OPTIC NERVE IMAGING TO PAPILLOEDEMA VS PSEUDOPAPILLOEDEMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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References:

1: Pardon et al (2019); Optom Vis Sci, 96, 599-608.

2: Dreesbach et al (2020); Transl Vis Sci Technol, 9, 24.

3: Jivraj et al (2021); J Neuroophthalmol, 41, e509-e515.

4: Malmqvist et al (2018); J Neuroophthalmol,

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Commercial relationships: None.

Purpose

- Due to the difficulty in differentiating the two conditions and the severe nature of papilledema (PP), many unnecessary referrals are made from the community into the hospital eye service for further assessment.
- This systematic review and meta-analysis was conducted to determine the ***most diagnostically accurate imaging test that distinguishes pseudopapilloedema from papilloedema***.

Aims

Primary outcomes were:

- **Sensitivity**
- **Specificity**
- **Area under receiver operating curve (AUC).**

Secondary outcomes were between-group differences in imaging parameters.

Meta-analysis used available quantitative data.

Methods

Searches were conducted in **Medline, Embase and CENTRAL.** Clinical studies that used non-invasive imaging techniques to distinguish papilloedema (PP) or pseudopapilloedema (pseudo-PP) or adult controls were used.

Details of the screening and inclusion process are reported in Figure 1.

Of these studies:

- 25/45 were focused on **OCT**
- 11/45 on **ultrasound**
- 2/45 on **MRI**
- 2/45 **scanning laser Ophthalmoscopy**
- 1/45 **fundus photography**
- 4/45 on **deep learning algorithms** for fundus photography

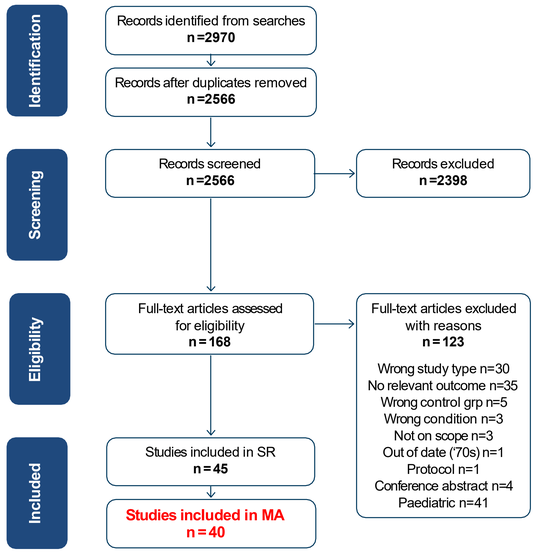
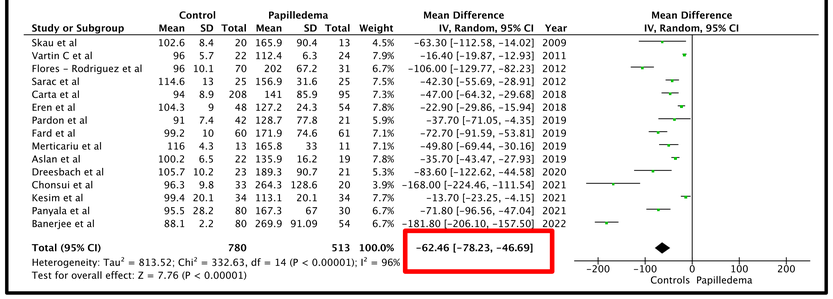


Figure 1. PRISMA flow chart for overall systematic review (SR) and meta-analysis (MA). 40 studies included in meta-analysis.

Results

PP showed thicker pRNFL than controls.

