

The Diagnostic Accuracy of Low-Dose Computed Tomography in Diagnosing Urolithiasis: A Systematic Review and Meta-Analysis

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Abstract

Background: Urolithiasis is a prevalent health issue all over the world, To evaluate the diagnostic accuracy of low-dose computed tomography (LDCT) for detecting urolithiasis.

Methods: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was followed. PubMed, EMBASE and The Cochrane Library were searched for original diagnostic studies to identify all relevant studies published prior to May 2020. The index test was LDCT, and the reference standards were comprehensive diagnosis or standard-dose CT (SDCT).

Results: 17 studies with 1,761 patients and 2,053 stones were included for the quantitative analysis. The pooled sensitivity was 0.95 (95%CI: 0.93-0.97) in patient-based studies and 0.86 (95%CI: 0.76-0.93) in urolithiasis-based studies. The pooled specificity of LDCT were 0.97 (95%CI: 0.95-0.99) in patient-based studies and 0.98 (95%CI: 0.63-1.00) in urolithiasis-based studies. The Fagan nomogram of LDCT for diagnosis of urolithiasis showed that the probability of urolithiasis is 98% if the LDCT scan is positive and 6% if the LDCT scan is negative. The likelihood ratio plot showed that the summary positive pooled likelihood ratio (LRP) and negative likelihood ratio (LRN) for LDCT was in the left upper quadrant (LUQ) area.

Conclusions: LDCT has excellent diagnostic value in urolithiasis. LDCT can detect the urolithiasis specifically, but is limited to differentiate the contents of the stones.

Background

Characterized by renal colic pain, urolithiasis is a prevalent health issue all over the world, with its incidence rates ranging from 7–13% in North America, 5–9% in Europe, and 1–5% in Asia[1]. As one of the most common disorders in urinary tract, the recurrence rate of urolithiasis is up to 30–50% within 10 years of the first stone episode[2].

Compared with intravenous urogram (IVU) and plain x-ray of kidneys (KUB), unenhanced computed tomography (CT) has excellent sensitivity and specificity of over 95% of diagnosing urolithiasis, therefore unenhanced CT of the abdomen and pelvis is the first choice for patients with acute renal colic pain and suspicion of urolithiasis[3–7]. Nevertheless, unenhanced CT also has a higher radiation dose than IVU or KUB, leading to a higher risk of radiation hazard such as cancer[6]. To reduce the risk caused by the high radiation dose, reducing radiation dose during the evaluation of urinary stone has become of interest in the field of urology[7]. It is reported that a CT protocol with over 85% dose reduction can identify patients who have highly suspected urolithiasis and require urologic intervention effectively and safely[8]. However, the quality of CT images such as noise and artifacts, which compromises the diagnostic performance, will be significantly degraded due to simply lowering the radiation dose of the CT[9].

The diagnostic accuracy of LDCT for urolithiasis has been investigated in the former studies[10–11]. However, neither of the two studies differentiate the evaluation methods between patient-based and urolithiasis-based studies. In the patient-based studies, LDCT was performed to confirm the diagnosis of urolithiasis in suspected patients, and number of confirmed cases were reported. This is to say, LDCT was used to diagnose whether the suspected patients were urolithiasis in the patient-based studies. In the urolithiasis-based studies, LDCT was performed to confirm whether the suspected stones were true positive urinary stones, which means LDCT was used to differentiate whether the images were truly stones rather than phlebolith or others, and the number of stones were reported. Therefore, the purpose of this meta-analysis was to evaluate the sensitivity and specificity of LDCT for the diagnosis of urolithiasis from both patient-based and urolithiasis-based studies. Additionally, subgroup analyses for ultra-low-dose computed tomography (ULDCT) (average effective dose \leq 1 mSv) and LDCT were performed in both patient-based and urolithiasis-based group.

Methods

This meta-analysis was performed and written in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses-Diagnostic Test Accuracy (PRISMA-DTA)[12], Statement.

Literature Search

Two authors (S. Liang and L. Chang) searched on PubMed, EMBASE and The Cochrane Library from January 2000 to May 2020 independently by using the terms: "urinary calculi" OR "urolithiasis" OR "ureteral calculi" OR "ureterolithiasis" OR "kidney calculi" OR "nephrolithiasis" OR "colic", "sensitivity and specificity" OR "diagnostic accuracy", "Computed tomography" OR "low-dose CT". The articles were included by the following inclusion criteria: (a) prospective comparative studies which performed LDCT to diagnose urolithiasis in comparison to acceptable reference standard; (b) the studies reported the sensitivity, specificity and True positive (TP), False positive (FP), False negative (FN), True negative (TN); (c) the studies were written in English. Studies with insufficient or unspecific data were excluded.

