Screening for Diabetic Retinopathy

Diabetic retinopathy is a highly specific vascular complication of both insulin-dependent (type I) and non-insulin-dependent (type II) diabetes mellitus. The prevalence of retinopathy is strongly related to the duration of diabetes. After 20 yr of diabetes, nearly all patients with type I diabetes and >60% of patients with type II diabetes have some degree of retinopathy. Diabetic retinopathy poses a serious threat to vision. In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), 3.6% of younger-onset patients (aged <30 yr at diagnosis, an operational definition of type I diabetes), and 1.6% of older-onset patients (aged ≥30 at diagnosis, an operational definition of type II diabetes) were legally blind. In the younger-onset group, 86% of blindness was attributable to diabetic retinopathy. In the older-onset group, where other eye diseases were more common, one-third of the cases of legal blindness were due to diabetic retinopathy. Overall, diabetic retinopathy is estimated to be the most frequent cause of new cases of blindness among adults aged 20–74 yr.

THE NATURAL HISTORY OF DIABETIC RETINOPATHY —

Screening strategies depend on the rates of appearance and progression of diabetic retinopathy and on risk factors that alter these rates. Vision-threatening retinopathy usually does not appear in type I patients in the first 5 yr of diabetes, nor before puberty. Over the subsequent two decades, nearly all type I patients develop retinopathy. Up to 21% of patients with type II diabetes have recently been found to have retinopathy at the time of first diagnosis of diabetes, and most develop some degree of retinopathy over subsequent decades.

In general, the progression of retinopathy is orderly, advancing from mild background abnormalities characterized by increased vascular permeability, to preproliferative retinopathy (moderately severe NPDR) characterized by vascular closure, to proliferative retinopathy characterized by the growth of new blood vessels on to the retina and posterior surface of the vitreous.

Vision loss with diabetic retinopathy results from several mechanisms. First, central vision may be impaired by macular edema or capillary nonperfusion. Second, the new blood vessels of proliferative retinopathy and contraction of their accompanying fibrous tissue can distort the retina and lead to tractional retinal detachment, producing severe and often irreversible vision loss. The new blood vessels may bleed adding the further complication of preretinal or vitreous hemorrhage.

There are several epidemiological studies describing the onset and progression of diabetic retinopathy. The WESDR can serve as the model. The WESDR attempted to identify all diabetic patients treated by physicians in an 11-county area in southern Wisconsin. Twelve hundred and ten patients with younger-onset diabetes and 1780 patients with older-onset diabetes were entered into the study between 1979 and 1980. Patients had several clinical assessments including seven-field stereofundus photographs and measurement of glycosylated hemoglobin. A 4-yr follow-up examination repeated the fundus photographs. The WESDR found the relationship described above between onset of retinopathy and duration of diabetes. It also established that progression of retinopathy was a function of baseline retinopathy. In particular, among type II diabetic patients, where there is a lower aggregate proliferative retinopathy or severe macular edema over 4 yr among patients whose baseline photographs showed no retinopathy. The WESDR epidemiological data were limited primarily to younger white Northern European extraction populations and may not be applicable to black or Hispanic populations or others with a high prevalence of hyperglycemia. The more severe the baseline retinopathy the greater the frequency of progression to vision-threatening retinopathy.

There has been extensive research on potential risk factors for retinopathy. There is now a large and consistent set of observational studies documenting the association of poor glucose control and retinopathy. In the WESDR a strong positive relationship between the incidence and progression of retinopathy and glucose control (i.e., measured by glycoslyated hemoglobin) was found after controlling for duration of diabetes, age, sex, and baseline retinopathy. Whether hyperglycemia is causal and whether tight glycemic control can prevent or ameliorate retinopathy is currently not known. But hyperglycemia is an indicator of risk for retinopathy. It also seems clear that proteinuria is associated with retinopathy. High blood pressure is an established risk factor for the development of macular edema and is associated with the presence of proliferative diabetic retinopathy. Preliminary observations indicate an association of serum lipid levels with

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lipid in the retina (hard exudates). In addition, several case series and a controlled prospective study suggest that pregnancy in type 1 diabetic patients may aggravate retinopathy. Beyond these clinical features, there are no well-substantiated risk factors for retinopathy.

THE EFFICACY OF LASER PHOTOCOAGULATION SURGERY

—The prime motivation for screening for diabetic retinopathy is the established efficacy of laser photocoagulation surgery in preventing visual loss. Two large National Institutes of Health–sponsored trials, the Diabetic Retinopathy Study (DRS) and the Early Treatment Diabetic Retinopathy Study (ETDRS) provide the strongest support for the therapeutic benefit of photocoagulation surgery.

The DRS tested whether scatter (panretinal) photocoagulation surgery could improve the prognosis of proliferative retinopathy. One thousand seven hundred and fifty-eight patients participated. By the 2-yr analysis, a dramatic benefit of photocoagulation was evident. Severe visual loss was seen in 15.9% of untreated eyes vs. 6.4% of treated eyes. The benefit was greatest among patients whose baseline evaluation revealed high-risk characteristics (HRC; chiefly vitreous hemorrhage with any retinal neovascularization or disc neovascularization). Twenty-six percent of control eyes with HRC progressed to severe visual loss versus 11% of treated eyes. The absolute benefit of photocoagulation was much smaller for eyes that did not have HRC. Given the risk of a modest loss of visual acuity and of contraction of visual field from panretinal laser therapy, such therapy has been primarily recommended for eyes approaching or reaching HRC.

