Abstract

Aim. – This study evaluated the incidence of diabetic retinopathy (DR) over a 3-year period in a French population that was followed by OPHDIAT®, and assessed the clinical and biological risk factors associated with incident retinopathy.

Methods. – The studied patients were screened for DR during hospitalization for their annual diabetes check-up in the endocrinology department by two examinations three years apart. DR screening used the OPHDIAT® telemedical network, and the examination included clinical and biological data.

Results. – A total of 254 patients were studied. At the 3-year follow-up, the incidence was 14.0%, (CI 9.5–18.4%). Longer duration of diabetes and the presence of micro- or macroalbuminuria were significantly associated with incident retinopathy ($P<0.05$). Other potential risk factors were not statistically significantly related to DR progression, and only treatment with insulin showed a trend towards significance ($P<0.20$).

Conclusion. – This study provides the first French data on the incidence of DR, which was estimated after a 3-year follow-up at 14.0%. Longer duration of time from the onset of diabetes and higher baseline albuminuria were the only statistically significant risk factors found for the incidence of DR after our 3-year study. Nevertheless, microalbuminuria should be more widely used in ophthalmological practice in the assessment of DR, as is already the case for both blood pressure and HbA1c.

Keywords: Diabetic retinopathy; Incidence; Risk factors; Screening; OPHDIAT®

Résumé

Étude de l’incidence durant trois ans de la rétinopathie diabétique dans une population suivie à l’hôpital Lariboisière à Paris.

Buts. – Évaluer l’incidence de la rétinopathie diabétique à trois ans dans une population hospitalière française issu du réseau OPHDIAT®, et estimer les facteurs de risques cliniques et biologiques associés à la progression de la rétinopathie.

Méthodes. – Lors d’une hospitalisation annuelle dans un service d’endocrinologie pour bilan annuel de leur diabète, les patients étudiés ont fait l’objet d’un dépistage de la rétinopathie diabétique à trois ans d’intervalle. Le dépistage a été effectué grâce au réseau OPHDIAT®, et les données cliniques et biologiques ont été étudiées.

Résultats. – Deux cent cinquante-quatre patients ont été étudiés. À trois ans, l’incidence était de 14,0 %, (IC 9,5–18,4). Une plus longue durée du diabète et la présence d’une micro- ou macroalbuminurie étaient significativement associées à l’incidence de la rétinopathie diabétique, $P<0.05$. Les autres facteurs de risques potentiels n’étaient pas significativement associés, et seul le traitement par insuline avait une tendance à être significative ($P<0.02$).
1. Introduction

Diabetic retinopathy (DR) is the primary cause of legal blindness in Western countries [1]. Better management of diabetic patients and, in particular, better glycemic control, lower blood pressure [2,3] and regular eye follow-up [4,5], have reduced both the incidence and progression of DR in several countries. However, screening for DR remains a major public-health issue because of the alarming increase in the prevalence of diabetes around the world. In France between 2000 and 2009, the number of people treated for diabetes increased from 2.6% to 4.4% of the population [6]. Access to an ophthalmologist is difficult in France, and this remains a genuine handicap for proper follow-up. In response to these two problems, the telemedical network OPHDIAT® was specifically designed to facilitate access to regular annual eye evaluations in patients with diabetes [7]. The network was set up in 2004 and, since then, it has continued to function routinely.

The purpose of the present study was to evaluate the incidence of DR over a 3-year period in a French population that was followed-up by this network, and to assess the clinical and biological risk factors associated with incident retinopathy.

2. Methods

2.1. Study population

This retrospective study included 254 diabetic patients, whatever their type of diabetes, who visited the endocrinology department of the Lariboisière Hospital in Paris, France, between 2004 and 2011. All of the patients studied were screened for DR during hospitalization for their annual diabetes check-up by two examinations three years apart.

2.2. Procedure

All patients in the study underwent complete examinations during hospitalization that included:

- a questionnaire detailing the time since diabetes onset, drug treatments for diabetes and treatment for hypertension — in particular, treatment with angiotensin-converting enzyme inhibitors (ACEI) and treatment by statins;
- clinical examination, in which blood pressure was measured using a Dinamap monitor or standard mercury sphygmonanometer, height and weight were recorded, body mass index (BMI) calculated, and screening for DR carried out using a non-mydriatic retinal camera (see below);
- and determinations of glycosylated haemoglobin (HbA1c), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides and creatinine in venous blood, and albuminuria in a sterile urine sample or a 24-h sample.

