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Presence and Risk Factors for Glaucoma in Patients with Diabetes

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Abstract

Diabetes mellitus represents a growing international public health issue with a near quadrupling in its worldwide prevalence since 1980. Though it has many known microvascular complications, vision loss from diabetic retinopathy is one of the most devastating for affected individuals. In addition, there is increasing evidence to suggest that diabetic patients have a greater risk for glaucoma as well. Though the pathophysiology of glaucoma is not completely understood, both diabetes and glaucoma appear to share some common risk factors and pathophysiologic similarities with studies also reporting that the presence of diabetes and elevated fasting glucose levels are associated with elevated intraocular pressure – the primary risk factor for glaucomatous optic neuropathy. While no study has completely addressed the possibility of detection bias, most recent epidemiologic evidence suggests that diabetic populations are likely enriched with glaucoma patients. As the association between diabetes and glaucoma becomes better-defined, routine evaluation for glaucoma in diabetic patients, particularly in the telemedicine setting, may become a reasonable consideration to reduce the risk of vision loss in these patients.

Keywords

Glaucoma; Diabetes Mellitus; Diabetic Retinopathy; Epidemiology; Risk Factors

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Conflict of Interest

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INTRODUCTION

Diabetes mellitus represents a significant public health issue which has become increasingly prevalent due to changes and trends in diet, lifestyle, and consequently, the rate of obesity [1]. Since 1980, the worldwide prevalence of diabetes has nearly quadrupled to an estimated 422 million affected persons in 2014 [2]. As a result, global health care expenditures for diabetes are expected to total as much as 490 billion United States dollars by the year 2030, comprising an estimated 12% of total health care costs [3].

The burden of diabetes on the health care system is manifest in many different ways. Diabetic patients require more outpatient visits, chronic medications, and are at risk for a number of systemic microvascular complications that result in end organ damage and associated complications: renal disease, cardiovascular disease, amputations, vision loss, and premature death [3]. In particular, vision loss from diabetic retinopathy (DR) represents one of the most devastating complications on quality of life and is the leading cause of blindness in working age and economically active adults [4–7]. An older survey among diabetic patients in the United States reported a prevalence of self-rated visual impairment as high as 24.8% [8]. Current estimates of the prevalence of DR have been estimated as 34.6% among all patients with diabetes (both type 1 and type 2) and as a result, the implications of diabetic eye disease are far-reaching [9]. In addition to retinopathy, diabetes has been associated with a number of other potentially vision-threatening ocular complications including cataract, uveitis, and glaucoma [10–13].

Glaucoma represents the leading cause of worldwide irreversible blindness, as defined by best-corrected central visual acuity of less than 3/60 or a visual field of less than 10° in the better seeing eye [14]. It is characterized by pathognomonic optic nerve changes which result in progressive visual field loss over time [14]. Primary open angle glaucoma (POAG) is the most common form of glaucoma and is associated with a number of risk factors such as family history, African ancestry, and elevated intraocular pressure (IOP) [15]. Of these, IOP is the only modifiable and effective target of therapy, and as a result, the mainstay of current glaucoma treatment is IOP reduction through the use of medications, laser, or surgery.

Whether or not an association exists between diabetes mellitus and glaucoma has been an issue of debate in the past, but findings from several studies in recent years seem to suggest that the risk of glaucoma among diabetic patients may be greater than once believed [11–13,15–19]. In this paper, we review the medical literature characterizing the proposed relationship and risk factors for glaucoma in patients with diabetes as well as the potential clinical implications of this association for diabetic individuals.

PATHOPHYSIOLOGIC FEATURES OF DIABETIC EYE DISEASE

A pooled analysis of population-based studies by Yau and colleagues estimates that the total number of people with DR worldwide is approximately 93 million and of these, 28 million (30.1%) have vision-threatening DR [9]. In general, DR is believed to be more common in patients with type 1 diabetes compared to type 2 diabetes. According to this report, the age-

standardized prevalence of DR in type 1 diabetic patients was 77.31%, whereas 25.16% of type 2 diabetic patients had DR. The higher rate of DR seen in type 1 diabetic patients is believed to be a result of the increased diabetes duration, hemoglobin A1c levels, and blood pressure typically observed in these patients [9].

