Purpose: To identify the most accurate diagnostic imaging modality for classifying pediatric eyes as papilledema (PE) or pseudopapilledema (PPE).

Design: Prospective observational study.

Subjects: Nineteen children between the ages of 5 and 18 years were recruited. Five children (10 eyes) with PE, 11 children (19 eyes) with PPE owing to suspected buried optic disc drusen (ODD), and 3 children (6 eyes) with PPE owing to superficial ODD were included.

Methods: All subjects underwent imaging with B-scan ultrasonography, fundus photography, autofluorescence, fluorescein angiography (FA), optical coherence tomography (OCT) of the retinal nerve fiber layer (RNFL), and volumetric OCT scans through the optic nerve head with standard spectral-domain (SD OCT) and enhanced depth imaging (EDI OCT) settings. Images were read by 3 masked neuro-ophthalmologists, and the final image interpretation was based on 2 of 3 reads. Image interpretations were compared with clinical diagnosis to calculate accuracy and misinterpretation rates of each imaging modality.

Main Outcome Measures: Accuracy of each imaging technique for classifying eyes as PE or PPE, and misinterpretation rates of each imaging modality for PE and PPE.

Results: Fluorescein angiography had the highest accuracy (97%, 34 of 35 eyes, 95% confidence interval 92%–100%) for classifying an eye as PE or PPE. FA of eyes with PE showed leakage of the optic nerve, whereas eyes with suspected buried ODD demonstrated no hyperfluorescence, and eyes with superficial ODD showed nodular staining. Other modalities had substantial likelihood (30%–70%) of misinterpretation of PE as PPE.

Conclusions: The best imaging technique for correctly classifying pediatric eyes as PE or PPE is FA. Other imaging modalities, if used in isolation, are more likely to lead to misinterpretation of PE as PPE, which could potentially result in failure to identify a life-threatening disorder causing elevated intracranial pressure and papilledema. Ophthalmology 2017; ●:1–10 © 2017 by the American Academy of Ophthalmology

Supplementary material available at www.aaojournal.org.

Papilledema (PE) in children can be the presenting sign of a life-threatening disorder such as meningitis or brain tumor. However, pseudopapilledema (PPE) has been mistaken for true PE in children in up to 76% of cases. The most common cause of PPE in children is optic disc drusen (ODD). Because ODD are buried and noncalcified early in life, and become more superficial and calcified over time, buried ODD in children may be more likely to simulate true PE and more difficult to detect. Misdiagnosis of PPE as true PE may subject children to an invasive, expensive, and unnecessary evaluation, including neuroimaging and lumbar puncture (LP). Conversely, misdiagnosis of PE as PPE can have life-threatening consequences. Moreover, ODD and PE can coexist, and the prevalence of drusen is increased in patients with idiopathic intracranial hypertension; ODD may be either a cause or a result of PE. Therefore, it is important for clinicians to be able to identify PE even in the presence of ODD.

In adults, the standard test for diagnosis of ODD is B-scan ultrasonography. Calcified ODD appear as hyperechogenic masses on the optic nerve head with posterior shadowing, persisting at low gain. However, in the subgroup of children and adults with suspected buried ODD and no surface drusen, ultrasonography was positive in only 39 of 82 (48%) eyes.

By fluorescein angiography (FA), ODD exhibit early and late nodular staining of the optic nerve head, in contrast to leakage that occurs with true optic disc edema (ODE).
Pineles and Arnold found early nodular staining in 25% and late nodular staining in 29% of eyes with buried ODD. Moreover, the absence of leakage excluded superimposed edema.

More recently, there has been interest in the use of optical coherence tomography (OCT) to diagnose ODD. Lee et al. found that the peripapillary retinal nerve fiber layer (RNFL) as measured by OCT was thicker in eyes with true ODE than in eyes with ODD. The authors also described the appearance of ODD on volumetric spectral-domain OCT (SD OCT) scans as focal hyperreflective subretinal masses with adjacent boot-shaped retinal elevation. Merchant et al. reported that volumetric, enhanced depth imaging OCT (EDI-OCT) identified significantly more eyes with suspected buried ODD than ultrasonography.