2.3. Assessment of retinopathy

Screening of DR used the OPHDIAT® (Ophthalmology Diabetes Telemedicine) network, which is based in the Ile-de-France region (around Paris) and includes 30 screening centres linked through a central server to an ophthalmological reading centre [7,8]. Retinal photographs were taken at baseline and at follow-up using a non-mydriatic funduscope camera (TOPCON TRC-NW6, Rotterdam, The Netherlands). Two 45° non-stereoscopic retinal digital photographs per eye were obtained without pupil dilatation: one was of the macula, and included the optic disc; and the other showed the nasal fields.

Trained orthoptists took the retinal photographs, which were then transmitted to the central server where they were read and graded by experienced ophthalmologists. DR was graded according to an international DR classification system [9].

Consultation with an ophthalmologist was recommended to patients for further fundal eye examination in cases of either moderate non-proliferative DR or a more severe diagnosis. Patients with a normal examination were asked to attend another eye screening the following year [5].

2.4. Statistical analysis

Statistical Analysis System software (SAS, version 9.2, SAS Institute Inc., Cary, NC, USA) was used for all data analyses. The incidence of retinopathy was presented as a percentage with a 95% confidence interval (CI). Other data were expressed as means ± SD for continuous variables and as a percentage for categorical variables, with comparisons between those with and without incidental retinopathy using t and χ² tests. The frequency of retinopathy (with standard error bars) has been presented according to time since onset of diabetes and the presence of micro- or macroalbuminuria in the figures.

3. Results

A total of 254 patients were studied. At baseline, 236 patients (93%) showed no DR whereas 18 patients (7%) did. These 18 patients were not included in the calculation of the incidence of DR. At the 3-year follow-up, retinopathy had developed in 33 of the 236 patients in whom retinopathy was not
Table 1
Presence of retinopathy in the studied population at baseline and at the 3-year follow-up.

<table>
<thead>
<tr>
<th>Retinopathy at baseline</th>
<th>Without (n)</th>
<th>With (n)</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without</td>
<td>203</td>
<td>33</td>
<td>236</td>
</tr>
<tr>
<td>With</td>
<td>2</td>
<td>16</td>
<td>18</td>
</tr>
</tbody>
</table>

205 patients had retinopathy present at baseline, thereby giving an incidence of 14.0% (CI: 9.5–18.4%; Table 1). Neither severe non-proliferative diabetic retinopathy (NPDR) nor any proliferative DR was found in our study.

On identifying the type of retinopathy, 29 patients (12%) had developed mild NPDR and four (2%) had moderate NPDR.

Table 2 shows the baseline characteristics of patients with and without incident retinopathy. As the data for some variables are missing, the number of patients studied is specified for each variable.

A longer duration of time since the onset of diabetes and the presence of micro- or macroalbuminuria were significantly associated with the incidence of DR ($P < 0.05$). Other potential risk factors were not statistically significantly related to its progression, and only treatment with insulin showed a trend towards significance ($P < 0.20$).

Fig. 1 shows that the incidence of DR increased progressively with the time since diabetes onset. The incidence was highest (30%) for the group with five to 20 years of diabetes whereas, paradoxically, the incidence was lower for those in whom diabetes (21%) had been present for above 20 years.

Fig. 2 shows the incidence of retinopathy according to albuminuria. In the group with no albuminuria (<30 mg/mL), the incidence was 12 ± 2% compared with 25 ± 8% and 50 ± 20% in the group with microalbuminuria (30–300 mg/mL) and macroalbuminuria (>300 mg/mL).
in the microalbuminuria and macroalbuminuria groups, respectively.

4. Discussion

Our present study showed the rate of incident retinopathy after three years of follow-up, while most epidemiological studies have used a 5-year follow-up timescale. For this reason and to compare studies, the incidences are presented here as annual rates.

