Morphological Diagnostics in Paediatric Glaucoma—Analysis of the Disc Damage Likelihood Scale by KOWA Non Mydriatic Fundus Camera and its Correlation to HRT and OCT

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Abstract

Title: Morphological diagnostics in paediatric glaucoma

Background: Morphological parameters vary in paediatric glaucoma with a minor knowledge on standard values available compared to an adult cohort. Accordingly, we designed a study to assess the objectively measured disc damage likelihood scale (DDLS) by KOWA stereophotography as a novel parameter in comparison to standard glaucoma diagnostics, HRT 3 and OCT.

Methods and Findings: Prospective study of 47 eyes (n=47) categorized into three groups; 14 normal optic discs (11 female, 3 male, 12.7 ± 6.1years), 15 glaucoma suspects (3f, 12m, 11.7 ± 3.1years) and 18 paediatric glaucoma (10f, 8m, 11.2 ± 2.5years). Stereometric measurements of the optic disc by KOWA camera, Moorfields regression analysis (MRA) and glaucoma probability score (GPS) of the HRT3 and retinal nerve fibre layer (RNFL) of the OCT were analysed. Results were split in 2 groups: Diagnosis 1 was defined as “outside normal limits”, Diagnosis 2 as “borderline or outside normal limits”.

Conclusions: The DDLS showed the highest predictive power for glaucomatous damage compared to glaucoma coefficients of the established devices. Additionally, the gold standard of optic nerve head assessment still includes the examination of the fundus photography. As stereo photography is an easy and timesaving instrument, it might be an additive tool in paediatric glaucoma.

Keywords: Paediatric glaucoma; Disc damage likelihood scale; Optic coherence tomography; Stereo photography; Heidelberg retina tomography

Abbreviations

DDLS-Disc Damage Likelihood Scale; GPS-Glaucoma Probability Score; HRT-Heidelberg Nerve Head; MRA-Moorfields Regression Analysis; OCT-Optic Coherence Tomography; POAG-Primary Open Angle Glaucoma; PSD-Pattern Standard Deviation; RNH-Retinal Nerve Head; RNFL-Retinal Nerve Fibre Layer; SD-OCT-Spectral Domain-Optic Coherence Tomography

Background

Various glaucoma parameters and new devices were developed for monitoring glaucoma patients and suspects recently [1-6]. These techniques were usually adapted to an adult cohort [1-3,6]. As paediatric glaucoma is still one of the leading causes for inability to work and blindness in young age, investigations of effective parameters for early detection, diagnosis and follow up have to be made [7]. Morphological optic nerve head (ONH) parameters such as the retinal nerve fibre layer (RNFL), Moorfields regression analysis (MRA), glaucoma probability score (GPS) and F.S. Mikelberg and R. Burk coefficients showed to be adequate in ONH evaluation in...
glaucoma patients [2,3,5,8-10]. Spectral Domain optical coherence tomography (SD-OCT) can be used to assess peripapillary RNFL thickness, macular thickness, and retinal layer thickness in children as young as 5 years [10]. SD-OCT was easier to obtain than Time Domain (TD)-OCT in children (n=83) [11]. Yanni et al. developed a data set for paediatric means and normative reference ranges that could be used as a standard with which to compare those children suspected of having retinal or optic nerve abnormalities [10]. Progressive disc tilting and the development or enlargement of peripapillary atrophy (PPA) are known factors during a myopic shift in children and must be taken into account when analysing infantile discs [12]. Eyes of childhood glaucoma patients, however, exhibited less significant changes in disc morphology during myopic shift compared to eyes with normal disc or enlarged cup-to-disc ratio [12].

See comment in PubMed Commons belowSee comment in PubMed Commons belowThe disc damage likelihood scale (DDLS) was devised by Spaeth et al. to incorporate the effect of disc size and foveal rim width into a clinical grading scale in 2002 [6,13]. It could be demonstrated that DDLS is highly correlated with glaucomatous visual field defects and showed a high interobserver reproducibility [6,13,14].

