Fundus Photography as a Screening Method for Diabetic Retinopathy in Children With Type 1 Diabetes

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HE WORLDWIDE INCIDENCE OF TYPE 1 DIABETES (T1D) in children has increased dramatically during the last 3 decades: The Diabetes Mondiale Study spanning the 1990s showed that the yearly incidence of T1D varied from 0.1 per 100,000 in China and Venezuela to 40.9 per 100,000 in Finland, which had the highest incidence of all 57 countries studied.1

In Finland, the incidence of T1D in children <15 years of age was even higher, 64.2 per 100,000 per year during the period from 1980 to 2005, growing fastest in the age group of 0–4 years.2 A new annual peak incidence of 64.9 per 100,000 was observed in 2006, but since then the incidence has reached a plateau.3 It has been estimated that over half a million Finns suffer from diabetes and that approximately 40,000 of them have T1D.4

Diabetic retinopathy (DR) is the most common complication of T1D. Almost all patients with an onset of T1D under the age of 30 years have some type of DR 20 years from diagnosis.5,6 DR is the leading cause of acquired visual impairment in the working age group in Finland.7 Because DR can progress despite being asymptomatic for a long time, regular screening of the ocular fundi to detect the onset and to follow the progression of DR is important.8

Mydriatic fundus photography is the most effective screening method for DR, with a sensitivity exceeding 80%.9 Screening is often carried out with a 45-degree fundus camera.10 However, stationary 60-degree cameras can also be used for better coverage of the fundus.11,12 A green filter and monochromatic photography enhance the detection of hemoglobin-containing changes, as compared with color images.13–16

The American Academy of Ophthalmology and Diabetes Association recommend that clinical ophthalmic examinations as a screening method for DR be started 3–5 years after a diagnosis of T1D, followed by annual reviews for pediatric patients older than 9 years.17 The National Health Service in the UK recommends both clinical fundus examination and fundus photography annually for all T1D patients aged 12 years and older.18

In Finland, photographic screening of children with T1D is recommended to commence at the age of 10 years regardless of the duration of T1D.16 This age was chosen as a compromise as compared to an individual onset of photography at the beginning of puberty, which is when DR usually starts to occur.19 DR has, however, been
photography session is successful in children, in terms of providing gradable fundus images in a clinical setting. We assessed this as a part of a study of DR in children with T1D. Our hypotheses were that (1) fundus photography is more difficult to perform in younger as compared with older patients, and (2) macula-centered (MC) images are more often gradable than optic disc–centered (DC) images. Furthermore, we assessed whether girls cooperate better than boys, whether those with better glycemic control cooperate better than those with worse control, and whether a younger age at the onset of T1D, or a longer duration of diabetes, was associated with imaging success.

RESULTS OF SUCCESS IN TERMS OF PROVIDING GRADABLE fundus images in children during their first-ever fundus photography session were reviewed as a retrospective, observational cohort study. The study was approved by the Coordinating Ethics Committee of the Hospital District of Helsinki and Uusimaa, and it was performed in accordance with the Declaration of Helsinki.

• ELIGIBILITY CRITERIA: The children who were eligible for inclusion in the study had been diagnosed with T1D during the period from 2000 to 2013 at Children's Hospital, Helsinki, Finland; were under the age of 16 years; resided in Helsinki; and underwent initial fundus photography during the period 2009–2013 when they were 9–17 years of age. The search for eligible patients was carried out at Children's Hospital, where all new T1D patients are registered. A total of 213 patients were identified, and all were enrolled in this study.

