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REVIEW ARTICLE

Diagnostic accuracy of AS-OCT vs gonioscopy for detecting angle closure: a systematic review and meta-analysis

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Abstract

Purpose This study aims to review the literature that compares the accuracy of Anterior Segment-Optical Coherence Tomography (AS-OCT) against gonioscopy in detecting eyes with angle closure. It is currently unclear how AS-OCT fits into clinical practice for detecting angle closure. This is a systematic review and meta-analysis.

Methods A literature search was performed on Medline, Embase, Scopus and the Cochrane Central Register of Controlled Trials to identify studies that investigated the diagnostic accuracy of AS-OCT in detecting eyes with angle closure as diagnosed by gonioscopy. Eligible studies included in the analysis met stringent inclusion criteria determining the sensitivity and specificity of AS-OCT.

Results The initial search identified 727 studies, of which 23 were included in the final analysis. We found substantial variation in the parameters being studied and methodologies. The sensitivity of AS-OCT ranged from 46 to 100% (median 87%). Twenty-one studies identified parameters that showed sensitivity above 80%. The specificity ranged from 55.3 to 100% (median 84%).

Conclusion AS-OCT demonstrates good sensitivity for detecting angle closure. It may provide an avenue to address high rates of undiagnosed angle closure, such as found in developing Asian countries. However, AS-OCT is not yet able to replace gonioscopy. Clinicians should consider whether the diagnostic accuracy of AS-OCT is acceptable for their specific clinical use before adopting it. More studies are needed to determine the utility of AS-OCT, including longitudinal studies to determine the significance of eyes classified to have closed angles by AS-OCT but open on gonioscopy.

Keywords Anterior segment optical coherence tomography · OCT · Glaucoma · Narrow angle · Gonioscopy · Screening

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Key messages

- It is currently unclear how AS-OCT fits into clinical practice for detecting angle closure.
- AS-OCT is sensitive for detecting angle closure.
- AS-OCT may be a good screening tool for angle closure.
- AS-OCT has a high rate of false positives when measured against gonioscopy.
- AS-OCT is not yet able to replace gonioscopy.

Introduction

Primary angle closure glaucoma (PACG) affects an estimated 23 million people worldwide, with over 80% of cases found in Asia [1]. PACG is a more aggressive form of glaucoma, and despite accounting for only around 26% of glaucoma cases, it causes almost half of the blindness [2]. It confers a three times higher risk of blindness compared to primary open angle glaucoma (POAG) [2–4]. Angle closure disease is significantly underdiagnosed worldwide, particularly in rural or developing areas, causing a significant burden of blindness. In China, over 90% of primary angle closure cases were undiagnosed in 2010 [5]. PACG is also frequently misdiagnosed, with up to two-thirds of cases misdiagnosed as POAG in one Indian study [6].

Identifying eyes with angle closure, including primary angle closure suspects (PACS), is critical for several reasons. Firstly, PACG is a more aggressive disease than POAG and there is a greater risk of vision loss if left untreated [2]. Almost 30% of eyes with angle closure and peripheral anterior synechiae or high pressures will progress to PACG within 5 years [7]. Secondly, the treatment for PACG is different to POAG. Treatment can effectively reduce the intraocular pressure and reduce risk of glaucomatous progression. Finally, it may identify eyes at higher risk of acute angle closure with mydriatic agents [8].

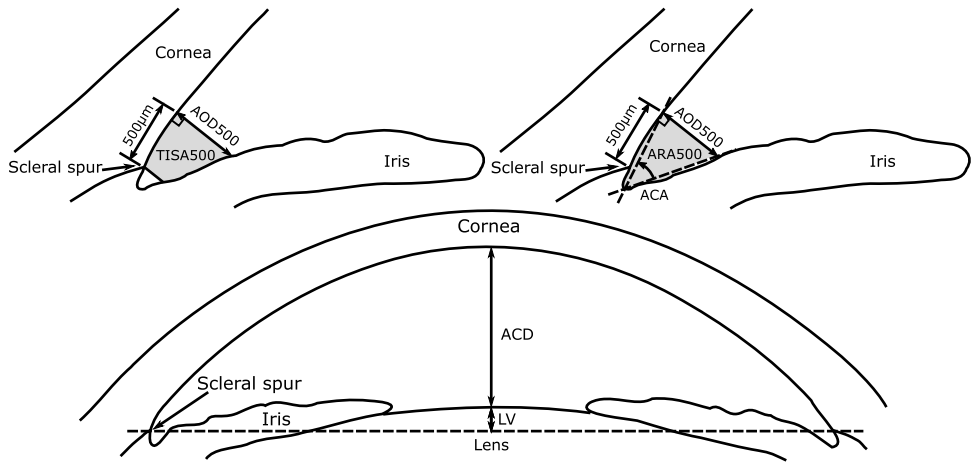

Fig. 1 Angle opening distance at 500 µm (AOD500)—the distance between the corneal endothelium and iris along a line drawn perpendicularly from a point on the corneal endothelium 500 microns anterior to the scleral spur. Trabecular-iris space area at 500 µm (TISA500)—the area enclosed by the AOD500 line, the anterior iris surface, the corneal endothelium/trabecular meshwork and a line drawn perpendicular from the scleral spur. Angle recess area at 500 µm (ARA500)—the area enclosed by the AOD500 line, anterior iris surface and the corneal endothelium/trabecular meshwork/ciliary body. Anterior chamber angle (ACA)—this may be formally defined using the trabecular-iris angle at 500 µm (TIA500). The angle subtended by the AOD500 line from the apex of the iris recess. Lens vault (LV)—the perpendicular distance between the anterior apex of the lens and the line that joins the two opposite scleral spurs. Anterior chamber depth (ACD)—the distance between the corneal endothelium and anterior surface of the lens along the central axis. Anterior chamber volume (ACV)—the volume of the anterior chamber. Iridotrabecular contact index (ITC index)—a parameter that reflects the circumferential extent of anterior angle with iridocorneal touch. Iridotrabecular contact length (ITC length)—the distance between the scleral spur and the anterior extent of iridocorneal touch. Iridotrabecular contact area (ITC area)—the total area of ITC in the eye, determined by ITC length around the circumference of the eye. Trabecular-iris circumference volume at 500 µm (TICV500)—the total volume of trabecular-iris space in the eye, determined by TISA500 around the circumference of the eye

Detection of angle closure relies on careful assessment of the anterior chamber angles. The gold standard method is gonioscopy [9]. This can be performed with basic equipment and allows 360-degree visualisation of the anterior chamber angle. However, it has several downsides including that it requires a significant amount of skill from the practitioner, compliance from the patients, contact with the eye and only fair repeatability [10]. The skill required is a significant barrier to effective detection of angle closure. Very few clinicians can perform gonioscopy well, contributing to the high rate of undiagnosed angle closure disease. In a USA-based study, optometrists were 46% less likely to diagnose angle closure disease than ophthalmologists [11]. Poorer countries are even less likely to have skilled clinicians and the equipment needed for assessment by gonioscopy. For these reasons, gonioscopy is not suitable for large scale screening. There is a need for better screening tools to improve detection rates of angle closure, especially in rural areas or developing countries [12].

Anterior segment optical coherence tomography (AS-OCT) is a computerised imaging technology that provides optical cross-sectional images of ocular structures. It has become an invaluable tool for assessing the anterior segment as it provides high-resolution visualisation of the cornea and anterior chamber as well as objective measures of anterior eye parameters (Fig. 1).

Although AS-OCT can provide excellent data on the structure of the anterior chamber angle, it remains unclear how it fits into clinical practice for detecting angle closure. The largest review by the American Academy of Ophthalmology was conducted on studies up from 2005 to 2011 and concluded that AS-OCT could provide useful supplemental information when used alongside gonioscopy [13]. A review by Porporato et al. (2018) found that AS-OCT had good sensitivity and diagnostic accuracy but did not include several studies of lower level of evidence [14]. Both reviews did not focus on collating sensitivity and specificity data to compare AS-OCT against gonioscopy. A review by Chansangpetch et al. (2018) did collate sensitivity and specificity data but did not conduct the review systematically [15]. A Cochrane review by Jindal et al. (2020) assessed non-contact tests for angle closure but did not compare against gonioscopy as a reference standard [16].

This study aimed to systematically review the literature investigating the diagnostic accuracy AS-OCT in the detection of angle closure, thus determining the utility of AS-OCT in clinical practice. This systematic review was conducted with a focus on reviewing the sensitivity and

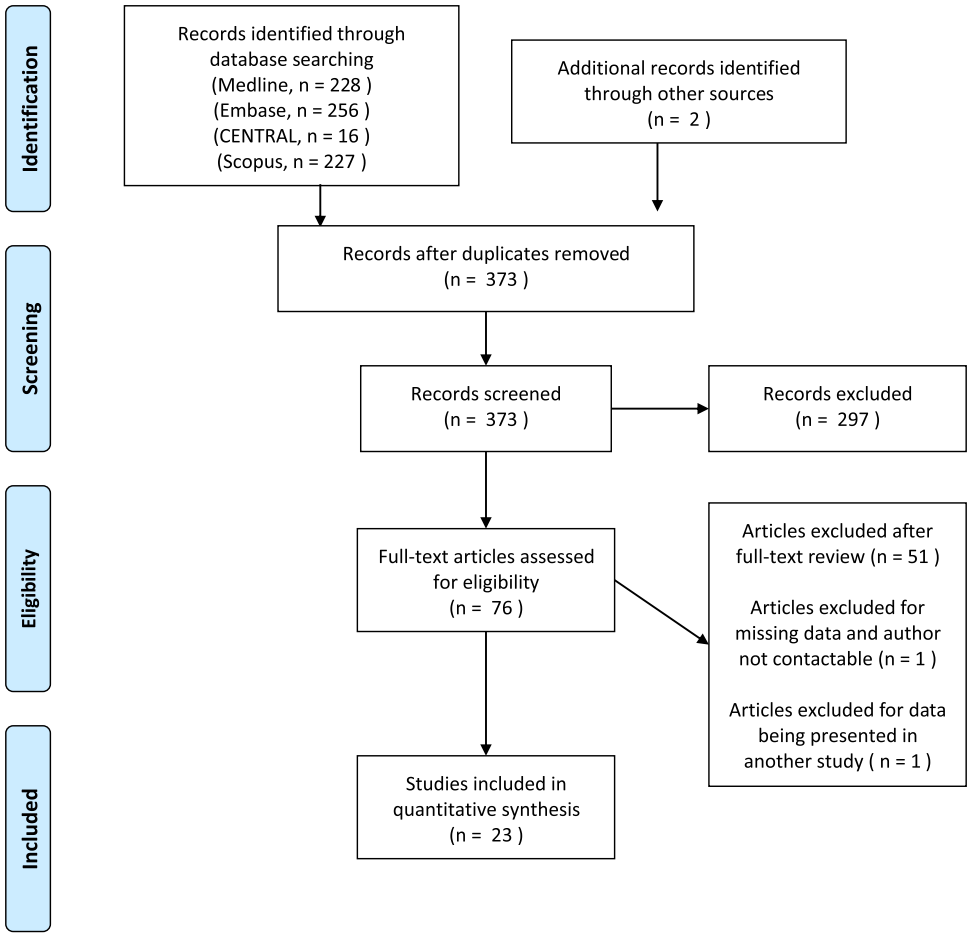

Fig. 2 Study selection flowchart following the PRISMA guidelines

specificity of parameters that can be measured with AS-OCT when compared against gonioscopy as the reference standard (Fig. 2).

