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Diagnostic Accuracy of Imaging Devices in Glaucoma: An Updated Meta-Analysis

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Abstract

Background: Different devices have diverse accuracy in diagnosing glaucoma, and therefore choosing the best device is challenging. Thereby, this study was conducted to evaluate the diagnostic sensitivity and specificity of imaging devices in glaucoma and explore the need for an updated meta-analysis on this issue.

Methods: In this systematic review and meta-analysis, PubMed, Scopus, and Web of Science databases were searched for articles published between January 2004 and 2022. Cross-sectional or diagnostic studies were selected, and sensitivity, specificity, positive predictive value, and negative predictive value were measured.

Results: A total of 28 cross-sectional studies were included for meta-analysis. Devices were divided into 2 groups, based on the optic nerve area and the macular area. For the nerve area, the pooled sensitivity was 77% (CI 95%, 70-83; I2, 90.01%) and the pooled specificity was 89% (CI 95%, 84-92, I2, 93.22%), and for the macular area, the pooled sensitivity was 87% (CI 95%, 80-92, I2, 91.79%), and the pooled specificity was 90% (CI 95%, 84-94; I2, 86.30%). We analyzed each device separately. For optical coherence tomography(OCT), the pooled sensitivity was 85% (CI 95%, 81-89; I2, 87.82%) and the pooled specificity was 89% (CI 95%, 85-92; I2, 84.39%); for Heidelberg retinal tomography (HRT), the pooled sensitivity was 72% (CI 95%, 57-83; I2, 88.94%) and the pooled specificity was 79% (CI 95%, 62-90; I2, 98.61%), and for optical coherence tomography angiography (OCTA), the pooled sensitivity was 82% (CI 95%, 66-91; I2, 93.71%) and the pooled specificity was 93% (CI 95%, 87-96; I2, 64.72%).

Conclusion: The macular area was more sensitive and specific than the optic nerve head. Furthermore, OCT had higher sensitivity, and OCTA had higher specificity when compared with other imaging devices.

Keywords: Diagnostic Imaging, Glaucoma, Heidelberg Retinal Tomography, Meta-analysis, Optical Coherence Tomography, Optical Coherence Tomography Angiography, Systematic Review

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Introduction

Glaucoma is the most common cause of irreversible blindness, affects the physical and mental health in the world, and reduces the life quality of people living with the disease. The disease is on the list of 10 debilitating factors in developed countries such as the United States (1, 2). Given the positive association between glaucoma prevalence and aging, glaucoma is expected to become a major health concern in the coming decades (3, 4). Glaucoma is defined as a group of optic neuropathies; their common feature is the acquired progressive degeneration of the optic

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↑What is "already known" in this topic:
There are some new technologies that detect glaucoma; however, specificity and sensitivity of these technologies are different. An older meta-analysis was done but the limitation of the previous study and the publishing of some new articles related to diagnosing glaucoma was a need for exploring again.

→What this article adds:
Our new comparison based on the type of imaging (Macular area and optic nerve head) and technologies (OCT, HRT, and OCTA) was done. Finally, we found that macular area imagings are more sensitive and specific; also, OCT is more sensitive and OCTA is more precise than the other devices.

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nerve head (ONH) along with pathological changes such as thinning of the neuroretinal rim, increase in the cup/disc ratio, disc cupping, and progressive excavation of the optic disc, which in open-angle glaucoma first results in loss of the visual field and finally irreversible blindness if left untreated (5-8).

In the last few years, imaging technologies such as optical coherence tomography (OCT), optical coherence tomography angiography (OCTA), Heidelberg retinal tomography (HRT), and scanning laser polarimetry (SLP or GDx) have all played a significant role in the diagnosis of glaucoma, allowing the measurement of retinal nerve fiber layer (RNFL) thickness and different morphological parameters of the optic disc. They identify a large number of affected people, based on various criteria; these technologies lead to early and more accurate diagnosis of patients in need of treatment, which can prevent the progression of the disease and the incidence of complications such as blindness (8-10). Determining the accurate diagnostic value of imaging technologies in glaucoma screening can be a valuable service to ophthalmologists, patients, and health policymakers to reduce the vision irreversible effects and costs imposed on society. A prior study examined this issue, but it has to be updated in light of recent research on cutting-edge technologies (11). The purpose of this meta-analysis was to review and compare relatively new techniques of ocular assessment such as OCT, OCTA, (HRT), and GDx in terms of sensitivity and specificity to diagnose primary open angle glaucoma from healthy individuals and confirm the diagnosis as well as other statistical parameters and finally evaluate the clinical course and disease progression, respectively.

Methods

This meta-analysis was performed according to the PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelies,. This systematic review and meta-protocol analysis was submitted to the world's first international prospective register of systematic reviews for registration (CRD42021293138).

Eligibility Criteria

In this study, the principles of PIRT (P, population, I, index test, R, reference test; T, target condition) were considered for the introduction of preliminary studies. Studies whose populations were general and whose diagnostic value indices (sensitivity, specificity, positive and negative predictive values) were calculated by HRT, GDx, OCT, OCTA (index tests) versus other reference tests, were entered into the meta-analysis.

Inclusion and Exclusion Criteria

Descriptive, cross-sectional, or diagnostic studies that were based on the eligibility criteria were included. Analytical types (case studies, cohorts), experimental studies, clinical trials, case reports, animal studies, review studies, or letters to the editor were excluded from this meta-analysis.

Study Parameters

The parameters included sensitivity, specificity, the positive predictive value, and the negative predictive value. After reviewing the selected preliminary studies, as reported in the sensitivity and specificity study results, the number of people with a positive result in both tests (true positive) was calculated, taking into account the total population of the study. In the case of non-reporting sensitivity and specificity indices, the positive and negative predictive values were calculated with the following formulas, using the results of preliminary studies:

$$Sensitivity: {True\ Positive}/{True\ Positive + False\ Negative}$$

$$Specificity: {True\ Negative}/{True\ Negative + False\ Positive}$$

$$Positive\ Predict\ Value: {True\ Positive}/{True\ Positive + False\ Positive}$$

$$Negative\ Predict\ Value: {True\ Negative}/{True\ Negative + False\ Negative}$$

Standard References

There is no recognized acknowledged method for glaucoma diagnosis. We agreed with the definition of glaucoma provided by study researchers.

Search Strategy

In this study, systematic review and diagnostic meta-analysis were performed to find studies on the accuracy of glaucoma diagnostic tools. An advanced search was conducted in PubMed, Scopus, and Web of Science databases using sensitive descriptors, terms, and words between 2004 and 2022. The applied keywords in the search strategy were as follows: ("Diagnosis" OR "Diagnoses" OR "Diagnose") AND ("Glaucoma" OR "Glaucomas" OR "Angle-Closure Glaucoma" OR "Open-Angle Glaucomas"), and related MESH and Emtree terms were added.

Data Extraction

Two authors (M.A. and A. M.) performed title-abstract and full-text screening independently. The disagreements between them were eventually resolved by a third author (Y.M.). After screening, the final selection of articles was made by evaluating the full text of the selected ones. The checklist of data extraction included the first author and colleagues, the year and country of the study, the number and the mean age of participants, the type of sampling, the index tests, and the reference standard, which were ext

racted and recorded from selected articles.