In this study the DDLS was objectively measured by the KOWA nonmyd WX 3D fundus camera. The aim of this study was to assess the correlation between the objective DDLS and the Heidelberg retina tomography (HRT) and OCT as widely used glaucoma diagnostic tools and to assess the predictability of glaucumatos damage in children.

Methods

This prospective study was completed under the agreement of the ethical committee of the Charite university medicine, Berlin. The criteria of the declaration of Helsinki were fulfilled. Written consent of all patients was obtained; three different versions of agreement forms for different ages were provided and a form for the parents/caretakers to sign it. Children of any age could understand the meaning and consequences of conducting in this study, however, all parents/guardians also signed the consent form. All consent forms were approved by the ethical committee of the Charite university medicine, Berlin.

A total of 47 eyes (n=47) were included. Patients were categorized into three groups; 14 normal optic discs (11 female, 3 male, age 12.7 ± 6.1 years), 15 glaucoma suspects (3 female, 12 male, age 11.7 ± 3.1 years) and 18 paediatric glaucoma diagnoses (10 female, 8 male, 11.2 ± 2.5 years), summarized in Table 1. The paediatric glaucoma cohort consists of 8 infantile glaucoma, 5 primary congenital glaucoma, 1 aniridia and 4 secondary glaucoma (2 pseudophacic glaucoma, 2 uveitic glaucoma).

Inclusion criteria were age >5years (able to absolve diagnostic tests), best corrected visual acuity of at least 20/200 (6/60), astigmatism <2.5 dpt and clear optic media. To avoid nationality based differences in optic disc morphology, a Caucasian cohort was used for this study [15]. Exclusion criteria included macrodiscs, microdiscs, higher spherical errors (>5 dpt.) and higher astigmatism >2.5 dpt., contact lenses, hazy optic media interfering with fundus examination, ocular trauma and patients with intraocular surgery for less than 3 months. Additionally, children with neurologic disorders and prematurity were excluded.

We recognised in this study cohort, that reliable visual field tests were obtained at the age of 11 years. Healthy eyes were selected out of the normal population and did not show distinctive structural or morphological features of glaucoma (if possible, mean defect (MD) <2dB, pattern standard deviation (PSD) <2dB). Glaucoma suspects were defined as having morphological and structural alterations (funduscropy, if possible, visual field test MD>2-4dB, PSD>2-4dB) of the optic disc and normal intraocular pressure or eyes with borderline/ high individual IOP and normal diagnostics (MD<2dB, PSD<2dB).

To be diagnosed as manifest paediatric glaucoma structural and morphological optic disc alterations were present. The optic disc was described according to the diagnostic criteria by Jonas in children >11years, which were able to repeat reliable visual field testing (MD>4dB, PSD>4dB) [16]. In addition especially in children, the increased IOP and wide diurnal IOP variations were a sensitive marker for glaucoma [17].

All patients were measured by the Kowa nonmyd WX 3D camera (2D/3D Nonmydriatic Retinal Camera, Kowa Company Ltd., Japan), the HRT3 (Heidelberg Engineering GmbH, Germany), and OCT (SD-OCT, Carl Zeiss Meditec, Dublin, CA, USA) by one examiner on the same day. The correlation of the CDR between KOWA, HRT3, and Funduscropy was analysed in the study cohort. All 3 devices graded the optic disc topography related to the predictability for glaucumatos damage in “healthy”, “borderline” and “outside normal limits” results. The study population was split into two groups: Diagnosis 1 “outside normal limits”, diagnosis 2 “borderline and outside normal limits”. Kowa nonmyd WX 3D.

The Kowa nonmyd WX 3D (2D/3D Nonmydriatic Retinal Camera, Kowa Company Ltd.) fundus camera recorded simultaneously two images (stereometric) of the optic disc which are at an angle of 34° to each other. The pupil diameter should not be smaller than a minimum diameter of 4 mm. Due to the different shooting angle a horizontal shift of the pixels (1600 x 1600 pixels) was obtained, which was highly reproducible. Based on the correlation coefficient of the red, green and blue channel images, the corresponding pixels of the two captured images could be identified and the disparity was calculated. This was correlated with the depth of the image and was specified via an algorithm. As a reference plane the retina was chosen. It was defined by a horizontal line through the centre of the papilla.

