Screening options for diabetic retinopathy

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Purpose of review

This review assesses the current status of the different methods used in screening for diabetic retinopathy. This update is particularly timely because the incidence of diabetes is rising rapidly and the number of patients with vision-threatening diabetic retinopathy is increasing.

Recent findings

We evaluate the different methods used and their results in improving the delivery of eye care to patients with diabetic retinopathy. In populations with poor access to ophthalmic care, screening techniques such as the nonmydriatic camera used in offices of primary care physicians may be useful in identifying lesions of diabetic retinopathy requiring treatment. One of the limitations is the lack of dilation and cataract formation, which may result in ungradable photographs. Patients with treatable lesions as well as those with ungradable photographs should be referred for comprehensive ocular examination.

Summary

Screening techniques do not replace the eye examination. Ophthalmologists can play an important role in diabetic care apart from treating eye disease. Counseling can be provided to patients regarding the importance of blood glucose and blood pressure control and may motivate patients to achieve strict glucose and blood pressure control.

Keywords

macular edema, nonmydriatic camera, proliferative retinopathy

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Abbreviation

CSME clinically significant macular edema

1040-8738

Introduction

Diabetic retinopathy is one of the leading causes of blindness in the US [1] despite highly effective treatment strategies developed over the past several decades [2,3]. The number of patients with diabetes referred by primary care physicians, diabetologists, endocrinologists, and others for ophthalmic care is far below the recommended guidelines of the American Academy of Ophthalmology and the American Diabetes Association [4]. As diabetes increases in prevalence in the coming years as the population in the US is becoming more obese and living longer, diabetic retinopathy will be an increasing burden on the affected individuals and on society. Worldwide, diabetes is projected to affect 300 million people by 2025, and 10% will likely develop visual impairment secondary to diabetic retinopathy (World Health Organization Media Centre; http://www.who.int/mediacentre/factsheets/fs236/en/print.html). We need to improve our ability to detect the onset of vision-threatening diabetic retinopathy by increasing our rates of screening of persons with diabetes.

Current status of ophthalmic examinations for diabetic retinopathy

Several organizations have advocated yearly comprehensive eye examinations with dilation for all persons with diabetes, beginning at diagnosis of diabetes for those with type 2 diabetes and after 5 years of diabetes for those with type 1 diabetes. At the enrollment of a community-based intervention trial [5], 35% of the participants did not follow the guidelines; two-thirds of this group reported no examinations in the year prior to enrollment and only one-third had had an undilated eye examination. In an epidemiologic study of more than 2000 persons [6], 11% with type 1 and 7% with type 2 diabetes were identified as having high-risk proliferative diabetic retinopathy, but they had not been seen by an ophthalmologist in the previous 2 years. Furthermore, 46% of these eyes with high-risk proliferative diabetic retinopathy had not received the necessary photocoagulation surgery. In the National Committee for Quality Assurance's Health Plan Employers Data Information Set 3.0 System [7], the average rate of annual eye examinations for patients was 38% across participating health plans. Among prepaid health plan enrollees such as the Kaiser Health Maintenance Organization, 77% of patients with diabetes received an eye examination over the 3-year study period.

Clearly, there is a need for improvement in the rates of eye examinations for all persons affected with diabetes.

In order to access patients and communities that have suboptimal or no ophthalmic care, other technologies are needed. Both geographic (rural) and sociocultural barriers make it difficult to reach some of these patients. With the burden of diabetic retinopathy growing worldwide, it will be important to develop ways of screening for diabetic retinopathy in settings such as the offices of the medical physicians who deliver medical care to patients with systemic diabetes. This report assesses the various types of screening conducted for the detection of diabetic retinopathy.

Rationale for screening

The importance of detecting clinically important lesions of retinopathy is to facilitate the timely administration of treatment strategies to prevent vision loss. The screening methods must have high sensitivity and specificity in detecting the two main causes of vision loss in diabetic retinopathy: the presence of either clinically significant macular edema (CSME) or of severe nonproliferative or proliferative diabetic retinopathy, when treatment would be considered. In cases of CSME, patients treated with focal laser photocoagulation have a 50% reduction in the risk of moderate visual loss [8]. Scatter (panretinal) laser photocoagulation along with vitrectomy has reduced the risk of severe vision loss in patients with severe nonproliferative and proliferative diabetic retinopathy by as much as 90% [2,9].