The aforementioned studies all included both adults and children; few studies have examined the ability of imaging to identify ODD specifically in children, in whom ODD have different characteristics. Therefore, the best imaging modality to differentiate between PE and PPE in children has not been established. We sought to compare the accuracy of B-scan ultrasonography, fundus photography, autofluorescence, FA, OCT RNFL analysis, and volumetric optic nerve OCT scans with standard SD OCT and EDI OCT in classifying pediatric eyes as PE or PPE.

**Methods**

This study was approved by the University of California, Los Angeles, Institutional Review Board and conformed to the requirements of the US Health Insurance Portability and Accountability Act and tenets of the Declaration of Helsinki. Informed consent from a parent or guardian was obtained for all subjects. Children between the ages of 5 and 18 years with a diagnosis of PPE (owing to superficial or suspected buried ODD) or true PE were recruited from the pediatric and neuro-ophthalmology clinics of 5 of the coauthors (M.Y.C., F.G.V., J.L.D., L.B., S.L.F.) at a single eye institute from September 2015 through February 2017. Diagnosis was established by the attending physician based on evaluation of the patient’s history and physical examination, as well as review of diagnostic testing such as neuroimaging and LP results, if available. None of the attending physicians who referred patients for this study participated as masked image interpreters. Given the lack of a gold-standard test for diagnosing PPE, patients diagnosed with PPE were followed for at least 6 months, to ensure stability of findings and reduce the possibility of misdiagnosis. All patients with PE underwent neuroimaging and LP, which was required to demonstrate elevated opening pressure (greater than 28 cm H₂O) for study inclusion. Patients with disorders of the optic nerve other than PPE owing to suspected buried or superficial ODD and PE were excluded. Additionally, we excluded patients with superimposed PE, the interpretation was recorded as PE rather than PPE. Images for each subject were presented to the neuro-ophthalmologists. These neuro-ophthalmologists did not examine the patients, and they had no clinical context (such as history, magnetic resonance imaging, or LP results) available when reviewing the images.

For each eye, at least 2 FA images (early and late) were selected for presentation to the image readers. If a third (midphase) image was available, this was also presented.

Images were captured with the Spectralis OCT (Heidelberg Engineering Inc, Heidelberg, Germany). For peripapillary RNFL analysis, scans were acquired using a standardized 3.4-mm-diameter circle around the optic disc. An automated algorithm identified the anterior and posterior aspects of the nerve fiber layer and calculated the average thickness and thickness in 4 quadrants (superior, inferior, temporal, nasal). Volumetric scans through the optic nerve head were performed with standard SD OCT and EDI OCT. The OCT protocol for volumetric scans through the optic nerve head consisted of 512 A-scans generating 25 horizontal B-scan sections, 240 µm apart, spanning an area of 20 by 20 degrees. The RNFL report was exported for each eye for presentation to the image readers. For both standard SD OCT and EDI OCT scans of the optic nerve head, all B-scans acquired for each eye through the optic nerve were presented to the image readers.

**Image Interpretation**

Three masked experienced neuro-ophthalmologists (A.A.C., A.A.S., P.A.Q.) evaluated images and interpreted them as representing either PPE or PE. PPE was defined as the absence of PE, because we expected that ODD may not be identifiable on some imaging modalities in young children with suspected buried ODD. Therefore, if an image reader believed an image represented ODD with superimposed PE, the interpretation was recorded as PE rather than PPE. Images for each subject were presented to the neuro-ophthalmologists in random order. The final image interpretation (PPE or PE) was based on the agreement of at least 2 of 3 neuro-ophthalmologists. These neuro-ophthalmologists did not examine the patients, and they had no clinical context (such as history, magnetic resonance imaging, or LP results) available when reviewing the images.