Methods

This paper was written in accordance with the 1964 Declaration of Helsinki and its later amendments. The University of Sydney ethics committee waived the need for ethics approval due to this paper being a literature review. Data was gathered by electronic searches of MEDLINE, EMBASE, Scopus and the Cochrane Central Register of Controlled Trials (CENTRAL). Search terms included, 'gonio*', 'optical coherence tomography', 'angle closure', 'narrow angle', 'diagnos*', 'identif*', 'screen*' and 'detect*'. The literature search was performed in April 2020. The reference lists of included studies were reviewed to search for any papers that may have been missed during this search. Only papers written in English were included in this review. Only studies performed on humans were included. Abstracts, case studies and expert opinions were excluded from this review.

Selection criteria included any trial that investigated the diagnostic accuracy of AS-OCT in detecting eyes with angle closure as diagnosed by gonioscopy. Only papers that provided enough data to determine the sensitivity and specificity of AS-OCT were included. Only papers that assessed the ability to detect an eye with angle closure (as opposed to a quadrant or individual with angle closure) were included.

After the literature search was performed, study selection, extraction of data and assessment of risk of bias were independently performed by two key investigators (TD and VT). For any papers with missing data, the corresponding author would be contacted to find the missing data. If no reply was received 2 weeks after initial contact, then the study would be excluded. An assessment of each studies risk of bias was performed using the QUADAS-2 tool [17]. We modified the QUADAS-2 tool to also consider whether each study analysed only one eye per participant. Any disagreement was discussed amongst the two investigators to resolve the discrepancy.

Data was extracted by two key investigators (TD and VT) for each index parameter in each study. We extracted the number true positives, false positives, false negatives and true negatives to construct 2×2 contingency tables. This approach allows calculation of sensitivity and specificity as well as positive and negative predictive values (PPV and NPV). We only reported PPV and NPV values for studies that did not use a case–control design. When data was given for both training and validation sets, only results from the validation set were extracted as we deemed them to be statistically more rigorous. When data were included in more than one publication, only data from the most recent publication were extracted for analysis. To present the most relevant data, analysis of studies with a longitudinal design was performed and reported separately. This was necessary because they had different approaches and aims when investigating the clinical question.

Data was entered into Revman 5.4 [18] to create the forest plots presented in this review. We performed a meta-analysis of the sensitivity and specificity data when there were data from 3 or more studies available for an index parameter. This was performed using a hierarchical summary receiver operator curve (ROC) model for each index parameter [19]. Results were calculated using the MetaDAS macro [20] in SAS for Windows, version 9.4 [21] and presented as an estimated summary ROC curve. The Cochrane Handbook outlines how estimation of a summary ROC curve is the most appropriate form of meta-analysis given the studies included in our review [19]. Unfortunately, it was not appropriate to calculate summary sensitivity and specificity points for any index parameters because there were few studies available or there was large heterogeneity in gonioscopy criteria and/or positivity threshold. If we were to calculate summary sensitivity and specificity values, they would represent diagnostic accuracy at an indeterminate average positivity threshold and be unusable in clinical practice [19].

Some studies provided data on more than one index parameter or at more than one positivity threshold. Our analysis only included a single data set per index parameter per study. When there was more than one data set available for an index parameter in a study, such as when multiple positivity thresholds were tested, the single data set with the highest Youden's *J* statistic was selected for analysis [22].

Comparison between index parameters was made directly by analysing studies that assessed more than one index parameter. Takwoingi et al. (2013) [23] showed that this approach is more reliable than indirect comparisons. We extended this to allow for direct comparison between studies by the same researchers that used the exact same patients and study design and only differed in the index parameter being studied. It was not possible to perform a formal statistical comparison between index parameters due to the small number of studies for each index parameter.

It was not possible to perform a quantitative heterogeneity analysis for any index parameter due to a small number of studies. Instead, we have presented a narrative description of the contributors to heterogeneity, aided by graphical presentation on the relevant summary ROC plot.

Results

The initial search gave 727 papers across the 4 databases. After removing duplicates, there were 373 papers to be reviewed. These papers were screened based on their title and abstract and after removing unsuitable studies, there

were 76 papers remaining for a full text screen. Twenty-five papers were found to be suitable for inclusion after full appraisal. Two further studies were excluded. One for missing data and the authors not contactable [24], and the other because there was a more in-depth reanalysis of the same data in another later study [25, 26].

Seven studies were performed by the same research group and used a common set of patients, labelled as Population A [26–32]. Another two studies used another common set of patients, labelled as Population B [33, 34]. These studies tested different index parameters; therefore, it was not necessary to entirely exclude any of the studies. Occasionally, some data were presented in more than one study. Accordingly, subsets of data from two studies were excluded to avoid double reporting of the data [27, 33].

A total of 5663 patients were included across all studies, excluding the duplicate patients that appeared in more than one study. Eighteen studies (78%) were based out of Asia, 3 out of the USA (13%), and 2 out of the UK (9%). Ten studies (43%) were conducted in a community setting, 12 (52%) were conducted in a secondary care setting, and in 1 study, it was unclear (4%). Two studies were longitudinal in nature and investigated the accuracy of AS-OCT in predicting eyes that would develop angle closure 4 years later [32]. Results from 7 different OCT devices were analysed between the included studies. Characteristics of each study are outlined in Table 1.

Gonioscopy criteria for diagnosing angle closure varied between studies. Non-visibility of posterior trabecular meshwork (PTM) was used as gonioscopy criteria for diagnosing angle closure in most studies. Non-visibility of ≥ 1, 2, 3 and 4 quadrants of PTM was used as a threshold in 5, 13, 6 and 1 studies, respectively. Six studies did not directly assess for visibility of PTM and used the Spaeth grading system or a modified Shafer grading system instead [37, 40]. One study analysed only three quadrants in each eye to determine angle closure by gonioscopy [47].

The risk of bias was found to be variable amongst the studies and summarised in Figs. 3 and 4. We identified two areas of study design that were frequently performed in a way that are likely to introduce bias. Eight studies did not avoid a case–control study design which falls under the 'Patient Selection domain'. Nine studies did not pre-specify a threshold for diagnosis of angle closure which falls

Table 1 Study characteristics

First Author	Date	No. of eyes	Location	Setting	Angle closure prevalence by gonioscopy (%)	Type of OCT
Porporato [34]	2019	1865 [B]	Singapore	Community	7.5	CASIA SS-1000, Tomey
Li [35]	2019	252[a]	China	Secondary	N/A	CASIA SS-1000, Tomey
Porporato [33]	2018	1857 [B]	Singapore	Community	5.17	CASIA SS-1000, Tomey
Nongpiur [32]	2017	342 [A]	Singapore	Community	N/A	Visante, Carl-Zeiss
Tun [36]	2017	202	Singapore	Secondary	24.8	CIRRUS 5000, Carl-Zeiss
Melese [37]	2016	189[b]	USA	Secondary	N/A	CASIA SS-1000, Tomey
Baskaran [31]	2015	342 [A]	Singapore	Community	N/A	Visante, Carl-Zeiss
Dabasia [38]	2015	78	UK	Secondary	N/A	Visante, Carl-Zeiss
Campbell [39]	2015	78	UK	Community	15	3D OCT-2000, Topcon
Qin [40]	2013	65	USA	Secondary	N/A	RTVue, Optovue
Nongpiur [26]	2013	1368 [A]	Singapore	Community	21.6	Visante, Carl-Zeiss
Baskaran [41]	2013	140	Singapore	Secondary	22.9	CASIA SS-1000, Tomey
Baskaran [42]	2012	97	Singapore	Secondary	39.8	Visante, Carl-Zeiss
Tan [30]	2012	1465 [A]	Singapore	Community	21.5	Visante, Carl-Zeiss
Grewal [43]	2011	265	India	Secondary	10.6	RTVue 100, Optovue
Chang [27]	2011	2047 [A]	Singapore	Community	19.3	Visante, Carl-Zeiss
Narayanaswamy [29]	2010	1465 [A]	Singapore	Community	21.5	Visante, Carl-Zeiss
Khor [28]	2010	1853 [A]	Singapore	Community	16.4–28.2	Visante, Carl-Zeiss
Hong [44]	2009	73	Korea	Unclear	N/A	SL-OCT, Heidelberg
Sakata [45]	2009	83	Singapore	Secondary	36.1	Visante and SL-OCT
Wong [46]	2009	153	Singapore	Secondary	30.1–33.3	Visante, Carl-Zeiss
Nolan [47]	2006	342	Singapore	Secondary	44.4	Prototype OCT, Carl-Zeiss
Radhakrishnan [48]	2005	31	USA	Secondary	N/A	Prototype OCT, Carl-Zeiss

[a]Seventy-five eyes in validation set. [b]Sixty-nine eyes in validation set. [A]Shared population A. [B]Shared population B

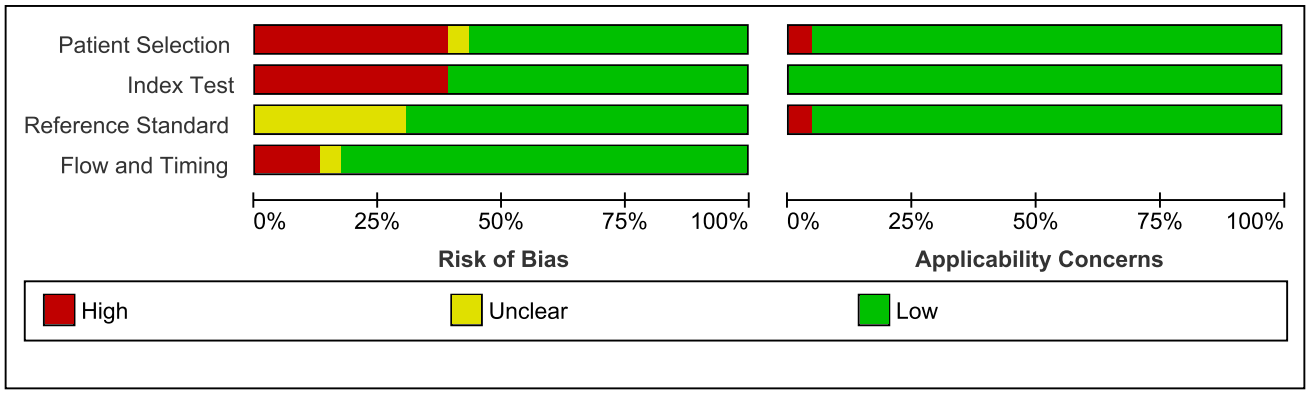

Fig. 3 Risk of bias and applicability concerns graph

under the 'Index Test' domain. Instead, they determined an ideal threshold to fit to the data after it had been collected.

