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Ophthalmic Technology Assessment

Imaging Methods for Differentiating Pediatric Papilledema from Pseudopapilledema

A Report by the American Academy of Ophthalmology

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Purpose: To review the published literature on the accuracy of ophthalmic imaging methods to differentiate between papilledema and pseudopapilledema in children.

Methods: Literature searches were conducted in January 2020 in the PubMed database for English-language studies with no date restrictions and in the Cochrane Library database without any restrictions. The combined searches yielded 354 abstracts, of which 17 were reviewed in full text. Six of these were considered appropriate for inclusion in this assessment and were assigned a level of evidence rating by the panel methodologist. All 6 included studies were rated as level III evidence.

Results: Fluorescein angiography, a combination of 2 OCT protocols, and multicolor confocal scanning laser ophthalmoscopy (Spectralis SD-OCT; Heidelberg Engineering, Heidelberg, Germany) demonstrated the highest positive percent agreement (92%–100%; 95% confidence interval [CI], 69%–100%) and negative percent agreement (92%–100%; 95% CI, 70%–100%) with a clinical diagnosis of papilledema in children. However, results must be interpreted with caution owing to methodologic limitations, including a small sample size leading to wide CIs and an overall lack of data (there was only 1 study each for the above methods and protocols). Ultrasonographic measures showed either a high positive percent agreement (up to 95%) with low negative percent agreement (as low as 58%) or vice versa. Autofluorescence and fundus photography showed a lower positive (40%–60%) and negative (57%) percent agreement.

Conclusions: Although several imaging methods demonstrated high positive and negative percent agreement with clinical diagnosis, no ophthalmic imaging method conclusively differentiated papilledema from pseudopapilledema in children because of the lack of high-quality evidence. Clinicians must continue to conduct thorough history-taking and examination and make judicious use of ancillary testing to determine which children warrant further workup for papilledema. *Ophthalmology 2020;127:1416-1423 © 2020 by the American Academy of Ophthalmology*

The American Academy of Ophthalmology prepares Ophthalmic Technology Assessments to evaluate new and existing procedures, drugs, and diagnostic and screening tests. The goal of an Ophthalmic Technology Assessment is to review systematically the available research for clinical efficacy, effectiveness, and safety. After review by members of the Ophthalmic Technology Assessment Committee, other Academy committees, relevant subspecialty societies, and legal counsel, assessments are submitted to the Academy's Board of Trustees for consideration as official Academy statements. The purpose of this assessment by the Ophthalmic Technology Assessment Committee Pediatric Ophthalmology/Strabismus Panel is to review the published literature on the accuracy of ophthalmic imaging methods to differentiate between papilledema and pseudopapilledema in children.

Background

Pediatric ophthalmologists often receive referrals for suspected papilledema in children. Papilledema is diagnosed when optic disc edema occurs in the setting of elevated intracranial pressure, whereas pseudopapilledema occurs when apparent optic disc swelling is secondary to other causes, typically structural factors such as optic disc drusen (ODD). The diagnostic distinction is critical in children because misdiagnosis of papilledema as pseudopapilledema has life-threatening implications. Conditions such as meningitis or an intracranial mass lesion may be overlooked. Conversely, misdiagnosing pseudopapilledema as papilledema will lead to unnecessary, invasive, and expensive further testing, typically involving neuroimaging and

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lumbar puncture, each requiring sedation in children.[1] No gold standard diagnostic test exists to distinguish between papilledema and pseudopapilledema. Thus, ophthalmologists frequently must rely on clinical judgment and absence of progression over time to support the diagnosis of pseudopapilledema. No consensus exists as to the duration of stability that is required to confirm the absence of true papilledema; however, several published studies required at least 3 to 6 months of follow-up without change in optic nerve appearance to meet the criteria for a pseudopapilledema diagnosis.[2–4]

Differentiating pseudopapilledema from papilledema in children is particularly difficult. For example, ODD, the most common cause of pseudopapilledema, may be clinically indistinct at a younger age. While ODD in children are buried, the clinical appearance mimics papilledema. Then, over time, as ODD become more superficial, they are detected more easily with ophthalmoscopy.[5] Furthermore, ODD in children are less likely to be calcified and are more difficult to detect using ultrasonography, the imaging method traditionally used for ODD detection in adults.[6] Because ODD in children frequently are buried within neural tissue, they are obscured and may be undetectable with autofluorescence and fluorescein angiography.[5–7]