The contour of the disc was marked by the inner margin of Elschng's scleral ring. The contour of the cup was assigned by the outer margin of the cup, which was indicated by the bending of the ONH vessels at the rim [18]. The observer determined
several points on the contour (usually 8-12), and the contour line was then automatically generated by software spline interpolation [18].

Stereometric parameters obtained were disc area, rim volume, cup volume, disc volume, vertical cup/disc ratio, cup disc area ratio, rim disc area ratio, height variation contour etceteras. In this study the items vertical cup/disc ratio, disc area and cup volume were used for further analysis. The rim/disc ratio was objectively quantified in the six quadrants of the optic nerve head.

Spectral domain-optical coherence tomography (SD-OCT)

The technique of optical coherence tomography is described in several papers.1 In summary, the OCT is an optical signal acquisition method [1,4]. It captured micrometre resolution, three-dimensional images from optical scattering media [4,5,10]. OCT is an interferometric technique using near-infrared light. The use of relatively long wavelength light allowed it to penetrate into the scattering medium. The OCT retinal nerve fibre layer thickness analysis was performed by fast retinal nerve fibre layer map protocols using an internal fixation target [4].

Heidelberg retina tomography (HRT 3)

Based on the confocal laser scanning ophthalmoscopy technique it displayed high-resolution optical images with depth selectivity [19]. In-focus images from selected depths could be acquired. Images were traced point-by-point and reconstructed with a software program allowing three-dimensional reconstructions of the objects. Moorfields regression analysis (MRA), glaucoma probability scores (GBS) and stereometric parameters were evaluated. Furthermore R Burk and FS. Mikelberg coefficients were analysed [2,3].

Disc damage likelihood scale (DDLS)

This scale incorporated the size of the disc and the radial width of the neuroretinal rim in evaluating the optic nerve head. The system categorised the optic nerve head (ONH) as small (<1.5 mm), medium (1.5-2.0 mm) or large (>2.0 mm).

This ensured that the disc size was measured thereby reducing misclassification bias based on disc size [6,14,20]. In this study, the KOWA fundus camera objectively measured the DDLS (Figure 1).

Figure 1: Normogram of the Disc Damage likelihood scale of the KOWA fundus camera adapted from Spaeth et al. 2002, Trans Am Ophthalmol Soc.

Statistical Analysis

Statistical data were calculated using Statistical Package for the Social Sciences (SPSS) version 20.0; from SPSS, Inc. linear regression analysis and descriptive statistics (mean, standard deviation, 95% limits of agreement and correlation quotients) were processed.

The relationship between DDLS, HRT3 parameters, and OCT RNFL was analysed with a c²-test. The area under the curve (Receiving operating characteristics ROC) was used to identify useful parameters to detect glaucomatous damage. A p-value of less than 0.05 indicated a statistically significant difference.

Results

Data of 14 healthy eyes, 15 glaucoma suspects and 18 paediatric glaucoma were analysed. Descriptive Statistics were presented in Table 1.

The disc area measured by HRT 3 was 2.39 ± 0.66 mm² and the mean disc area of the KOWA was 3.19 ± 0.48 mm² in healthy patients (p=0.01).

The mean disc area of the HRT was 2.38 ± 0.41 mm², whereas the mean disc area of the KOWA was 3.25 ± 0.70 mm² in glaucoma suspects (p=0.01).

The mean disc area of the HRT was 3.41 ± 1.05 mm², whereas the mean disc area of the KOWA was 3.45 ± 0.84 mm² in paediatric glaucoma (p=0.80).
Correlation of the KOWA rim/disc ratio compared to the RNFL, MRA and GPS in the six quadrants of the optic nerve head was summarized in Table 2.