Between all 23 studies, the sensitivity ranged from 46 to 100% (median 87%) and the specificity ranged from 55.3 to 100% (median 84%). There were 21 (91%) and 17 (74%) studies that identified a parameter that had sensitivity and specificity over 80%, respectively. The four studies that showed the best diagnostic accuracy for AS-OCT all used a case–control study design [37, 35–48]. It is likely that this artificially improved their results. Summarised data from all 23 studies was collated and presented in Table 2 (available online).

AOD and TISA

AOD and TISA are two parameters that were often analysed together. Six studies assessing AOD were included in the analysis for a total of 1970 participants (Figs. 5 and 6). Five studies assessing TISA were included in the analysis for a total of 1905 participants (Figs. 7 and 8).

The largest study to analyse AOD and TISA was performed by Narayanaswamy et al. in 2010 [29]. They reported that the most powerful parameters were AOD750 nasally (sensitivity 82.5%, specificity 84.0%) and AOD750 temporally (sensitivity 90.2%, specificity 77.4%). This study reported the lowest specificity for AOD and was the only study conducted in a community setting.

We considered 4 studies to be at high risk of bias in the patient selection domain for not avoiding a case–control design [37, 40, 35, 48]. This includes the 3 studies with the highest reported sensitivity for AOD and TISA. We considered 4 studies to be at high risk of bias in the index test domain because they did not pre-specify a positivity threshold [29, 40, 48, 43]. We also considered two studies to be at increased risk of bias for analysing more than one eye per patient [40, 48].

Iridotrabecular touch

Seven studies assessing for the presence of iridotrabecular touch were included in analysis for a total of 2808 participants (Figs. 9 and 10). The best evidence comes from a study by Khor et al. (2010)[28]. They found that it was most effective when assessing for touch in the inferior quadrant, reaching a sensitivity as high as 87.8%. However, specificity was less than 73%. The results for this study sit directly on the summary ROC curve. The risk of bias amongst the studies was generally low. All of the studies avoided a case–control design, apart from one study by Campbell et al. (2015) where it is uncertain [39]. The study by Nolan et al. (2006) was considered to be at an increased risk of bias for including more than one eye per patient [47].

ITC index

Three studies assessing ITC index were included in the analysis for a total of 2074 patients (Figs. 11 and 12). One study does not appear in the analysis as data from the same patients were also presented in an earlier study [33, 34]. The data from the later study were essentially identical but used different gonioscopy criteria and had a lower Youden's *J* statistic.

Porporato et al. (2018) assessed ITC index in a community based study and showed a NPV of over 96% for all tested thresholds [33, 34]. Baskaran et al.(2013) used a hospital-based population which generally showed similar specificity but higher sensitivity [41]. Melese et al. (2016) showed an improved result over both other studies (sensitivity 93%, specificity 84%) [37].

The studies by Porporato et al. (2018) and Baskaran et al.(2013) were both considered to have low risk of bias in all domains. The study by Melese et al. (2016) used a

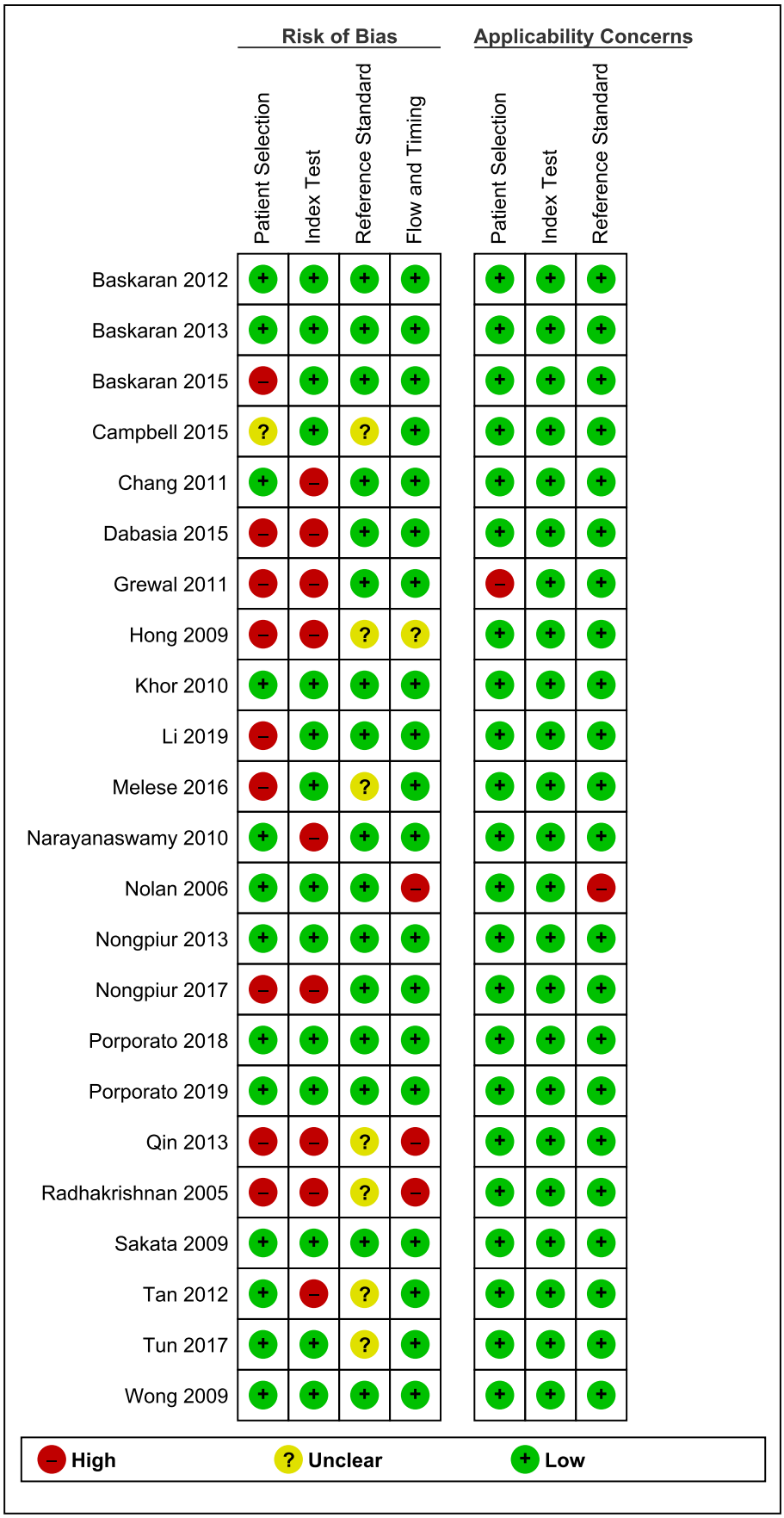

Fig. 4 Risk of bias and applicability concerns summary

Table 2 Summarised data of all included studies

First author	Gonioscopy criteria	AS-OCT criteria	Threshold value	Sensitivity	Specificity	PPV	NPV
Porporato [34]	Posterior PTM not visible in ≥ 2 quadrants	ITC index	**≥ 35%**	**82.1 (74.8–88.1)**	**78.4 (76.4–80.4)**	**23.6 (21.5–25.8)**	**98.2 (97.4–98.7)**
			≥ 50%	75.7 (67.8–82.6)	84.2 (82.4–85.9)	28.0 (25.2–31.0)	97.7 (97.0–98.3)
			≥ 75%	60.7 (52.1–68.9)	90.8 (89.3–92.1)	34.8 (30.5–39.5)	96.6 (95.9–97.2)
Li [35]	Posterior PTM not visible in > 180 degrees	AOD500 @ Temporal (mm)	0.221 (0.215, 0.270)	97.5	65.7		
		AOD500 @ Nasal (mm)	0.192 (0.184, 0.213)	97.4	80.0		
		AOD500 @ Superior (mm)	0.106 (0.085, 0.146)	95.0	85.3		
		AOD500 @ Inferior (mm)	0.150 (0.097, 0.186)	97.4	74.3		
		AOD750 @ Temporal (mm)	**0.240 (0.232, 0.301)**	**97.5**	**85.7**		
		AOD750 @ Nasal (mm)	0.231 (0.222, 0.300)	95.0	77.1		
		AOD750 @ Superior (mm)	0.106 (0.085, 0.146)	92.5	88.2		
		AOD750 @ Inferior (mm)	0.217 (0.196, 0.258)	92.5	77.1		
		TISA500 @ Temporal (mm^2)	0.077 (0.068, 0.080)	87.5	80.0		
		TISA500 @ Nasal (mm^2)	0.073 (0.039, 0.086)	94.9	77.1		
		TISA500 @ Superior (mm^2)	0.015 (0.002, 0.038)	85.0	91.2		
		TISA500 @ Inferior (mm^2)	0.050 (0.015, 0.067)	100.0	80.0		
		TISA750 @ Temporal (mm^2)	0.153 (0.134, 0.200)	92.5	60.0		
		TISA750 @ Nasal (mm^2)	0.123 (0.099, 0.128)	95.0	77.1		
		TISA750 @ Superior (mm^2)	**0.065 (0.032, 0.117)**	**95.0**	**85.3**		
		TISA750 @ Inferior (mm^2)	0.106 (0.054, 0.133)	97.4	62.9		
		ACD (mm)	**2.28 (2.04, 2.37)**	**92.5**	**88.6**		
		ACV (mm^3)	**98.1 (89.2, 118.1)**	**90.0**	**97.1**		
Porporato [33][a]	Posterior PTM not visible in ≥ 3 quadrants	ITC index	≥ 35%	84.7 (76.0–91.2)	77.0 (75.0–78.0)	16.7 (15.1–18.4)	98.9 (98.3–99.3)
			≥ 50%	**84.7 (76.0–91.2)**	**77.1 (75.0–78.0)**	**16.7 (15.1–18.4)**	**98.9 (98.3–99.3)**
			≥ 75%	61.2 (50.8–70.7)	89.7 (88.2–91.0)	24.3 (19.2–30.2)	97.7 (96.8–98.4)
Nongpiur [32]	Posterior TM not visible in ≥ 2 quadrants	**LV**	**> 0.56 mm**	**64.6 (49.5–77.8)**	**78.3 (73.0–83.0)**		
		AOD750	**≤ 0.31 mm**	**95.8 (85.7–99.5)**	**60.1 (54.2–65.9)**		
		Stepwise logistic regression using LV and AOD750	**abs value > 1.99**	**91.7 (80.0–97.7)**	**63.0 (57.1–68.6)**		
		Angle closure score as defined by Nongpiur et al	abs value > 3.11	79.2 (65.0–89.5)	73.2 (67.6–78.3)		
Tun [36]	Posterior TM not visible in ≥ 2 quadrants	**≥ 2 quadrants with any irido-corneal contact anterior to scleral spur**		**0.68 (0.53–0.80)**	**0.86 (0.78–0.92)**	**0.71 (0.59–0.80)**	**0.85 (0.78–0.89)**

Table 2 (continued)