• FUNDUS PHOTOGRAPHY AND CLASSIFICATION OF PHOTOGRAPHIC SUCCESS: Two 60-degree fundus images of each eye, 1 centered on the macula (MC) and the other on the optic disc (DC), were taken after pupillary dilation with 0.5% tropicamide drops during regular outpatient visits by 1 of 3 trained nurses. All images were taken with a digital Canon CF-60UD fundus camera (Canon Inc, Tokyo, Japan). Images were monochromatic (black-and-white), obtained with a green filter (ie, red-free), and stored using IMPAX Client software (Agfa HealthCare, Greenville, South Carolina, USA). Photographic success was graded by 1 observer (T.G.) using a slightly modified classification of the Atherosclerosis Risk in Communities (ARIC) Study (Supplemental Table). An image was classified as “gradable” when it had good focus and clarity, it adhered to the field definitions, the macula and optic disc were fully visible and gradable, and there were no artifacts (Supplemental Table). An image was classified as “gradable” when it was at least of fair quality with regard to field definitions, focus, and clarity, allowing for minor artifacts but no obscuration of the macula or optic disc. An image was considered “ungradable” if the above criteria were not met. Furthermore, if the macula was not visible owing to more nasal centralization in an otherwise “gradable” DC image, it was classified as “partially gradable.”

Photography was graded as a “complete success” if both images of both eyes were gradable and as “partial success” when the 2 images of only 1 eye were gradable. When at least 1 MC image was gradable, photography was graded “macula-centered image(s) only,” and when neither of the MC images was gradable, photography was considered to have been “unsuccessful.” In addition, an alternative grading of “qualified complete success” was achieved when the outcome was “complete success” except for the DC image(s) being “partially gradable.”

Grading of photographic success did not specify other situations in which the DC image of 1 eye was gradable in addition to the MC image of the other eye. Rather, these images were labeled as “macula-centered image(s) only.” Furthermore, if the DC images of both eyes but no MC images were gradable, photography was classified as “unsuccessful.”

Baseline data (sex, date of birth, date of diagnosis of T1D, and glycohemoglobin 1A [HbA1c] level at the time of the initial photography session) were entered from patient charts into an Excel file (Microsoft, Seattle, Washington, USA). The date of the initial fundus photography session was taken from the IMPAX Client database.

• STATISTICAL METHODS: Data were imported from Excel and analyzed using statistical IBM SPSS software for Windows (version 22; SPSS Inc, Chicago, Illinois, USA). Continuous variables are expressed as median and range. Exact binomial 95% confidence intervals (CI) are given for the main findings. The association between age and the outcome of fundus photography was evaluated using age as a continuous variable or, alternatively, by dividing the study population in 3 age groups on the basis of age at the initial photography session.
The Pearson $\chi^2$ test and the Kruskal-Wallis test were used to compare unordered and singly ordered contingency tables, respectively. The Mann-Whitney $U$ test was used to compare the distribution of continuous variables. Differences between 2 dependent categorical variables were assessed with the McNemar test. The Bonferroni correction was used when appropriate to adjust for multiple comparisons. A $P$ value of $< .05$ was considered statistically significant.

**RESULTS**

Of the 213 patients, 121 (57%) were male. The median age of all patients at the time of the T1D diagnosis was 8.7 (range, 1–15) years. Age at the time of the initial fundus photography was 11.2 (range, 9–17) years. At this time, the median duration of T1D was 2.3 (range, 0.2–9.6) years, and the median HbA1c was 8.5% (6.3%–13.8%). The number of patients in the 3 defined age groups of 9–10, 11–12, and
SUCCESS OF FUNDUS PHOTOGRAPHY: Complete success with the initial fundus photography was obtained in 97 patients (46%; 95% CI, 39%-52%), whereas partial success was achieved in 56 patients (26%; 95% CI, 21%-33%). Thus, at least partial success was reached in 153 patients (72%; 95% CI, 65%-78%). Macula-centered imaging was successful in 47 cases (22%; 95% CI, 17%-28%), so at least 1 gradable MC image was obtained in 200 patients (94%; 95% CI, 90%-97%). In 13 patients (6%; 95% CI, 3%-10%), the initial fundus photography session was unsuccessful. At least qualified complete success was reached in 136 patients (64%; 95% CI, 57%-70%).