Data extraction and quality assessment

Data were extracted by the same two independent readers (S. Liang and L. Chang) who performed the literature search and study selection. Disagreements were solved by a third reader (X. Li), who is a specialist in urinary imaging.

The two reviewers extracted the following information independently: the first author, the published year, the inclusion interval of patients, reference standard of urolithiasis, the characteristics of urolithiasis patients (number, average age, BMI and stone number), the characteristics of LDCT (slice, reconstruction technique, mAs, kVp and average dose) the values (true positives, false positives, true negatives, and false negatives) and urolithiasis character from each

included study. The Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool was then applied by S. Liang, L. Chang, and C. Wang independently. When there were differences in QUADAS scores between S. Liang and L. Chang, X. Li served as a third reviewer to settle discrepancies. The QUADAS is a 14-item scale designed to assess the quality of studies of diagnostic accuracy included in meta-analysis. The results of the quality assessment were summarized with RevMan version 5.3.5 (The Cochrane Collaboration, Copenhagen, Denmark)

Statistical Analysis

Statistical heterogeneity was assessed using I square test. Heterogeneity was interpreted as absent (I^2 : 0–25%), low (I^2 : 25.1–50%), moderate (I^2 : 50.1–75%), or high (I^2 : 75.1–100%). A random effects model was applied to estimate the continuous outcome data if the p value < 0.1 and an I^2 value > 50%, which indicates statistical heterogeneity[13]. Otherwise, a fixed-effects model was used.

Meta-Analysis

The index test was LDCT, and the reference standards were comprehensive diagnosis (including clinical passage, surgical removal, other imaging, other clinical information) or standard-dose CT (SDCT). The studies were divided into patient-based and urolithiasis-based group. Subgroup analysis of LDCT (average effective dose range 1 mSv to 3.5 mSv) and ULDCT (average effective dose \leq 1 mSv) was also divided into patient-based and urolithiasis-based group. The sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR) and 95% confidence intervals (95%CI) for the accuracy of LDCT were pooled via Stata version 14.0 (The StataCorp LP, Texas City, USA). The high pooled DOR reflects the high accuracy.

We used Deek test to examine the publication bias of the included studies. Stata version 14.0 (The StataCorp LP, Texas City, USA) were used to draw the forest plots providing the assessments of sensitivity and specificity, and summary receiver operating characteristic curves (SROC) in order to acquire the area under the curve (AUC) reflecting the diagnostic accuracy of LDCT. Results were compiled using PRISMA.

Results

Literature Search and Study Selection

819 full texts were retrieved after duplicates removed. Then the titles and abstracts of 381 studies were screened, of which 356 were excluded due to the following reasons: meta-analysis and systematic reviews (n = 13), reviews (n = 9), case reports (n = 30), editorial comments (n = 4), other topics (n = 299). 8 full-text articles were later excluded due to these reasons: retrospective studies (n = 4), without specific number of TP, FP, FN, TN (n = 3), without effective dose (n = 1). Finally, a total of 17 unique articles with 1,761 patients (mean age: 46.40) and 2,053 stones were included[14–30] for the quantitative analysis. 13 studies[14–26] were included in the former studies[10–11], and 4 studies[27–30] were new studies. Of the 17 studies, 12 studies were included in patient-based group and 5 studies were included in urolithiasis-based group. The process of the study selection is shown in Supplemental Fig. 1.

Quality Assessment

All of the 17 included articles were prospective studies. Generally, most of the quality indicators of the QUADAS-2 tool were met in these included studies.