First author	Gonioscopy criteria	AS-OCT criteria	Threshold value	Sensitivity	Specificity	PPV	NPV
Melese [37][b]	Spaeth grade A or B. Clinical judgement used for Spaeth grade C		(95% CI)	(min, max)	(min, max)		
		AOD500 @ Temporal (mm)	0.28 (0.17–0.39)	1.00 (1.00, 1.00)	0.79 (0.58, 0.97)		
		AOD500 @ Nasal (mm)	0.23 (0.14–0.32)	1.00 (1.00, 1.00)	0.87 (0.69, 1.00)		
		AOD500 @Superior (mm)	0.15 (0.08–0.21)	0.87 (0.61, 1.00)	0.92 (0.71, 1.00)		
		AOD500 @ Inferior (mm)	0.24 (0.21–0.26)	1.00 (1.00, 1.00)	0.84 (0.65, 1.00)		
		AOD750 @ Temporal (mm)	0.37 (0.29–0.46)	0.97 (0.82, 1.00)	0.84 (0.66, 0.97)		
		AOD750 @ Nasal (mm)	0.39 (0.33–0.46)	1.00 (1.00, 1.00)	0.79 (0.58, 0.95)		
		AOD750 @ Superior (mm)	0.24 (0.19–0.29)	0.97 (0.84,1.00)	0.87 (0.66, 1.00)		
		AOD750 @ Inferior (mm)	**0.31 (0.25–0.37)**	**1.00 (1.00, 1.00)**	**0.92 (0.76, 1.00)**		
		TISA500 @ Temporal (mm^2)	0.079 (0.045–0.113)	0.97 (0.85, 1.00)	0.76 (0.58, 0.96)		
		TISA500 @ Nasal (mm^2)	0.070 (0.037–0.103)	0.87 (0.59, 1.00)	0.84 (0.68, 1.00)		
		TISA500 @ Superior (mm^2)	0.028 (0.012–0.043)	0.87 (0.61, 1.00)	0.87 (0.68, 1.00)		
		TISA500 @ Inferior (mm^2)	0.054 (0.045–0.064)	1.00 (1.00,1.00)	0.84 (0.65, 1.00)		
		TISA750 @ Temporal (mm^2)	0.162 (0.031–0.101)	0.97 (0.85, 1.00)	0.79 (0.58, 0.97)		
		TISA750 @ Nasal (mm^2)	0.134 (0.079–0.190)	0.94 (0.70, 1.00)	0.84 (0.66, 0.98)		
		TISA750 @ Superior (mm^2)	0.073 (0.042–0.103)	0.87 (0.61, 1.00)	0.89 (0.68, 1.00)		
		TISA750 @ Inferior (mm^2)	**0.120 (0.098–0.142)**	**1.00 (1.00, 1.00)**	**0.84 (0.65, 1.00)**		
		TICV500 (microL)	1.92 (1.26–2.57)	1.00 (1.00, 1.00)	0.87 (0.70, 1.00)		
		TICV750 (microL)	**4.00 (2.95–5.06)**	**1.00 (1.00, 1.00)**	**0.87 (0.70, 1.00)**		
		ITC length @ Temporal (mm)	0.030 (0.000–0.112)	0.80 (0.56, 1.00)	0.84 (0.66, 0.98)		
		ITC length @ Nasal (mm)	0.017 (0.000–0.089)	0.61 (0.35, 0.90)	0.94 (0.82, 1.00)		
		ITC length @ Superior (mm)	0.159 (0.067–0.250)	0.80 (0.45, 1.00)	0.79 (0.43, 0.95)		
		ITC length @ Inferior (mm)	**0.054 (0.000–0.112)**	**0.87 (0.58, 1.00)**	**0.79 (0.56, 0.95)**		
		ITC index (%)	**36.9 (23.1–51.1)**	**0.93 (0.73, 1.00)**	**0.84 (0.63, 0.98)**		
		ITC area (mm^2)	**3.27 (1.40–5.15)**	**0.93 (0.73, 1.00)**	**0.87 (0.68, 1.00)**		

Table 2 (continued)

First author	Gonioscopy criteria	AS-OCT criteria	Threshold value	Sensitivity	Specificity	PPV	NPV
Baskaran [31]	Posterior TM not visible in ≥ 2 quadrants	≥ 1 quadrant with any iridotrabecular contact anterior to scleral spur		100.0 (92.6–100.0)	22.1 (17.4–27.4)		
		≥ 2 quadrants with any iridotrabecular contact anterior to scleral spur		**75.0 (60.4–86.4)**	**56.5 (50.5–62.3)**		
		≥ 3 quadrants with any iridotrabecular contact anterior to scleral spur		41.7 (27.6–56.8)	89.1 (84.9–92.5)		
		4 quadrants with any iridotrabecular contact anterior to scleral spur		16.7 (7.48–30.2)	97.2 (94.5–98.8)		
	Posterior TM not visible in ≥ 3 quadrants	≥ 1 quadrants with any iridotrabecular contact anterior to scleral spur		100.0 (87.7–100)	20.7 (16.3–25.6)		
		≥ 2 quadrants with any iridotrabecular contact anterior to scleral spur		82.1 (63.1–93.9)	55.1 (49.3–60.8)		
		≥ 3 quadrants with any iridotrabecular contact anterior to scleral spur		**50.0 (30.7–69.4)**	**87.9 (83.7–91.3)**		
		4 quadrants with any iridotrabecular contact anterior to scleral spur		25.0 (10.7–44.9)	97.1 (94.5–98.6)		
Dabasia [38][c]	**Posterior TM not visible in ≥ 270 degrees**	**ACA (°)**	**≤ 20.7**	**87.2 (72.6–95.7)**	**86.8 (71.9–95.6)**		
	Expert opinion after dynamic gonio assessment		≤ 18.6	100 (80.5–100.0)	66.7 (53.3–78.3)		
	Posterior TM not visible in ≥ 270 degrees	ACD (mm)	≤ 2.50	71.8 (55.1–85.0)	84.6 (69.5–94.1)		
	Expert opinion after dynamic gonio assessment		**≤ 2.38**	**82.3 (56.6–96.2)**	**83.6 (71.9–91.8)**		
Campbell [39]	Posterior TM visible for less than 270 degrees	Iridotrabecular touch in nasal or temporal quadrant	**Visit 1**	**46 (17—77)**	**87 (76—94)**	**36**	**90**
			Visit 2	25 (6—57)	89 (79—96)	31	86
Qin [40]	Modified Shaffer grade ≤ 1 in all quadrants	**AOD-Schwalbe's Line @ Nasal (mm)**	**0.29**	**80**	**87**		
		AOD-Schwalbe's Line @ Temporal (mm)	0.29	85	77		

Table 2 (continued)

First author	Gonioscopy criteria	AS-OCT criteria	Threshold value	Sensitivity	Specificity	PPV	NPV
Nongpiur [26]	Posterior PTM not visible in ≥ 180 degrees	Stepwise logistic regression model	0.5	96	75	51	99
			0.26	**89**	**89**	**69**	**97**
Baskaran [41]	Posterior PTM not visible in ≥ 1 quadrants	ITC index	> 35%	69.1 (52.9–82.4)	88.8 (80.8–94.3)	72.5 (55.9–85.5)	87.0 (78.8–92.9)
			≥ 50%	42.9 (27.7–59.0)	94.9 (88.5–98.3)	78.3 (55.7–92.8)	79.5 (71.0–86.4)
			> 70%	21.4 (10.3–36.8)	99.0 (94.4–100.0)	90.0 (55.5–99.7)	74.6 (66.2–81.8)
	Posterior PTM not visible in ≥ 2 quadrants		> 35%	71.9 (53.3–86.3)	84.3 (76.0–90.6)	57.5 (40.9–73.0)	91.0 (83.6–95.8)
			≥ 50%	43.8 (26.4–62.3)	91.7 (84.8–96.1)	60.9 (38.5–80.3)	84.6 (76.7–90.6)
			> 70%	25.0 (11.5–43.4)	98.1 (93.5–99.8)	80.0 (42.2–97.9)	81.5 (73.8–87.8)
	Posterior PTM not visible in ≥ 3 quadrants		> 35%	71.0 (52.0–85.8)	83.5 (75.2–89.9)	55.0 (38.5–70.7)	91.0 (83.6–95.8)
			≥ 50%	45.2 (27.3–64.0)	91.7 (84.9–96.2)	60.9 (38.0–80.7)	85.5 (77.8–91.3)
			> 70%	25.8 (11.9–44.6)	98.2 (93.5–99.8)	80.0 (44.4–97.5)	82.3 (74.6–88.4)
	Posterior PTM not visible in 4 quadrants		**> 35%**	**92.3 (64.0–99.8)**	**78.0 (69.7–84.8)**	**30.0 (16.6–46.5)**	**99.0 (94.5–100.0)**
			≥ 50%	76.9 (46.2–95.0)	89.8 (83.1–94.4)	43.5 (23.2–65.5)	97.4 (92.7–99.5)
			> 70%	46.2 (19.2–74.9)	96.9 (92.1–99.1)	60.0 (26.2–87.8)	94.6 (89.2–97.8)
Baskaran [42]	Posterior PTM not visible in ≥ 2 quadrants	Any iridotrabecular touch anterior to the SS in ≥ 1 quadrants		95	61	61.7	94.9
		Any iridotrabecular touch anterior to the SS in ≥ 2 quadrants		92	65	63.5	92.5
		Any iridotrabecular touch anterior to the SS in ≥ 3 quadrants		**84**	**75**	**68.1**	**88.0**
		Any iridotrabecular touch anterior to the SS in ≥ 4 quadrants		77	76	68	83.3
Tan [30]	Posterior TM not visible in ≥ 180 degrees	**LV (mm)**	**≥ 0.576**	**85.7**	**77.5**	**51**	**95.2**
Grewal [43]	Shaffer grade ≤ 1 in all quadrants	AOD500 @ Nasal (mm)	≤ 0.34	78.6 (59.0–91.7)	71.3 (65.1–77.0)	19.5 (11.3–30.1)	97.1 (93.4–99.0)
		AOD500 @ Temporal (mm)	**≤ 0.32**	**67.9 (47.7–84.1)**	**88.2 (83.4–92.0)**	**33.3 (18.6–51.0)**	**96.3 (92.8–98.4)**
		TISA500 @ Nasal (mm^2)	≤ 0.20	64.3 (44.1–81.3)	78.7 (72.8–83.8)	18.3 (9.50–30.4)	95.3 (91.2–97.8)
		TISA500 @ Temporal (mm^2)	**≤ 0.21**	**71.4 (51.3–86.7)**	**81.0 (75.4–85.8)**	**22.8 (12.8–35.8)**	**96.4 (92.7–98.5)**
Chang [27]	**Shaffer grade ≤ 1 in ≥ 2 quadrants**	**AOD750 if SS visible. If not, subjective assessment (mm)**	**≤ 0.258**	**83.0 (78.9–86.5)**	**78.2 (76.1–80.2)**	**48.4 (44.6–52.3)**	**94.9 (93.6–96.0)**

Table 2 (continued)