Challenges in screening

Several challenges exist in screening for diabetic retinopathy. Where would be the most likely place to capture the highest yield of patients requiring screening? Who should be screened? Which technology should be considered in the screening? Who should be implementing the screening? Will there be expertise to adjudicate the results of the screening? Will the screening result in a timely referral of patients who urgently need care for their sight-threatening diabetic retinopathy? Who will provide the funds for such screening and perhaps care as well? It is not feasible to address all the challenges in this short report, and there are no easy answers for some of the issues raised.

Most experts would consider the offices of primary care physicians treating patients with systemic diabetes to be an ideal place for screening. Mass screenings at health fairs or screening by optometrists or ophthalmologists of the general population with fundus photographs are not likely to capture a high yield of patients with diabetic retinopathy. The targeted population should be persons with diabetes in the primary care setting.

In patients with CSME, the challenge is to detect the elevation of the retina in fovea by photographic means. This would require either viewing or photographing the affected eye using stereoscopic methods. Both CSME and proliferative diabetic retinopathy may require dilated eye examinations to obtain adequate ophthalmoscopy or quality photographs to assess for the presence of these fine vessels.

Methods of screening for diabetic retinopathy

The traditional screening has been the one-on-one examination of the patient with diabetes by the ophthalmologist. The increasing rate of diabetes is burdensome, and it will be difficult in many countries, including the US, to meet the need for annual ophthalmologic examinations among all persons with diabetes who have been advised to have them. One of the barriers is the low rate of referrals from primary care physicians and diabetologists treating patients with diabetes for eye examinations by ophthalmologists familiar with the management of diabetic retinopathy. Should the responsibility for screening be shared among the clinicians treating the patient: primary care physicians, endocrinologists, diabetologists, general ophthalmologists, and vitreoretinal specialists? The interobserver differences among the different clinicians, general ophthalmologists, retinal specialists, ophthalmic nurses, and ophthalmic photographers on the grading of a single image of the retina shows only fair agreement [10]. Retinal specialists had the best agreement among the groups (kappas 0.58 and 0.63 for retinopathy severity and macular edema and for appropriate referrals of those requiring therapy). When all readers were compared with the consensus of retinal specialists, agreement was poor: 0.35, 0.28, and 0.29 for retinopathy severity, macular edema, and need for referrals to the ophthalmologist.

A growing number of studies have been conducted with digital photography as clinical practice has converted to digital for many ophthalmologists. The ease of performance as well as the ease in storage make digital photography more desirable. The gold standard for the documentation of diabetic retinopathy consists of the stereoscopic photography of seven standard fields on color film established in the Early Treatment Diabetic Retinopathy Study – Classification of Diabetic Retinopathy [11]. Studies [12,13] have been conducted showing the comparability of digital fundus photography with film-based fundus photography of the seven stereo fields. Monochromatic fundus photography has been suggested in a case series [14] to be more sensitive than ophthalmoscopy for the detection of diabetic retinopathy. The results of a study in England suggest that the use of fundus photography of seven stereo fields provides more reliable and accurate information than the clinical examination using ophthalmoscopy [15]. The sensitivity of detection of eye disease by photography was 89% (95% confidence interval [CI]: 80–98%), significantly better than for direct ophthalmoscopy (65%; 95% CI: 51–79%). With the addition of stereoscopic macular photography,

the analysis of patients with false-negative results indicated possible improvement of photographic sensitivity to 93%. Specificity of detection of sight-threatening eye disease was 86% (95% CI: 82–90%) for photography and 97% (95% CI: 95–99%) for direct ophthalmoscopy. Other investigators [16] have also concluded that conducting direct ophthalmoscopy in addition to performing fundus photography of seven stereo fields provides very little additional information.