**Statistical Analysis**

Image interpretations were compared with the gold standard of clinical diagnosis. Accuracy of each imaging modality for classifying eyes as PPE or true PE was calculated as:

\[
\text{Accuracy} = \frac{(\text{Number of eyes correctly categorized as PPE or true PE})}{(\text{Total number of eyes imaged})} \times 100\%
\]

The rate of misinterpretation of true PE as PPE was calculated for each imaging modality as follows:

\[
\text{Misinterpretation rate (PE)} = \frac{(\text{Number of eyes with PE misinterpreted as PPE})}{(\text{Total number of eyes with PE})} \times 100\%
\]
Similarly, the rate of misinterpretation of PPE as PE was calculated for each imaging modality. Accuracy and rates of misinterpretation were computed including all eyes with PPE and PE. The calculations were repeated using only 1 eye per patient; if both eyes qualified for the study, then the right eye was selected for this analysis.

The accuracy and rates of misinterpretation for each individual image reader on each imaging modality were calculated separately. The consistency of interpretation among the 3 neuro-ophthalmologists was assessed using multirater kappa. Additionally, the accuracy and rates of misinterpretation were separately computed for children younger than 12 years of age and children 12 years and older. The accuracy of each imaging modality for detecting suspected buried and superficial ODD was also calculated. The mean RNFL thickness measurements by OCT for eyes with suspected buried ODD, superficial ODD, and true PE were compared using Student t test. P values less than 0.05 were considered significant.

Results

We recruited 14 children with PPE and 5 children with PE. Two children with PPE had a known family history of ODD. The cause of PE was idiopathic intracranial hypertension in 4 patients and meningitis in 1 patient. Intracranial pressure (ICP) was elevated in all patients with PE (mean 39 cm H2O, range 30–50 cm H2O). Of the patients with PPE, 11 had suspected buried ODD and 3 had superficial ODD. Two patients with PPE underwent LP before referral to our eye institute, and this revealed normal opening pressure. The patients with PPE, 11 had suspected buried ODD and 3 had superficial ODD. Two patients with PPE underwent LP before referral to our eye institute, and this revealed normal opening pressure. The mean age of patients with suspected buried ODD was signifi-

![Image 1](https://example.com/image1)

![Image 2](https://example.com/image2)

![Image 3](https://example.com/image3)

Table 1. Comparison of 5 Children with Papilledema and 14 Children with Pseudopapilledema Owing to Suspected Buried or Superficial Optic Disc Drusen Who Were Included in This Study

<table>
<thead>
<tr>
<th>Group</th>
<th>No. Eyes Included</th>
<th>Mean Age in Years (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papilledema, n = 5</td>
<td>10</td>
<td>10 (5–16)</td>
</tr>
<tr>
<td>Pseudopapilledema, n = 14</td>
<td>25</td>
<td>11 (6–17)</td>
</tr>
<tr>
<td>Suspected buried ODD, n = 11</td>
<td>19</td>
<td>11 (6–13)</td>
</tr>
<tr>
<td>Superficial ODD, n = 3</td>
<td>6</td>
<td>17 (16–17)</td>
</tr>
</tbody>
</table>

ODD = optic disc drusen.

*P = 0.0029, t test comparing age of subjects with suspected buried vs. superficial ODD.

On FA, eyes with PPE owing to suspected buried ODD generally showed absence of hyperfluorescence both early and late (Fig 1D and E). Eyes with superficial ODD demonstrated early and late nodular staining of the optic nerve, with no change in the area of hyperfluorescence over time (Fig 1G and H). Eyes with PE showed early and late hyperfluorescence of the optic nerve that increased in area over time, consistent with leakage (Fig 1D and E).

On B-scan ultrasonography, superficial ODD were seen as hyperechoic lesions on the optic nerve head, with posterior shadowing, which remained at low gain (Fig 3G). In most cases, eyes with suspected buried ODD showed elevation of the optic nerve head, without a hyperechoic mass (Fig 3G). However, a hyperechoic mass on the optic nerve head consistent with calcified ODD was identified in 6 of 19 (32%) eyes with suspected buried ODD. Eyes with PE showed elevation of the optic nerve head without a hyperechoic mass (Fig 2G), and the B-scan ultrasonographic appearance was indistinguishable from eyes with suspected buried ODD without calcification.