The recently completed ETDRS assessed the value of argon laser surgery and aspirin in early proliferative (PDR), moderate to severe nonproliferative diabetic retinopathy (NPDR), and diabetic macular edema (a complication seen in the presence of both PDR and NPDR). The ETDRS established the benefit of focal laser photocoagulation in eyes with macular edema, particularly those with clinically significant macular edema. In the part of the ETDRS that studied macular edema, 1490 eyes with macular edema were randomized to deferral of photocoagulation (until proliferative retinopathy with HRC occurred) and 754 eyes were randomized to immediate focal photocoagulation. Among patients with clinically significant macular edema after 2 yr, 20% of untreated eyes had experienced a doubling of the visual angle to (e.g., 20/40 or 20/50 to 20/100) compared with 8% of treated eyes. In recent results from the ETDRS, aspirin did not prevent the development of high-risk proliferative retinopathy and did not reduce the risk of visual loss nor did it increase the risk of vitreous hemorrhage. The relative risk of vitreous or preretinal hemorrhage for patients assigned to aspirin compared with patients assigned to placebos in eyes that had new vessels definitely present at baseline was 1.05 (99% confidence interval 0.81–136). This included patients in the referral group who in follow-up had scatter laser photocoagulation on reaching HRC. These findings suggest there are no ocular contraindications to aspirin when required for cardiovascular disease or other medical indications.

Other results from ETDRS indicate that provided careful follow-up can be maintained, scatter photocoagulation is not recommended for eyes with mild or moderate nonproliferative diabetic retinopathy. When retinopathy is more severe, scatter photocoagulation should be considered and usually should not be delayed if the eye has reached the high-risk proliferative stage.

Laser photocoagulation surgery in both the DRS and ETDRS was beneficial in preventing further visual loss, but generally not beneficial in reversing already diminished acuity. This preventive effect and the fact that patients with proliferative retinopathy or macular edema may be asymptomatic provide strong support for a screening program to detect diabetic retinopathy.

Currently, there are no other interventions that have been clearly shown to benefit diabetic retinopathy, and therefore no other therapies to consider in fashioning a screening strategy.

MANAGEMENT OF PATIENTS WITH DIABETES

—Diabetic retinopathy is only one of several potentially serious complications of diabetes that requires diligent attention by health-care professionals. Because they have a multisystem chronic disease, patients with diabetes are best monitored and managed by highly skilled physicians whose training and experience help to ensure early detection and appropriate treatment of the serious complications of the disease, including diabetic retinopathy. In ideal circumstances, patients with diabetes will have their disease under good control and be monitored frequently by physicians knowledgeable in the care of diabetes. These physicians, in turn, will ensure that their patients receive timely care by other health-care professionals whose expertise will allow for continued optimal functioning and prolonged lives of their patients. Clearly, in this regard, a team approach to screening, diagnosing, treating, and monitoring the complex facets of this systemic disease will serve the best interests of the patient. In particular, patients with diabetes must be examined routinely for the development of diabetic retinopathy.

COST-EFFECTIVENESS OF SCREENING

—There have been several cost-effectiveness analyses of screening for diabetic retinopathy. The currently published analyses have assessed yearly and semiannual screening programs. Although the modeling techniques and the component costs have differed substantially, the basic message of all these analyses is the same. Screening for diabetic retinopathy saves vision at a relatively low cost, and even this cost is often less than the disability payments pro-

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vided to people who would go blind in the absence of a screening program.

SUMMARY AND RECOMMENDATIONS—Timely laser photocoagulation therapy can prevent loss of vision in a large proportion of patients with severe nonproliferative and proliferative diabetic retinopathy. Patients with vision-threatening retinopathy may not have symptoms. As a result, ongoing evaluation for retinopathy is a valuable strategy. The most sensitive screening technique is stereofundus photography and this might provide the basis for more efficient screening strategies in the future. However, it has not been widely used for screening. Currently, yearly dilated ophthalmoscopic examination seems the best approach.

Guidelines

1. Patients with type I diabetes should be screened annually for retinopathy beginning 5 yr after the onset of diabetes. In general, screening is not indicated before the start of puberty.

2. Patients with type II diabetes should have an initial examination for retinopathy shortly after the diagnosis of diabetes is made. If dilated ophthalmoscopy is used, then examinations should be repeated annually. If skilled reading of seven-field stereo photographs is available and reveals no retinopathy at the initial screen, then the next screening exam does not need to be done for 4 yr. Care should be taken not to lose these patients to follow-up. After this 4-yr exam, subsequent screening with stereo photographs or dilated ophthalmoscopy should be performed annually. Patients with persistent very elevated glucose levels (e.g., mean plasma glucose <280 mg/dl) or proteinuria should have yearly examinations regardless of screening technique.

3. When planning pregnancy, women with preexisting diabetes should be counseled on the risk of development and/or progression of diabetic retinopathy. Women with diabetes who become pregnant should have a comprehensive eye examination in the first trimester and close follow-up throughout pregnancy. This does not apply to women who develop gestational diabetes, because such individuals are not at increased risk for diabetic retinopathy.

4. Patients with macular edema, moderate to severe nonproliferative retinopathy, or any proliferative retinopathy require the prompt care of an ophthalmologist who is knowledgeable and experienced in the management of diabetic retinopathy.

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