Because of these difficulties, recent investigators have assessed the use of OCT to help identify ODD in children.[8,9] The high resolution and depth of penetration of OCT, particularly enhanced depth imaging (EDI) OCT, potentially could overcome the barriers to detecting buried, noncalcified ODD in children and could facilitate differentiation of pseudopapilledema from papilledema.[10] In adults, the features of ODD on EDI OCT have been delineated carefully, and a consensus protocol for the diagnosis of ODD in adults using EDI OCT has been outlined by the Optic Disc Drusen Studies Consortium.[11,12] No such consensus recommendations exist for using OCT to diagnose ODD, pseudopapilledema, or papilledema in children. Moreover, various OCT measures have been used to identify suspected papilledema, including retinal nerve fiber layer (RNFL) thickness, anterior bowing of Bruch's membrane, and absence of direct visualization of ODD on volumetric optic nerve OCT scans.[2–4,13]

Considering the recent interest in new imaging methods, as well as the lack of agreement in the literature on the optimal imaging choice, the panel reviewed the current evidence on the accuracy of ophthalmic imaging methods for differentiating papilledema and pseudopapilledema in children.

Questions for Assessment

The focus of this assessment was to address the following question: What diagnostic imaging method has the highest accuracy in discriminating between pseudopapilledema and papilledema in children?

The panel considered the following imaging methods: ultrasonography, OCT, autofluorescence, fluorescein angiography, fundus photography, and multicolor confocal scanning laser ophthalmoscopy (cSLO; Spectralis SD-OCT, Heidelberg Engineering, Heidelberg, Germany). Multicolor cSLO, available only on the Spectralis SD-OCT platform, uses 3 wavelengths of laser (blue, green, and near infrared) that penetrate tissues to varying depths to highlight different retinal layers.[14] All 3 wavelengths are acquired simultaneously with OCT scanning, and thus, minimal additional time is required to perform multicolor cSLO with OCT.

Description of Evidence

Literature searches were conducted last in January 2020 in the PubMed database for English-language studies with no date restrictions and in the Cochrane Library database without any restrictions. The following terms were used, along with publication and language filters: *papilledema*, *pseudopapilledema*, *papilledema*[mh], *papilloedema*, *pseudopapilloedema*, *optic nerve head edema*, *OCT*, *optical coherence tomography*, *tomography*, *optical coherence* [mh], *enhanced depth imaging*, *EDI*, *ss OCT*, *swept source OCT*, *ss*, *swept source*, *optic disk imaging*, *optic disk/diagnostic imaging*[mh], *optical imaging*, *diagnostic techniques*, *ophthalmological*, *fundus photography*, *fundus, photograph**, *fluorescein angiography*, *fluorescein, angiograph**, *autofluorescence*, *ultrasonography*, *multicolor imaging*, *multicol* imaging*, *confocal scanning laser tomography*, *Bruch's membrane*, *Bruch's membrane opening*, *shape analysis*, *optic nerve head*, *peripapillary*, *retinal pigment epithelium*, and *RPE*.

Searches yielded 354 articles (i.e., 86 articles when the search was restricted to pediatric patients and an additional 268 articles without age restriction). Abstracts were selected for full-text review if they met the following inclusion criteria: (1) at least 1 of the predefined ophthalmic diagnostic imaging methods (ultrasound, OCT, fluorescein angiography, fundus photography, autofluorescence, or multicolor cSLO) was assessed, (2) at least 2 patient groups were included (papilledema and pseudopapilledema), and (3) most or all patients were children. The review of studies was limited to those that focused on children because of the differing characteristics of ODD, the most common cause of pseudopapilledema, in this age group. Articles about patients with papilledema who were not compared directly with those with pseudopapilledema were excluded (e.g., the comparison group included patients with pseudopapilledema in addition to controls or other diagnoses).