As in other organ systems affected by diabetes, microvascular abnormalities are central to the development of DR. Though the exact mechanism by which hyperglycemia causes DR is not completely understood, several factors have been implicated: sorbitol accumulation, oxidative stress, accumulation of advanced glycation end products (AGEs), protein kinase C (PKC) activation, and angiogenic factors [20–38].

The biochemical processes associated with chronic hyperglycemia ultimately lead to vascular abnormalities that result in endothelial and metabolic dysfunction both at the level of the eye as well as other organ systems. Loss of retinal pericytes, capillary basement membrane thickening, and vascular endothelial cell dysfunction are some of the early changes that have been described in DR [20,39–41]. Impaired retinal vascular autoregulation is seen in part, due to pericyte loss, and disruptions in vascular permeability represent key features that are central to the development of both DR and diabetic macular edema (Figure 1) [42,43]. In addition, increased leukocyte adhesion and retinal leukostasis are believed to play a role in capillary nonperfusion [20,44].

Over time, retinal ischemia leads to an uptake of angiogenic growth factors, namely VEGF, which contributes to pathologic processes causing diabetic macular edema as well as retinal neovascularization – the pathognomonic feature of proliferative diabetic retinopathy [45,46]. Overexpression of VEGF under hypoxic conditions is not limited to retinal vascular endothelial cells, but is present in all retinal cell types including retinal pigment epithelial cells and ganglion cells and studies have shown dysfunction in all layers of the diabetic retina [47–51]. Over the past decade, therapies targeted at inhibiting VEGF have emerged as highly effective drugs for treating retinal disease have been proven effective. Intravitreal injection of these medications, such as aflibercept, bevacizumab and ranibizumab have demonstrated remarkable efficacy in treating retinal leakage and neovascularization and have become the new standard of care for diabetic macular edema and an alternative treatment for proliferative diabetic retinopathy [52–54].

PATHOPHYSIOLOGIC FEATURES OF GLAUCOMA

Glaucoma is a neurodegenerative disorder of the optic nerve in which retinal ganglion cell (RGC) death leads to characteristic patterns of visual field loss. By the year 2020, it is estimated that the worldwide prevalence of glaucoma will approach 80 million people with 11.2 million being bilaterally blind from glaucoma [55]. Though elevated IOP is the primary risk factor for the development of POAG, over half of all patients in the Baltimore Eye Survey had a screening IOP below the upper limit of normal (21 mmHg) [56]. In addition, glaucoma occurring at IOPs within the normal range (10–21 mmHg) is more common than previously believed, particularly among certain East Asian populations where as many as 92% of glaucoma patients have been reported to have normal IOPs in the Tajimi Study, for example [57].

Previously, it was believed that the primary mechanism by which glaucoma occurred was mechanical stress from elevated IOP. Unlike in angle closure glaucoma where narrowing of the iridocorneal angle causes mechanical obstruction of the trabecular meshwork to block aqueous humor outflow, IOP elevation in POAG is believed to be the result of resistance to aqueous outflow. Though IOP elevation is directly related to RGC death, multiple other mechanisms are thought to contribute to the development of glaucomatous optic neuropathy including genetics, impaired microcirculation, and abnormalities in cerebrospinal fluid pressure [58].

Mechanical stress from elevated IOP is thought to occur primarily at the level of the lamina cribrosa – the point at which the optic nerve fibers penetrate the posterior sclera [59]. The optic nerve fibers form the axons of the RGCs, but IOP-induced mechanical stress causes posterior bowing and thinning of the lamina, which disrupts axonal transport [59–62]. As a result, the RGCs undergo apoptotic cell death in conjunction with loss of neuroretinal rim tissue of the optic disc and corresponding enlargement of the optic cup (Figure 2) [63].

A growing number of genetic abnormalities have been implicated in the pathogenesis of POAG. The myocilin (*MYOC*) gene in the locus for primary open angle glaucoma on chromosome 1 (*GLC1A*), was the first reported gene to be associated with juvenile and early adult forms of POAG [64,65]. Such cases are sometimes referred to as “myocilin glaucoma” [66]. Other genes that have been implicated with increased POAG include *CDKN2BAS*, *SIX1/SIX6*, *TMCO1*, *AFAP1, FOXC1, ABCA1, ATXNN2, GAS7, TXNRD2,* and *CAV1/CAV2* [67–71]. In addition, variants in the *OPTN*, *TBK1*, *and C12orf23* genes have been implicated in open angle glaucoma occurring at normal IOP levels (i.e. normal tension glaucoma) [71–74].

