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First Incidence and Progression Study for Diabetic Retinopathy in Portugal, the RETINODIAB Study

Evaluation of the Screening Program for Lisbon Region

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Purpose: To estimate the 5-year incidence and progression of diabetic retinopathy (DR) among persons with type 2 diabetes mellitus (DM).

Design: Population-based, prospective, cohort study.

Participants: The RETINODIAB (Study Group for Diabetic Retinopathy Screening) program was implemented in the Lisbon and Tagus Valley area between July 2009 and December 2014. A total of 109 543 readable screening examinations were performed and corresponded to 56 903 patients who attended the screening program at entry. A total of 30 641 patients (53.85%) had at least 1 further screening event within the study period and were included in the analysis.

Methods: Participants underwent two 45° nonstereoscopic retinal digital photographs per eye according to RETINODIAB protocol. All images were graded according to the International Clinical Diabetic Retinopathy Scale. Referable diabetic retinopathy (RDR) was defined for all patients graded as moderate nonproliferative DR (NPDR), severe NPDR, or proliferative DR (PDR), with or without maculopathy or mild NPDR with maculopathy. Nonparametric estimates of the annual and cumulative incidences were obtained by Turnbull's estimator. Associations between the potential risk factors and the time to onset/progression of retinopathy were assessed through a parametric survival analysis for interval-censored data.

Main Outcome Measures: The authors estimated the onset and progression incidence rates of DR.

Results: Yearly incidence of any DR in patients without retinopathy at baseline was 4.60% (95% confidence interval [CI], 3.96−4.76) in the first year, decreasing to 3.87% (95% CI, 2.57−5.78) in the fifth year. In participants with mild NPDR at baseline, the progression rate to RDR in year 1 was 1.18% (95% CI, 0.96−1.33). Incidence of any DR and RDR and DR progression rate were associated with known duration of diabetes, age at diagnosis, and use of insulin treatment.

Conclusions: This longitudinal epidemiologic study provides the first Portuguese incidence DR data in a large-scale population-based cohort of type 2 diabetes after a 5-year follow-up. Duration of diabetes, age at diagnosis, and insulin treatment were associated with increasing risk of incidence and progression of DR. A personalized schedule distribution of screening intervals according to the individual patient's profile should be implemented, with resulting benefits in terms of health costs. *Ophthalmology 2015;■:1−9 © 2015 by the American Academy of Ophthalmology.*

Diabetic retinopathy (DR) remains a major cause of visual impairment and represents an ongoing and worrying worldwide public health issue.[1−3] In 2013, 382 million people had diabetes; this number is expected to increase to 592 million by 2035, according to the International Diabetes Federation.[4] Most people with diabetes live in low- and middle-income countries, and these will experience the greatest increase in cases of diabetes over the next 22 years.[5]

Diabetic retinopathy is a highly specific vascular complication of both type 1 and 2 diabetes, with incidence strongly related to the duration of diabetes.[6−8] It is well established that effectiveness of the laser treatment depends on the accurate and timely treatment of DR among patients with diabetes mellitus (DM), particularly those with a high risk of DR.[9]

This type of retinopathy represents an excellent paradigm for screening as laid out in the principles for screening of human disease described by Wilson and Jungner in 1968.[10] Indeed, from a public health standpoint, screening for DR has been shown to be cost-effective in health economic terms.[11]

To decrease by approximately 30% the new cases of blindness caused by diabetes, the declaration of St. Vincent

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(1989) called for the implementation of national strategies for DR screening in a systematic manner.[12] The World Health Organization, the International Diabetes Federation, and the Portuguese Directorate-General of Health (DGS) co-organized in 1997 the Fourth Meeting in Lisbon for the Implementation of the St. Vincent Declaration, which was attended by delegates from 60 countries.[13] This conference reinforced, once again, the need for greater engagement from all signatory countries. This international challenge was strengthened at the Liverpool meeting in 2005.[14] Despite all this, it has been only in the last decade that significant progress has been made in implementing DR screening programs.

Portugal currently has a population of 10.6 million, who are predominantly white, and the majority (~8.5 million) are located on the western coast.[15] According to the National Observatory for Diabetes, approximately 1 million Portuguese have diabetes, the equivalent of 13% of the population aged 20 to 79 years (2013).[16]

After a pilot regional DR screening program that was launched in 2008, the Diabetic Retinopathy Screening Service for Lisbon and Tagus Valley, RETINODIAB, was commissioned and driven by the Portuguese Diabetes Association (APDP) in 2009. This screening program was supported by the Regional Health Administration of Lisbon and Tagus Valley under the auspices of the DGS, which is a public health branch of the Ministry of Health. The major aim of this project was to identify all undiagnosed sight-threatening DR to ensure timely onward referral to Lisbon area hospital eye services.

