Original article

Use of retinal photography in the diagnosis of diabetic macular edema

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ABSTRACT

Objective: To determine the validity of retinal photography in the diagnosis of diabetic macular edema. Determine the number and size of the photographs for its correct diagnosis.

Methods: Cross-sectional observational study consisting of 420 eyes of patients with diabetic retinopathy, using a combination of retinography (simple, stereoscopic, red-free light), after expansion, to determine its validity in the diagnosis of diabetic macular edema. Sensitivity, specificity, positive and negative predictive values and the correlation with the gold standard test (optical coherence tomography) were calculated. The retinographs were evaluated by three experts and their results were analyzed using the statistical program SPSS 15.0 Windows.

Results: Sensitivities were below 80% in simple photographs and above 80% in the stereoscopic retinography, whereas those associated with red-free filters, reaching the 30° green stereoscopic photography, showed a sensitivity of 94.3%. The specificity was 95% in color and red-free stereoscopic retinography of 45° and 30°. The positive predictive value was greater than 95% and the negative value was greater than 90% with a coefficient of agreement of 80%, and a degree of consistency with the benchmark of over 80%.

Conclusions: The results of the stereoscopic retinographs are sufficient to enable them to be used in screening for diabetic macular edema. The use of a green filter and its combination with visual acuity improves the results in the diagnosis of this disease.

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Utilidad de las retinografías en el diagnóstico del edema macular diabético

RESUMEN

Objetivo: Determinar la validez de las retinografías en el diagnóstico del edema macular diabético. Fijar el número y amplitud de las fotografías necesarias para su correcto diagnóstico.

Métodos: Estudio observacional transversal constituido por 650 ojos de pacientes con retinopatía diabética, a los que se realizó una combinación de retinografías (simples,
Introduction

Diabetic macular edema is the main cause of diminished visual acuity (VA) in diabetes. Central vision is involved from early stages of the retinopathy and it expresses more frequently in elderly patients with diabetes mellitus type II. In addition, the complications of diabetic retinopathy are largely preventable although early detection is crucial as it could reach severe stages without exhibiting symptoms.

Traditionally, slit lamp biomicroscopy has been used in clinical practice to diagnose diabetic macular edema. Research studies have utilized retinal stereo photographs focused on the posterior pole. However, these methods only provide quantitative and subjective information about retinal thickening but are relatively insensitive to detect retinal thickness changes. It has been estimated that an increase of 150–160% of the normal sickness is required for detection using said methods.

Technological developments have given rise to new technologies which have revolutionized diabetic macular edema management, enabling easy and precise retinal thickness measurements. Of these technologies, optic coherence tomography (OCT) is the reference test for diagnosing diabetic macular edema.

Diabetic retinopathy classification is based on clinical examinations which are highly sensitive and specific even though retinographs provide highly valuable data because they are able to document and compare the severity of the process, its progress and the effects of treatment. However, for diagnosing diabetic macular edema, a flat photograph is not as efficient as in other retinal injuries because a simple photograph does not facilitate retinal thickness measurements. At presence, some retinal cameras are equipped with special devices which can take stereoscopic images which exhibits advantages over simple images as they allow a more effective analysis of retinal thickness.

The objective of this study is to assess the usefulness of stereoscopic retinographs for diagnosing diabetic macular edema.

Subjects, materials and methods

A transversal prospective study which comprised 650 eyes of 325 diabetic patients who exhibited some degree of retinopathy between 2005 and 2009. In accordance with the Helsinki Declaration, all patients expressed their informed consent after being explained the characteristics of the study and receiving guarantees about the confidentiality of the results.

A personal record was made for each patient for subsequent epidemiological study. In addition, an in-depth ophthalmological examination was carried out which included refraction and visual acuity measurements following the protocol proposed and published by the Early Treatment Diabetic Retinopathy Study Research Group (ETDRS) as well as slit lamp examination to verify the absence of contraindications for dilation. The patients exhibiting ophthalmic and/or systemic diseases as well as opacity in ocular media which could jeopardize the quality of the tests were excluded.

Subsequently, retinographs were taken focused on the posterior pole of patients and utilizing the TRC-6W mydriatic retinograph (Topcon, Topcon Corporation, Tokyo, Japan), establishing 8 types of different photographic assemblies of the retinographs depending on whether they were simple or stereoscopic, in color (Fig. 1) or with green filters (anerithra light) (Fig. 2) and on the increases thereof at 45° or 30°.

The retinographs were analyzed by 3 experts, establishing the diagnostic of macular edema on the basis of the criteria established by the ETDRS. Sensitivity, specificity, positive and negative predictive value and the matching (κ index) were obtained for each examination. The results were analyzed by the SPSS 15.0 statistical software (SPSS Inc., Chicago, USA) for Windows.