The graphical display of the risk of bias and applicability assessment is shown in Supplemental Fig. 2, the details are shown in Supplemental Table 1. 5 studies[15, 20, 23, 29, 32] were at unclear risk of bias in patient selection, of which, 4 studies[15, 23, 29, 32] were due to the fact that the diagnosis of some patients were unclear and whether the patient samples enrolled met the criteria for continuance was not reported. Besides, one study[20] differentiated the patient selection inappropriately since patients already underwent CT scan of known urinary stones. What is more, 12 studies [15–21, 23, 25, 29–30] were at unclear risk of bias of concerning the results of LDCT examination because that the use of threshold was unclear. 4 studies[16, 17, 20, 28] were at unclear risk of bias in the flow and timing for the reasons that the information about the duration interval was unclear. There was unclear applicability concerns of patient selection because inappropriate exclusions were avoided in one study[22]. The conduct or interpretation of the index test had unclear risk in 3 studies[15, 23, 29] because whether the results of the index test obtained with the knowledge of the reference standard is unclear. There was unclear applicability concerns regarding the reference in the 2 studies[23, 29], because whether the results of the reference standard obtained with the knowledge of the index test is unclear. because the results comparing without the knowledge of the results of the index test. The result of Deek test to examine the publication bias of the included studies is that $p = 0.98 > 0.1$, which represents that there is no public bias (Supplemental Fig. 3).

Data Extraction and Meta-Analysis

Study characters were shown in Tables 1 and 2 \times 2 table, sensitivity, specificity and prevalence was shown in Supplemental Table 2. Taking all the 17 studies into consideration, the sensitivity estimates ranged from 0.70 to 0.98 and the specificity estimates ranged from 0.39 to 1.00. The result of heterogeneity test showed that 3 studies[20, 26, 30] have obvious heterogeneity (Supplemental Fig. 4).

Table 1
Summary of characteristics of the included studies.

Author	Inclusion interval	Patients				Reference standard	Low-dose CT			
		Number	Average Age	Average BMI	Stone Number		Slices	Reconstruction technique	mAs	kVp
Liu2000(14)	December 1996-July 1997	60	42	NR	37	Comprehensive diagnosis (Intravenous urography,IVU)	1	NR	280	120
Hamm2002(15)	November 2000-February 2001	109	49	NR	80	Comprehensive diagnosis (retrograde ureteropyelography)	4	NR	70	120
Tack2003(16)	October 2000-March 2001	106	45	26.2	38	Comprehensive diagnosis	4	NR	30	120
Kim2005(17)	January 2002-June 2003	116	44	NR	116	standard-dose CT	4	NR	50	120
Kluner2006(18)	March 2004-October 2004	142	47	NR	102	Comprehensive diagnosis (Ultrasound)	16	NR	20	120
Poletti2006(19)	NR	125	45	NR	184	standard-dose CT	16	NR	30	120
Mulkens2007(20)	June 2004-May 2005	150	50.23	24.87	158	Comprehensive diagnosis	6\16	NR	51\70	110\120
Fracchia2012(21)	March 2011-October 2011	101	53.4	NR	84	standard-dose CT	64	NR	30.9	120
Moore2014(22)	February 2012-May 2013	201	43.6	29.1	102	standard-dose CT	64	NR	NR	NR
Park2014(23)	May 2013-July 2013	69	48.7	24.37	101	standard-dose CT	NR	IR,MBIR	NR	NR
Kwon2015(24)	December 2012-February 2013	116	48.9	NR	197	standard-dose CT	256	IR	60	100
Malkawi2015(25)	August 2011-December 2011	18	41	28.7	27	standard-dose CT	64	IR	NR	NR
Park2015(26)	June 2003-September 2013	103	49.9	24.9	276	standard-dose CT	256	FBP,IMR	20	100
Fontarensky2015(27)	February 2013-October 2013	118	42.9	25.3	79	standard-dose CT	64	ASIR,MBIR	NR	80,100,120

*Comprehensive diagnosis includes clinical passage, surgical removal, other imaging and other clinical information

Author	Inclusion interval	Patients				Reference standard	Low-dose CT			
		Number	Average Age	Average BMI	Stone Number		Slices	Reconstruction technique	mAs	kVp
Koteshwar2016(28)	January 2011-December 2013	100	39.25	21.7	138	Comprehensive diagnosis	64	NR	70	120
Ahn2017(29)	January 2015-May 2015	92	50.8	NR	240	standard-dose CT	128	FBP,ADMIRE	60	80
Chi2018(30)	March 2014-August 2015	35	40.4	24.4	94	Comprehensive diagnosis	256	IR	60	100