First author	Gonioscopy criteria	AS-OCT criteria	Threshold value	Sensitivity	Specificity	PPV	NPV
Narayanaswamy [29][d]	Posterior PTM not visible in ≥ 180 degrees	AOD250 @ Temporal (mm)	0.144	77.1 (72.5–81.8)	68.2 (65.6–70.9)	37.7 (33.8–41.6)	92.2 (90.4–94.0)
		AOD250 @ Nasal (mm)	0.138	75.6 (70.8–80.3)	70.6 (68.0–73.2)	39.1 (35.1–43.1)	92.0 (90.2–93.8)
		AOD500 @ Temporal (mm)	0.191	88.9 (85.4–92.3)	74.6 (72.1–77.1)	46.6 (42.5–50.7)	96.4 (95.1–97.6)
		AOD500 @ Nasal (mm)	0.177	85.1 (81.1–89.0)	76.1 (73.7–78.6)	47.1 (42.8–51.3)	95.3 (93.9–96.6)
		AOD750 @ Temporal (mm)	**0.258**	**90.2 (86.9–93.4)**	**77.4 (74.9–79.8)**	**49.9 (45.6–54.2)**	**96.9 (95.8–98.0)**
		AOD750 @ Nasal (mm)	0.225	82.5 (78.3–86.7)	84.0 (81.9–86.2)	56.3 (51.6–61.0)	95.0 (93.7–96.3)
		TISA500 @ Temporal (mm^2)	0.103	88.2 (84.7–91.8)	59.1 (56.3–62.0)	35.0 (31.6–38.5)	95.2 (93.6–96.7)
		TISA500 @ Nasal (mm^2)	0.076	73.3 (68.4–78.2)	75.2 (72.7–77.7)	42.4 (38.1–46.7)	91.8 (90.0–93.5)
		TISA750 @ Temporal (mm^2)	**0.151**	**83.5 (79.4–87.6)**	**76.7 (74.3–79.2)**	**47.3 (43.0–51.6)**	**94.8 (93.4–96.2)**
		TISA750 @ Nasal (mm^2)	0.134	80.3 (75.9–84.7)	77.5 (75.1–79.9)	47.2 (42.8–51.8)	94.0 (92.5–95.5)
		ARA750 @ Temporal (mm^2)	**0.191**	**84.1 (80.1–88.2)**	**69.2 (66.5–71.9)**	**40.6 (36.7–44.4)**	**94.5 (93.0–96.0)**
		ARA750 @ Nasal (mm^2)	0.154	74.0 (69.1–78.8)	75.8 (73.3–78.3)	43.2 (38.9–47.5)	92.0 (90.3–93.7)
Khor [28]		Any iridotrabecular touch anterior to the SS in ≥ 1 quadrants of quadrants tested					
	Posterior TM not visible in ≥ 1 quadrants	Inferior only		79.5	72.7	53.4	90.0
		Inferior, nasal and temporal		82.2	68.3	50.5	90.7
		Nasal and temporal only		40.8	89.0	59.3	79.3
	Posterior TM not visible in ≥ 2 quadrants	Inferior only		83.9	68.8	41.0	94.3
		Inferior, nasal and temporal		87.4	64.8	39.0	95.2
		Nasal and temporal only		46.8	87.6	49.3	86.5
	Posterior TM not visible in ≥ 3 quadrants	**Inferior only**		**87.8**	**67.0**	**34.3**	**96.6**
		Inferior, nasal and temporal		90.8	62.8	32.4	97.2
		Nasal and temporal only		49.2	86.4	41.5	89.7
Hong [44]	TM visible in < 90 degrees	ACA (°)	**31.8**	**75.0**	**97.6**		
		ACD (mm)	**2.45**	**87.5**	**97.6**		
Sakata [45]	Posterior TM not visible in ≥ 1 quadrants	Any iridotrabecular touch anterior to the SS in ≥ 1 quadrants					
		Visante data		97 (83–100)	51 (37–65)	53 (46–60)	96 (79–99)
		SL-OCT data		**90 (73–98)**	**64 (50–77)**	**59 (49–68)**	**92 (79–97)**

Table 2 (continued)

First author	Gonioscopy criteria	AS-OCT criteria	Threshold value	Sensitivity	Specificity	PPV	NPV
Wong [46]	**Posterior TM not visible in ≥ 1 quadrants**	Any iridotrabecular touch anterior to the SS in ≥ 1 quadrants		84	58	50	88
		Any iridotrabecular touch anterior to the SS in ≥ 2 quadrants		**68**	**75**	**58**	**82**
		Any iridotrabecular touch anterior to the SS in ≥ 3 quadrants		43	86	61	75
	Posterior TM not visible in ≥ 2 quadrants	Any iridotrabecular touch anterior to the SS in ≥ 1 quadrants		83	55	44	88
		Any iridotrabecular touch anterior to the SS in ≥ 2 quadrants		65	72	50	83
		Any iridotrabecular touch anterior to the SS in ≥ 3 quadrants		46	86	59	79
Nolan [47][e]	Spaeth 0° in ≥ 1 quadrants, assessing temporal, nasal and inferior quadrants only	Any iridotrabecular touch anterior to the SS in ≥ 1 quadrants out of the 3 temporal, nasal and inferior quadrants		**94.1 (88.7–97.1)**	**55.3 (47.9–62.4)**	**62.7 (58.8–66.4)**	**92.1 (85.4–95.7)**
Radhakrishnan [48]	Shaffer grade ≤ 1 in 4 quadrants	**AOD500 (mm)**	**0.191**	**100.0**	**87.5**		
		ARA500 (mm^2)	**0.12**	**87.0**	**100**		
		ARA750 (mm^2)	0.17	91.3	87.5		
		TISA500 (mm^2)	**0.11**	**87.0**	**100**		
		TISA750 (mm^2)	0.17	91.3	87.5		

95% Confidence intervals indicated in brackets

Parameter with the highest Youden-*J* value in bold

[a]Excluded duplicate data from Porporato (2019)

[b]Data from validation set only

[c]Excluded per individual analysis

[d]PPV/NPV values given for 20% prevalence

[e]Excluded per individual analysis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Grewal 2011	19	28	9	209	0.68 [0.48, 0.84]	0.88 [0.83, 0.92]
Qin 2013	22	5	6	32	0.79 [0.59, 0.92]	0.86 [0.71, 0.95]
Narayanaswamy 2010	284	260	31	890	0.90 [0.86, 0.93]	0.77 [0.75, 0.80]
Li 2019	37	5	1	32	0.97 [0.86, 1.00]	0.86 [0.71, 0.95]
Radhakrishnan 2005	8	3	0	20	1.00 [0.63, 1.00]	0.87 [0.66, 0.97]
Melese 2016	31	3	0	35	1.00 [0.89, 1.00]	0.92 [0.79, 0.98]

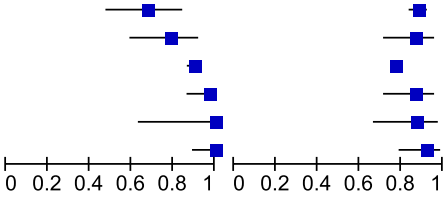

Fig. 5 Forest plot for studies investigating AOD

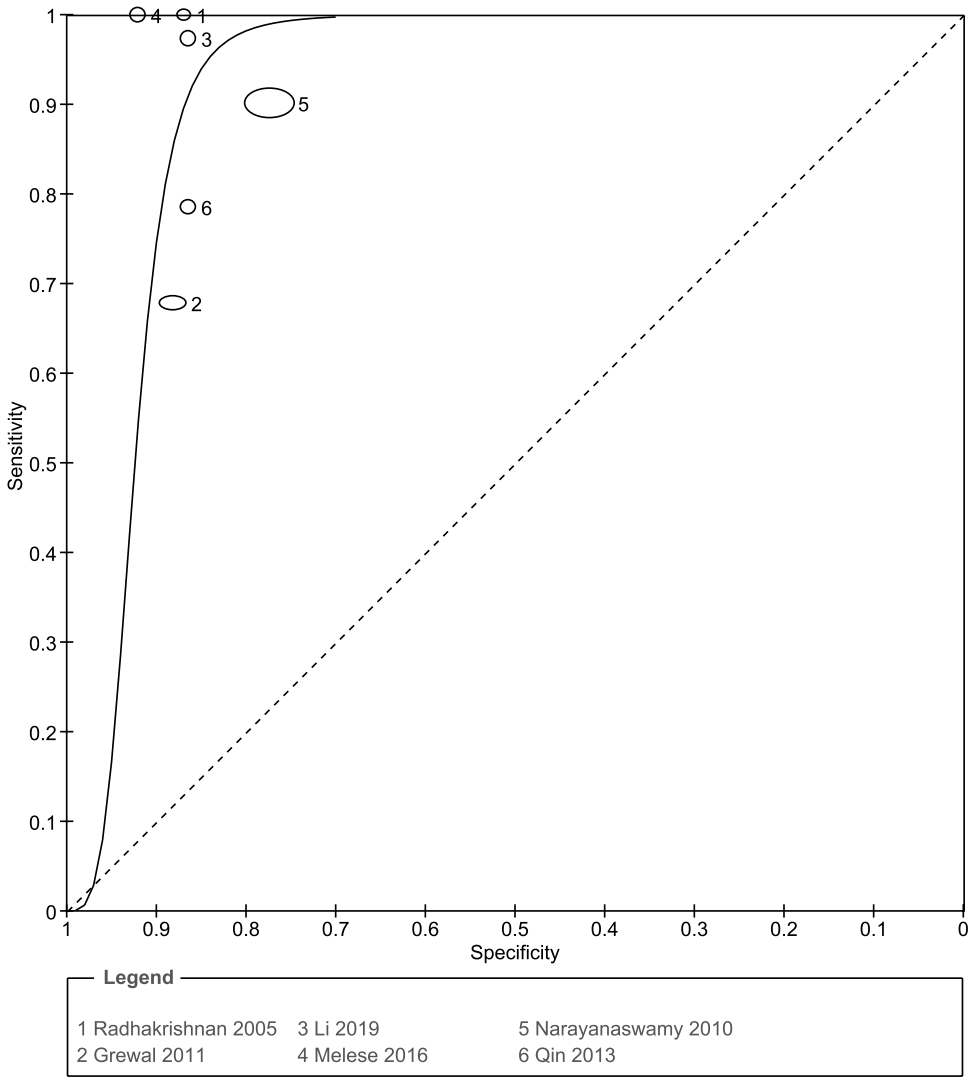

Fig. 6 Summary ROC plot for studies investigating AOD

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Grewal 2011	20	45	8	192	0.71 [0.51, 0.87]	0.81 [0.75, 0.86]
Narayanaswamy 2010	263	268	52	882	0.83 [0.79, 0.87]	0.77 [0.74, 0.79]
Radhakrishnan 2005	7	0	1	23	0.88 [0.47, 1.00]	1.00 [0.85, 1.00]
Li 2019	36	5	2	32	0.95 [0.82, 0.99]	0.86 [0.71, 0.95]
Melese 2016	31	6	0	32	1.00 [0.89, 1.00]	0.84 [0.69, 0.94]

