.

Figure 14 Proliferative diabetic retinopathy with extensive fibro-vascular membranes.

have been published concerning prevention of post-injection endophthalmitis. Recent studies reported very low rates of post-injection endophthalmitis of less than 1 in 8000 injections performed in an operating theater setting after diligent disinfection of the conjunctiva with povidone-iodine, using sterile gloves and wearing face-masks[56,57]. Other studies report somewhat higher rates of infectious endophthalmitis after intravitreal injection, both after procedures performed in an office-setting and in a theater-setting[58]. The effect of meticulous povidone-iodine prophylaxis on the conjunctival bacterial load and contamination of needles used for injection prophylaxis has been shown in several studies[59-62].

Apart from anti-VEGF medication intravitreal steroids have been evaluated for the treatment of diabetic macular edema. Compared to anti-VEGF medication, steroids have additional anti-inflammatory effects and sustained-release devices can lengthen the intervals between re-treatments[63]. In Europe, a non-absorbable implant containing 190 μg fluocinolone acetonide has been approved as second-line treatment of chronic diabetic macular edema not responding to other therapeutic options. Also approval of an absorbable dexamethasone implant for the treatment of diabetic macular edema is expected by the end of 2014. While

intravitreal steroids are effective in reducing diabetic macular edema, patients need to be informed about possible progression of cataract and increased intraocular pressure[64-67].

Proliferative diabetic retinopathy

In early proliferative diabetic retinopathy, pan-retinal laser photocoagulation is effective in reducing the risk of visual loss, while surgery needs to be performed in very advanced proliferative diabetic retinopathy[68]. The suggested screening intervals of patients with diabetes are intended to enable the treating ophthalmologist to detect proliferation amendable for laser treatment early. Pan-retinal laser photocoagulation should be performed when retinal neovascularization is detected during fundoscopy or *via* fluorescein angiography in order to prevent complications of proliferative diabetic retinopathy such as vitreous hemorrhage or tractional retinal detachment (Figure 13)[68]. Pan-retinal laser photocoagulation aims at eliminating non-perfused parts of the retina, thus reducing ischemia, intravitreal VEGF-levels, and the stimulus for proliferation. The efficacy of pan-retinal laser photocoagulation in reducing the risk of loss of vision has already been shown more than 30 years ago[68]. However, patients need to be informed about side-effects of pan-retinal laser treatments such as constriction of visual fields and reduced dark-adaption due to loss of rod function. These side-effects may also interfere with the patients' driving ability.

Pars-plana vitrectomy is performed in advanced cases of proliferative diabetic retinopathy, the presence of extensive tractional membranes, vitreous hemorrhage, and tractional retinal detachment (Figure 14). About ten years ago trans conjunctival sutureless 23 gauge vitrectomy started to replace conventional 20 gauge technique and offers comparable safety and efficacy as well as reduced surgery-times and faster rehabilitation of patients[69].

Combination of diabetic macular edema and proliferative diabetic retinopathy

In patients with diabetic macular edema and proliferation, treatment of macular edema should be performed before pan-retinal laser photocoagulation in order to prevent worsening of macular edema due to peripheral pan-retinal laser photocoagulation.

CONCLUSION

In patients with diabetes, regular retinal exams are essential. While laser photocoagulation is effective, if performed in time, advanced stages of diabetic retinopathy need to be treated by vitreo-retinal surgery and have limited visual prognosis. Even though new therapeutic options such as intravitreal medical therapy and sutureless pars-plana vitrectomy have improved ophthalmic care of patients with diabetes, interdisciplinary care remains essential. Good metabolic and blood pressure control is indispensable for reducing the risk of

ophthalmic complications.

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