Results

For the macular edema, analysis sensitivities below 80% were obtained for color photographs at 45°, green at 45°, color at 30°, and above 80% in color stereoscopic photographs at 45°.
stereoscopic green at 45°, stereoscopic in color at 30°, stereoscopic green at 30%, with stereoscopic green photographs reaching a sensitivity of 94.3%. In what concerns specificity, values above 90% were obtained in color and red-free stereoscopic photographs at 45° and 30° (Table 1). The positive predictive value approached 95% in green light retinographs at 45° and 30° or above in the rest. A diagnostic safety degree above 85% was obtained in stereoscopic photographs at 45° and 30°, and a precision of 90% in stereoscopic color retinography at 30° and red-free at 45° and 30°.

Analyzing the combination of the VA with retinographs, increased diagnostic sensitivity was observed. In simple photographs it increased 72.6% in 45° color retinographies and 77.1% in 30° color photographs at a sensitivity of 82% and 87% respectively. For stereoscopic photographs sensitivity values increased 18.2% in 45° color retinographs and values of 89% and 87.6% in 30° color photographs up to 93%. In the case of red-free retinographs, sensitivities of approximately 79.2% in photographs at 45° and of 89.5% in photographs at 30° increased to approximately 88% and 95% respectively. Finally, the combinations of green filter stereoscopic retinographies increased from 18.9% in associations of 2 retinographies at 45° and 94.3% of 2 photographs at 30° up to 93% 96% respectively when associating the VA capture (Fig. 3).

Table 1 – Indices, coefficients and probability values for comparing retinal photographs with OCT diagnostic for macular edema.

<table>
<thead>
<tr>
<th></th>
<th>Color 45°</th>
<th>2 Color 45°</th>
<th>Green 45°</th>
<th>2 Green 45°</th>
<th>Color 30°</th>
<th>2 Color 30°</th>
<th>Green 30°</th>
<th>2 Green 30°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>72.6%</td>
<td>80.2%</td>
<td>79.2%</td>
<td>89.6%</td>
<td>77.1%</td>
<td>87.6%</td>
<td>89.5%</td>
<td>94.3%</td>
</tr>
<tr>
<td>Specificity</td>
<td>93.5%</td>
<td>95.2%</td>
<td>92.1%</td>
<td>91.9%</td>
<td>93.3%</td>
<td>94.9%</td>
<td>91.7%</td>
<td>91.5%</td>
</tr>
<tr>
<td>Positive predictive value (PPV)</td>
<td>95.1%</td>
<td>96.6%</td>
<td>94.4%</td>
<td>95.0%</td>
<td>95.3%</td>
<td>96.8%</td>
<td>94.9%</td>
<td>95.2%</td>
</tr>
<tr>
<td>Negative predictive value (NPV)</td>
<td>66.7%</td>
<td>74.1%</td>
<td>72.5%</td>
<td>83.8%</td>
<td>70.0%</td>
<td>81.2%</td>
<td>83.3%</td>
<td>90.0%</td>
</tr>
<tr>
<td>True positives (TP)</td>
<td>77</td>
<td>85</td>
<td>84</td>
<td>95</td>
<td>81</td>
<td>92</td>
<td>94</td>
<td>99</td>
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<tr>
<td>False positives (FP)</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>True negatives (TN)</td>
<td>58</td>
<td>60</td>
<td>58</td>
<td>57</td>
<td>56</td>
<td>56</td>
<td>55</td>
<td>54</td>
</tr>
<tr>
<td>False negatives (FN)</td>
<td>29</td>
<td>21</td>
<td>22</td>
<td>11</td>
<td>24</td>
<td>13</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Exactitude (Pc)</td>
<td>80%</td>
<td>86%</td>
<td>84%</td>
<td>90%</td>
<td>83%</td>
<td>90%</td>
<td>90%</td>
<td>93%</td>
</tr>
<tr>
<td>Diagnostic safety (J)</td>
<td>0.66</td>
<td>0.75</td>
<td>0.71</td>
<td>0.82</td>
<td>0.70</td>
<td>0.83</td>
<td>0.81</td>
<td>0.86</td>
</tr>
<tr>
<td>Positive certainty (L+)</td>
<td>11.26</td>
<td>16.84</td>
<td>9.98</td>
<td>11.11</td>
<td>11.57</td>
<td>17.23</td>
<td>10.74</td>
<td>11.13</td>
</tr>
<tr>
<td>Negative certainty (L−)</td>
<td>0.29</td>
<td>0.21</td>
<td>0.23</td>
<td>0.11</td>
<td>0.24</td>
<td>0.13</td>
<td>0.11</td>
<td>0.06</td>
</tr>
<tr>
<td>Estimated prevalence</td>
<td>16%</td>
<td>16%</td>
<td>16%</td>
<td>16%</td>
<td>16%</td>
<td>16%</td>
<td>16%</td>
<td>16%</td>
</tr>
<tr>
<td>Probability of positive post-test (PPPT)</td>
<td>68.2%</td>
<td>76.2%</td>
<td>65.5%</td>
<td>67.9%</td>
<td>68.8%</td>
<td>76.6%</td>
<td>67.2%</td>
<td>67.9%</td>
</tr>
<tr>
<td>Probability of negative post-test (PNPT)</td>
<td>5%</td>
<td>4%</td>
<td>4%</td>
<td>2%</td>
<td>4%</td>
<td>2%</td>
<td>2%</td>
<td>1%</td>
</tr>
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</table>
Discussion

The British Diabetic Association\(^9\) establishes that, in order to utilize a technique as a screening test for diabetic retinopathy, it should have a sensitivity of at least 80% and a specificity of 95% against the reference test, with a percentage of true positives of 55% and under 5% of failures.