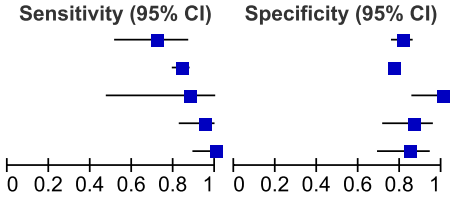

Fig. 7 Forest plot for studies investigating TISA

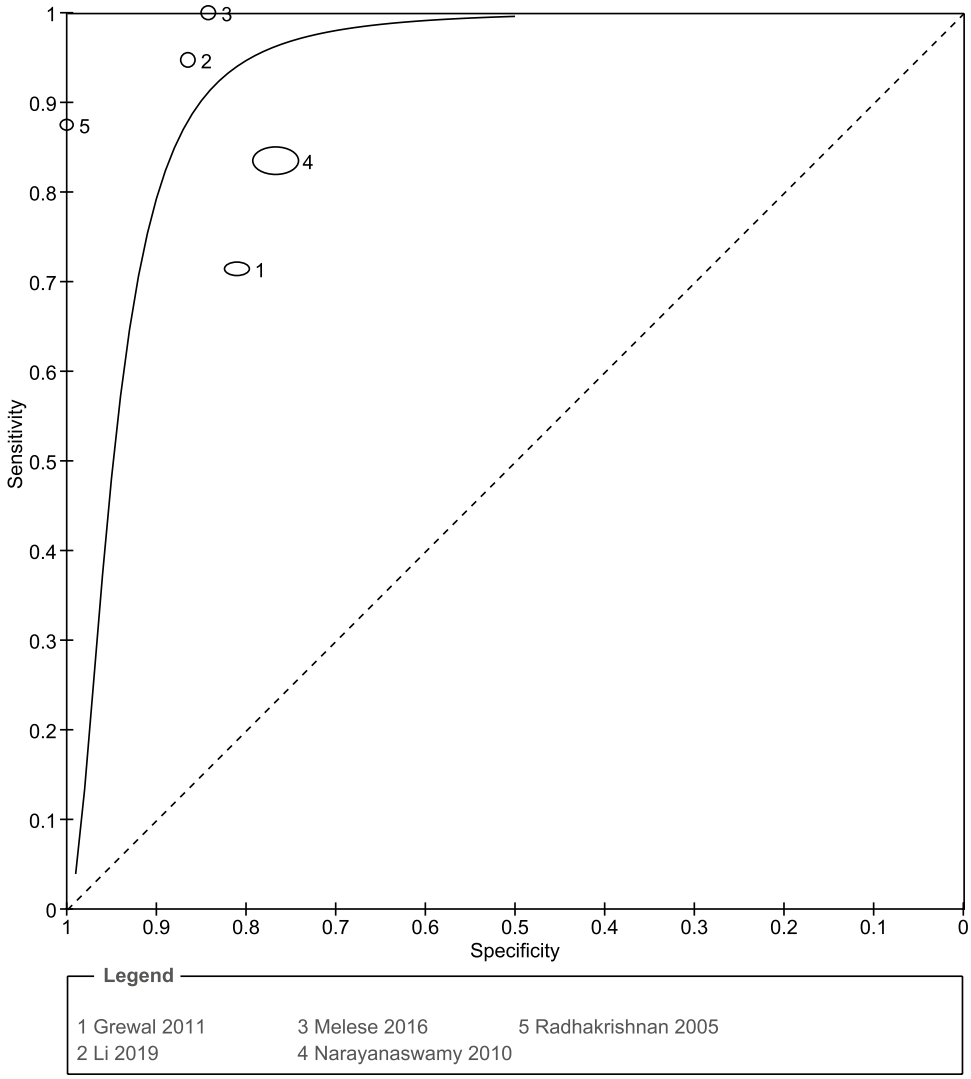

Fig. 8 Summary ROC plot for studies investigating TISA

case–control design so we considered it to be at high risk of patient selection bias.

ACD

Three studies assessing ACD have been included in the analysis for a total of 226 participants (Figs. 13 and 14) [35, 44, 38]. Overall, the evidence investigating ACD is weak due to all 3 studies using a case–control design and small sample sizes. Results showed variable sensitivity (ranging from 71.8 to 92.5%) and specificity (ranging from to 83.6 to 97.6%).

Remaining index parameters

The remaining index parameters had few studies to draw data from as shown in the forest plot in Fig. 15. Data has

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Campbell 2015	5	9	6	58	0.45 [0.17, 0.77]	0.87 [0.76, 0.94]
Tun 2017	34	14	16	138	0.68 [0.53, 0.80]	0.91 [0.85, 0.95]
Wong 2009	35	25	16	77	0.69 [0.54, 0.81]	0.75 [0.66, 0.83]
Baskaran 2012	32	15	6	44	0.84 [0.69, 0.94]	0.75 [0.62, 0.85]
Khor 2010	266	511	37	1039	0.88 [0.84, 0.91]	0.67 [0.65, 0.69]
Sakata 2009	27	19	3	34	0.90 [0.73, 0.98]	0.64 [0.50, 0.77]
Nolan 2006	143	85	9	105	0.94 [0.89, 0.97]	0.55 [0.48, 0.62]

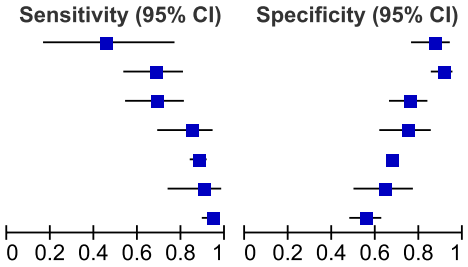

Fig. 9 Forest plot for studies investigating Iridotrabecular touch

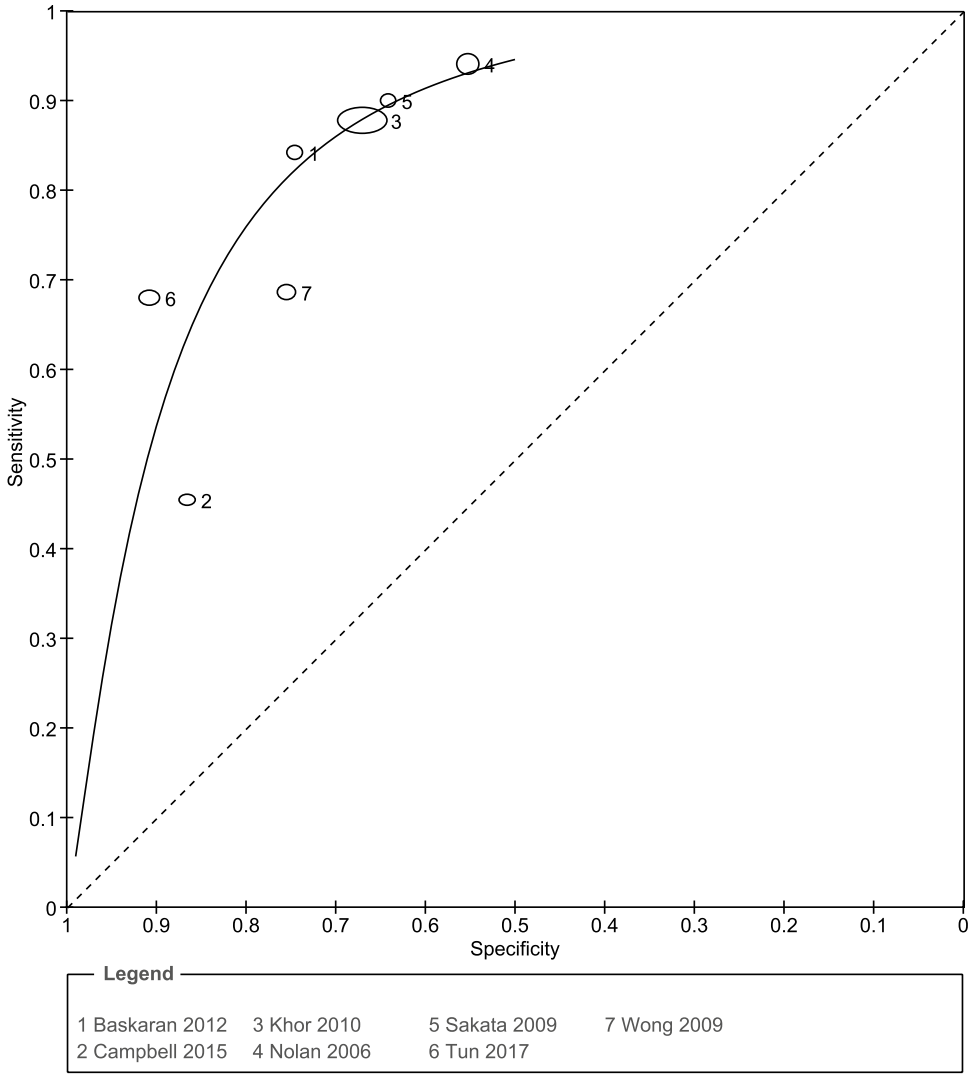

Fig. 10 Summary ROC plot for studies investigating iridotrabecular touch

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Porporato 2018	318	340	58	1141	0.85 [0.81, 0.88]	0.77 [0.75, 0.79]		
Baskaran 2013	12	28	1	99	0.92 [0.64, 1.00]	0.78 [0.70, 0.85]		
Melese 2016	29	6	2	32	0.94 [0.79, 0.99]	0.84 [0.69, 0.94]		

Fig. 11 Forest plot for studies investigating ITC index

not been shown on a summary ROC plot to avoid facilitating an inappropriate indirect comparison between index parameters. Li et al. (2019) found that ACV showed a sensitivity of 90.0% and specificity of 97.1% [35]. ACA was analysed in two studies and the results varied significantly [44, 38] with sensitivity ranging from 75.0 to 100.0% and specificity ranging from to 66.7 to 97.6%. LV has been assessed in a single community based study by Tan et al. (2012) with 1465 eyes [30]. The results showed a reasonable ability to detect angle closure (sensitivity 85.7%, specificity 77.5%, PPV 51.0%, NPV 95.2%). TICV, ITC area and ITC length were analysed by Melese et al. (2016) [37]. TICV achieved 100% specificity and 87% specificity. ITC area had good results (sensitivity 93%, specificity 87%). The results for ITC length were more the modest. ARA has only been assessed in two studies with variable sensitivity (range 74.0–91.3) and specificity (range 69.2–100).