***Comprehensive diagnosis includes clinical passage, surgical removal, other imaging and other clinical information**

The pooled results of sensitivity were 0.95 (95%CI: 0.93–0.97) in patient-based studies and 0.86 (95%CI: 0.76–0.93) in urolithiasis-based studies, respectively. The pooled specificity of LDCT were 0.97 (95%CI: 0.95–0.99) in patient-based studies and 0.98 (95%CI: 0.63–1.00) in urolithiasis-based studies, respectively. The forest plots were shown in Fig. 1 and the SROC curves were shown in Fig. 2. The heterogeneity was almost absent in the patient-based studies but high in the urolithiasis-based studies. The AUC were 0.99 (95%CI: 0.98–0.99) and 0.93 (95%CI: 0.91–0.95) in patient-based and urolithiasis-based studies. Additionally, the pooled PLR, NLR, DOR and the result of subgroup analysis were depicted in Supplemental Table 3.

The pooled sensitivity of the patient-based group was 0.97 in ULDCCT and 0.94 in LDCT, respectively. The pooled specificity of the patient-based group was 0.95 in ULDCCT and 0.97 in LDCT, respectively. The pooled sensitivity of the urolithiasis-based group was 0.85 in ULDCCT and 0.90 in LDCT, respectively. The pooled specificity of the urolithiasis-based group was 0.85 in ULDCCT and 0.96 in LDCT, respectively. The numbers were shown in Supplemental Table 4.

The Fagan nomogram of LDCT for diagnosis of gout showed the PLR and NLR, presenting the result that the probability of urolithiasis is 98% if the LDCT scan is positive and 6% if the LDCT scan is negative (Fig. 3), which means providing a patient is from a population with an average of 50% pre-test probability of urolithiasis, then a positive test result yields on average a post-test probability of 98%, and a negative test result yields on average a post-test probability of 6%. The likelihood ratio plot showed that the summary pooled likelihood ratio positive(LRP) and likelihood ratio negative(LRN) for LDCT was in the left upper quadrant(LUQ) area, which means LDCT can both exclude and confirm the urolithiasis(Fig. 4).

Discussion

The pooled sensitivity and specificity reflect that LDCT could be a useful test for diagnosing urolithiasis, with no major difference in the reference standard. What is more, ULDCCT also has an excellent clinical use according to the subgroup analysis. However, we found that the specificity appears to be low in line with the average effective dose. In our study, ULDCCT was defined as effective dose < 1.0 mSv. Similar to ours, a systematic review defining ULDCCT as effective dose < 1.9 mSv reported that LDCT and ULDCCT have high diagnostic accuracy, sensitivity and specificity despite significant radiation dose reduction in comparison to SDCT[31], though they may not be as effective in detecting stones < 3 mm in size or in patients with a BMI of > 30 kg/m²[32]. Both SDCT and LDCT have high diagnostic accuracy of ureteral uric acid stones, while the detection of uric acid stones is reduced when LDCT is at ≤ 15mAs[33]. Nevertheless, how low can the effective dose actually be still remains unknown.

In addition, the subgroup analysis of patient-based and urolithiasis-based studies shows that the pooled sensitivity of urolithiasis-based studies is much lower than that of the patient-based studies, indicating that the LDCT diagnoses urolithiasis accurately. However, LDCT may be problematic with small stones and evidence of distal ureteral obstruction[34]. The size and location of the stones may cause false-positive and false-negative findings, affecting the sensitivity and specificity. In the studies reporting the size of stone, the sensitivity declines when the size of stone declines[14, 17, 19]. Nevertheless, the thresholds of the stone were 5mm[14], 3mm[19] and 2mm[17] respectively. The specific value of the stone threshold remains uncertain. Phlebolith may cause the false-positive and false-negative findings, especially in distal ureter and VUJ[20, 28]. What is more, heterogeneity of renal stroma may also make it difficult to differentiate between hyperdense pyramids and small calculus, thus causing false-positive findings[19]. In addition, passed off calculus should be taken into consideration as no calculus was detected on CT with haematuria and positive urine analysis[28].