Quality Evaluation of Articles

The revised tool for the quality assessment of diagnostic accuracy studies checklist was used to evaluate and control the quality of articles to assess the applicability and risk of bias. This tool includes 4 main areas as follows: (1) patient selection; (2) the index test; (3) the reference standard; and (4) the patient status during the study and the time interval between the index test and the reference standard, which is divided as yes, no, and unspecified. This tool's objective is to assess the methodological quality of the research and the

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methods used to introduce errors into the studies.

Statistical Analysis

All statistical analyses were performed with STATA Version 16.

This statistic is a single overall indicator of diagnostic accuracy that indicates how much more frequently (expressed as odds) a positive test result occurs among patients with the condition of interest compared with patients without the condition. To compare diagnostic accuracy among instruments and among parameters within each instrument, a meta-analysis considering the hierarchical summary receiver operating characteristic (HSROC) model was performed. This model takes proper account of the sample size regarding diseased and non-diseased cases in each study and allows estimation for random effects and accuracy effects. Results from the HSROC models were graphically represented using SROC curves. The significance level was set at $P < 0.05$, and 95% confidence intervals were calculated for sensitivity and specificity. Pairwise comparisons were used considering the Tukey method for correcting type I error in multiplicity contrasts. Forest plots were used to show the sensitivity and specificity of each instrument and study and to determine evidence of heterogeneity within sensitivity and specificity. The Deek funnel plot was used to quantify publication bias, and the Deek asymmetry test was used to determine whether bias was present (12-14).

Sensitivity Analysis

Sensitivity analysis was not performed in this study because all studies were cross-sectional or diagnostic and were almost identical in methodology.

Results

Study Selection

As a result of searching the electronic databases, 3668 studies were obtained, of which 2034 remained after removing duplicates. In the last stage, 23 studies were selected for inclusion in the research after reviewing titles, abstracts, and full texts and considering the inclusion and exclusion criteria (Figure 1) (15-37). The characteristics of the studies included in this meta-analysis are reported in Table 1.

Quality Assessment Result

Assessment of the included research revealed minimal bias risk across the board, although 20% of the studies had severe bias in terms of patient selection (Figure 2).

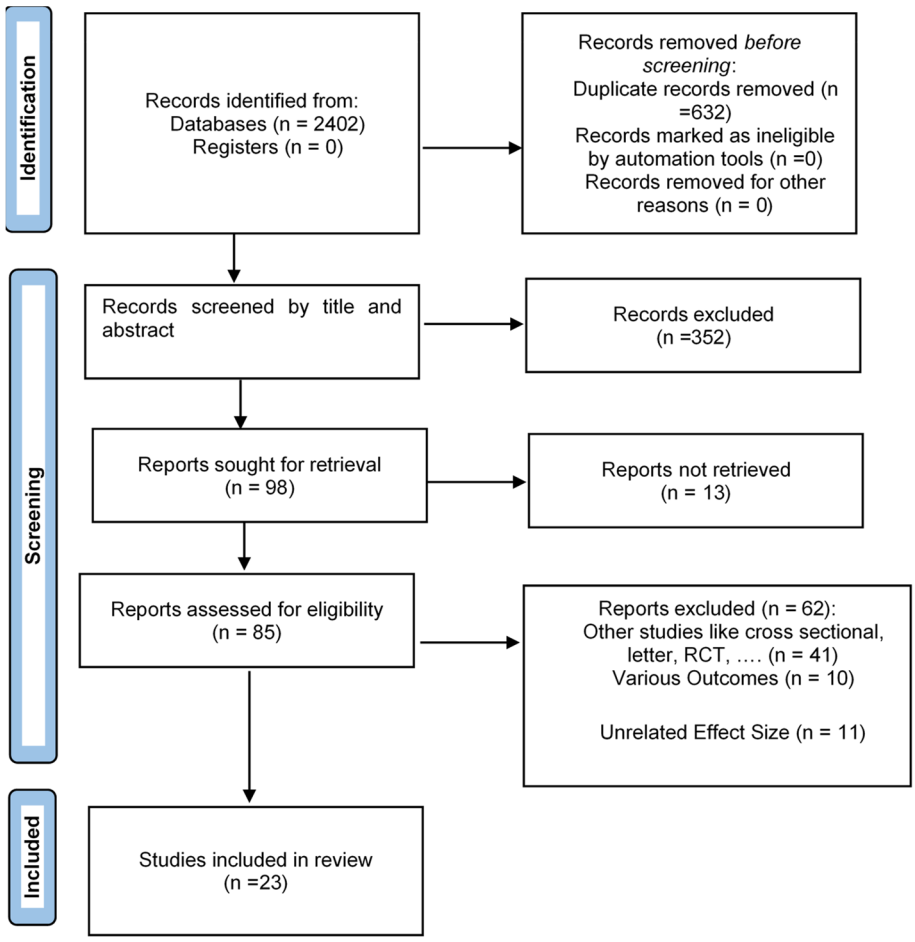

Figure 1. PRISMA 2020 flow diagram for new systematic reviews included in the study

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Table 1. Characteristics of included studies

Authors (Years)	Type of study	Study population	Sample size (people)	Type of sampling	Type of glaucoma (Level)	country	Reference test	Index test (Criterion)	Outcome			
									TP	FP	FN	TN
Dabasia. P, et al (2015) (15)	Cross-sectional	aged ≥60 years	505	Convenience	primary open-angle glaucoma (Early, moderate and advanced)	(United Kingdom)	Visual field testing (Humphrey Field Analyzer) +biomicroscope +Goldman applanation tonometer +gonioscopy +ophthalmoscopy and fundus photography	iVue-OCT (GCC)	21	58	5	421
								iVue-OCT (RNFL)	23	54	3	425
Dave. P, et al (2015) (16)	Cross-sectional	Mean age= 62	156(unilateral)	Convenience	primary open-angle glaucoma (early)	(India)	visual acuity +manifest refraction + Goldmann applanation tonometry + slit-lamp biomicroscopy +gonioscopy +stereoscopic examination + photograph	SD-OCT (RNFL thickness)	44	1	32	79
								SD-OCT (Number of black squares=5)	32	8	44	72
Hood. D, et al (2016) (17)	Cross-sectional	---	102	from a larger cohort	open-angle glaucoma (early)	(Columbia)	visual field (VF) +spherical refractive error	SS-OCT (with VF Information)	56	3	1	42
								SS-OCT (without VF Information)	56	1	1	44
Lee. K, et al (2016) (18)	Cross-sectional	Mean age= 60	120	Convenience	primary open-angle glaucoma (early)	(Korea)	Goldman applanation tonometry +refraction tests +slit- lamp +biomicroscope +gonioscopy +dilated stereoscopic examination of the optic disc perimetrically	SD-OCT (Macular inner retinal layer)	51	19	9	41
								SS-OCT (Macular inner retinal layer	47	22	13	38
Malik. R, et al (2016) (19)	Cross-sectional	Mean age= 62	130	Convenience	primary open-angle glaucoma (-) (Myopic eyes)	(Canada)	+visual acuity +ocular biometry + Goldman applanation tonometry	SD-OCT (BMO-MRW) (RNFL thickness)	50	21	6	53
							+slit-lamp and fundus examination	CSLT (DM-RA)	50	52	6	22