Univariate analysis did not show an association between the presence or absence of complete success vs sex, age at diagnosis, HbA1c level, duration of diabetes, and age at photography (Table 1).

The percentages of gradable MC and DC images of the right and left eye for the 3 age categories were comparable (Table 2). MC images of both eyes were gradable in 78 patients in the youngest group (81%), 47 in the intermediate group (82%), and 52 patients in the oldest group (87%), and the MC image of 1 eye only was gradable in 10 (10%), 9 (16%), and 4 patients (7%), respectively. DC images of both eyes were gradable in 46 (48%), 28 (49%), and 29 patients (48%) in the 3 age groups, and both DC images were ungradable in 19 (20%), 14 (25%), and 22 patients (37%), respectively.

Complete success was reached equally often in the 3 age categories (43 [45%], 26 [46%], and 28 patients [47%], respectively) (Figure 2). No difference in the percentages of patients with unsuccessful photography (8%, 2%, and 7%, respectively) was apparent. However, 32% of patients in the youngest age group reached partial success, as compared with 28% in the intermediate and 15% in the oldest group (P = .093, Kruskal-Wallis test with Bonferroni correction for 4 comparisons; Figure 2). The frequency of gradable MC image(s) only increased with increasing age (15%, 25%, and 32%, respectively; P = .043, Kruskal-Wallis test).

QUALITY OF MACULA-CENTERED VERSUS OPTIC DISC-CENTERED IMAGES: MC image field definition reached good grade in both eyes of 192 patients (90%), and no one had a poor grade field in either eye (Table 3). Furthermore, the macula was fully visible and gradable in both eyes of 201 patients (94%), and the optic disc was free of obscurations in both eyes of 206 patients (97%). The focus and clarity grade was good in both eyes of 131 patients (62%), and in 1 eye only of 55 patients (26%). At least fair focus and clarity grade were achieved in both eyes of 184 patients (86%). Artifacts in the MC images of both eyes were seen in 43 patients (20%), and of 1 eye only in 65 patients (31%).

As regards DC images, 15 patients (7%) achieved field definition of good grade in both eyes, and 59 (28%) in 1 eye only. Half of the DC images were of fair grade in both eyes. Fifteen patients (7%) failed to reach at least fair field definitions in either eye. The optic disc was
gradable in 170 patients (80%) in both eyes and in 28 patients (13%) in 1 eye only, and the macula was gradable in 120 (56%) and 51 patients (24%), respectively. Focus and clarity were of good grade in 92 patients (43%) in both eyes and in 53 patients (25%) in 1 eye only. Artifacts were visible in 64 patients (30%), equally often in both eyes and in 1 eye only.

A single DC image was less often of gradable quality as compared with a single MC image in the right and left eyes (Table 2; P < .001 for all comparisons, McNemar test with Bonferroni correction for 2 comparisons). The MC images of both eyes were more often gradable than the DC images, in 177 (83%; 95% CI, 77%-88%) and 103 patients (48%; 95% CI, 41%-55%), respectively (P < .001, McNemar test). The MC image was gradable in 1 eye only in 23 patients (11%). The 13 patients (6%) with ungradable MC images in both eyes were outnumbered by the 55 patients (26%) with ungradable DC images in both eyes (P < .001). Altogether, 147 patients (69%) had partially gradable DC images for both eyes. Taking into consideration the partial gradability of DC images, the difference in gradability between MC and DC images remained significant (P < .001).