**Table 1:** Demographic and descriptive statistics (mean, standard deviation, median) of different glaucoma parameters in the three study cohorts.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Age</th>
<th>CDR Examiner</th>
<th>GAT</th>
<th>Phakic</th>
<th>Pseudo</th>
<th>Cup volume KOWA</th>
<th>Cup volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Mean ± st dev</td>
<td>12.7 ± 6.10</td>
<td>0.37 ± 0.11</td>
<td>17.82 ± 3.46</td>
<td>12</td>
<td>2</td>
<td>0.22 ± 0.14</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>10.6</td>
<td>0.4</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glaucoma suspects</td>
<td>Mean ± st dev</td>
<td>11.7 ± 3.10</td>
<td>0.49 ± 0.12</td>
<td>16.08 ± 2.72</td>
<td>15</td>
<td>0.32 ± 0.21</td>
<td>0.25 ± 0.10</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>12.8</td>
<td>0.5</td>
<td>16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glaucoma</td>
<td>Mean ± st dev</td>
<td>11.2 ± 2.50</td>
<td>0.76 ± 0.07</td>
<td>18.47 ± 4.34</td>
<td>16</td>
<td>2</td>
<td>0.47 ± 0.30</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>10.8</td>
<td>0.8</td>
<td>18</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Table 2:** Correlation of the KOWA rim/disc ratio compared to retinal nerve fibre layer (RNFL), Moorfields regression analysis (MRA) and glaucoma probability score (GPS) in six quadrants of the optic nerve head.

<table>
<thead>
<tr>
<th>Kowa rim/disc ratio, Correlation coefficient, p value</th>
<th>Normal</th>
<th>Glaucoma suspects</th>
<th>Manifest Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RNFL</td>
<td>MRA</td>
<td>GPS</td>
</tr>
<tr>
<td>Temporal</td>
<td>r=0.446</td>
<td>r=0.583</td>
<td>r=0.253</td>
</tr>
<tr>
<td></td>
<td>p=0.110</td>
<td>p=0.130</td>
<td>p=0.545</td>
</tr>
<tr>
<td>Superotemporal</td>
<td>r=0.244</td>
<td>r=0.808</td>
<td>r=0.162</td>
</tr>
<tr>
<td></td>
<td>p=0.40</td>
<td>p=0.015</td>
<td>p=0.701</td>
</tr>
<tr>
<td>Superonasal</td>
<td>r=0.213</td>
<td>r=0.108</td>
<td>r=0.020</td>
</tr>
<tr>
<td></td>
<td>p=0.465</td>
<td>p=0.800</td>
<td>p=0.963</td>
</tr>
<tr>
<td>Inferotemporal</td>
<td>r=0.188</td>
<td>r=0.161</td>
<td>r=0.026</td>
</tr>
<tr>
<td></td>
<td>p=0.520</td>
<td>p=0.702</td>
<td>p=0.952</td>
</tr>
<tr>
<td>Inferonasal</td>
<td>r=0.237</td>
<td>r=0.493</td>
<td>r=0.181</td>
</tr>
<tr>
<td></td>
<td>p=0.436</td>
<td>p=0.214</td>
<td>p=0.668</td>
</tr>
<tr>
<td>Nasal</td>
<td>r=0.106</td>
<td>r=0.173</td>
<td>r=0.026</td>
</tr>
<tr>
<td></td>
<td>p=0.719</td>
<td>p=0.682</td>
<td>p=0.952</td>
</tr>
</tbody>
</table>

**Correlation of the cup/disc ratio between KOWA, HRT and funduscopy**

In healthy patients, the CDR of the KOWA compared to CDR by HRT 3 (r=0.689 p=0.059) and to the CDR of the examiner (r=0.618 p=0.032) showed a good correlation. Further the CDR of the HRT 3 compared to the CDR of the examiner showed a good correlation (r=0.624 p=0.098).

In glaucoma suspects, the CDR of the KOWA compared to CDR by HRT 3 showed a good correlation (r=0.761 p=0.136), whereas the CDR of the KOWA (r=0.161 p=0.568) and the CDR by HRT 3 (r=0.107 p=0.864) compared to the CDR of the examiner showed a poor correlation.