The APDP is the world's oldest diabetes association and a senior member of the International Diabetes Federation. Since its foundation in 1926, the APDP has been driven by a single overarching objective: to improve the quality of life of people with diabetes.

In Portugal, so far, there are no accurate data on the incidence of DR, based on a large-scale screening community-based program, over a period of time.

We describe the first incidence and progression study for DR in a Portuguese population among persons with type 2 DM. We estimated the annual and cumulative DR incidence and the DR rate progression over a 5-year period, and explored the association between the development of retinopathy and its putative risk factors.

Methods

The RETINODIAB Network

RETINODIAB (Study Group for Diabetic Retinopathy Screening) is a telemedical screening system carried out by the APDP that has focused on clinical aspects of DR screening. Its primary aim was to promote the advance of knowledge on all aspects of DR through an active cooperation between ophthalmologists and other specialists, such as endocrinologists, internists, and neurologists. Currently, more than 200,000 people nationwide have benefited from integrated and specialized healthcare services provided by the APDP in a range of diabetes-related fields: diabetology, ophthalmology, pediatrics, nutrition, cardiology, podiatry, nephrology, urology, women's health, and mental health.

Working under the auspices of Regional Health Administration of Lisbon and the Tagus Valley protocol (Portuguese Ministry of Health), the Association's clinical services were integrated into the public healthcare network around Lisbon and Tagus Valley. Moreover, the APDP has fostered the development of important scientific studies in epidemiology and diabetology in Portugal.[17–19] The APDP has carried out relevant scientific work in collaboration with international institutions of reference.

Lisbon and Tagus Valley Area

Lisbon and Tagus Valley is 1 of the 5 regions of Portugal termed as "Nomenclature of Territorial Units for Statistics" (NUTS II subdivisions). The region corresponds to 13% of the Portuguese territory including the capital, Lisbon; it has a population of 3.7 million (34% of the total population); and, according to the Centre for Regional Dynamics Observation (2009), it represents 44% of the national gross domestic product.

There are 15 primary health center groups in this area, organized according to the 5 existing NUTS III (subregions: Greater Lisbon, Setubal Peninsula, Middle Tagus, Lezíria, and West Coast). Their mission is to ensure the provision of Primary Health Care in a particular geographic area, enhancing health gains accomplished by Family Health Units or other primary care units.

Nonmydriatic Digital Camera for Diabetic Retinopathy Screening

Currently, teleophthalmology based on digital imaging system provides a credible and efficient DR screening service. Indeed, it allows a sensitivity of 92% and a specificity of 90%, thus justifying its use in terms of cost/benefit and gains to health.[20] Furthermore, it offers several advantages, such as instant photography display, ease of storage and consultation of iconography available, and a remote transmission via Internet. The advance of telemedicine in ophthalmology screening of DR has a broader application, especially in remote ophthalmologic-assistance areas.

Portuguese Diabetes Association Screening Protocol

The RETINODIAB screening program was held in several health units covered by the APDP protocol. It encompasses several screening centers located in the primary care units of 15 primary health center groups. Each screening center is equipped with a nonmydriatic camera (model CR-2, Canon, Tokyo, Japan). Persons with type 2 diabetes who are registered with a general practitioner in the Lisbon and Tagus Valley area and not already under the care of hospital eye services for DR-related reasons are required to be referred to RETINODIAB program. Only patients with no history of documented DR or mild DR were referred for screening. All persons invited for examination are sent an appointment letter with a date, time, and medical center for screening. The devices were allocated—geographic distribution among different health centers—in a regular and systematic manner to improve the interaction with general practitioners, thus optimizing system referral and screening. All images were classified according to The International Clinical Diabetic Retinopathy Scale.[21]

This International Clinical Classification System categorizes DR severity in 5 levels, which include 3 stages of low risk (none, mild, and moderate NPDR), a fourth stage of severe NPDR, and a fifth stage of PDR, in the presence or absence of diabetic macular edema, which is graded separately. Referable diabetic retinopathy (RDR) was defined for all patients graded as moderate NPDR; severe NPDR or PDR, with or without maculopathy; or mild NPDR with maculopathy. This category (RDR) relates to those