Impaired microcirculation is also believed to be a contributing factor in the development of glaucoma since it was first reported by Harrington in 1959, and subsequent studies have provided further evidence that abnormalities in ocular perfusion may be contributory in the development of glaucomatous optic neuropathy, particularly in cases of normal IOP [75–84]. More recent research has also focused on the possibility of low cerebrospinal fluid pressure as a contributing mechanism through an increased translaminar pressure gradient which may exacerbate cupping of the optic nerve head [85–88].

GLAUCOMA RISK FACTORS AND CORRELATION WITH DIABETES

Common Pathophysiologic Mechanisms in Glaucoma and Diabetes

Several common mechanisms have been postulated to contribute to the possible link between glaucoma and diabetic retinopathy. Diabetes and hyperglycemia is associated with glycation of lipids and abnormalities of lipid metabolism which may increase oxidative stress and promote cellular apoptosis – the same mechanism by which RGC loss occurs in glaucoma [89–98].

Vascular dysregulation has been described in both diabetic eye disease and glaucoma, and upregulation of nitric oxide, a potent vasodilator, has been reported in both conditions [99–102]. Nitric oxide is a known regulator of not only vascular tone, but also apoptosis

[101,103]. In addition, reactive nitrogen species have been shown to contribute to inflammatory responses via oxidative stress and optic nerve degeneration as well [103,104,105]. The contributory role of PKC in the pathophysiology of diabetic retinopathy has also been established and there is evidence to suggest that elevated PKC may also be associated with abnormalities of matrix metalloprotease in the trabecular meshwork causing impaired aqueous outflow and elevated IOP [88,105,106]. In addition, overexpression of matrix metallprotease-9 has been associated with structural optic nerve head changes in diabetic patients, thus providing another potential link between diabetes and glaucoma [89,108,109].

Other pathways by which investigators have linked diabetes and glaucoma include glial cell dysfunction and impairment of retrograde axonal transport [89]. Glial cells, such as astrocytes, are non-neuronal cells that support and protect neurons in the central nervous system, including the retina and optic nerve. Dysfunction of these cells has been demonstrated in animal models of diabetes and glaucoma and is believed to contribute to neuroinflammatory pathways of apoptosis [110–116]. In addition, it has been postulated that alterations in connective tissue remodeling due to diabetes may affect both the lamina cribrosa and the trabecular meshwork, thereby potentially increasing susceptibility to glaucoma through biomechanical changes at the optic nerve and impairment of aqueous humor outflow affecting IOP homeostasis [89].

Diminished neurotrophic factor delivery secondary to abnormalities in axonal transport has been demonstrated in both diabetic peripheral neuropathy and the optic nerve in glaucoma [117–120]. Alterations in neurotrophic factor expression, such as insulin-like growth factor and neurotrophin-3, are also seen in the presence of elevated intraocular pressure, the primary risk factor for glaucomatous optic neuropathy [121]. In particular, insulin-like growth factor is necessary for proper glucose metabolism in the central nervous system and resistance to insulin may be a contributor to neurodegenerative processes as a result [122–125]. With regard to the eye and glaucoma, insulin and insulin-like growth factor have been shown to play a role in RGC survival [122,126–128]. In addition, insulin has been reported to affect IOP with lower IOP being associated with insulin-induced hypoglycemia while increased IOP has been associated with insulin resistance [129,140]. Clinically, a large retrospective cohort of diabetic patients with open angle glaucoma reported that metformin, a first-line agent used to treat insulin-resistance in type 2 diabetes, is associated with a decreased risk of developing open angle glaucoma even after accounting for variations in glycemic control [131]. In addition, genetic polymorphisms related to pancreatic beta-cell function in type 2 diabetes mellitus were associated with increased risk of POAG and provide further support for these findings [132].