In paediatric glaucoma, the CDR of the KOWA compared to CDR by HRT 3 showed a very good correlation (r=0.850 p=0.002). Additionally the CDR of the KOWA (r=0.558 p=0.059) compared to the CDR of the examiner showed a good correlation. In contrast, the CDR by HRT 3 (r=0.198 p=0.609) compared to the CDR of the examiner showed a poor correlation.
Glaucoma diagnostic analysis in normal patients

Referring to diagnosis 1 (“outside normal limits”)
Figure 2

DDLS did not show a significant correlation with MRA (p=0.565), GPS (p=0.108) and RNFL (p=0.907).

Referring to diagnosis 2 (“borderline or outside normal limits”)

The GPS (p=0.076), MRA (p=0.801) and RNFL (p=0.610) did not correlate significantly compared to DDLS. Between DDLS 0-4 and R. Burk (p=0.126) and F.S. Mikelberg coefficient (p=0.053) a statistically significance could not be reached.

Glaucoma diagnostic analysis in glaucoma suspects

Referring to diagnosis 1 (“outside normal limits”)
Figure 3

DDLS did not show a significant correlation with MRA (p=0.082), GPS (p=0.233) and RNFL (p=0.448).

Referring to diagnosis 2 (“borderline or outside normal limits”)

DDLS did not correlate significantly with MRA (p=0.082), GPS (p=0.082) and RNFL (p=0.343). No significant correlation between DDLS Grading 0-4 and R. Burk (p=0.167) and F.S. Mikelberg coefficient (p=0.073) was found.

Figure 2: Scatterplots of the relationship between Disc damage likelihood scales (DDLS) compared to the Moorfields Regression Analysis (MRA), Glaucoma Probability Score (GPS) of the HRT 3 and Retinal Nerve fibre Layer (RNFL) of the SD OCT in the healthy cohort.

Figure 3: Scatterplots of the relationship between Disc damage likelihood scale (DDLS) compared to the Moorfields Regression Analysis (MRA), Glaucoma Probability Score (GPS) of the HRT 3 and Retinal Nerve fibre Layer (RNFL) of the SD OCT in the glaucoma suspects.

Glaucoma diagnostic analysis in paediatric glaucoma

Referring to diagnosis 1 (“outside normal limits”)
figure 4

DDLS did not show a significant correlation with MRA (p=0.108), glaucoma probability score analysis (p=0.108) and RNFL (p=0.447).

Figure 4: Scatterplots of the relationship between Disc damage likelihood scale (DDLS) compared to the Moorfields regression analysis (MRA), the glaucoma probability score (GPS) of the HRT 3 and retinal nerve fibre layer (RNFL) of the SD OCT in the glaucoma cohort.
Referring to diagnosis 2 ("borderline or outside normal limits")

DDLS did not correlate significantly with MRA (p=0.072), glaucoma probability score analysis (p=0.108) and RNFL (p=0.064). No significant correlation between DDLS Grading 0-4 and R. Burk (p=0.508) and F.S. Mikelberg (p=0.064). No significant correlation between DDLS considering Diagnosis 1 and 2 (MRA-Diagnosis 2 results (Table 3 and Figure 5).

Using the area under the curve (ROC) comparing R.Burk and F.S. Mikelberg and DDLS for Diagnosis 1+2, the DDLS had the best predictive power in comparison to HRT 3 and OCT apart from the MRA Diagnosis 2 results (Table 3 and Figure 5).

**Table 3**: Value of area under the curve for ROC for F S Mikelberg coefficient (FSM), R Burk coefficient (RB), Disc damage likelihood scale (DDLS) considering Diagnosis 1 and 2 (MRA-Moorfields Regression Analysis, GPS-Glaucoma Probability Score, OCT-Optic Coherence Tomography).