RNFL thickness by OCT was increased in eyes with PPE owing to suspected buried ODD and PE (Figs 1H and 2H), and on average decreased in eyes with superficial ODD (Fig 3H). The average RNFL thickness values by OCT are shown in Figure 4 for eyes with true PE, all eyes with PPE, and eyes with suspected buried ODD and superficial ODD. There was no significant difference in average RNFL thickness between eyes with true PE and eyes with PPE (142 vs. 116 μm, P = 0.11). However, eyes with suspected buried ODD had a thinner average RNFL than eyes with suspected buried ODD (87 vs. 125 μm, P < 0.05). On volumetric SD OCT and EDI OCT scans, both PPE and PE showed elevation of the optic nerve head (Figs 1C, F; 2C, F; and 3C, F). Eyes with PPE owing to superficial and suspected buried ODD demonstrated irregular hyperreflective and hyporeflective areas suggestive of ODD (Figs 1C, F, and 3C, F). However, eyes with PE also displayed similar findings, simulating ODD (Figs 2C, F, and 3).

The multirater kappa for agreement among the 3 neuro-ophthalmologists for each imaging modality is shown in Table 2. The image readers had the best consistency of interpretation for FA (0.60). Agreement was low for the other imaging modalities (kappa range 0.17–0.43).

The accuracy of each imaging modality in classifying pediatric eyes as PPE or true PE, and rates of misinterpretation of PE and PPE, are displayed in Table 3. The accuracy and misinterpretation rates of each individual image reader are shown in Table S1 (available at www.aoajournal.org). FA had the best accuracy (97%; 34 of 35 eyes; 95% confidence interval, 92%–100%), and no FA images of PE were misinterpreted as PPE. The other imaging modalities all had similar accuracy (ranging from 62% to 74%) and had substantial misinterpretation rates for PE (range 30%–70%, or 3–7 of 10 eyes) by the image readers. All modalities, except EDI OCT, were more accurate at classifying
eyes as PPE or true PE in children 12 years of age or older than in younger children. Similar results were obtained when only 1 eye per patient was included for analysis (Table S2, available at www.aaojournal.org).

The accuracies of each imaging technique for identifying suspected buried and superficial ODD are compared in Table 4. All imaging modalities except OCT RNFL were better at detecting superficial than suspected buried ODD. With the exception of OCT RNFL analysis, all imaging techniques identified 100% of superficial ODD.

**Discussion**

FA had the greatest accuracy for classifying pediatric eyes as PPE or PE. No cases of PE were misinterpreted on FA. FA images were also interpreted most consistently by the image readers. Of the other imaging modalities, fundus photography had the lowest rate of misinterpretation of PE, which was still considerable at 30% (3 of 10 eyes). Ultrasound, autofluorescence, and all OCT protocols had an even higher (40%—70%, or 4—7 of 10 eyes) rate of misinterpretation of PE as PPE by the image readers. All imaging modalities except OCT RNFL were better at detecting superficial compared with suspected buried ODD. Additionally, all imaging modalities except EDI OCT were more accurate in children 12 years of age and older than in younger children.

The superiority of FA for classifying eyes as PPE or PE was likely owing to the existence of leakage as a clear and relatively easily evaluated marker for true edema on FA.
However, the accuracy rate of individual neuro-ophthalmologists was lower than the consensus accuracy rate (consensus rate, 97%; individual rates ranged from 83% to 97%, Table S1). Figure S1, top row (available at www.aaojournal.org), shows an example FA of an eye with PE that was misinterpreted as PPE by 1 image reader but correctly identified as PE by the other 2 neuro-ophthalmologists. This shows that FA is not infallible, and reliance on a single test, even the most accurate test in this study, may lead to misdiagnosis without the appropriate clinical context. Furthermore, FA cannot be used to distinguish between PE and other causes of ODE such as inflammatory or infectious optic neuritis, as these would all show leakage of the optic disc on FA.

In this study, ophthalmic imaging modalities other than FA did not display findings specific to PE, leading to the inability to distinguish between buried or noncalcified ODD and true PE. For example, on B-scan ultrasonography, both buried noncalcified ODD and PE exhibited optic nerve head elevation, without a hyperechogenic mass (Figs 1G and 2G). Similarly, on autofluorescence, both buried ODD and PE were characterized by the absence of hyperautofluorescent lesions on the optic nerve head (Figs 1B and 2B).