Neurodegeneration and Ganglion Cell Apoptosis

RGC apoptosis and retinal nerve fiber layer (RNFL) thinning are characteristic structural findings seen in glaucoma that have also been described in diabetic retinopathy. In conjunction with RNFL loss, excavation or cupping at the level of the optic nerve head is the pathognomonic finding that is most commonly associated with glaucoma. However, a similar appearance of the optic nerve head may also be seen in the presence of anterior

ischemic optic neuropathy, which occurs more frequently in diabetic patients in some studies, or after laser photocoagulation treatment for proliferative diabetic retinopathy [133–136]. Structural optic nerve abnormalities have also been reported in an experimental rat model of diabetes, which also showed corresponding RGC dysfunction as measured by electroretinogram [137]. Such similarities can present challenges in distinguishing glaucomatous from non-glaucomatous optic neuropathy, especially in the presence of both conditions.

Though diabetic retinopathy is generally considered primarily a microvascular complication of diabetes, it is now known that neurodegeneration is also a significant component in its pathophysiology and may even precede the microvascular changes that are typically seen in diabetic eye disease [138–140]. In a recent study by Sohn and colleagues, progressive loss of both the nerve fiber layer and RGC/inner plexiform layer was observed using optical coherence tomography (OCT) in 45 patients with no or minimal diabetic retinopathy. In the same study, they also demonstrated progressive inner retinal thinning and RGC loss in a streptozotocin-induced mouse model of type 1 diabetes on both OCT and immunohistochemistry [141]. These findings are consistent with earlier work from the same investigators, who reported selective thinning limited to the inner retina in type 1 diabetic patients [142,143]. Cross-sectional human studies from other groups comparing RNFL thickness in healthy subjects and patients with preclinical diabetic retinopathy have also demonstrated mean and superior quadrant RNFL thickness to be reduced in diabetic patients when measured by OCT [144,145]. As a result, neurodegeneration in diabetic eye disease appears to occur in the same location of the neural retina as glaucomatous optic neuropathy.

In addition, neurodegeneration in both glaucoma and diabetic eye disease is believed to be relatively nonselective, affecting all RGC types. In general, RGCs can be classified based on their functional features and projections from the optic nerve head to layers of the lateral geniculate nucleus. Studies in experimental primate models of glaucoma have shown that RGC loss of all types occurs by apoptosis with greater loss occurring as a direct function of IOP [146–148]. Specifically, loss of neurons in the magnocellular and parvocellular pathways has been demonstrated in glaucoma, which has also been reported in a histologic study of human retinas with diabetic retinopathy by Meyer-Rusenberg and colleagues as well [147,149].

Functional Abnormalities in Glaucoma and Diabetes

From a functional standpoint, it is well-established that RGC loss in glaucoma is associated with visual field deterioration and loss [150–152]. Several animal and human electrophysiologic studies have reported a variety of abnormalities in the presence of both diabetic retinopathy and glaucoma compared to normal eyes [153–163]. A recent study of visual field profiles for POAG from the Nurses' Health Study found that early peripheral, as opposed to paracentral, visual field loss was more common in POAG patients with diabetes mellitus [164]. While the diagnosis of diabetes in this study was based on patient self-report and did not exclude diabetic patients with retinal laser photocoagulation (which can also produce peripheral visual field loss), chart review in a subset of these subjects demonstrated that self-report was a valid method for accurate classification of diabetes among health

professionals. Nevertheless, these findings suggest that there may be important phenotypic differences in glaucoma patients depending on diabetes status. Similarly, Kim et al. have also reported differences in the location and rate of deterioration of visual field defects in glaucoma patients based on diabetes status [165].

Cardiovascular Risk Factors in Glaucoma and Diabetes

Hypertension and hyperlipidemia have long been considered significant contributory risk factors for the development and progression of DR, and assessment and management of both hypertension and dyslipidemia in diabetic persons are considered the standard of care by the American Diabetes Association [166–174]. However, the contributory role of cardiovascular disease in the development or progression of glaucoma is less clear.