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Table 1. Continued

Authors (Years)	Type of study	Study population	Sample size (people)	Type of sampling	Type of glaucoma (Level)	country	Reference test	Index test (Criterion)	Outcome			
									TP	FP	FN	TN
Schweitzer. C, et al (2016) (20)	Cross-sectional	Mean age= 65	532	population-based	open angle glaucoma (3categories based on the specific definition)	(France)	noncontact tonometer + nonmydriatic radiophotograph + central corneal thickness measurement + optic disc color photography	SD-OCT (RNFL thickness)	31	60	9	432
Caglar. C, et al (2017) (21)	Cross-sectional	Mean age= 53	148	Convenience	primary open-angle glaucoma (-)	(Turkey)	Gonioscopy + slit-lamp biomicroscopic + Goldman applanation tonometry + Humphrey automatic perimetry	HRT-3 (GPS)	66	25	9	48
								HRT-3 (MRA)	54	13	21	60
Chen. X, et al (2017) (22)	Cross-sectional	Mean age= 59	45	Convenience	primary open-angle glaucoma (early)	(China)	visual acuity + slit-lamp biomicroscope + refraction + gonioscopy + Goldman applanation tonometry + visual field analysis	OCT (GCILP)	18	3	7	17
Khoueir. Z, et al (2017) (23)	Cross-sectional	Mean age= 68	180	Convenience	open angle glaucoma (Early (31) And other types)	(USA)	visual acuity testing + refraction + Goldman applanation tonometry + slit-lamp biomicroscope + gonioscopy + ultrasonic pachymetry +dilated ophthalmoscopy + stereo disc photography +visual field (VF) testing	OCT (2D RNFL thickness)	93	2	20	65
								OCT (3D RNFL thickness)	102	12	9	55

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Table 1. Continued

Authors (Years)	Type of study	Study population	Sample size (people)	Type of sampling	Type of glaucoma (Level)	country	Reference test	Index test (Criterion)	Outcome			
									TP	FP	FN	TN
Pazos. M, et al (2017) (24)	Cross-sectional	Mean age= 66	80	Convenience	open angle glaucoma (early)	(Spain)	visual acuity + pachymetry + slit-lamp biomicroscope +Goldman applanation tonometry + gonioscopy +optic nerve head retinography	SD-OCT (mRNFL)	38	11	2	29
Rao. H, et al (2017) (25)	Cross-sectional	Mean age= 65	72	Convenience	primary open-angle glaucoma (-)	(USA)	slit-lamp biomicroscope + Goldman applanation tonometry + gonioscopy +dilated fundus examination + visual field (VF) examination + stereoscopic optic disc photography	OCTA (Vessel density)	26	7	13	26
								SD-OCT (RNFL thickness)	34	7	5	26
Kim. Y. W, et al (2018) (26)	Cross-sectional	Mean age= 32	254	consecutive	open-angle glaucoma	(Korea)	visual acuity + slit-lamp biomicroscope + gonioscopy + Goldman applanation tonometry + refraction + dilated fundus examination + disc stereophotography + red-free fundus photography and standard automated perimetry	SD-OCT (RNFL Thickness)	54	22	7	171
								SD-OCT (3D-NRR Thickness)	50	14	11	179
Wan. K. H, et al (2018) (27)	Cross-sectional	Mean age= 53	150	consecutive	primary open-angle glaucoma (Mild, moderate, advanced)	(China)	partial coherence laser interferometry + ultrasonographic pachymetry + Goldman applanation tonometry + biomicroscope examination of the optic disc and gonioscopy	OCTA (Inner Macular Vessel Density)	55	3	60	32
								OCT (Inner Macular Thickness)	89	3	26	32

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Table 1. Continued

Authors (Years)	Type of study	Study population	Sample size (people)	Type of sampling	Type of glaucoma (Level)	country	Reference test	Index test (Criterion)	Outcome			
									TP	FP	FN	TN
Brusini. P, et al (2018) (28)	Cross-sectional	Mean age= 67	378	convenience	chronic open-angle glaucoma	(Italy)	SAP + GDx VCC + HRT and sd- OCT (no gold standard methods to compare with)	OCT GSS	177	16	9	176
Bambo. M. P, et al (2020) (29)	Cross-sectional	Mean age= 64	68	sequential	Early primary open-angle glaucoma	(Spain)	Best corrected visual acuity + Goldmann applanation tonometer + slit-lamp examination + OCT(pRNFL)	OCT(BMO-MRW)	26	1	8	33
Chen. A, et al (2020) (30)	Cross-sectional	Mean age= 66	83	convenience	primary open-angle glaucoma (early, moderate, sever)	(USA)	---	OCTA (LPA)	44	2	3	31
								OCTA (FPL)	44	2	3	31
								OCTA (NFLPCD)	38	2	9	31
Akil. H, et al (2017) (31)	Cross-sectional	Mean age= 64	48	convenience	primary open-angle glaucoma	(USA)	Refraction + intraocular pressure measurement + gonioscopy + anterior segment examination + dilated fundus examination + fundus photography + standard automated perimetry + peripapillary and macular OCT	OCTA (Vessel density of SRL)	17	1	7	23
								OCTA (Vessel density of DRL)	22	0	2	24

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Table 1. Continued

Authors (Years)	Type of study	Study population	Sample size (people)	Type of sampling	Type of glaucoma (Level)	country	Reference test	Index test (Criterion)	Outcome			
									TP	FP	FN	TN
Maupin. E, et al (2020) (32)	Cross-sectional	Mean age= 82	1033	electoral rolls	primary open-angle glaucoma, primary angle-closure glaucoma, secondary glaucoma	(France)	Best corrected visual acuity + noncontact tonometer + photograph of the optic disc and the macula visual field testing + SD-OCT (RNFL thickness)	SD-OCT (Neuro-retinal rim width) ISNT rule	88	477	5	463
								SD-OCT (Neuro-retinal rim width) IST rule	65	122	28	818
								SD-OCT (Neuro-retinal rim width) IS rule	29	91	64	849
Li. M, et al (2020) (33)	Cross-sectional	Mean age= 43	171	convenience	primary open angle glaucoma	(China)	best-corrected visual acuity + slit-lamp examination + gonioscopy + fundus photography + SD-OCT + standard automated perimetry	SS-OCT (Scleral spur length, Method I)	61	17	17	76
								SS-OCT (Scleral spur length, Method II)	62	24	16	69
								SS-OCT (Scleral spur length, Method III)	71	49	7	44
								SS-OCT (Scleral spur opening width)	61	33	17	60
Sun. S, et al (2020) (34)	Cross-sectional	---	777 (Testing data set = 156)	convenience	primary open-angle glaucoma (Early, moderate, Severe)	(Korea)	best-corrected visual acuity + refraction + slit-lamp biomicroscope +gonioscopy + Goldman applanation tonometry + dilated stereoscopic examination of optic disc + digital color stereo disc photography + red-free RNFL photography + Cirrus HD-OCT	SD-OCT (RNFL)	87	3	6	60
								SD-OCT (GCIPL)	77	5	16	58
								ensemble model	81	2	12	61
Saito. H, et al (2009) (35)	Cross-sectional	Mean age= 64	2297	Convenience	Glaucoma	(Japan)	refraction + visual acuity + central corneal + slit-lamp biomicroscopy + Goldmann applanation tonometry + fundus examination + IMAGEnet digital fundus camera system + frequency doubling technology (FDT) screener	HRT II (FSM)	39	297	27	1934
								HRT II (MRA)	26	87	40	2144
								HRT II (GPS)	43	379	23	1852