The literature review identified 6 articles on children and 11 articles that included both adults and children for full-text review. Six articles were selected for inclusion in the final assessment and were assigned a level of evidence rating by the panel methodologist (R.H.T.) based on the Oxford Center for Evidence-Based Medicine—Levels of Evidence.[15] A level I rating was assigned to well-designed and well-conducted randomized clinical trials; a level II rating was assigned to well-designed case-control and cohort studies and lower-quality randomized studies; and a level III rating was assigned to case series, case reports, and lower-quality cohort and case-control studies. All 6 articles were rated as level III evidence.

Table 1. Positive and Negative Percent Agreement of Imaging Methods with Clinical Diagnosis of Papilledema in Children, Presented by Study

Authors (Year)	Level of Evidence	Study Design	Criteria Used to Identify Papilledema on Imaging	No. of Papilledema Patients	No. of Pseudopapilledema Patients	Mean Age (Range)*	Follow-up Duration	Positive Percent Agreement (95% Confidence Interval)	Negative Percent Agreement (95% Confidence Interval)
Ultrasonography									
Chang et al (2017)[4]	III	Prospective	Absence of drusen (hyperechoic mass with posterior shadowing at low gain on ON head)	5	14	11 (5–17)	At least 6 mos for pseudopapilledema	40% (7%–77%)	86% (60%–97%)
Dahlman-Noor et al (2018)[19]	III	Retrospective	ON sheath dilation	3	58	Median, 11 (interquartile range, 8–13)	Up to 3 mos	33% (2%–88%)	100% (94%–100%)
Neudorfer et al (2013)[17]	III	Prospective	ON width >3.3 mm	20	24	12.7 (2–30), 89% younger than 18	Mean, 18 mos (range, 2 days–83 mos)	85% (64%–95%)	63% (43%–79%)
Neudorfer et al (2013)[17]	III	Prospective	ON width >3.0 mm	See above	See above	See above	See above	95% (76%–100%)	58% (39%–76%)
OCT									
Chang et al (2017)[4]	III	Prospective	RNFL thickness	5	14	11 (5–17)	At least 6 mos for pseudopapilledema	40% (7%–77%)	71% (45%–88%)
Chang et al (2017)[4]	III	Prospective	SD OCT volumetric scan (absence of drusen)	See above	See above	See above	See above	40% (7%–77%)	92% (69%–99%)
Chang et al (2017)[4]	III	Prospective	EDI OCT volumetric scan (absence of drusen)	See above	See above	See above	See above	40% (7%–77%)	85% (60%–97%)
Dahlmann-Noor et al (2018)[19]	III	Retrospective	RNFL thickness >75th percentile in superonasal, nasal, and/or temporal sectors	3	58	Median, 11 (interquartile range, 8–13)	Up to 3 mos	67% (12%–98%)	91% (81%–96%)
Dahlmann-Noor et al (2018)[19]	III	Retrospective	Anterior bowing of BM	See above	See above	See above	See above	33% (2%–88%)	97% (88%–99%)
Martinez and Ophir (2011)[2]	III	Retrospective	RNFL thickness >300 μm in ≥3 clock hours	9	6	15 (9–20)	At least 3 mos for pseudopapilledema	89% (56%–99%)	100% (61%–100%)
Thompson et al (2018)[3]	III	Prospective	BMO >1718 μm	19	58	12 (standard deviation, 3)	At least 6 mos for pseudopapilledema	68.4% (46%–85%)	82.8% (71%–90%)
Thompson et al (2018)[3]	III	Prospective	RNFL thickness >131 μm	See above	See above	See above	See above	84.2% (62%–94%)	91.4% (81%–96%)
Thompson et al (2018)[3]	III	Prospective	Anterior bowing of BM	See above	See above	See above	See above	21.1% (9%–43%)	94.8% (86%–99%)
Thompson et al (2018)[3]	III	Prospective	RNFL >131 μm + BMO >1718 μm	See above	See above	See above	See above	91.7% (69%–98%)	92.2% (81%–96%)
Autofluorescence									
Chang et al (2017)[4]	III	Prospective	Absence of drusen (hyperautofluorescent lesions on ON head)	5	14	11 (5–17)	At least 3 mo. for pseudopapilledema	40% (7%–77%)	57% (33%–79%)
Fluorescein angiography									
Chang et al (2017)[4]	III	Prospective	ON leakage	See above	See above	See above	See above	100% (72%–100%)	93% (80%–100%)

Table 1. (Continued.)