A positive correlation between systemic hypertension and glaucoma has been reported in the Blue Mountain Eye Study, the Rotterdam Study, and the Egna-Neumarkt Study [175–177]. However, the Barbados Eye Study and the Early Manifest Glaucoma Trial did not find a correlation between systemic hypertension and incidence or progression of glaucoma, although the Early Manifest Glaucoma Trial did find that a history of cardiovascular disease was a significant predictor of glaucoma progression [178–180]. The Los Angeles Latino Eye Study reported somewhat conflicting results when they reported that both low diastolic and high systolic and mean arterial blood pressures were associated with a higher prevalence of open angle glaucoma even after controlling for IOP [181]. The authors of the study postulate that low diastolic blood pressure can lead to decreased ocular perfusion pressures, which is consistent with the vascular hypothesis of glaucomatous optic neuropathy, whereas changes associated with chronic systemic hypertension, such as arteriosclerosis, can also decrease ocular perfusion [181]. A recent meta-analysis of 16 studies found that individuals with systemic hypertension had a pooled odds ratio of 1.2 for the development of glaucoma compared to normotensive individuals [182]. Several studies have, however, shown a positive correlation between IOP and systemic hypertension, particularly elevated systolic blood pressure [80,175,183–189]. Though the Barbados Eye Study did not find a correlation between hypertension and incident glaucoma, elevated systolic blood pressure, diabetes history, and age were positively associated with elevated IOP [183]. While elevated IOP is a risk factor for glaucoma, evidence from the population-based studies above would suggest that these changes in IOP may not always increase the risk of incident glaucoma.

The relationship between glaucoma and dyslipidemia has not been studied as extensively as its relationship with hypertension or diabetes. As in the case of systemic hypertension, there are published reports that dyslipidemia may be associated with increases in IOP [190–194]. However, the Beijing Eye Study found that despite a positive correlation between dyslipidemia and IOP, there was no association with glaucoma [194]. Kang and colleagues also found no relationship between risk of POAG and total cholesterol, but consumption of a high ratio of n-3 to n-6 polyunsaturated fat was associated with an increased risk of POAG [195]. Likewise, Ko and colleagues found an association between self-reported diabetes and glaucoma in the National Health and Nutrition Examination Survey, but this association was not significant after adjustment for triglyceride levels [13].

Metabolic Syndrome and Insulin Resistance in Glaucoma and Diabetes

Metabolic syndrome is a cluster of clinical risk factors, including hypertension and dyslipidemia, which is a significant predictor of diabetes [196,197]. Insulin resistance is thought to be involved in the pathophysiology of metabolic syndrome and as a result, the components of metabolic syndrome are comprised of significant systemic risk factors for either elevated IOP or glaucoma [198].

In a study examining individual components of metabolic syndrome, Newman-Casey and colleagues found that hyperlipidemia alone in the absence of diabetes or glaucoma was not a risk factor for open angle glaucoma. However, both diabetes mellitus and systemic hypertension, either alone or in combination, were associated with an increased hazard of open angle glaucoma [199]. A subsequent study from the same investigators found that among patients with hyperlipidemia, the use of 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors, commonly referred to as “statins”, were associated with a significant reduction in the risk of POAG. The authors postulate that it is not treatment of hyperlipidemia but the effect of these medications on pathways that contribute to IOP lowering and neuroprotection that reduces POAG risk [200].

With regard to insulin resistance, a recent study comparing IOP changes in diabetic and non-diabetic individuals found reported that hyperglycemia during oral glucose tolerance testing has a positive correlation with IOP [201]. Similarly, data from the Korean National Health and Nutrition Examination Survey also reported higher mean IOP to be positively correlated with estimated insulin resistance in addition to the presence of diabetes mellitus, hypertension, metabolic syndrome, and lipid abnormalities [192]. However, neither of these studies examined the relationship between insulin resistance and glaucoma. In a study of normal tension glaucoma patients and components of metabolic syndrome, Kim and colleagues found hypertension and impaired glucose tolerance were associated with a significantly higher prevalence of normal tension glaucoma [202]. However, a slightly lower prevalence of glaucoma was seen among participants with metabolic syndrome in the Singapore Malay Eye Study and neither pre-diabetes or metabolic syndrome were consistently associated with glaucoma in a cross-sectional study of subjects from the 2005–2008 National Health and Nutrition Examination Survey [12,203]. Recently, a study using healthcare claims data reported a dose-dependent reduction in POAG risk among diabetic persons using metformin, the first-line medication used to treat patients with type 2 diabetes mellitus and improve insulin sensitivity. In addition, those subjects with a higher Hemoglobin A_{1c} had an increased risk of glaucoma, suggesting that glycemic control and insulin sensitivity may contribute to glaucoma risk [204]. When considered together, many of the risk factors associated with diabetes may also be contributory to glaucoma as well.