Nongpiur et al. (2013) assessed a stepwise logistic regression model that uses multiple parameters to determine an angle closure score and estimate a probability of angle closure [25, 26, 32]. Data for two different thresholds were presented, with one weighted toward a higher sensitivity of

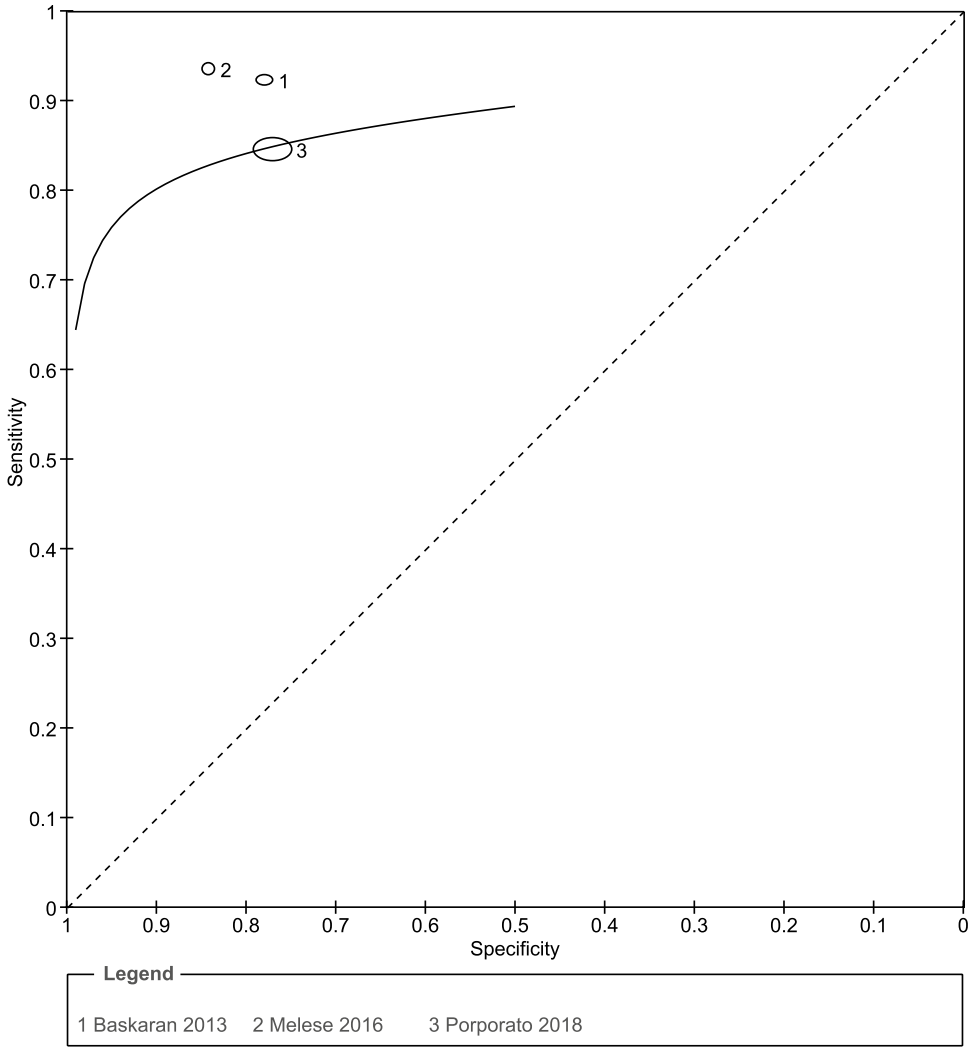

Fig. 12 Summary ROC plot for studies investigating ITC index

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Dabasia 2015	14	10	3	51	0.82 [0.57, 0.96]	0.84 [0.72, 0.92]		
Hong 2009	36	1	5	31	0.88 [0.74, 0.96]	0.97 [0.84, 1.00]		
Li 2019	35	4	3	33	0.92 [0.79, 0.98]	0.89 [0.75, 0.97]		

Fig. 13 Forest plot for studies investigating ACD

96% (NPV 99%) and the other weighted toward a higher specificity of 89% (PPV 69%).

Ability to predict development of angle closure at 4 years

Nongpiur et al.(2017) and Baskaran et al.(2015) assessed models that use baseline AS-OCT measurements to predict angle closure by gonioscopy four years later (Fig. 16) [31, 32]. The two studies were conducted at the same community clinic in Singapore and used the exact same participants ($n = 342$). The participants were limited to those that did not have angle closure by gonioscopy at baseline. Nongpiur et al. (2017) showed the sensitivity of LV and AOD750 to be 64.6% and 95.8% respectively. Baskaran et al. (2015) assessed for the number of quadrants with presence of iridotrabecular touch. When 1 quadrant was used as the threshold, the sensitivity was 100%. When 4 quadrant was used as the threshold, the specificity was above 97%.

Comparisons between index parameters

In the paired studies by Narayanaswamy et al. (2010) [29] and Tan et al. (2012) [30], AOD, TISA and LV were shown

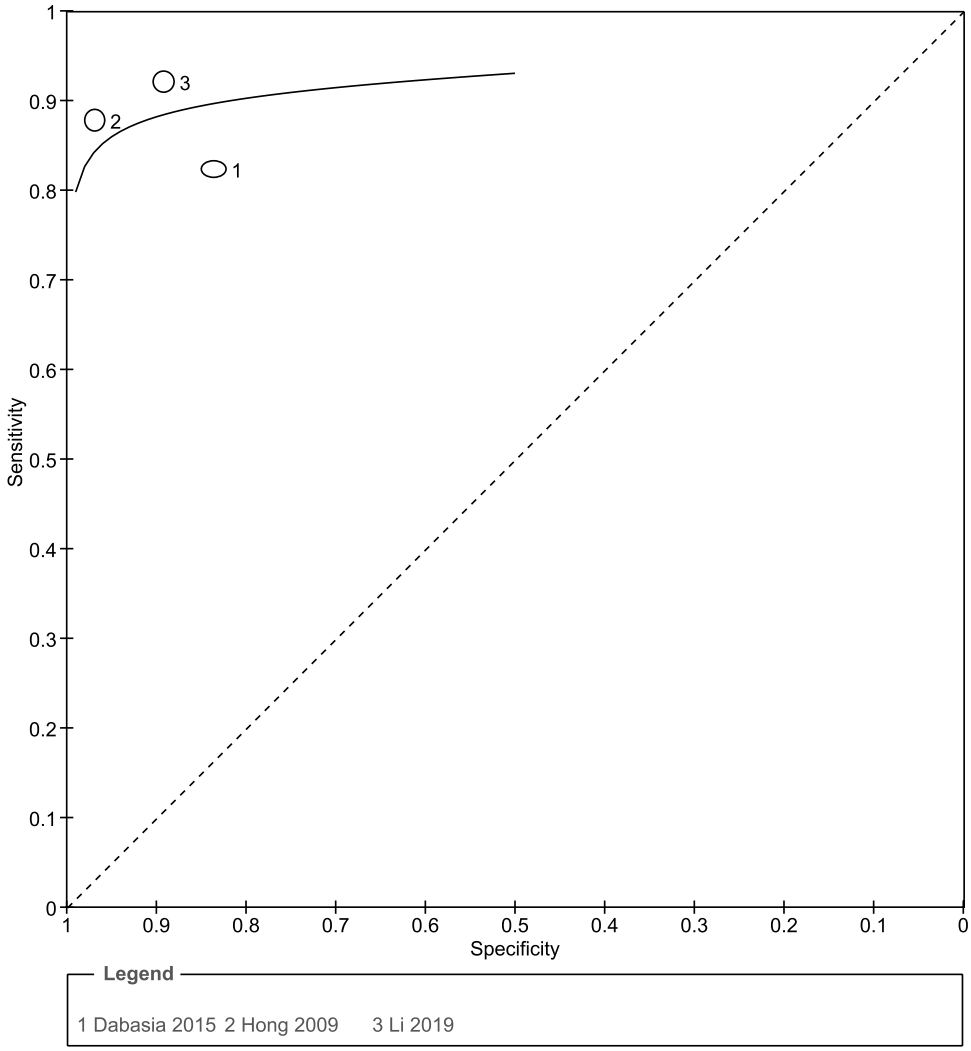

Fig. 14 Summary ROC plot for studies investigating ACD

to be significantly more specific than ARA (AOD: 0.77 (95% CI 0.75–0.80), TISA: 0.77 (95% CI 0.74–0.79), LV: 0.77 (95% CI 0.75–0.80), ARA: 0.69 (95% CI 0.66–0.72)). The two longitudinal studies showed that LV was more specific than all other tested parameters, but it was less sensitive than AOD and a stepwise logistic model. However, Nongpiur et al. (2017) did not find a significant difference between parameters when comparing AUC values. These conclusions are only applicable at the specific positivity thresholds used in the studies. There is not enough information to make any further conclusions about the relative accuracy of index parameters.

Discussion

Optical coherence tomography has made an incredible impact in the field of ophthalmology. It is proven to be cost-effective and has become a key imaging modality for many eye conditions including glaucoma and neovascular age-related macular degeneration [49, 50]. Our systematic review focused on the evidence of the diagnostic accuracy of AS-OCT in detecting angle closure. We were able to produce summary ROC curves and show that AS-OCT may reach above 90% in sensitivity or specificity for detecting angle closure as defined by gonioscopy. However, the studies that showed the best results for AS-OCT were at often high risk of bias due to their study design. There is not enough evidence to conclude that any individual parameter is significantly better or worse for detecting angle closure. Similarly, there is not enough evidence to conclude that horizontal, vertical or circumferential AS-OCT scans perform differently.

AS-OCT allows excellent visualisation of the anterior angle and has several key advantages over gonioscopy. It is non-contact, more comfortable for the patient and requires little training to use. The objective measurements are ideal for ongoing monitoring of glaucoma patients and suspects. However, AS-OCT cannot replace gonioscopy which remains the reference standard as it is useful for