**QUALITY OF IMAGES OF RIGHT VERSUS LEFT EYE:** The MC images of the right eyes of all patients were available for grading, whereas 1 left eye image was missing and 1 failed in field definition (Table 3). Half of the MC images were of excellent quality in both eyes, and MC images were equally often gradable in 187 (88%) and 190 (89%) of the right and left eyes, respectively (P < .001). The MC image was ungradable mainly because they were out of focus (8% and 9% for the right and left eye, respectively). The most common reason for not reaching excellent quality was presence of artifacts in 77 (36%) right and 74 (35%) left eye images, followed by less than good grade of focus and clarity in 77 (36%) right and 74 (35%) left eye images, respectively (P < .001, McNemar test with Bonferroni correction for 2 comparisons). The most common reason for the DC images not reaching excellent quality was less than good field definition, with only 37 (17%) right eye and 52 (24%) left eye images, respectively, reaching good grade. The DC images of the left eye were

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**TABLE 2. Percentage of Gradable Initial 60-Degree Red-Free Monochromatic Fundus Images in 3 Age Groups of 213 Children With Type 1 Diabetes**

<table>
<thead>
<tr>
<th>Image</th>
<th>9-10 Years, N (%; 95% CI)</th>
<th>11–12 Years, N (%; 95% CI)</th>
<th>13–17 Years, N (%; 95% CI)</th>
<th>Total N (%; 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMC</td>
<td>83 (86; 78–93)</td>
<td>51 (89; 76–96)</td>
<td>53 (88; 77–95)</td>
<td>187 (88; 83–92)</td>
</tr>
<tr>
<td>RDC</td>
<td>68 (71; 61–80)</td>
<td>35 (61; 48–74)</td>
<td>36 (60; 47–72)</td>
<td>139 (65; 58–72)</td>
</tr>
<tr>
<td>LMC</td>
<td>83 (86; 78–93)</td>
<td>52 (81; 61–97)</td>
<td>55 (92; 82–97)</td>
<td>190 (89; 84–93)</td>
</tr>
<tr>
<td>LDC</td>
<td>55 (57; 47–67)</td>
<td>36 (63; 49–76)</td>
<td>31 (52; 38–65)</td>
<td>122 (57; 50–64)</td>
</tr>
</tbody>
</table>

CI = confidence interval; LDC = left optic disc centered; LMC = left macula centered; RDC = right optic disc centered; RMC = right macula centered.

**FIGURE 2.** The percentage of 213 children with type 1 diabetes, divided into 3 age groups, reaching different levels of overall photographic success at their initial fundus photography screening using 2 60-degree monochromatic images from each eye.
more likely to have disturbing artifacts than to be artifact free (Table 3). Gradability tended to be more frequent in the right eye (139, 65%) than in the left one (122, 57%; \( P = .06 \), McNemar test with Bonferroni correction for 2 comparisons; Table 2). The images were ungradable mainly because of obscuration of the macula (39, 18% and 62, 29% for the right and the left eye, respectively; Table 3).

The overall photographic success did not differ between the right and left eyes: 131 (62%; 95% CI, 55%-68%) patients had gradable MC and DC images of the right eye, and 119 (56%; 95% CI, 49%-63%) patients of the left eye, respectively (\( P = .14 \), McNemar test).

### DISCUSSION

In this study, we observed that almost half of the diabetic children achieved complete success of their initial fundus photography, and at least partial success was achieved by over 70%. Most of the remaining 28% of patients had at least 1 gradable MC image, and thus we failed to obtain images that provide reliable information regarding the presence of possible DR only for 6% of all patients. We view this as a favorable result, considering that it was the first session of dilated retinal photography and that 45% of our study population was not older than 9–10 years of age.

Our hypothesis that older age at the time of initial fundus photography would be associated with better outcome was not supported. Complete success or unsuccessful photography was equally common in all 3 age groups. The patients in the youngest age group, surprisingly, tended to reach partial success most often, and the oldest age group most frequently had gradable MC image(s) only. This may imply better cooperation in the youngest age group, as partial success requires at least 1 gradable DC image, which is in terms of fixation more demanding than an MC image.