EPIDEMIOLOGY OF GLAUCOMA IN DIABETIC POPULATIONS

Many epidemiologic studies have examined the relationship between diabetes and glaucoma risk with somewhat mixed results [11–13,15–19,199,205–211]. Some of these discrepancies may be related to the study sample, sample size, patient drop-out, detection bias, reverse causation, and variations in the diagnostic criteria and methods for defining glaucoma and diabetes. In addition, these studies were not designed with a primary endpoint of evaluating

the association between glaucoma and diabetes. For example, the Ocular Hypertension Treatment Study, a randomized trial that examined the safety and efficacy of IOP lowering medications in delaying or preventing the development of POAG, initially reported that diabetes was protective against the conversion from ocular hypertension (elevated IOP without optic neuropathy) to glaucoma [212]. However, the diagnosis of diabetes was made by patient self-report and further analysis showed that the study sample was underpowered to find an effect of diabetes on the development of glaucoma [213]. Despite these discrepancies, the majority of the evidence suggests an increased risk of POAG in persons with diabetes.

A recent meta-analysis of 47 studies by Zhao and colleagues reported a pooled relative risk of glaucoma of 1.48 in patients with diabetes compared to those without diabetes [11]. In addition, there was an increasing relative risk of glaucoma that was positively associated with diabetes duration. Though elevated IOP alone is a significant risk factor for but is not diagnostic for glaucoma, diabetic patients had a pooled average increase in IOP of 0.09 mmHg for every 10 mg/dl increase in fasting glucose [11]. Using a different approach than the epidemiologic studies above, findings by Goldacre and colleagues seem to provide further evidence for a possible link between glaucoma and diabetes. By studying a large data set of hospital linkage records from the United Kingdom, they found that the rate ratio for glaucoma among inpatients admitted for diabetes was substantially increased at 2.47 compared to the reference cohort. Interestingly, the risk of glaucoma among inpatients admitted for hypertension was only modestly elevated at 1.07 [214].

The global prevalence of glaucoma among all people, including both diabetic and nondiabetic persons, is estimated to be approximately 3%. However, this figure can vary significantly by age and race [14,215]. In contrast, the prevalence of glaucoma that has been reported specifically in diabetic populations ranges from 2.5% to 15.6% [13,204,210,216–221]. In total, the majority of these studies suggest that glaucoma prevalence is approximately two to three times higher in diabetic populations compared to nondiabetic populations.

IMPLICATIONS FOR CLINICAL CARE

The American Diabetes Association currently recommends that all patients with diabetes undergo annual dilated funduscopic examinations to evaluate for the presence of retinopathy, although eye examinations may be performed every 2 years at the discretion of the eye care provider if no retinopathy is present. For newly diagnosed patients with type 1 diabetes mellitus, an initial eye examination is recommended within five years after diagnosis. For type 2 diabetes mellitus, eye examinations are recommended at the time of diagnosis [222]. However, compliance with eye examination guidelines are modest at best, especially in the absence of eye abnormalities. Computerized billing records from a single tertiary eye care facility reported a compliance rate of just 31% among diabetic patients without retinopathy [223]. One potential proposal to improve compliance with eye examination guidelines is integration of a telemedicine program, which has been shown to increase compliance rates when integrated within primary care centers [224].

Current guidelines for glaucoma screening are more controversial. In 2013, the United States Preventive Services Task Force stated that there is insufficient evidence to support routine screening for primary open angle glaucoma among visually asymptomatic adults [225]. These recommendations have initiated much debate about the utility of glaucoma screening efforts as a result [226,227]. However, glaucoma has many features that would be amenable to effective screening. Affected patients are often asymptomatic, especially in earlier stages of the disease. Many patients experience a relatively slow rate of progression and studies have shown that higher treatment costs are associated with management of more advanced stages of the disease [228,229]. In addition, glaucoma is a condition with effective and proven treatments and the Early Manifest Glaucoma Trial has shown that therapies that reduce IOP are effective in delaying the progression of glaucomatous vision loss [230].