Our results are similar to those of the Blue Mountains Eye Study (BMES), which had an incidence at five years of 22.2% [10], but are significantly higher than those of the Australian Diabetes, Obesity and Lifestyle (AusDiab) study [11] and the Melbourne Visual Impairment Project (Melbourne VIP) [12], which had incidence rates of 11% and 14%, respectively, at five years. The incidences in the Liverpool Diabetic Eye Study [13,14] and the DIRECT-Prevent 1 trial [15] exceeded 30% at five years. There are several possible reasons for these differences in incidences. The time since diabetes onset and rises in blood glucose or HbA1c levels are considered to be the most important risk factors for the incidence of DR. In our present study, the mean time since the onset of diabetes was 11.8 ± 6.9 years in patients with incident retinopathy, higher than in other studies: the time since diabetes onset was five years in the AusDiab study [11] and 7.4 years in the BMES [10]. However, it was clearly lower than that of the Liverpool Diabetic Eye Study, which studied type-1 diabetes patients whose durations of time since the onset of diabetes was 15.7 years in those with background retinopathy and 18.4 years in those with mild pre-proliferative retinopathy [14]. In the Melbourne VIP, diabetes had been present for more than 10 years in 43% of the participants but, in that diabetic population, only 15.3% of patients were treated with insulin vs 39.4% of the patients in our present study [12]. In the DIRECT-Prevent 1 study, the incidence was very high, but all of the patients were type-1 diabetics and the screening method used was different, with seven-field retinal photography vs two fields in our study [15]. Also, no cases of severe NPDR or proliferative DR were seen in our study for a number of reasons. First, ours was a relatively small population (n = 254) compared with, for example, the Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) study and the Liverpool Diabetic Eye Study, and the follow-up duration was only three years. Second, patients with NPDR that was moderate or worse were excluded from screening by OPHDIA®©, as consultation with an ophthalmologist was recommended instead.

The OPHDIAT®© is a telemedical network that uses digital non-mydriatic cameras linked to a central reading centre for ophthalmological assessment of DR. Use of the OPHDIAT®© network has increased the proportion of patients undergoing fundus examination during hospitalization while reducing the mean time taken by an ophthalmologist per diagnosis of DR [8]. In addition, every month, the network has to meet quality-assurance procedural objectives and has to undergo evaluation of its performance, yet almost all of the predetermined quality-assurance standards for screening and grading are achieved. The proportion of non-gradable photographs is below the quality-assurance requirement (<10%), and agreement between graders ranges from 92% to 99%, making the OPHDIAT network a reliable technique for DR screening [16].

However, in our present study, only two factors were found to be associated with the incidence of retinopathy: the time since the onset of diabetes; and the presence of micro- or macroalbuminuria. Other risk factors typically associated with retinopathy, such as insulin treatment, HbA1c and blood pressure, were not statistically significant. This can be explained by recruitment bias. Our studied population was one that attended hospital clinics and underwent regular monitoring. The average HbA1c in the groups with and without incident retinopathy showed good therapeutic management. This was also true for hypertension, as 60% of our patients treated for hypertension had average systolic and diastolic blood pressures below the standard levels required for diabetic patients. Of our patients treated for hypertension, 87% of those without retinopathy and 100% of those with retinopathy were treated with an ACEI. The DIRECT-Prevent 1 study [15] showed that treatment with candesartan reduced the incidence of retinopathy, albeit not significantly (P = 0.058), which could explain the low incidence of DR even with the longer duration since onset of diabetes.

Microalbuminuria describes the urinary excretion of small amounts of albumin. Many studies have shown that this is a marker of cardiovascular and renal risks in type-2 diabetes patients [17], and that it may also be considered a marker of generalized endothelial dysfunction. Indeed, microalbuminuria has been linked to increases in transcapillary albumin leakage, and in von Willebrand factor and other markers of endothelial dysfunction [18]. Several studies have reported an association between microalbuminuria and the presence of DR, including the WESDR study [19], which involved a large sample of diabetic patients (＞1300 patients) and, more recently, cross-sectional studies from Iran (590 patients) [20] and Brazil (1214 patients) [21].

The present study has several limitations. It was a retrospective study with a small sample population, including only a small number of patients with DR. In addition, our diabetic patients were from a hospital population and not the general population, so they may have received better follow-up and more aggressive treatment than those in the general population. Furthermore, the population studied was predominantly an urban population from the Île-de-France and, thus, not comparable to a rural population.

In summary, the present study provides the first French data on the incidence of DR, which was estimated after a 3-year follow-up at 14.0% (CI: 9.6–18.4%). A longer time since the onset of diabetes and higher baseline albuminuria were the only statistically significant risk factors found for the incidence of DR over the 3-year period of our study. Nevertheless, testing for microalbuminuria should be more widely used in ophthalmological practice for the assessment of DR, as is already the case for both blood pressure and HbA1c. In addition, the results of our study highlight the fact that the use of a telemedical network such as OPHDIAT®© allows for effective screening of DR, thereby effectively compensating for the lack of ophthalmologists in France.
Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References