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Table 1. Continued

Authors (Years)	Type of study	Study population	Sample size (people)	Type of sampling	Type of glaucoma (Level)	country	Reference test	Index test (Criterion)	Outcome			
									TP	FP	FN	TN
To´th, et al (2008) (36)	Cross-sectional	Mean age= 64	118	Convenience	primary open-angle glaucoma + normal pressure glaucoma +Exfoliative glaucoma + chronic angle-closure glaucoma (mild, moderate and severe)	(Hungary)	visual acuity testing +slit-lamp examination +Goldmann applanation tonometry +stereoscopic evaluation of the optic nerve head	GDx-VCC (NFI)	5	8	8	97
To´th, et al (2008) (36)	Cross-sectional	Mean age= 64	118	Convenience	primary open-angle glaucoma + normal pressure glaucoma +Exfoliative glaucoma + chronic angle-closure glaucoma (mild, moderate and severe)	(Hungary)	visual acuity testing +slit-lamp examination +Goldmann applanation tonometry +stereoscopic evaluation of the optic nerve head	HRT II (GPS)	9	22	4	83
To´th, et al (2007) (37)	Cross-sectional	Mean age= 61	181	Convenience	primary open-angle glaucoma + normal pressure glaucoma +Exfoliative glaucoma + chronic angle-closure glaucoma + Pigmentary glaucoma	(Hungary)	visual acuity testing +slit-lamp examination +Goldmann applanation tonometry +stereoscopic evaluation of the optic nerve head	GDx-VCC (NFI)	6	5	18	152

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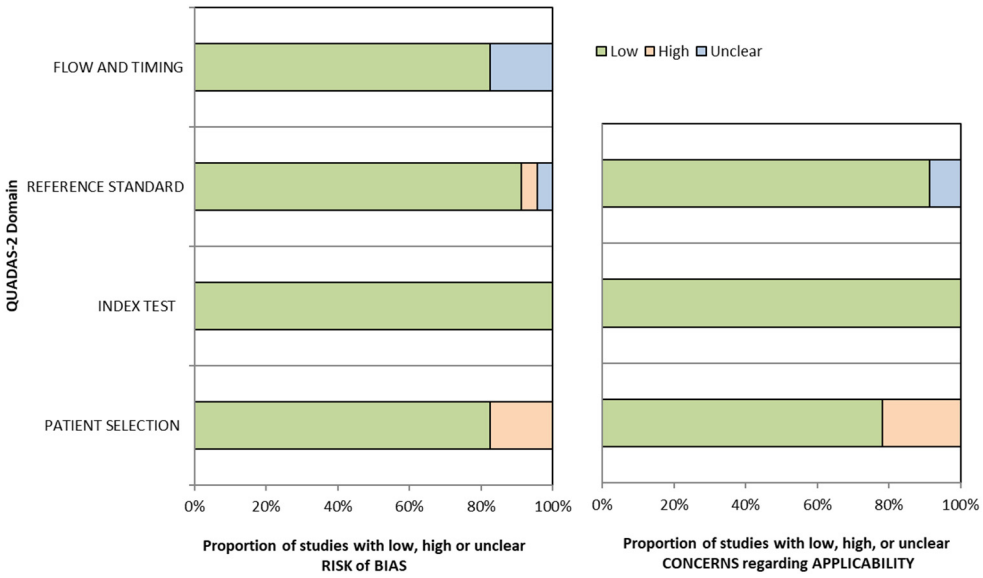

Figure 2. Quality assessment of included studies based on the revised tool for the quality assessment of diagnostic accuracy studies checklist

Study Characteristics

OCT, HRT 2, 3, GDx, and OCTA were among the tools investigated in this study. RNFL thickness, BMO-MRW, GCIPL, 3D NRR thickness, inner macular thickness, and scleral spur length were among the parameters assessed by the OCT device. GPS, FSM, MRA, and DM-RA were measured by the HRT device. NFI was measured by the SLP(GDx) and OCTA devices. LPA, FPL, NFLD, and vessel density were all included. The final papers included 4 studies from the United States, 3 from China, 3 from the Republic of Korea, 2 from each of Spain, India, France, and Hungary, and 1 from fro each of Colombia, Canada, Japan, Turkey, Italy, and Britain.

Accuracy of Nerve Area Devices in Glaucoma Diagnosis

Initially, the devices were divided into 2 groups, based on the nerve area and the macular area. A total of 27 cross-sectional studies were performed to determine the accuracy of the group of nerve area devices (criteria related to the optic nerve) in the diagnosis of glaucoma. The lowest level of sensitivity belonged to the study of Tooth et al, with a sensitivity of 25% (CI 95%, 10-47), and the highest level of sensitivity belonged to the study of Brusini et al, with a sensitivity of 95% (CI 95%, 91-98). The lowest level of specificity belonged to the study of Malik et al, with a specificity of 30% (CI 95%, 20-41), and the highest level of specificity belonged to the study of Dave et al, with a specificity of 99% (CI 95%, 93-100). After combining the results of these cross-sectional studies, the pooled sensitivity was 77% (CI 95%, 70-83), and the pooled specificity was 89% (CI 95%, 84-92) (Figure 3). In this category, the values of the positive likelihood ratio and the negative likelihood ratio were calculated as 7 and 0.26, respectively, and also the value of pretest probability was changed from 25% to positive posttest probability 69%, and negative posttest probability 8%, respectively (Figure 3). Of note, the Deek funnel plot test results showed symmetrical distribution, which suggests no publication bias.

Accuracy of Macular Devices in Glaucoma Diagnosis

Sixteen cross-sectional studies determined the accuracy of the group of macular devices (criteria related to the macular) in the diagnosis of glaucoma. The lowest level of sensitivity belonged to the study of Wan K. H et al, with a sensitivity of 48% (CI 95%, 38-57), and the highest level of sensitivity belonged to the study of Hood. D et al, with a sensitivity of 98% (CI 95%, 91-100). The lowest level of specificity belonged to the study of Lee K et al, with a specificity of 63% (CI 95%, 50-75) and the highest level of specificity belonged to the study of Akil H et al, with a specificity of 100% (CI 95%, 86-100). After combining the results of these cross-sectional studies, the pooled sensitivity was 87% (CI 95%, 80-92), and the pooled specificity was 90% (CI 95%, 84-94) (Figure 4). Also, in this category, the values of the positive likelihood ratio and the negative likelihood ratio were 9 and 0.14, respectively. The value of pretest probability was changed from 25% to a positive posttest probability of 75%, and a negative posttest probability of 5%, respectively (Figure 4). Of note, the Deek funnel plot test showed symmetrical distribution which suggests no publication bias.