As a result, some have argued that an opportunistic, case-finding approach to glaucoma screening may be of value in high-risk populations [227,231]. In this regard, the implications of the purported glaucoma risk associated with diabetes are significant. A recent study by Silva and colleagues examining the prevalence of non-diabetic ocular findings in a diabetes telemedicine program reported that the rate of glaucomatous and glaucoma-suspicious optic nerves on funduscopic imaging ranged from 8.9 to 9.9% depending on the imaging device used [232]. Consequently, there may be reasonable cost-benefit in developing and incorporating effective glaucoma screening methods for diabetic patients, particularly those who already undergo fundoscopic imaging in teleretinal programs where simultaneous optic nerve evaluation for glaucoma may increase the diagnostic yield of potentially blinding eye disease.

CONCLUSION

Both diabetes and glaucoma represent significant public health issues in the aging population. Several epidemiologic studies suggest that diabetic individuals are at increased risk for the development of glaucoma and there may be pathophysiologic similarities to support an association between these two conditions [11–13,15–19,205–211]. Given the potential to utilize early detection and treatment efforts to significantly reduce vision loss from both glaucoma and diabetic retinopathy in at-risk individuals, the possible role of routine glaucoma evaluation in diabetic persons warrants further consideration as we continue to learn more about the association between these two blinding conditions.

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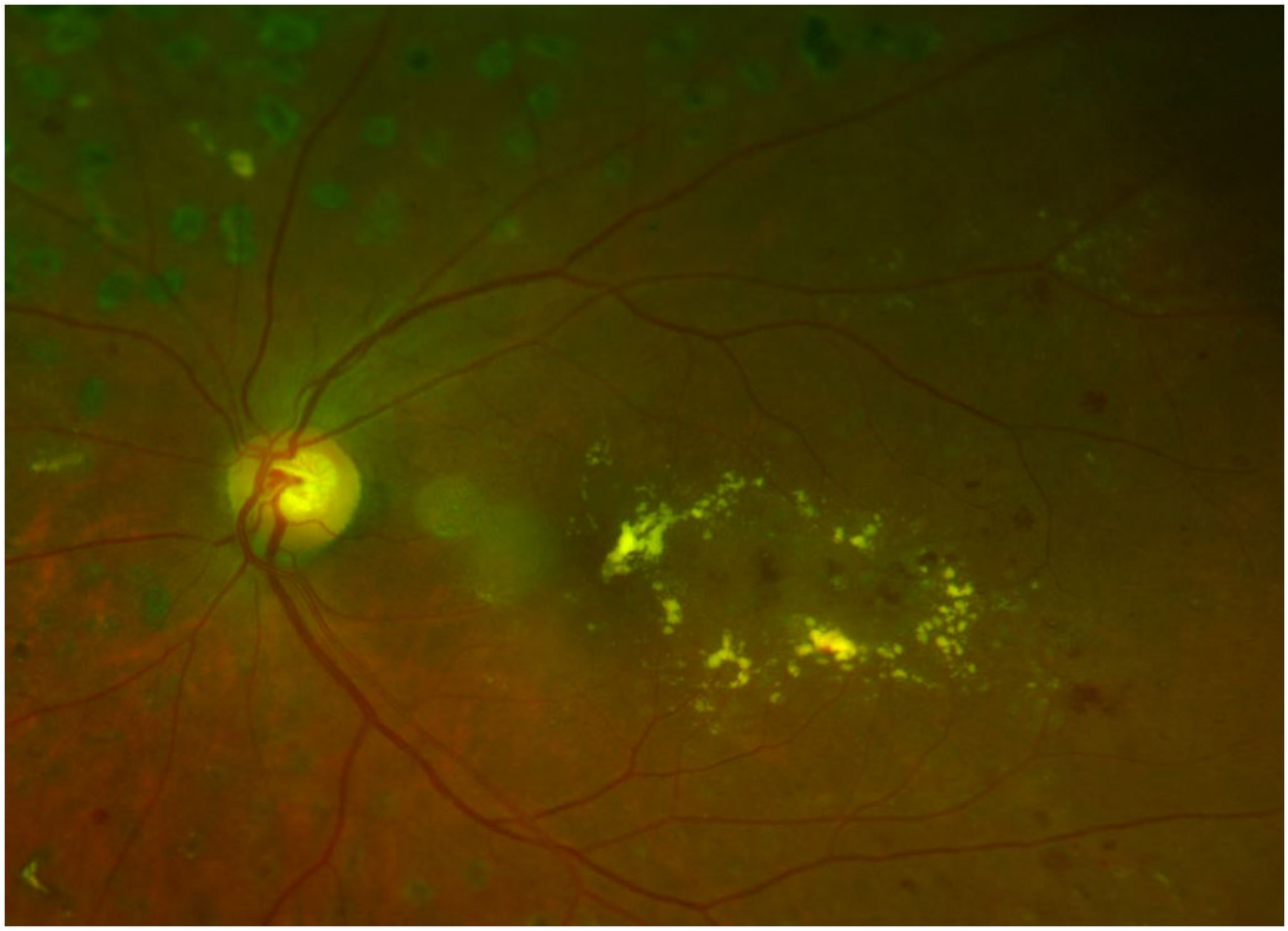