There are no similar prior studies with which to compare our results. However, a recent study from Atlanta, Georgia, assessed the reliability of nonmydriatic fundus photography in children examined by non-professionals. The participants had either normal eyes or various retinal pathologies. At least 1 (MC or DC) fundus photograph was obtained in...
90% of 212 children aged 1–18 years, and 13% had gradable photographs for neither eye. These numbers are only marginally worse as compared to our study, with 94% gradable MC images of at least 1 eye and 6% with unsuccessful photography. The differences likely reflect the different settings, nonmydriatic vs mydriatic, DR vs diverse retinal pathologies, and trained vs neophyte photographers. Nonmydriatic cameras in general require less training for the operator than mydriatic cameras. We had stringent criteria for a gradable image concerning field definitions, focus, and clarity, because images taken for screening DR must be able to resolve subtle changes such as single microaneurysms.

Our hypothesis that MC images are more often gradable than DC ones was supported. This is in contrast to the Atlanta study, in which DC images were of better quality than MC ones.23 The same observation was made in a study examining the feasibility of nonmydriadic fundus photography for detecting papilledema in adults by emergency physicians.24 Even during routine ophthalmoscopy and fundus examination at the slit lamp, it is easier to assess the optic disc than the macula when the pupil is not dilated. The examination of the optic disc does not dazzle the patient as much because the blind spot of the visual field is illuminated. We had, however, exactly the opposite experience. This difference may be related to mydriasis. In our study, a significant difference in favor of MC images was observed, most commonly owing to obscurations of the macula and worse field definitions of the DC images. MC retinal images seem to be highly successful even in young children, with over 80% of patients reaching gradable images of both eyes as compared with less than half of DC images. A likely explanation for this difference is ease of fixation when taking MC images. Of note, only 1 MC image has been used as a screening method,25,26 although a single MC nonmydriatic 45-degree image is sufficient for determining DR and not for establishing its grade.27

As fixation seems to easily become more nasal than needed when taking DC images, we defined “partial gradability” for such an otherwise gradable DC image and qualified complete success as an additional photographic success category for allowing more nasal centralization of otherwise gradable DC images. Consequently, at least qualified complete success was reached in 64% of patients as compared with complete success of 46%. The benefit of such a wider field combined with a loss of additional view of the macular area from 2 separate images will be assessed in further studies. The additional view of the macula is regarded as beneficial because it would improve the detection of subtle changes in the central fundus and would help in separating them from potential artifacts.

The success between the right and left eyes differed only in that the DC images were more often of excellent quality in the left eyes. The reason for this is not known, but it might be attributable to a learning effect because the right eye is generally imaged first. On the other hand, some children may have lost their patience, leading to more frequently ungradable DC images from the left eyes. There was, however, no difference in the overall success of photography of the right vs left eye in our study.

Our study has some limitations. First of all, it is a clinical experience of a single country and center. Thus, as to the generalizability of our results, there may well be culture-specific differences. In general, photographic success was defined in this study as the ability to obtain gradable fundus images and actually depends on a multitude of patient- and system-related factors. On the patient side, this may include the ability to cooperate, which has been taken into consideration because age at photography, duration of diabetes, and glycemic control were used as indicators for overall cooperation. Another important factor in achieving photographic success is pupil size, which is usually not a problem with young persons, and mydriatics were used in all. On the system side, photographic success may depend on the photographers’ skills, the type of camera used, and the image acquisition protocol. The experience of the photographer was not controlled for in this study. Technical skill with the mydriatic camera and skill in dealing with children may vary. There was, however, no specific assignment of patients (eg, according to age) to any of the 3 photographers. Because all photographers were experienced diabetic nurses at Children’s Hospital, they were familiar with the children, which likely increases the chances of a good photographic outcome. However, as such they were not part of a team taking photographs in adults with full-time engagement in fundus photography. Furthermore, the classification of image quality created for research purposes is strict as compared to the clinical setting requirements.

In conclusion, even when using the stringent classification of image quality created for research purposes in assessing the success of the initial fundus photography in diabetic children, this study showed quite favorable outcomes. It thus seems worthwhile to communicate our experience to a wider audience, as the number of diabetic patients in the pediatric population is increasing worldwide.1,2
REFERENCES