Accuracy of OCT Devices in Glaucoma Diagnosis

Then, the OCT device was examined. In this research, 27 cross-sectional studies, including SD-OCT, SS-OCT, and iVue-OCT, which were performed to determine the accuracy of the OCT device in diagnosing glaucoma, were included. After combining the results of these cross-sectional studies, the pooled sensitivity was 85% (CI 95%, 81-89). The lowest level of sensitivity belonged to the study of Dave et al, with a sensitivity of 42% (CI 95%, 31-54), and the highest level of sensitivity belonged to the study of

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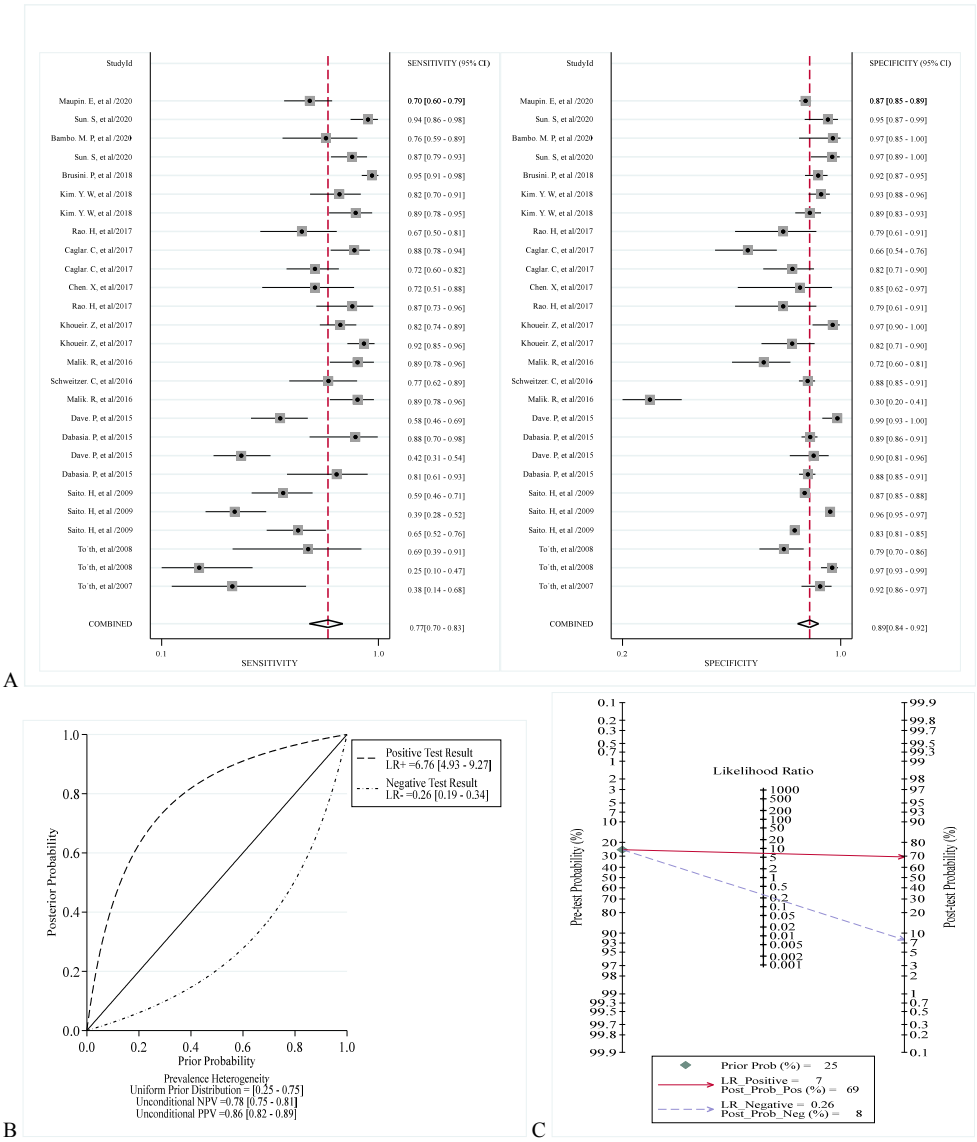

Figure 3. Meta-analysis plots of the diagnostic accuracy of the optic nerve area to diagnose glaucoma. (A) Pooled Sensitivity and Specificity. (B) Hierarchical summary receiver operating characteristic curve. (C) Likelihood ratio.

Hood et al, with a sensitivity of 98% (CI 95%: 91-100). The pooled specificity was 89% (CI 95%, 85-92). The lowest level of specificity belonged to the study of Lee et al, with the odds ratio of 63% (CI 95%, 50-79), and the highest level of specificity belonged to the study of Hood et al, with a specificity of 99% (CI 95%, 93-100) (Figure 5). Of note, the Deek funnel plot test showed a symmetrical distribution, which suggests no publication bias. In OCT, the positive likelihood ratio and the negative likelihood ratio were calculated 8 and 0.17, respectively. The pretest probability value was changed from 25% to a positive posttest probability of 72% and a negative posttest probability of 5%, respectively (Figure 5). The aggregated results for the RNFL parameter data were calculated. The pooled sensitivity was 93% (CI 95%, 89-95), and the pooled specificity was 92% (CI 95%, 87-96). The positive likelihood ratio and the negative likelihood ratio were calculated as 12 and 0.08, respectively. The subgroup analysis for the RNFL thickness parameter was performed. The pooled sensitivity was 82% (CI 95%, 70-90), and the pooled specificity was 88% (CI 95%, 76-95). The positive likelihood ratio and the negative likelihood ratio were calculated as 7.06 and 0.20, respectively.

Accuracy of HRT Devices in Glaucoma Diagnosis

Seven studies involving 2693 participants examined HRT. Four studies used HRT-2, and 2 studies used HRT-3. The lowest level of sensitivity belonged to the study of Saito. H et al, with a sensitivity of 39% (CI 95%, 28-52), and the highest level of sensitivity belonged to the study of Malik R et al, with a sensitivity of 89% (CI 95%, 78-96). The lowest level of specificity belonged to the study of Malik R et al, with a specificity of 30% (CI 95%, 20-41) and the highest level of specificity belonged to the study of Saito H et al, with a specificity of 96% (CI 95%, 95-97). After combining the results of these cross-sectional studies,