<table>
<thead>
<tr>
<th>Diagnosis1_MRA</th>
<th>Diagnosis2_MRA</th>
<th>Diagnosis1_GPS</th>
<th>Diagnosis2_GPS</th>
<th>Diagnosis1_OCT</th>
<th>Diagnosis2_OCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area</td>
<td>0.1</td>
<td>0.05</td>
<td>0.223</td>
<td>0.208</td>
<td>0.619</td>
</tr>
<tr>
<td>Std. Error</td>
<td>0.063</td>
<td>0.041</td>
<td>0.106</td>
<td>0.096</td>
<td>0.139</td>
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<tr>
<td>FSM</td>
<td>0.227</td>
<td>0.142</td>
<td>0.246</td>
<td>0.25</td>
<td>0.595</td>
</tr>
<tr>
<td>RB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DDLS</td>
<td>0.785</td>
<td>0.733</td>
<td>0.669</td>
<td>0.8</td>
<td>0.833</td>
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</table>

**Discussion**

Paediatric glaucoma is a severe disease with high intraocular pressure peaks and wide diurnal variations [17]. Paediatric glaucoma showed characteristics that differ compared to the primary open angle glaucoma (POAG) in adults. For example, cup reversal, topographic improvement of the optic disc after glaucoma therapy, and different genetic mutations can be observed in paediatric but not POAG glaucoma [21-23]. The most difficult diagnostic process is to detect beginning glaucomatous changes in children before irreversible damage occurs. To improve the clinical management of paediatric glaucoma various diagnostic tools were described using the analysis of perimetry, IOP devices, fundus photography, optical coherence tomography, HRT and fundoscopy [8,9,11,24-27]. Larsson et al. stated that HRT could be used in children between 5 and 16 years of age [24]. Children of this study fell within this age range. Additionally, the SD-OCT showed reliable results of RNFL and retinal layer thickness in children up to 5 years [10]. Another approach to assess early glaucomatous changes is the estimate of circumpapillary and macular retinal ganglion cell counts which enable us to discriminate different stages of glaucoma [26]. However, all the established devices rely on normative databases, which did not include morphological differences and age related alterations of children.

This study presented the first objectively measured DDLS compared to both widely used glaucoma diagnostic tools SD-OCT and HRT3 in children. Before an objective analysis was developed determination of the CDR and the DDLS stage was made by using a slit lamp examination with a 66-90 dpt. Lens [6,13].

**Stereometric parameters**

We found a significant difference in the disc area evaluation of the KOWA camera compared to the HRT 3 in the healthy subjects and glaucoma suspects (p=0.01). In the paediatric glaucoma cohort the difference did not show statistically significance (p=0.80). Januschowsky et al. found a significant mean difference of the disc area between KOWA and HRT III of 0.33 mm² in adult normal and glaucomatous subjects [28]. In contrast, the findings in this paediatric study outweighed the results of Januschowsky (mean differences 0.8 mm² in healthy eyes and 0.87 mm² in glaucoma suspects), which might be due to the different magnifying factor of the HRT and KOWA camera. However, the disc area of KOWA and HRT was closely related (mean difference 0.04 mm²) in glaucoma patients. This relationship of KOWA and HRT in manifest glaucoma, in contrast to the difference in glaucoma suspects, may be used for observing progression in manifest glaucoma. Population-based studies using fundus photography have found that the area of the ONH ranged from 2.09 to 2.94 mm² [18,29].

Furthermore Januschowsky’s results showed a mean difference of the cup volume of 0.03 mm³ in normal adults compared to the mean difference of 0.06 mm³ in healthy children [28]. In glaucomatous eyes the mean difference of the cup volume was 0.08 mm³ in adults and 0.07 mm³ in children (Table 1). So the measurements showed a closer congruence in...
manifest glaucoma between adults and children. No age matched analysis was found for comparative statistics in a paediatric cohort.

**Glaucoma diagnostics**

In this study the DDLS showed no statistically significant correlation in all three study cohorts compared to glaucoma probability score, Moorfields regression analysis and RNFL. It is known that children may have morphologic abnormalities of the optic nerve [24,30]. These abnormalities do not cause visual acuity or functional decreases, but might be the reason for the missing correlation [30]. According to the correlation between the disc damage likelihood scale and R. Burk and F.S. Mikelberg coefficient, no statistical significance was present.