Authors (Year)	Level of Evidence	Study Design	Criteria Used to Identify Papilledema on Imaging	No. of Papilledema Patients	No. of Pseudopapilledema Patients	Mean Age (Range)*	Follow-up Duration	Positive Percent Agreement (95% Confidence Interval)	Negative Percent Agreement (95% Confidence Interval)
Fundus photography									
Chang et al (2017)[4]	III	Prospective	Obscuration of blood vessels at ON margin, peripapillary hemorrhages, hyperemia	See above	See above	See above	See above	60% (23%–93%)	57% (33%–79%)
Multicolor confocal scanning laser ophthalmoscopy									
Malem et al (2016)[18]	III	Prospective	Green shift, obscuration of blood vessels, blurring of disc margins	11	9	11 (5–16)	None reported	100% (74%–100%)	100% (70%–100%)

BM = Bruch's membrane; BMO = Bruch's membrane opening; EDI = enhanced depth imaging; ICP = intracranial pressure; ON = optic nerve; RNFL = retinal nerve fiber layer; SD = spectral domain.
*In years.

Because no gold standard exists to differentiate pediatric papilledema from pseudopapilledema, published studies compared diagnostic tests with final clinical diagnoses. Based on Food and Drug Administration recommendations, reporting of sensitivity and specificity are not appropriate in the absence of a reference standard; instead, candidate tests should be compared using positive percent agreement and negative percent agreement.[16] Positive and negative percent agreement data were extracted from the 6 articles, and 95% confidence intervals (CIs) were calculated (GraphPad Prism software version 8.0.1 for Mac; GraphPad Software, San Diego, CA). Positive percent agreement was defined as the proportion of patients clinically diagnosed with papilledema for whom the diagnostic test results were positive for papilledema. Negative percent agreement was defined as the proportion of patients clinically diagnosed with pseudopapilledema for whom the diagnostic test results were negative for papilledema.

Published Results

Of the 6 studies included in this assessment, 2 evaluated OCT only[2,3]; 1 assessed ultrasonography only[17]; 1 evaluated multicolor cSLO only[18]; 1 used OCT and ultrasonography[19]; and 1 evaluated ultrasonography, OCT, autofluorescence, fluorescein angiography, and fundus photography.[4]

The published studies were heterogeneous with regard to 3 main characteristics: (1) study design (retrospective or prospective); (2) participant characteristics, including diagnoses considered (ODD only or all pseudopapilledema; idiopathic intracranial hypertension only or all papilledema), diagnostic criteria, and severity of diagnoses (mild papilledema only vs. all grades of papilledema); and (3) image interpretation, particularly the number and masking of image readers.

A variety of outcome measures were reported by the authors, including sensitivity, specificity, and accuracy of classifying eyes with papilledema and pseudopapilledema, "misinterpretation rates" of papilledema and pseudopapilledema, positive and negative predictive values, the area under the receiver operating characteristic curves, and multirater κ values (agreement among multiple image graders). As described previously, these data were used to calculate positive and negative percent agreement between diagnostic tests and clinical diagnosis.

Review of Studies

Table 1 summarizes the 6 level III studies that assessed ophthalmic imaging methods for differentiating between pediatric papilledema and pseudopapilledema. The positive and negative percent agreement are reported for each imaging method by study.

In a prospective study by Chang et al,[4] 19 children (age range, 5–17 years) were imaged, 5 with papilledema and 14 with pseudopapilledema secondary to ODD, using ultrasonography, 3 types of OCT analysis (RNFL thickness, standard spectral-domain [SD] OCT volumetric scans through the optic nerve, and EDI OCT volumetric optic nerve scans), autofluorescence, fluorescein