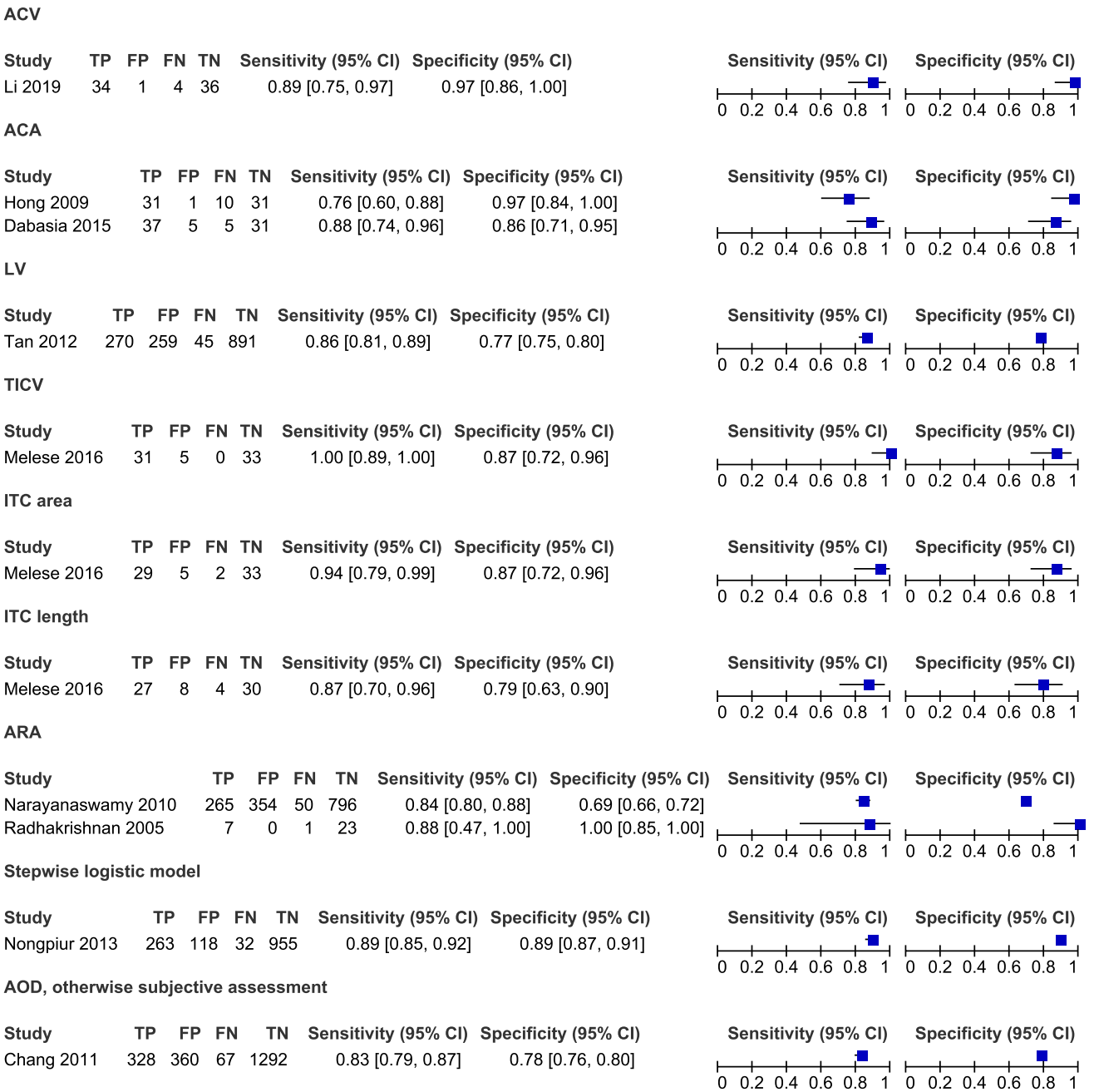

Fig. 15 Forest plot for studies investigating remaining parameters

purposes other than detecting angle closure including assessment of neovascularisation, peripheral anterior synechiae, pigment dispersion syndrome and angle recession. A dynamic assessment with indentation is also only possible with a gonioscopy lens. Furthermore, gonioscopy facilitates 360-degree visualisation of the anterior angle, whereas AS-OCT often only provides a small number of axis scans, preventing a complete assessment.

Time for data acquisition using the AS-OCT varies with different anterior angle parameters and is an important factor for clinicians from a practical perspective. AOD and TISA currently require manual input from the clinician to locate the scleral spur which may slow down the testing procedure, especially if multiple quadrants are assessed. This requirement for subjective input may also introduce error. The practicality of AOD and TISA is further reduced by frequently poor visualisation of the scleral spur. The largest study by Narayanaswamy had to exclude 25% of eyes from their analysis for this reason [29]. However, the OCT device software is improving over time and it may

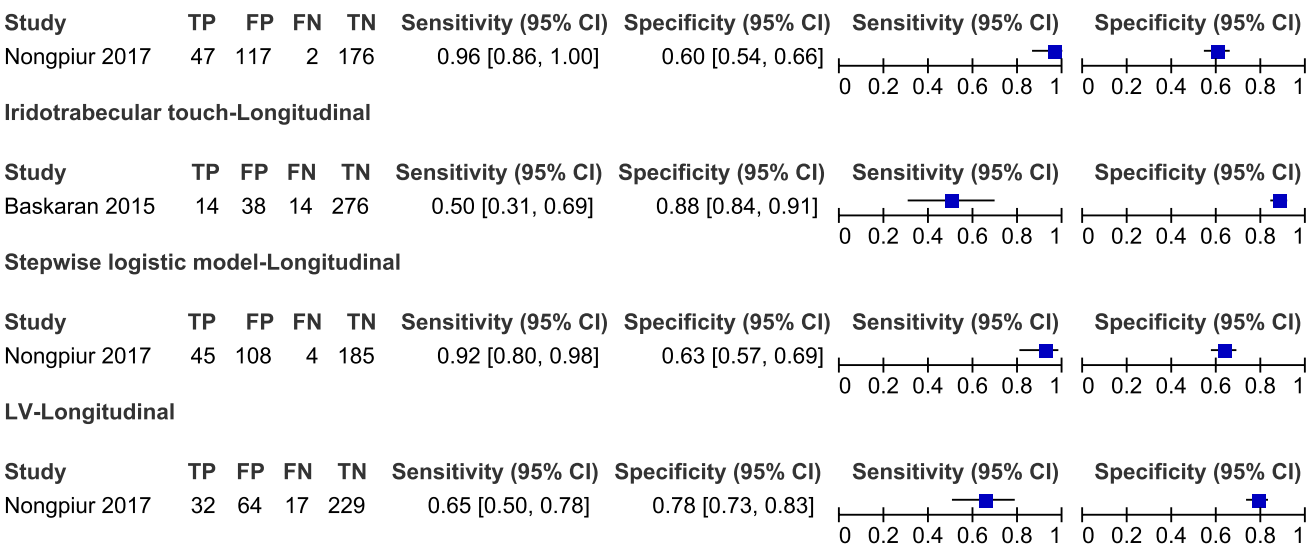

Fig. 16 Forest plot for longitudinal studies

soon be possible that results for all parameters are generated automatically.

The two included longitudinal studies showed that iridotrabecular touch and AOD750 have sensitivity above 95% for detecting eyes that would develop closed angles by gonioscopy 4 years later [31, 32]. However, they reported a high false-positive rate, leading to poor specificity. The longitudinal design allows us to analyse the natural history of eyes that are classified to have closed angles by AS-OCT but open by gonioscopy. These eyes correspond to false-positive data points in other studies. The results suggest that the eyes determined to have angle closure by AS-OCT should be carefully monitored as they are at higher risk of developing angle closure on gonioscopy.

Our review gives insight into possible clinical applications for AS-OCT in detecting angle closure. The good sensitivity corresponds to a strong NPV (reaching above 95%) and suggests that there might be a place for AS-OCT in ruling out angle closure. A negative result could be very reassuring in situations where a practitioner skilled in gonioscopy is not available. Potential use cases include telehealth consultations or in primary care practice. These situations are particularly relevant in the context of the COVID-19 pandemic when this review was written.

When the condition being tested for has a low prevalence in the population being tested, it is ideal if the specificity is high otherwise the PPV will be low. Despite AS-OCT generally showing specificity above 80%, the prevalence of angle closure is low enough that the PPV was often less than 50%. A positive result becomes difficult to interpret and would necessitate further testing.

We do not currently know if these false-positive errors are truly errors or if they represent eyes at greater risk of angle closure and glaucomatous damage. This uncertainty is partially caused by using gonioscopy to define angle closure. Nolan et al. (2006) have argued that gonioscopy may not be the most appropriate reference standard as it may miss cases of angle closure [47]. That if gonioscopy was being tested against AS-OCT as the reference standard, it would be shown to have low sensitivity and high specificity.

Another possible interpretation of the false-positive errors is that they represent pre-gonioscopic angle closure; that the eyes only determined to have angle closure by AS-OCT are at higher risk of glaucoma but have not yet progressed to angle closure by gonioscopy. Specifically, AS-OCT could allow for early detection of angle closure. This is supported by the two longitudinal studies that showed AS-OCT was very sensitive in detecting eyes that would progress from open to closed on gonioscopy [31, 32]. More longitudinal studies are needed to better determine the long-term risk of glaucoma and angle closure for patients that are deemed to be closed on AS-OCT but open by gonioscopy.

Due to its strong NPV, ease of use, objective measurements and possibility for earlier detection, AS-OCT may be ideal for initial assessment of patients at higher risk of angle closure. This may include patients from higher risk populations such as Asians, or those with structural risk factors. As an added benefit, AS-OCT gives information on iris configuration and anterior eye structure. This enables assessment of structural risk factors including pupillary block, large lens vault and large iris area [51–53].

When assessing the utility of AS-OCT for detecting angle closure, we should consider the shortcomings of our current tools. Many eyes with angle closure disease go unrecognised in developed countries and the rates are even worse in developing Asian countries. There are not enough clinicians skilled in gonioscopy to adequately assess for angle closure on a large scale. In this context, AS-OCT provides a tool for screening where there is very little else available. This provides an avenue to detect currently undiagnosed angle closure and reduce the long-term burden of blindness. Unfortunately, developing countries are currently unlikely to have access to an OCT device due to the prohibitive cost. However, this may change as the cost of technology decreases with time. Clinicians should consider the strengths and limitations of AS-OCT to determine how it may be safely used for their specific clinical needs.

Our review has been the first to perform a meta-analysis of data that assesses the accuracy of AS-OCT for detecting angle closure against gonioscopy as a reference standard. A review by the American Academy of Ophthalmology (2013) identified that AS-OCT may provide supplemental information when used alongside gonioscopy [13], whereas we found that AS-OCT has a strong NPV and may have a place in screening for angle closure. We found that AS-OCT may have specificity above 80% when certain parameters and thresholds are used. This contrasts with a review by Porporato et al. (2018) that reported the specificity to be low [14]. Despite this, we agreed that the PPV was often poor. It remains to be seen how the clinical utility of AS-OCT compares against other anterior chamber analysis modalities including Scheimpflug photography and Scanning Peripheral Anterior Chamber Depth Analyser.

There were several limitations of our review. There was substantial variation between studies in areas including gonioscopy criteria, AS-OCT positivity threshold and OCT device being used. We were therefore limited in what statistical analyses we were able to perform, making it difficult to draw firm conclusions on the utility of AS-OCT. We were unable to determine summary sensitivity and specificity values for each index parameter. We were also unable to perform a quantitative analysis of heterogeneity or quantitative comparison between index parameters.

To reduce heterogeneity, future studies should consider using non-visibility of 2 quadrants of PTM as the gonioscopy criterion if it matches clinical practice. Another approach would be to include results for several gonioscopy criteria as some studies have done. Future studies should analyse data using positivity thresholds established in previous studies if possible. If a new threshold is established, they should also validate their results using a separate population or by using a cross-validation procedure. Future studies should also avoid a case–control design.

Conclusion

Although the current literature is heterogenous in methodology, AS-OCT demonstrates good sensitivity and NPV. There are not enough clinicians skilled in gonioscopy to adequately assess for angle closure on a large scale, particularly in developing Asian countries. In this context, AS-OCT allows for earlier detection and provides a tool for screening where there is very little else available. This provides an avenue to detect currently undiagnosed angle closure and reduce the long-term burden of blindness. However, AS-OCT is not yet able to replace gonioscopy. Clinicians should consider whether the diagnostic accuracy of AS-OCT is acceptable for their specific clinical use before adopting it. More studies are needed to determine the utility of AS-OCT, including longitudinal studies to determine the significance of eyes classified to have closed angles by AS-OCT but open on gonioscopy.

Appendix 1

Full search strategy for Medline database.o

1. gonio*.mp. or exp Gonioscopy/
2. exp Tomography, Optical Coherence/ or optical coherence tomography.mp.
3. OCT.mp.
4. 2 or 3
5. narrow angle.mp.
6. closed angle.mp.
7. angle closure.mp.
8. Glaucoma, Angle-Closure/
9. 5 or 6 or 7 or 8
10. detect*.mp.
11. diagnos*.mp.
12. identif*.mp.
13. screen*.mp.
14. 10 or 11 or 12 or 13
15. 1 and 4 and 9 and 14

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Declarations

Ethics approval The need for ethics approval was waived by the institutional review board as this is a systematic review of existing literature.

Consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interest.

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