In our patients, OCT of the RNFL was unable to accurately classify eyes as PPE or PE. Eyes with suspected buried ODD demonstrated thickening of the RNFL (mean, 125 μm; range, 98–162 μm), which overlapped with the values for RNFL thickness in patients with PE (mean, 142 μm; range, 91–199 μm). Eyes with superficial ODD did show RNFL thinning in some cases (mean, 87 μm; range, 34–203 μm), but this also overlapped with and was not significantly different from RNFL thickness in eyes with
Our findings differ from those of Lee et al., who reported that RNFL thickness by OCT was higher in eyes with ODE than in those with ODD. This may be attributable to their inclusion of eyes with more severe ODE (mean RNFL thickness, 174 μm) than our patients. Diagnostic uncertainty is more likely to occur in cases of mild than severe ODE. In comparing eyes with mild PE with those with PPE, Karam and Hedges found, similar to the present study, that OCT analysis of the RNFL was unable to distinguish between the 2 entities.

In this study, volumetric OCT scans (SD OCT and EDI OCT) had high rates of identifying ODD (misinterpretation rate for PPE was 13%–14%). However, these modalities also had the highest rates of misinterpretation of PE as PPE (60%–70%, or 6–7 of 10 eyes). This was owing to nonspecific hyperreflective and hyporeflective areas in the OCT of eyes with edema that simulated ODD (Fig 2C and F, and Fig 5). In the literature, 3 different appearances of ODD on OCT have been described: (1) peripapillary hyperreflective masses, causing focal elevation of the adjacent retina in a boot shape; (2) hyporeflective ovoid regions with hyperreflective margins; and (3) horizontal hyperreflective bands, with or without a hyporeflective core. There is no consensus as to which of these 3 criteria is best for identifying ODD on OCT, and the neuroophthalmologists interpreting images for this study used a
variable combination of criteria. It has been suggested that the different OCT appearances of drusen represent a continuum in the development of ODD—initially the druse begins as a hyperreflective peripapillary mass representing axoplasmic stasis; stasis causes extrusion of calcified mitochondria, which are seen as hyperreflective bands or “granular” drusen on OCT; and, finally, calcium deposition leads to hyporeflective masses with hyperreflective margins. However, it is unknown how to best distinguish these hyperreflective and hyporeflective regions on OCT from swelling of the optic nerve, as occurs in ODE, or from normal structures of the optic nerve head, such as blood vessels. Similar to the present study, Kulkarni et al found that volumetric SD OCT scans through the optic nerve could not distinguish between buried ODD and mild PE, owing to irregular hyperreflective areas in eyes with PE that mimicked drusen. We extend these findings and report that EDI OCT did not improve the ability to distinguish between PE and PPE owing to suspected buried or superficial ODD.

An alternative reason for the high rate of misinterpretation of OCT images of PE as PPE is that there were ODD underlying the edema. Although we excluded patients clinically suspected to have both ODD and PE, we cannot eliminate the possibility that some patients with PE had underlying ODD that were only visible on OCT. However, when image readers suspected the coexistence of ODD and PE, the interpretation was recorded as PE (this only occurred in 1 case). Images were read as PPE only in the absence of findings of PE. Therefore, the misinterpretation rate of PE reflected all eyes with PE that were missed, even if there were underlying ODD.

In our study, children as young as 5 years of age were able to cooperate with all diagnostic tests. Only 2 images from 2 different patients, 1 OCT RNFL and 1 EDI OCT, were excluded owing to poor image quality. Venipuncture was performed by a dedicated FA nurse without anesthesia. In ophthalmology clinics without the ability to perform intravenous FA (IVFA) in children, oral FA may be considered as a substitute. However, oral FA may be less sensitive for detection of PE, and requires imaging at 30 and
60 minutes after contrast ingestion for detection of optic disc leakage.\(^{18}\)