angiography, and fundus photography. All patients with papilledema underwent lumbar puncture that documented elevated opening pressure; the patients diagnosed with pseudopapilledema who did not have lumbar puncture were followed up for at least 6 months to confirm the stability of the findings. Three masked image readers (neuro-ophthalmologists) interpreted the scans. Positive percent agreement of imaging methods ranged from 40% to 100%, whereas negative percent agreement ranged from 57% to 93%. Fluorescein angiography had the highest positive percent agreement at 100% (95% CI, 72%−100%) and negative percent agreement at 93% (95% CI, 80%−100%). The authors speculated that this was because of the presence of optic disc leakage in eyes with papilledema, in contrast to staining or no hyperfluorescence in eyes with pseudopapilledema. Importantly, the degree of optic disc leakage on fluorescein angiography corresponds to the grade of papilledema,[20] and eyes with mild papilledema may show mild leakage, making leakage difficult to distinguish from staining. In this study, the authors did not report papilledema grade. Thus, they may have overestimated the papilledema detection rate on fluorescein angiography if the papilledema grades were uniformly high. Other than leakage on fluorescein angiography, the authors did not identify any other imaging findings specific to papilledema. They did not assess optic nerve sheath width on ultrasonography and did not use a standard protocol to identify ODD on OCT. Fluorescein angiography had the highest multirater κ value (0.60) for agreement among the 3 masked image readers. When children younger than and older than 12 years were analyzed separately, fluorescein angiography remained the most accurate imaging method in each group. Among eyes with suspected buried ODD, fluorescein angiography also showed the highest accuracy. However, among eyes with superficial ODD, all imaging methods were 100% accurate, with the exception of OCT RNFL thickness.

In a retrospective study, Dahlmann-Noor et al[19] evaluated ultrasonography and OCT findings in 61 children (median age, 11 years) referred for "suspicious discs," 3 of whom ultimately were diagnosed with papilledema and 58 of whom ultimately were diagnosed with pseudopapilledema. All children with pseudopapilledema had ODD; the authors did not indicate whether they were superficial or buried but noted that 71% showed "small linear" ODD and 29% showed "gross" ODD. The 3 cases of papilledema were the result of intraventricular astrocytoma causing obstructive hydrocephalus, craniosynostosis, and central nervous system involvement of acute lymphocytic leukemia. However, the authors note that the patient with acute lymphocytic leukemia may have had leukemic infiltration rather than papilledema. At presentation, 1 patient (33%) showed optic nerve sheath dilation on ultrasonography, 2 patients (67%) showed OCT RNFL thickening of more than the 75th percentile of all right eyes in this study, and 1 patient (33%) showed anterior bowing of Bruch's membrane on OCT.

In a prospective study, Neudorfer et al[17] performed ultrasonography on all individuals with bilateral optic discs that appeared swollen on funduscopy during a 4-year period. They included 20 patients diagnosed with papilledema and 24 with pseudopapilledema. Although this study included adults, 89% of patients were younger than 18 years (mean age, 12.7 years; age range, 2−30 years). All patients with papilledema underwent lumbar puncture. Patients with pseudopapilledema who did not undergo lumbar puncture were followed up for an average of 22 months with stable findings. A single highly experienced ultrasound operator (masking was not reported) acquired all images. The authors found that optic nerve width of more than 3.0 mm was associated with 95% positive percent agreement and 58% negative percent agreement with clinical diagnosis of papilledema. Increasing the optic nerve width cutoff to more than 3.3 mm reduced the positive percent agreement to 85% and increased the negative percent agreement to 63%. Funduscopy by an ophthalmologist (the method and criteria for diagnosing pseudopapilledema and suspected papilledema by funduscopy were not reported) showed a higher negative percent agreement (71%), but lower positive percent agreement (63%), than ultrasonography with either cutoff value. Of 24 patients with pseudopapilledema, 11 were diagnosed with ODD (diagnostic criteria not stated). The authors did not analyze separately the usefulness of ultrasound in eyes with pseudopapilledema resulting from ODD versus other causes. They also did not evaluate whether age affected their results. This is an important limitation, because the age range (2−30 years) encompassed both young children, in whom pseudopapilledema resulting from buried ODD is more difficult to differentiate from papilledema, and older individuals.