- Sensitivity 77% - 100%
- Specificity 70% - 100%



Study or Subgroup	Control Mean	Control SD	Control Total	Papilledema Mean	Papilledema SD	Papilledema Total	Weight	Mean Difference IV, Random, 95% CI	Year
Skau et al	102.6	8.4	20	165.9	90.4	13	4.5%	−63.30 [−112.58, −14.02]	2009
Vartin C et al	96	5.7	22	112.4	6.3	24	7.9%	−16.40 [−19.87, −12.93]	2011
Flores – Rodriguez et al	96	10.1	70	202	67.2	31	6.7%	−106.00 [−129.77, −82.23]	2012
Sarac et al	114.6	13	25	156.9	31.6	25	7.5%	−42.30 [−55.69, −28.91]	2012
Carta et al	94	8.9	208	141	85.9	95	7.3%	−47.00 [−64.32, −29.68]	2018
Eren et al	104.3	9	48	127.2	24.3	54	7.8%	−22.90 [−29.86, −15.94]	2018
Pardon et al	91	7.4	42	128.7	77.8	21	5.9%	−37.70 [−71.05, −4.35]	2019
Fard et al	99.2	10	60	171.9	74.6	61	7.1%	−72.70 [−91.59, −53.81]	2019
Mertiçariu et al	116	4.3	13	165.8	33	11	7.1%	−49.80 [−69.44, −30.16]	2019
Aslan et al	100.2	6.5	22	135.9	16.2	19	7.8%	−35.70 [−43.47, −27.93]	2019
Dreesbach et al	105.7	10.2	23	189.3	90.7	21	5.3%	−83.60 [−122.62, −44.58]	2020
Chonsui et al	96.3	9.8	33	264.3	128.6	20	3.9%	−168.00 [−224.46, −111.54]	2021
Kesim et al	99.4	20.1	34	113.1	20.1	34	7.7%	−13.70 [−23.25, −4.15]	2021
Panyala et al	95.5	28.2	80	167.3	67	30	6.7%	−71.80 [−96.56, −47.04]	2021
Banerjee et al	88.1	2.2	80	269.9	91.09	54	6.7%	−181.80 [−206.10, −157.50]	2022
Total (95% CI)			**780**			**513**	**100.0%**	**−62.46 [−78.23, −46.69]**	

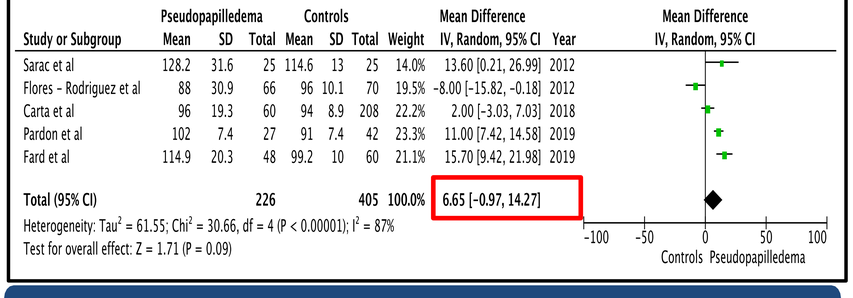
Heterogeneity: $Tau^2 = 813.52$; $Chi^2 = 332.63$, df = 14 ($P < 0.00001$); $I^2 = 96\%$

Test for overall effect: $Z = 7.76$ ($P < 0.00001$)

Figure 2. Forest plot for mean pRNFL thickness for PP versus Controls. Differences were also significant for quadrant specific measures.

Meta-analaysis found NO clinical significance in pRNFL thickness between pseudo-PP and controls.

- Heterogeneity was high between studies.



Study or Subgroup	Pseudopapilledema Mean	Pseudopapilledema SD	Pseudopapilledema Total	Controls Mean	Controls SD	Controls Total	Weight	Mean Difference IV, Random, 95% CI	Year
Sarac et al	128.2	31.6	25	114.6	13	25	14.0%	13.60 [0.21, 26.99]	2012
Flores – Rodriguez et al	88	30.9	66	96	10.1	70	19.5%	-8.00 [-15.82, -0.18]	2012
Carta et al	96	19.3	60	94	8.9	208	22.2%	2.00 [-3.03, 7.03]	2018
Pardon et al	102	7.4	27	91	7.4	42	23.3%	11.00 [7.42, 14.58]	2019
Fard et al	114.9	20.3	48	99.2	10	60	21.1%	15.70 [9.42, 21.98]	2019
Total (95% CI)			**226**			**405**	**100.0%**	**6.65 [-0.97, 14.27]**	

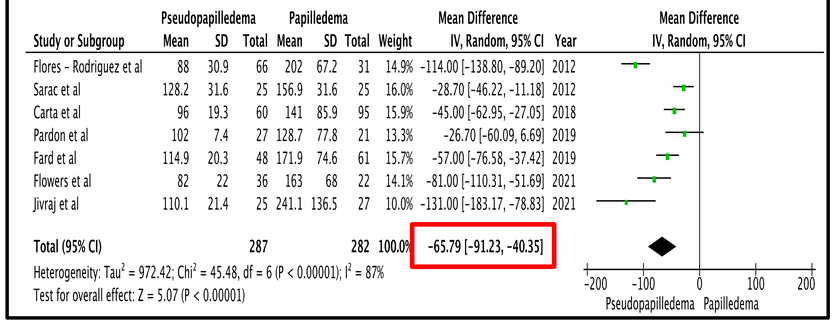
Heterogeneity: $Tau^2 = 61.55$; $Chi^2 = 30.66$, df = 4 ($P < 0.00001$); $I^2 = 87\%$

Test for overall effect: $Z = 1.71$ ($P = 0.09$)

Figure 4. Forest plot for mean pRNFL thickness for pseudo-PP vs controls. No significant difference found.