Fig 1.

Nonmydriatic ultrawide field image of the left eye of a patient with quiescent proliferative diabetic retinopathy. A circinate ring of hard exudates is seen in the macula along with numerous dot-blot hemorrhages and microaneurysms consistent with diabetic macular edema. Previous laser photocoagulation scars are present in the upper left.

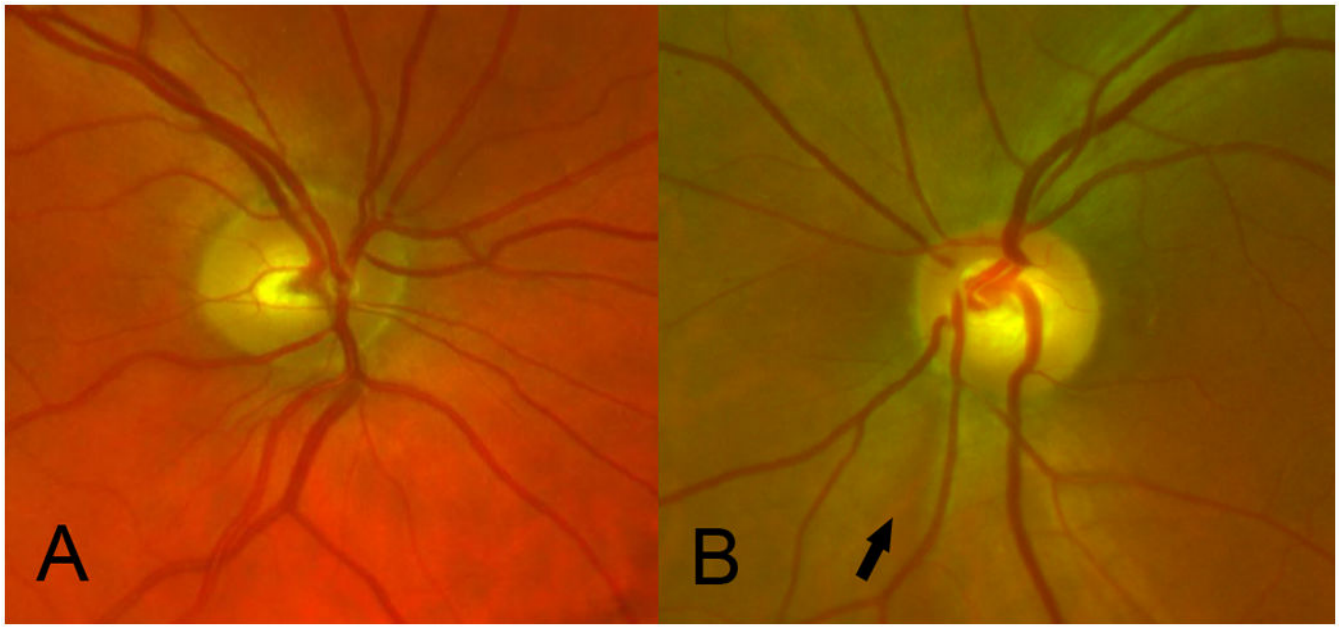

Fig 2.

(A) Optic nerve photograph from the right eye of a diabetic patient without glaucoma. A healthy neuroretinal rim and a normal cup to disc ratio is seen. **(B)** Left eye optic nerve photograph from a diabetic patient with glaucoma. Note the enlarged cup to disc ratio and the loss of retinal nerve fibers inferiorly (black arrow).