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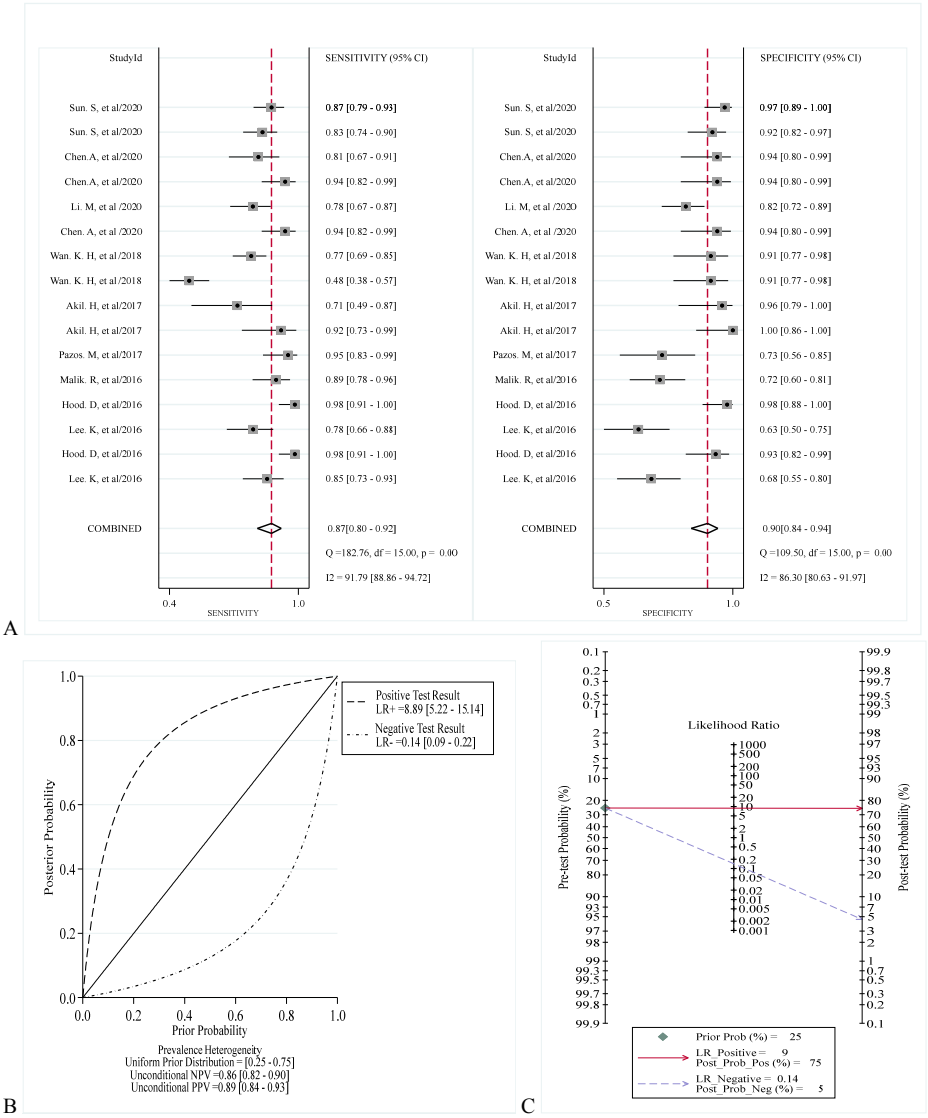

Figure 4. Meta-analysis plots of the diagnostic accuracy of the optic macular area to diagnose glaucoma. (A) Pooled sensitivity and specificity. (B) Hierarchical summary receiver operating characteristic curve. (C) Likelihood ratio.

the pooled sensitivity was 72% (CI 95%, 57-83), and the pooled specificity was 79% (CI 95%, 62-90) (Figure 6). Of note, the Deek funnel plot test showed a symmetrical distribution, which suggests no publication bias. Also, in this category, the positive likelihood ratio and the negative likelihood ratio were calculated as 3 and 0.36, respectively. The pretest probability value was changed from 25% to a positive posttest probability of 53% and a negative posttest probability of 11%, respectively (Figure 6).

Accuracy of OCTA Devices in Glaucoma Diagnosis

Seven studies involving 353 participants examined OCTA. The lowest level of sensitivity belonged to the study of Wan K H et al, with a sensitivity of 48% (CI 95%, 38-57) and the highest level of sensitivity belonged to the study of Chen A et al, with a sensitivity of 94% (CI 95%, 82-99). The lowest level of specificity belonged to the study of Rao H et al, with a specificity of 79% (CI 95%, 61-91) and the highest level of specificity belonged to the study of Akil H et al, with a specificity of 100% (CI 95%, 86-100). After combining the results of these cross-sectional studies, the pooled sensitivity was 82% (CI 95%, 66-91), and the pooled specificity was 93% (CI 95%, 87-96) (Figure 7). The Deek funnel plot test showed publication bias for these studies, which can lead to an overestimation of the diagnostic performance of OCTA. Also, in this category, the positive likelihood ratio and the negative likelihood ratio were calculated as 12 and 0.20, respectively. Also, the pretest probability value was changed from 25% to a positive posttest probability of 80% and a negative posttest probability of 6%, respectively (Figure 7).

Discussion

According to the main findings of our study, the macular area was more sensitive and specific than ONH. Furthermore, OCT had higher sensitivity and OCTA had higher specificity when compared with other imaging devices.

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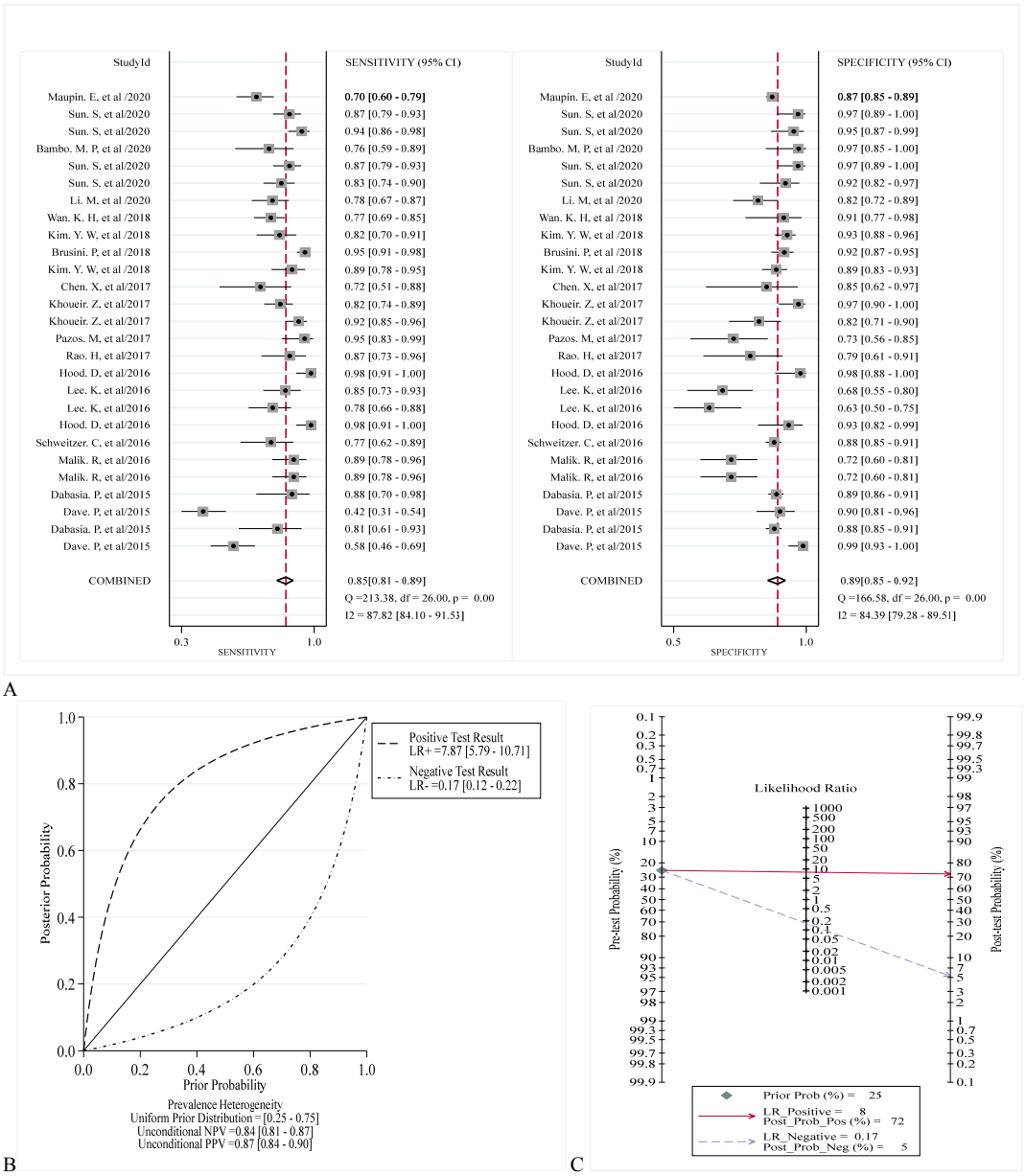