The main limitation of our study was use of clinical diagnosis as the gold standard for comparison with imaging tests. Because there is no standard imaging modality for detecting ODD in children, clinical diagnosis was considered the best indicator of the true diagnosis. All children diagnosed with PE had LP with documented elevated opening pressures. Patients with PPE were followed up for at least 6 months, to ensure stability of diagnoses of ODD appearance on OCT in the literature.\(^{14}\)

we cannot exclude the possibility of misdiagnosis in some patients, especially because not all children clinically diagnosed with PPE had LP showing normal opening pressure, and mildly elevated ICP can be associated with a stable appearance over 6 months. Other limitations of the study include relatively small sample size and inconsistency of criteria among our neuro-ophthalmologists in diagnosing ODD on volumetric OCT, which reflects the varying descriptions of ODD appearance on OCT in the literature.\(^{14}\)

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### Table 2. Agreement among 3 Masked Neuro-ophthalmologists Who Interpreted the Images, by Multirater Kappa

<table>
<thead>
<tr>
<th>Modality</th>
<th>Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasonography</td>
<td>0.39</td>
</tr>
<tr>
<td>Fundus photography</td>
<td>0.43</td>
</tr>
<tr>
<td>Autofluorescence</td>
<td>0.25</td>
</tr>
<tr>
<td>Fluorescein angiography</td>
<td>0.60</td>
</tr>
<tr>
<td>OCT RNFL</td>
<td>0.29</td>
</tr>
<tr>
<td>SD OCT</td>
<td>0.31</td>
</tr>
<tr>
<td>EDI OCT</td>
<td>0.17</td>
</tr>
</tbody>
</table>

EDI OCT = enhanced depth imaging optical coherence tomography; OCT = optical coherence tomography; RNFL = retinal nerve fiber layer; SD OCT = spectral-domain optical coherence tomography.

### Table 3. Accuracy of Imaging Modalities in Distinguishing between Pseudopapilledema and True Papilledema, and Rates of Misinterpretation by the Image Readers\(^*\)

<table>
<thead>
<tr>
<th>Modality</th>
<th>Accuracy, % (95% CI)</th>
<th>Papilledema Misinterpreted as PPE, % (95% CI)</th>
<th>Pseudopapilledema Misinterpreted as PE, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasonography</td>
<td>74 (60–89)</td>
<td>60 (30–90)</td>
<td>12 (0–25)</td>
</tr>
<tr>
<td>Younger than 12 years</td>
<td>63 (39–86)</td>
<td>50 (10–90)</td>
<td>30 (2–58)</td>
</tr>
<tr>
<td>12 years and older</td>
<td>84 (68–100)</td>
<td>75 (33–100)</td>
<td>0</td>
</tr>
<tr>
<td>Fundus photography</td>
<td>66 (50–81)</td>
<td>30 (16–58)</td>
<td>36 (17–55)</td>
</tr>
<tr>
<td>Younger than 12 years</td>
<td>50 (26–75)</td>
<td>17 (0–46)</td>
<td>70 (42–98)</td>
</tr>
<tr>
<td>12 years and older</td>
<td>79 (61–97)</td>
<td>50 (1–99)</td>
<td>13 (0–31)</td>
</tr>
<tr>
<td>Autofluorescence</td>
<td>62 (45–78)</td>
<td>50 (19–81)</td>
<td>33 (14–52)</td>
</tr>
<tr>
<td>Younger than 12 years</td>
<td>50 (26–75)</td>
<td>33 (0–71)</td>
<td>60 (30–90)</td>
</tr>
<tr>
<td>12 years and older</td>
<td>72 (52–93)</td>
<td>75 (33–100)</td>
<td>14 (0–33)</td>
</tr>
<tr>
<td>Fluorescein angiography</td>
<td>97 (92–100)</td>
<td>0</td>
<td>4 (0–12)</td>
</tr>
<tr>
<td>Younger than 12 years</td>
<td>94 (82–100)</td>
<td>0</td>
<td>10 (0–29)</td>
</tr>
<tr>
<td>12 years and older</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>OCT RNFL</td>
<td>69 (53–84)</td>
<td>50 (19–81)</td>
<td>20 (4–36)</td>
</tr>
<tr>
<td>Younger than 12 years</td>
<td>69 (46–91)</td>
<td>33 (0–71)</td>
<td>30 (2–58)</td>
</tr>
<tr>
<td>12 years and older</td>
<td>69 (48–89)</td>
<td>75 (33–100)</td>
<td>13 (0–31)</td>
</tr>
<tr>
<td>SD OCT</td>
<td>71 (55–87)</td>
<td>60 (30–90)</td>
<td>14 (0–29)</td>
</tr>
<tr>
<td>Younger than 12 years</td>
<td>64 (39–89)</td>
<td>67 (29–100)</td>
<td>13 (0–35)</td>
</tr>
<tr>
<td>12 years and older</td>
<td>76 (56–97)</td>
<td>50 (1–99)</td>
<td>15 (0–35)</td>
</tr>
<tr>
<td>EDI OCT</td>
<td>67 (51–83)</td>
<td>70 (42–98)</td>
<td>13 (0–27)</td>
</tr>
<tr>
<td>Younger than 12 years</td>
<td>71 (48–95)</td>
<td>50 (10–90)</td>
<td>0</td>
</tr>
<tr>
<td>12 years and older</td>
<td>63 (41–85)</td>
<td>0</td>
<td>20 (0–40)</td>
</tr>
</tbody>
</table>