The quality of the CT images may significantly degrade due to the lower radiation dose, therefore reconstruction techniques were implied in CT images. LDCT of urolithiasis can be feasible in overweight patients with a BMI between 25 and 35 kg/m² with iterative image reconstruction algorithms[35]. Time has witnessed the development of the reconstruction algorithms during these years. Conventional filtered back projection (FBP) reconstruction technique has been well received due to its quick imaging technology for decades[36]. Iterative reconstruction (IR) algorithms have been introduced to improve image quality with less image noise[37–38]. Advanced modeled IR (ADMIRE), adaptive statistical IR (ASIR), iterative model reconstruction (IMR), sinogram-affirmed iterative reconstruction (SAFIRE), are widely used in current clinical field[39]. Additionally, artificial intelligence (AI), which uses various data mining algorithms such as machine learning, deep learning, and cascading convolutional neural network model, has also been widely applied as feasible and highly-accurate ways in the diagnosis of urolithiasis[40–41].

The first step of managing urolithiasis is accurate diagnosis, and after it is to figure out the components of the stones[42]. The most common urinary stones, calcium oxalate stones, accounts for 75–80%, and then it is uric acid stone and cystine stone taking up for 7–10% and 1%, respectively[43]. However, in a recent meta-analysis including 21 studies found that dual-energy CT (DECT), with pooled sensitivity of 0.88 and specificity of 0.98, is an accurate test for

diagnosis of uric acid stones[44]. In general, LDCT is highly accurate for diagnosis of urolithiasis, whereas DECT can accurately differentiate uric acid from non-uric acid stones.

Conclusions

LDCT has excellent diagnostic value in urolithiasis given the high sensitivity and specificity of patient-based and urolithiasis-based groups. Our meta-analysis highlights the difference of the results between patient-based and urolithiasis-based groups, indicating that LDCT can detect the urolithiasis specifically, but is limited to differentiate the contents of the stones. At the meantime, the exact dose of ULDCCT remains controversial, inadequate studies about ULDCCT may contribute to inevitable error in the subgroup analysis. Therefore, future studies should focus on the composition of the stones and ULDCCT.

Abbreviations

DECT
dual-energy CT; IVU = intravenous urogram; KUB = plain x-ray of kidneys; LDCT = low-dose CT; SDCT = standard-dose CT; ULDCCT = ultra-low-dose CT

Declarations

Acknowledgments

Not applicable.

Authors' contributions

S. Liang: conception and design, project development, article research, article review, pictures production, manuscript writing and revising; L.Chang : conception and design, project development, article research, article review, pictures production, manuscript writing and revising; C. Wang: project development and manuscript revising; S. Lu: project development and manuscript revising; C. Sun: project development, supervision and manuscript revising; R. Zhao: project development, supervision and manuscript revising; X.Li:conception and design, project development, supervision and manuscript revising. All authors have read and approved the final manuscript.

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Availability of data and materials

The datasets in this work is available from the corresponding author.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