In paediatric glaucoma a significant correlation of the glaucoma probability score compared to KOWA rim/disc ratio was found in all six quadrants (Table 2). Strikingly the only strong correlation that was found was between the KOWA rim/disc ratio and the only parameter of the HRT that does not depend on disc size, GPS. As GPS is determined automatically, the question arises, how much the subjective examiner input is influencing the outcome of detecting glaucomatous damage in children.

Regarding the area under the ROC curve the highest predictive power was demonstrated by the objectively measured DDLS (0.669-0.833) in comparison to R.Burk (0.142-0.595) and F.S. Mikelberg (0.050-0.619) coefficients considering all devices (Table 3 and Figure 5). There were no comparative studies in children regarding ROC curves after an extensive pubmed research. Majid et al. stated following results for the subjectively obtained DDLS in adults. In POAG, the DDLS had the best predictive power (0.917), followed by the PSD (0.895) and RNFL (0.864) [31]. Danesh Meyer stated that the subjective DDLS (area under the curve 0.95) had the best predictive power, followed by the clinical examination of C/D ratio (0.84), and HRT-II Moorfields analysis (0.68) [20]. The predictive values reached higher levels in the comparative studies than our results. According to the known difficulties in diagnosing paediatric glaucoma the objectively measured DDLS seemed to be an effective additional tool.

As a limitation of our study it must be addressed that there is still no gold standard of objective parameters to detect glaucoma disease in children [32]. To reduce this bias in our study the optic nerve head was defined in healthy eyes, suspects or glaucomatous eyes before recruitment and the objective diagnostic analysis. Additionally, reliable visual field testing in children is based on a certain age. The mean age of our study cohort was 11-12 years, so we could report about generally reproducible visual field tests. Already El Dairi et al. stated that in the absence of reliable visual field data on many children with suspected or known glaucoma, ONH cup evaluation was essential for determining the presence and severity of glaucoma [32]. Further limitation of the present study could be the missing differentiation of the impact of birth weight, length, head circumference and sex of term infants on the optic nerve head parameters and their future risk on developing a glaucomatous damage [15,33,34]. We excluded preterm children as they exhibit different characteristics of optic nerve head parameters (increased rim volume, smaller cup shape, increased height variation contour, increased cup depth) with HRT III analysis [35].

**Conclusion**

In conclusion, studies have shown that OCT and HRT could distinguish between glaucomatous damage and healthy optic nerve heads in children. The objectively measured DDLS showed the highest predictive power for glaucomatous damage compared to Mikelberg and Burk coefficients in the established devices. Further studies seem to be sensible to use the KOWA camera for diagnosis of childhood glaucoma. In addition to the optic disc analysis with HRT and OCT, the gold standard of ONH assessment does still include the examination of the fundus photography. As stereophotography is an easy and timesaving instrument, it might be an additive, helpful tool in diagnosis and follow-up of paediatric glaucoma.

**Declarations**

**Ethics approval:** This prospective study was completed under the agreement of the ethical committee of the Charité university medicine, Berlin. The criteria of the declaration of Helsinki were fulfilled.

**Consent for publication:** Written consent of all patients was obtained; three different versions of agreement forms for different ages were provided and a form for the parents/caretakers to sign it. Children of any age could understand the meaning and consequences of conducting in this study, however, all parents/guardians also signed the consent form. All consent forms were approved by the ethical committee of the Charité university medicine, Berlin.

**Availability of data and materials:** All data generated or analysed during this study are included in this published article. The rest of datasets generated and/or analysed during the current study are not publicly available due but are available from the corresponding author on reasonable request.

**Competing interests:** No financial interest is reported by any of the authors.

**Authors’ contributions:** MP is the corresponding author, a major contributor in planning the study setting, examining the children and writing the manuscript. A-K MW, NT, MK, EB and SW collected, analysed and interpreted the data. A-K MW, NT, MK, EB and SW collected, analysed and interpreted the patient data with the inclusion, exclusion criteria. CE interpreted glaucomatous changes and was involved in the setup of this study (inclusion, exclusion criteria). All authors read and approved the final manuscript.

**References**


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