CI = confidence interval; EDI OCT = enhanced depth imaging optical coherence tomography; OCT = optical coherence tomography; PE = papilledema; PPE = pseudopapilledema; RNFL = retinal nerve fiber layer; SD OCT = spectral-domain optical coherence tomography.

\(^*\)Accuracy and misinterpretation rates are reported for all children (gray), and separately for children younger and older than 12 years of age.
Finally, for technical reasons, we were unable to perform OCT analysis of the ganglion cell layer, which may be superior to RNFL for detection of buried ODD, or quantitative analysis of the configuration of the peripapillary Bruch membrane and retinal pigment epithelium, which have been shown to be bowed inward in eyes with PE. We did not qualitatively observe this phenomenon in most of the eyes in our study with PE, although we did not perform principal component analysis, which has been used to demonstrate this finding in other studies. We also did not assess maximal anterior retinal projection on optic nerve OCT, which has been shown to distinguish between eyes of normal children and those with intracranial hypertension but has not been used in children with PPE. Finally, although we were able to obtain IVFA in children as young as 5 years of age without anesthesia, not all young children will cooperate with IVFA and not all clinics have personnel experienced in performing IVFA in children.

In conclusion, we report that FA had the highest accuracy for classifying pediatric eyes as PPE or PE. Ophthalmic imaging tests other than FA, including fundus photography, B-scan ultrasonography, autofluorescence, and OCT volumetric scans and RNFL analysis, had a substantial likelihood of misinterpretation of PE as PPE in children. We recommend the use of FA to rule out PE in cases of clinical uncertainty. In this study, 2 of 14 children with PPE (14%) underwent LP, showing normal opening pressure. FA showed absence of optic disc leakage in both patients. If FA had been performed as the initial test when the clinician was uncertain as to whether the patients had PPE or PE, this invasive testing could have been avoided. However, if the FA is consistent with ODE in cases of clinical ambiguity, neuroimaging and LP should be performed to evaluate for elevated ICP. Some children already have neuroimaging before ophthalmologic evaluation; in these cases, the magnetic resonance images should be examined for signs of elevated ICP. Brodsky and Vaphiades described 6 occult neuroimaging signs of elevated ICP that together identified 90% of adults and children with pseudotumor cerebri. Importantly, PPE owing to ODD may coexist with PE, and we recommend the use of FA to assess for optic disc leakage in children with PPE even when ODE are identified, if there are signs or symptoms suggestive of increased ICP.

References

Footnotes and Financial Disclosures

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Overall responsibility: Chang, Velez, Demer, Bonelli, Quiros, Arnold, Sadun, Pineles

Abbreviations and Acronyms:

EDI OCT = enhanced depth imaging optical coherence tomography; FA = fluorescein angiography; ICP = intracranial pressure; IVFA = intravenous fluorescein angiography; LP = lumbar puncture; OCT = optical coherence tomography; ODD = optic disc drusen; ODE = optic disc edema; PE = papilledema; PPE = pseudopapilledema; RNFL = retinal nerve fiber layer; SD OCT = spectral-domain optical coherence tomography.

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