The previously described examinations and fundus photography usually require the dilation of the pupils, making the assessment more difficult to conduct in locations outside of an ophthalmologist's office. Bursell *et al.* [12] have studied use of the nonymydriatic cameras. The use of nonmydriatic cameras was employed especially in locations such as the offices of medical physicians treating patients with diabetes. The photographs obtained from a nonmydriatic camera were compared with those taken via dilated photography with seven stereo fields, and correlation was relatively good [12]. There was reasonable agreement (kappa = 0.65) between the clinical level of diabetic retinopathy assessed via the undilated nonmydriatic images and the dilated Early Treatment Diabetic Retinopathy Study photographs. Agreement was excellent (kappa = 0.87) for suggested referral to ophthalmology specialists for eye examinations. The use of nonmydriatic cameras was tested in a clinical program [17] and was found to have good sensitivity and specificity. The assessment of the clinical level of diabetic retinopathy agreed exactly with clinical findings in 388 eyes (72.5%) or within one level in 478 eyes (89.3%). The nonmydriatic photographic system's referral based on most severe diagnosis in either eye matched retinal specialist–recommended follow-up in 248 of 268 patients (92.5%). A total of 136 of 525 (25.9%) of the screened patients had nondiabetic ocular abnormalities requiring referral. The investigators' recommended follow-up based on the photographic imaging compared favorably with clinical examination by a retinal specialist. In fact, this system was better at detecting even the nondiabetic lesions found in patients with diabetes, compared with the clinical fundus examination [18••]. Another digital system is designed for the screening of diabetic retinopathy [19].

The next step in the research is to simplify the seven stereo fields to a smaller number of images and to conduct the photography without dilation in the offices of nonophthalmologists. In one study [20], the use of two-field mydriatric digital images was compared with use of a single-field nonmydriatic digital image. The investigators found that mydriatic digital photography produced a sensitivity of 87.8%, a specificity of 86.1%, and a technical failure rate of 3.7%. Having a technician perform ophthalmoscopy did not alter the sensitivity or the specificity. For nonmydriatic photography, the sensitivity was 86.0%, specificity 76.7%, and technical failure rate 19.7%. The investigators concluded that the photographs with the dilation were superior to those obtained using nonmydriatic procedures.

The use of graders has been raised in a study [21] in which the detection of retinopathy is done using a computer-assisted automated system designed to detect red lesions on digitized fundus photographs. Although good sensitivity and specificity were demonstrated for the detection of the presence of diabetic retinopathy, further evaluation is necessary by an experienced grader. Other investigators have conducted studies [22] in which endocrinologists performed fundus photography using a nonmydriatic camera. Two endocrinologists and ophthalmologists with retinal expertise graded the fundus photographs. The kappas were 0.661, 0.647, and 0.676 for the two endocrinologists and ophthalmologists (gold standard), respectively. The number of ungradeable images centered around the macula decreased significantly when the pupil was dilated (42% to 5%). The exact agreement for diagnosis of macular edema between images was still poor with dilation, with kappas of 0.248, 0.234, and 0.278 for the two endocrinologists and the ophthalmologists, respectively. The number of gradable fundus photographs increased markedly when the pupils of these study patients were dilated.

To address the adequacy of coverage of the retina to detect the presence of proliferative diabetic retinopathy, fundus images obtained as a 60° field were compared with the standard seven stereoscopic fields of the peripheral retina [23]. The results showed that one such image was not adequate in coverage to detect peripheral retinal neovascularization or to detect severe nonproliferative diabetic retinopathy.

Frequency of screening remains controversial. Although the American Diabetes Association and the American Academy of Ophthalmology have both recommended annual eye examinations [24], other countries have advocated longer intervals between eye examinations; in Iceland [25], for example, biannual examinations are recommended.

Conclusion

Despite the increased research interest in digital photography techniques, the sensitivity and specificity of these techniques may not be as high as traditional standard seven-field stereoscopic 30° fundus photography for determining the level of diabetic retinopathy [26].

These techniques may eventually prove useful in future studies of screening and treatment trials. No studies at this time, however, have proven that photographic

screening programs achieve a greater reduction in vision loss compared with routine community care in areas of easy access. The screening examination does not replace an eye examination.

Ophthalmologists can play an important role in diabetic care apart from treating eye disease. Counseling can motivate patients regarding the importance of blood glucose and blood pressure control and help alleviate microvascular complications. Of course, such screening programs have great value in circumstances in which access to ophthalmic care is limited. Currently, these screening technologies are not considered a replacement for a comprehensive eye examination by an ophthalmologist experienced in managing diabetic retinopathy.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 576).

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