PP showed thicker pRNFL than pseudo-PP.

- Heterogeneity was high between studies.



Study or Subgroup	Pseudopapilledema Mean	Pseudopapilledema SD	Pseudopapilledema Total	Papilledema Mean	Papilledema SD	Papilledema Total	Weight	Mean Difference IV, Random, 95% CI	Year
Flores – Rodriguez et al	88	30.9	66	202	67.2	31	14.9%	−114.00 [−138.80, −89.20]	2012
Sarac et al	128.2	31.6	25	156.9	31.6	25	16.0%	−28.70 [−46.22, −11.18]	2012
Carta et al	96	19.3	60	141	85.9	95	15.9%	−45.00 [−62.95, −27.05]	2018
Pardon et al	102	7.4	27	128.7	77.8	21	13.3%	−26.70 [−60.09, 6.69]	2019
Fard et al	114.9	20.3	48	171.9	74.6	61	15.7%	−57.00 [−76.58, −37.42]	2019
Flowers et al	82	22	36	163	68	22	14.1%	−81.00 [−110.31, −51.69]	2021
Jivraj et al	110.1	21.4	25	241.1	136.5	27	10.0%	−131.00 [−183.17, −78.83]	2021
Total (95% CI)			**287**			**282**	**100.0%**	**−65.79 [−91.23, −40.35]**	

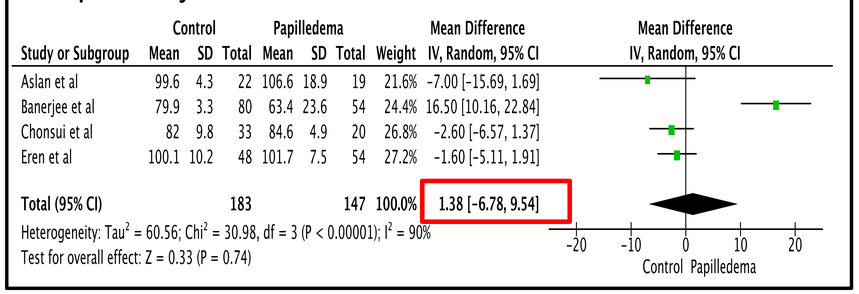
Heterogeneity: $Tau^2 = 972.42$; $Chi^2 = 45.48$, df = 6 ($P < 0.00001$); $I^2 = 87\%$

Test for overall effect: $Z = 5.07$ ($P < 0.00001$)

Figure 3. Forest plot for mean pRNFL thickness for PP versus pseudo-PP. Differences were also significant for quadrant-specific measures.

Optic nerve sheath diameter (ONSD) was larger in PP compared to controls.

- Sensitivity 68 % - 100%
- Specificity 54% - 100%



Study or Subgroup	Control Mean	Control SD	Control Total	Papilledema Mean	Papilledema SD	Papilledema Total	Weight	Mean Difference IV, Random, 95% CI
Aslan et al	99.6	4.3	22	106.6	18.9	19	21.6%	-7.00 [-15.69, 1.69]
Banerjee et al	79.9	3.3	80	63.4	23.6	54	24.4%	16.50 [10.16, 22.84]
Chonsui et al	82	9.8	33	84.6	4.9	20	26.8%	-2.60 [-6.57, 1.37]
Eren et al	100.1	10.2	48	101.7	7.5	54	27.2%	-1.60 [-5.11, 1.91]
Total (95% CI)			**183**			**147**	**100.0%**	**1.38 [-6.78, 9.54]**

Heterogeneity: $Tau^2 = 60.56$; $Chi^2 = 30.98$, df = 3 ($P < 0.00001$); $I^2 = 90\%$

Test for overall effect: $Z = 0.33$ ($P = 0.74$)

Figure 5. Forest plot for mean ONSD for PP vs Controls.

CONCLUSION

OCT and ultrasound are valuable adjuncts in suspected papilloedema.

Thicker pRNFL and greater ONSD support assessment, but diagnostic accuracy remains imperfect.

The quality of included studies was generally poor with substantial heterogeneity.

Standardised studies are required. Imaging should complement history and examination.

DIPP study