Martinez and Ophir[2] retrospectively analyzed imaging findings obtained from 15 patients 20 years of age and younger who were newly diagnosed with either bilateral papilledema or pseudopapilledema and underwent OCT. All patients underwent neuroimaging. Patients diagnosed with papilledema either underwent lumbar puncture demonstrating elevated opening pressure or demonstrated reduction in disc edema during follow-up. Patients with pseudopapilledema underwent lumbar puncture with a normal opening pressure or were followed up for at least 3 months with no change in funduscopic findings. Of the patients with pseudopapilledema, none was diagnosed with ODD, but diagnostic criteria for ODD were not reported. The authors assessed RNFL thickness in each clock hour and arbitrarily chose a cutoff value of 300 μm to differentiate papilledema from pseudopapilledema. Of 9 patients with papilledema, 8 (i.e., positive percent agreement of 89%) demonstrated RNFL thickening of more than 300 μm in at least 3 clock hours in at least 1 eye. All 6 patients with pseudopapilledema (i.e., negative percent agreement of 100%) showed RNFL thickness of less than 300 μm in every clock hour in both eyes. The patients with papilledema generally showed high intracranial pressure (average, 46.2 cm H_2O among those who underwent lumbar puncture), and thus the results may not be applicable to children with lower intracranial pressure and milder papilledema. Furthermore, time-domain OCT was used in this study, and the findings may not translate directly to patients evaluated with more modern SD OCT, because time-domain

OCT measurements are less reproducible and differ significantly from those acquired by SD OCT.[21] Finally, no analysis was carried out of the effect of age on OCT results.

Thompson et al[3] prospectively collected optic nerve OCT images in children with pseudopapilledema resulting from ODD (n = 58), those with mild (grade 1−2) papilledema secondary to idiopathic intracranial hypertension (n = 19), and controls (n = 13). Most children (89%) with pseudopapilledema harbored buried ODD. The mean age in both groups was 12 ± 3 years. The authors evaluated 3 OCT measures: (1) average circumferential RNFL thickness; (2) the size of Bruch's membrane opening, manually calculated by a masked ophthalmologist; and (3) the angulation of Bruch's membrane. The papillary height also was measured, but was not included in this assessment because it did not differ between eyes with papilledema and pseudopapilledema, and positive and negative percent agreement could not be calculated from the data reported. Based on their data, the authors determined that the optimal thresholds to classify eyes as papilledema were Bruch's membrane opening of more than 1718 μm and RNFL thickness of more than 131 μm. Using these cutoff values, the positive and negative percent agreement with clinical diagnosis of papilledema were 91.7% (95% CI, 69%−98%) and 92.2% (95% CI, 81%−96%), respectively. The authors then applied these OCT thresholds to a second prospective cohort of 22 eyes of 11 patients with pseudopapilledema and 16 eyes of 8 patients with mild papilledema, which resulted in accurate classification of 92% of eyes (positive percent agreement, 87% [95% CI, 64%−98%]; negative percent agreement, 95% [95% CI, 78%−100%]). Although results were not stratified by age, the authors used a multivariate logistic regression model including age, race, and gender, and they showed that the cutoff values remained associated significantly with mild papilledema relative to pseudopapilledema.

Finally, Malem et al[18] prospectively collected multicolor cSLO imaging data in 20 consecutive children (age range, 5−16 years) with suspected papilledema, of whom 11 were diagnosed with papilledema and 9 were diagnosed with pseudopapilledema. In this study, the underlying diagnosis in children with pseudopapilledema was ODD in 4 patients and anomalous, crowded, or hypermetropic discs in the remaining 5 patients. Patients with true papilledema showed neuroimaging evidence of intracranial pathologic features causing elevated intracranial pressure (such as intracranial tumor or venous sinus stenosis), or they underwent lumbar puncture that indicated elevated opening pressure. Two of 9 patients with pseudopapilledema underwent lumbar puncture that indicated normal opening pressure; the authors did not report follow-up of patients who did not undergo lumbar puncture. The images were evaluated by a medical retina specialist (masking not reported) who found that eyes with papilledema were characterized by an elevated hyperreflective green ring around the optic nerve, best seen on the blue and green reflectance images, in addition to indistinct disc margins and obscuration of vasculature at the disc margin. The authors reported that these findings were present in all eyes with papilledema and none of the eyes with pseudopapilledema. Thus, positive percent agreement was 100% (95% CI, 74%−100%), and negative percent agreement also was 100% (95% CI, 70%−100%). Results were not analyzed separately by age or underlying cause of pseudopapilledema.