Figure 5. Meta-analysis plots of the diagnostic accuracy of optical coherence tomography to diagnose glaucoma. (A) Pooled sensitivity and specificity. (B) Hierarchical summary receiver operating characteristic curve. (C) Likelihood ratio.

Therefore, our results confirm the existence of strong evidence for the clinical utility of OCT for glaucoma screening, OCTA for its diagnosing, and macular region was the most promising area for diagnosing glaucoma in imaging devices.

Glaucoma patients typically do not exhibit symptoms until the end of the disease process. If diagnosed early and appropriately treated, vision loss can be slowed or prevented. During the last decades, the use of imaging devices in clinical glaucoma practice has dramatically increased. The images and data obtained from HRT, GDx, OCT, and OCTA have improved our understanding of glaucoma and our ability to detect it and could aid in the refinement of the disease definition. Therefore, it is critical to examine the diagnostic accuracy of such devices in detail to integrate them into clinical practice properly. As a result, a glaucoma screening device for the general public would be beneficial. Unfortunately, glaucoma screening in the general population is currently ineffective. However, it may be more valuable and cost-effective in a specific high-risk population, such as elderly African Americans and Hispanics or those with a family history of glaucoma (38). In our study, OCT had higher sensitivity among imaging devices, indicating a reliable option for disease screening. Similarly, OCT demonstrated higher sensitivity than GDx and HRT in research comparing the utility of imaging equipment for glaucoma screening (39).

For a definite diagnosis of glaucoma, OCTA with a higher specificity compared with other devices in our study showed the most reliable option for disease diagnosis but

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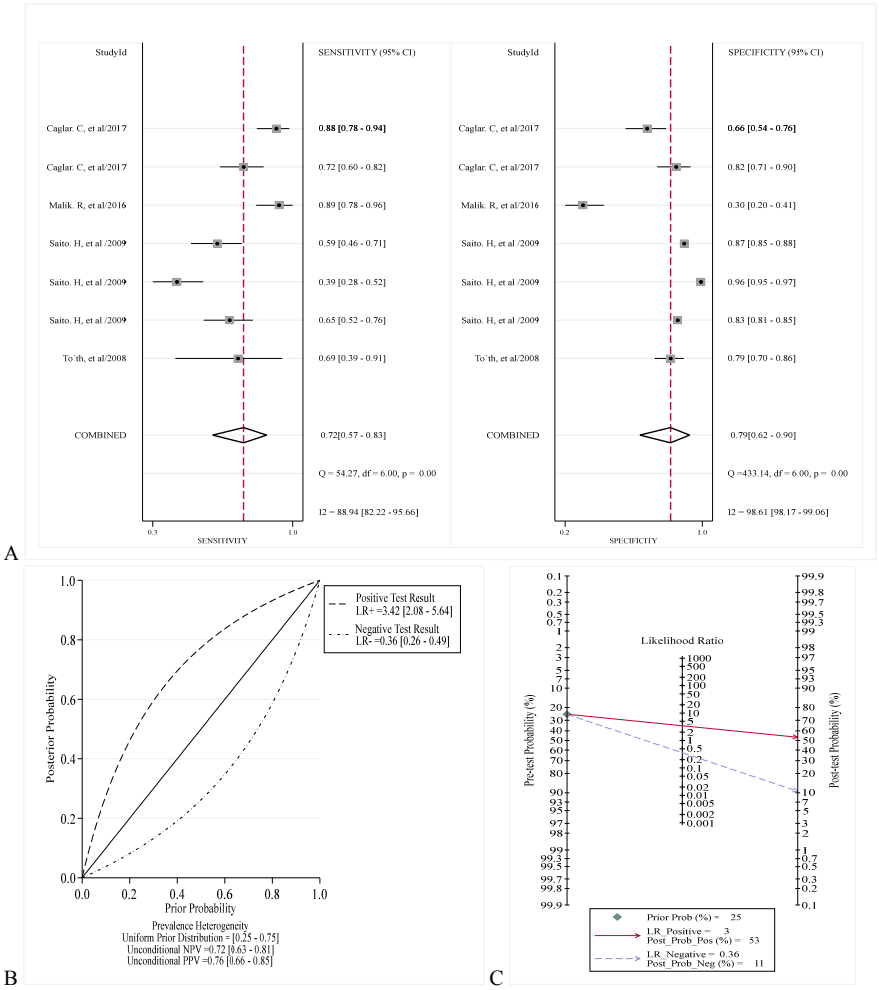

Figure 6. Meta-analysis plots of the diagnostic accuracy of Heidelberg retinal tomography to diagnose glaucoma. (A) Pooled sensitivity and specificity. (B) Hierarchical summary receiver operating characteristic curve. (C) Likelihood ratio.

not for screening. Recent literature about the diagnostic ability of OCTA supported our findings in which high specificity was found through their analysis (40-42). In a review study about OCTA diagnostic ability in glaucoma, their findings have suggested that vessel density measurements may offer advantages in early diagnosis for open-angle glaucoma, where vascular dysregulation frequently plays a role in disease progression; however, structural parameters perform better in angle-closure glaucoma, where intraocular pressure elevation plays a major or exclusive pathophysiological role (43). Furthermore, a previous metanalysis on the diagnostic performance of OCTA in glaucoma has revealed that OCTA may aid in diagnosing glaucoma by demonstrating that the VD in glaucoma patients is significantly lower than that in healthy controls in all locations evaluated (44).OCTA is a noninvasive device that has shown promise in glaucoma detection. It could elucidate vascular changes in glaucoma and, consequently, sooner detect glaucoma (44, 45). Additionally, a literature analysis on OCTA revealed several additional advantages, which are as follows: (1) a high level of repeatability and reproducibility in both normal and glaucoma eyes; (2) significantly lower OCTA parameters in glaucoma eyes; (3) equivalent discriminatory ability compared with OCT in distinguishing normal and glaucoma eyes, in which combining the 2 procedures produce a superior area under the curve than either technique alone; (4) a high spatial association between OCTA, OCT, and the visual function evaluated by visual field testing; (5) OCTA parameters have a better correlation with visual field mean deviation than do OCT parameters; (6) the equal discriminatory power of OCTA parameters in the peripapillary area compared with OCT parameters in distinguishing between glaucoma suspects/preperimetric glaucoma and normal eyes; (7) due to a less significant floor effect in OCTA than in OCT, OCTA measurements in the peripapillary area seem to be better biomarkers in progressive glaucoma; and (8) OCTA can detect progression (46).