In the instant study, the macular edema analysis obtained sensitivities exceeding 80% in stereoscopic photographs, in color photographs at 45\(^{\circ}\), stereo photograpbs green at 45\(^{\circ}\), stereoscopic in color at 30\(^{\circ}\) and stereoscopic green at 30\(^{\circ}\), with green stereoscopic photographs at 30\(^{\circ}\) achieving a sensitivity of 94.3%.

As regards specificity, values approaching 95% or above were obtained in color and red-free stereoscopic photographs at 45\(^{\circ}\) and 30\(^{\circ}\). The coefficients agreed by experts were of 80%, exhibiting a high match.

The positive predictive value exceeded 95% and the negative predictive value was in the area of 80%, demonstrating its usefulness to confirm or discard the diagnostic.

The pondered K coefficients in the 3 experts were close to 0.9 or above in stereoscopic retinographies in color and in green at 30\(^{\circ}\), with a high match with the reference test (OCT), indicating a high degree of agreement between observers (Fig. 4). The degree of precision approached 90% and the Youden J index (diagnostic certainty) was above 70% for stereoscopic retinographies, indicating a high proportion of success of these examinations and high overall quality of the tests for diagnostic.

The above results are consistent with those obtained by several authors such as Lin et al.\(^{10}\) who compared simple color retinographies with clinic and exploration for screening diabetic retinopathy, reaching a sensitivity of 78% and specificity of 86% but with a poor matching rate (\(\kappa\) 0.40).

Virgili et al.\(^{11}\) carried out a systematic review of studies, comparing stereo photographs and biomicroscopy with non-contact lenses for diagnosing macular edema with OCT.

They obtained sensitivity values of 0.79 and specificity of 0.88, emphasizing the role of OCT to identify slight increases in central retinal thickness comprised between 230 and 300 \(\mu\) which went unnoticed in routine clinical explorations.

Other studies such as the one by Liesenfeld et al.\(^{12}\) compared digital photographs obtained through telemedicine with standard retinal photographs and the clinical assessments were performed by ophthalmologists, obtaining 62% sensitivity in the diagnostic of clinically significant macular edema (CSME).

Stellingwerf et al.\(^{13}\) compared two 45\(^{\circ}\) stereoscopic photographs with the clinical assessments carried out by the ophthalmologist (considered to be the reference test) for screening diabetic retinopathy and achieved 95% sensitivity in treatable retinopathy and 83% in screening.

Yang et al.\(^{14}\) compared 30\(^{\circ}\) stereoscopic photographs with the Retinal Thickness Analyzer (RTA) for detecting retinal thickening. The interpretation of the retinograph by the

Fig. 4 – Retinograph matching degree with the reference test (OCT), in the diagnostic of diabetic macular edema.

![Fig. 4 – Retinograph matching degree with the reference test (OCT), in the diagnostic of diabetic macular edema.](http://www.elsevier.es)

Fig. 5 – Retinograph sensitivity in the diagnostic of diabetic macular edema and retinograph sensitivity associated with visual acuity measurement. VA: visual acuity; S: sensitivity.

![Fig. 5 – Retinograph sensitivity in the diagnostic of diabetic macular edema and retinograph sensitivity associated with visual acuity measurement. VA: visual acuity; S: sensitivity.](http://www.elsevier.es)
retinologist identified 78.8% of areas with retinal thickening and was significantly higher when the disease was present (89.6%) compared to when it was not present (78.4%). The retinography specificity was of 58%, which enabled the researchers to conclude that macular edema diagnosed by a retina specialist utilizing stereoscopic photography is sensitive but not specific in comparison to edema detected by RTA.

Nowadays, demand for attention has increased to the point that it is necessary to develop safe, faster and efficient screening methods. If we take into account that this type of retinograph is not available in most hospitals or health centers and that most available retinographs are not able to set up a photographic assembly to achieve stereopsis and identify the existence of retinal thickening, and also that the use of filters increases the cost of said tests and requires trained personnel with sufficient experience to interpret the photographs, it is easy to see that efficient alternatives are needed to enable the validity of screening tests.

For the above reasons and as proposed in the algorithm, the authors believe that the combination of VA (which, despite not being a highly sensitive method, is the most economic procedure to suspect its presence) with different simple retinographs (which are available in most hospitals) could provide a degree of detectability achieving sufficient sensitivity to be used as a screening test in the early diagnostic of diabetic macular edema (Fig. 5).

Conflict of interests
No conflict of interests has been declared by the authors.

REFERENCES