Conclusions

This review of level III evidence suggests that fluorescein angiography and multicolor cSLO both are potentially useful ancillary imaging methods in differentiating between papilledema and pseudopapilledema in children. Both were reported to have 100% positive percent agreement and more than 90% negative percent agreement with a clinical diagnosis of papilledema.[4,18] However, each method was evaluated by only 1 study that had a small number of participants, leading to wide CIs for both positive and negative percent agreement (range, 70%−100%). Additionally, the study of multicolor cSLO had other significant limitations, including only a single image reader with no masking reported and no reported follow-up of children with pseudopapilledema, which is important when a lumbar puncture is not performed to confirm stability of findings and reduce the possibility of misdiagnosis.

Of the imaging methods included in this assessment, OCT was evaluated by the most studies with the most participants.[2−4,19] Unfortunately, significant heterogeneity was present in the OCT measures used by the various studies, so the results cannot be compared directly. However, it seems that combining 2 OCT measures, Bruch's membrane opening size and average RNFL thickness, holds promise for differentiating between pediatric papilledema and pseudopapilledema.[3]

Ultrasonography, although widely used to diagnose pseudopapilledema resulting from ODD in adults,[6] was found to be suboptimal for the diagnosis of suspected papilledema in children. Various ultrasonographic measures had either high positive or negative percent agreement, but not both.[4,18,20] However, given the relative ease with which ultrasonography may be performed in young and uncooperative children, unlike the other imaging methods assessed here, it may be reasonable to consider ultrasonography for screening of papilledema if the clinician is aware of its limitations. For example, optic nerve width of more than 3.0 mm on ultrasound has high positive but low negative percent agreement with the clinical diagnosis of pediatric papilledema,[17] whereas detection of ODD on ultrasonography has high negative but low positive percent agreement.[4] This technology assessment included only studies of ocular ultrasound being performed by ophthalmologists or ocular ultrasonographers and not bedside ultrasonography performed by other medical specialists, such as emergency medicine physicians. However, the limitations of ultrasound in diagnosing papilledema discussed above would extend to nonophthalmologists as well. The other 2 imaging methods assessed, autofluorescence and fundus

photography, each were evaluated by only 1 study and showed lower positive (40%−60%) and negative (57%) percent agreement with the clinical diagnosis of papilledema in children.[4]

Given the lack of high-quality evidence to support the usefulness of any ophthalmic imaging method in isolation to differentiate pediatric papilledema from pseudopapilledema, clinicians must continue to rely on comprehensive history-taking and an ophthalmologist's examination with the judicious use of auxiliary tests to determine which children require further workup for suspected papilledema.

Future Research

Future research on the use of ophthalmic imaging tests to differentiate pediatric papilledema and pseudopapilledema must be of higher quality than studies identified in the current literature. Prospective studies with rigorous adherence to accepted definitions of papilledema and pseudopapilledema are necessary. Moreover, image interpretation ideally should be performed by more than 1 masked grader. Larger participant samples also are needed, and this may require multiinstitutional collaboration to recruit adequate numbers. Acquisition of OCT imaging data should be standardized, given the difficulty in comparing time-domain OCT, standard SD OCT, EDI OCT, and swept-source OCT. Moreover, the usefulness of newer OCT algorithms, such as 3-dimensional analysis to quantify ODD volume, should be evaluated.[22] The diagnosis of ODD, the most common cause of pseudopapilledema, by OCT in children also should be standardized, although clinicians must recognize that ODD and papilledema may coexist.[7] Future investigators should consider designing studies that evaluate a combination of imaging methods, because this potentially could improve diagnostic accuracy. Finally, future studies should assess whether age, cause of pseudopapilledema (ODD vs. other structural anomalies), and grade of papilledema affect the accuracy of ophthalmic imaging methods in differentiating between pediatric papilledema and pseudopapilledema.

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Abbreviations and Acronyms:
CI = confidence interval; **cSLO** = confocal scanning laser ophthalmoscopy; **EDI** = enhanced depth imaging; **ODD** = optic disc drusen; **RNFL** = retinal nerve fiber layer; **SD** = spectral-domain.

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