The macular region in our study was the most reliable area for diagnosing glaucoma. Still, despite conflicting reports, several studies suggest segmented macular and ONH parameters are comparable to RNFL parameters in diagnostic performance (38, 47, 48). Furthermore, our results indicated that the macular area was more reliable than ONH parameters based on their high sensitivity and specificity,

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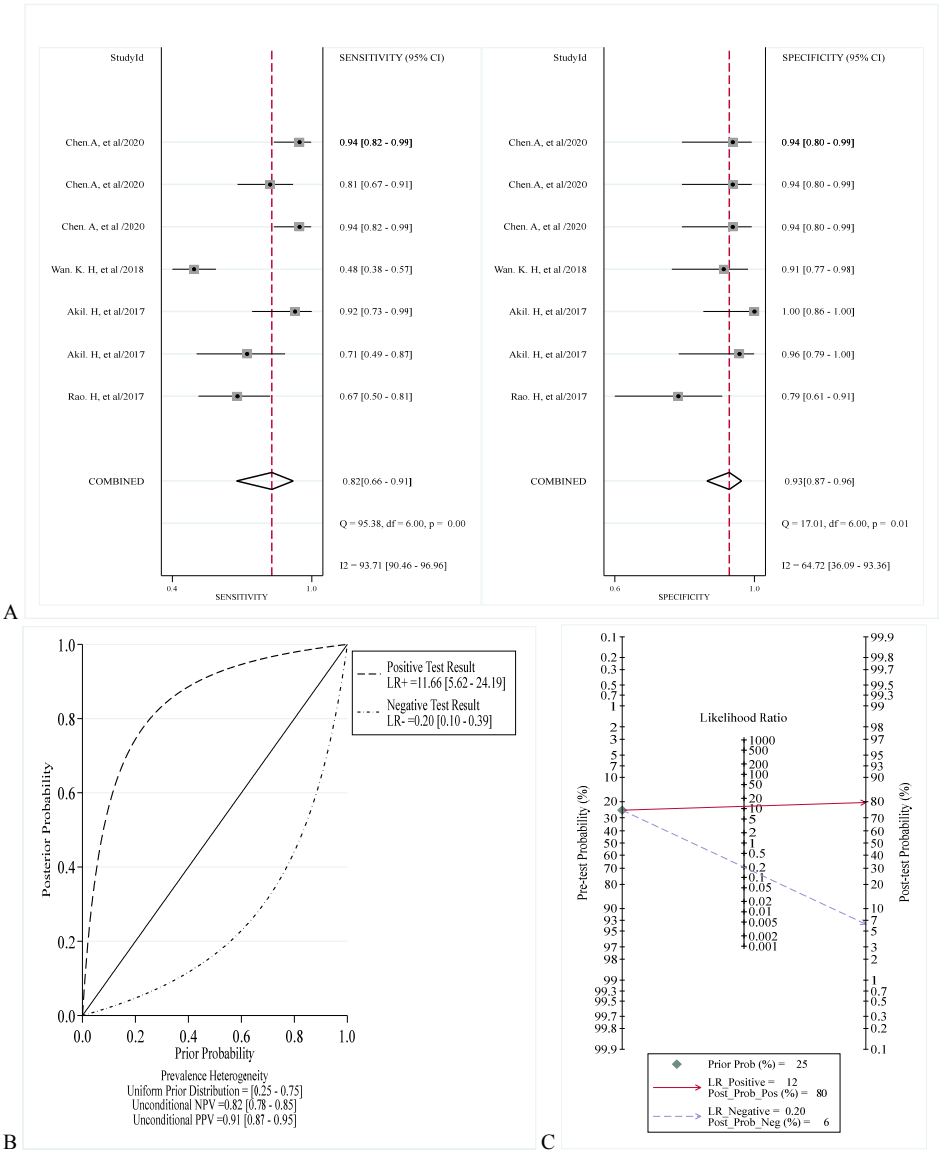

Figure 7. Meta-analysis plots of the diagnostic accuracy of optical coherence tomography angiography to diagnose glaucoma. (A) Pooled sensitivity and specificity. (B) Hierarchical summary receiver operating characteristic curve. (C) Likelihood ratio.

implying compelling evidence for their ability to differentiate between normal and glaucomatous eyes. Individual layers in the macular region, which are particularly impacted by glaucomatous damage, such as macular RNFL (mRNFL), the ganglion cell layer with the inner plexiform layer (GCIPL), and the ganglion cell complex (GCC = mRNFL+ GCIPL) can now be quantified using SD-OCT segmentation algorithms. Recent studies found that the diagnostic capability of GCIPL was comparable to RNFL and ONH parameters in an area under the receiver operating characteristics (49, 50). Also, the minimum macular GCIPL has been reported to be the most sensitive for diagnosing glaucoma among the various GCIPL-specific parameters (average, minimum, sectoral) (51, 52). Thus, our result may be due to many studies that used SD-OCT.

The fact that the majority of the I-squares are very high is one of the drawbacks of our meta-analysis. This restriction can be attributed to multiple research using different sampling techniques and defining the phenomenon under consideration differently, which makes it difficult to combine information in a useful way. Another drawback was the employment of different tools in primary investigations to estimate the index and frequency of the variables under consideration (like a true positive, false positive, true negative, and false negative).

Conclusion

As in the present study, imaging devices and the first technology-based evaluation could increase the number of detected cases while lowering screening expenses. Among mentioned devices in this study, OCT was the best option for disease screening and OCTA for glaucoma diagnosis. Furthermore, because of their high sensitivity and specificity, macular parameters were shown to be more reliable

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than ONH parameters, providing scientific support for their capacity to distinguish between normal and glaucomatous eyes.

Authors Contribution

M.A., A.M., and Y.M. conceptualized the idea for this review, formulated the review question and objectives, assisted with developing the final search strategy, contributed to the data analysis/interpretation, and wrote the manuscript. M.P. and L.R. contributed to formulating the review objectives and writing the manuscript. All authors read and approved the final manuscript.

Ethical Approval

This work was recorded in the Research of Kurdistan University of Medical Sciences (IR.MUK.REC.1401.002).

Acknowledgment

Not applicable.

Conflict of Interests

The authors declare that they have no competing interests.

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