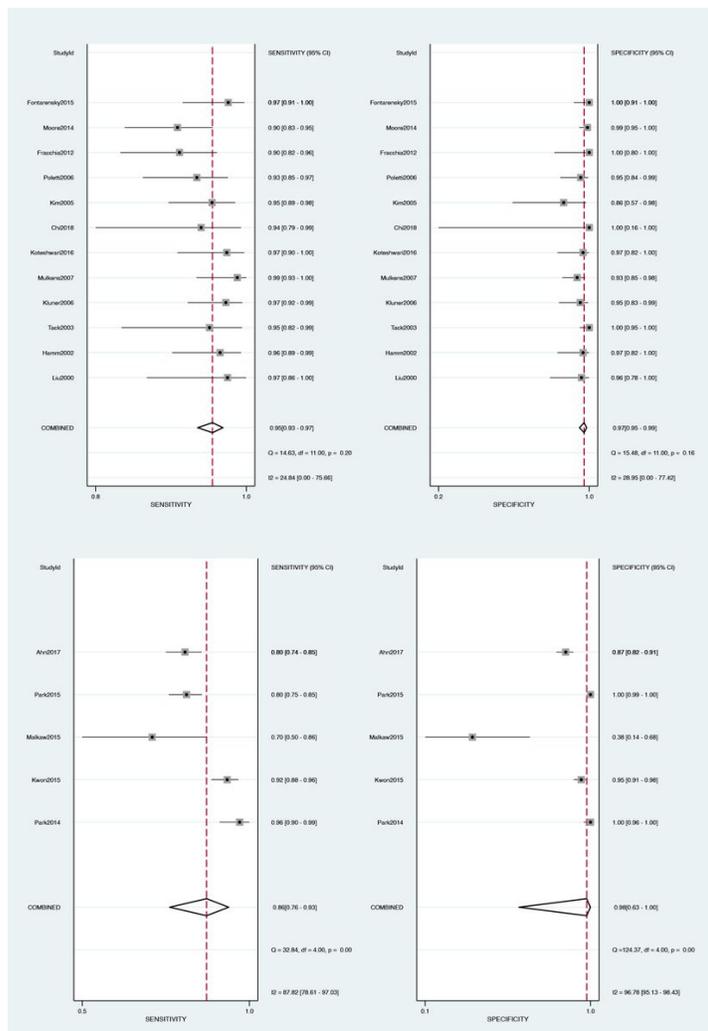


Figure 1

Figure 1

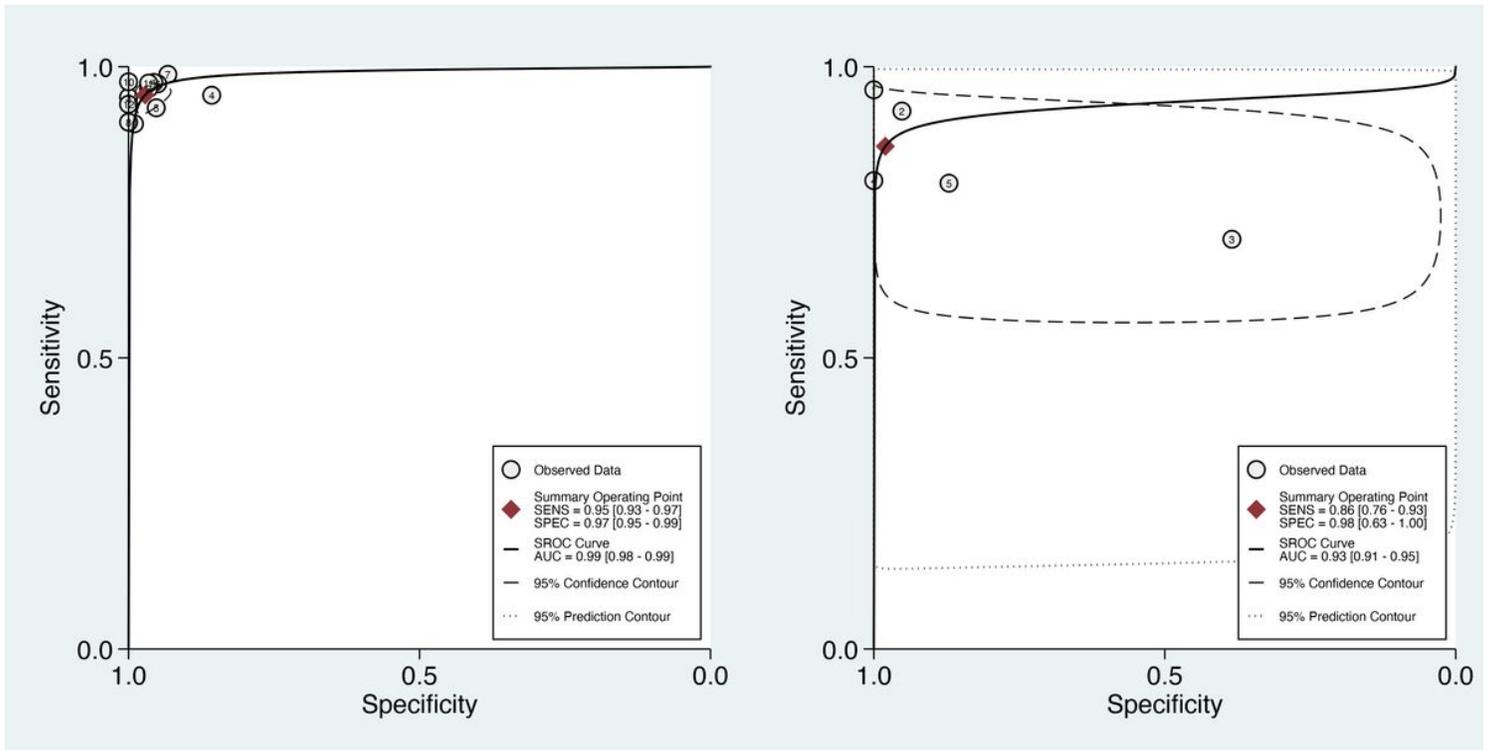


Figure 2

Figure 2

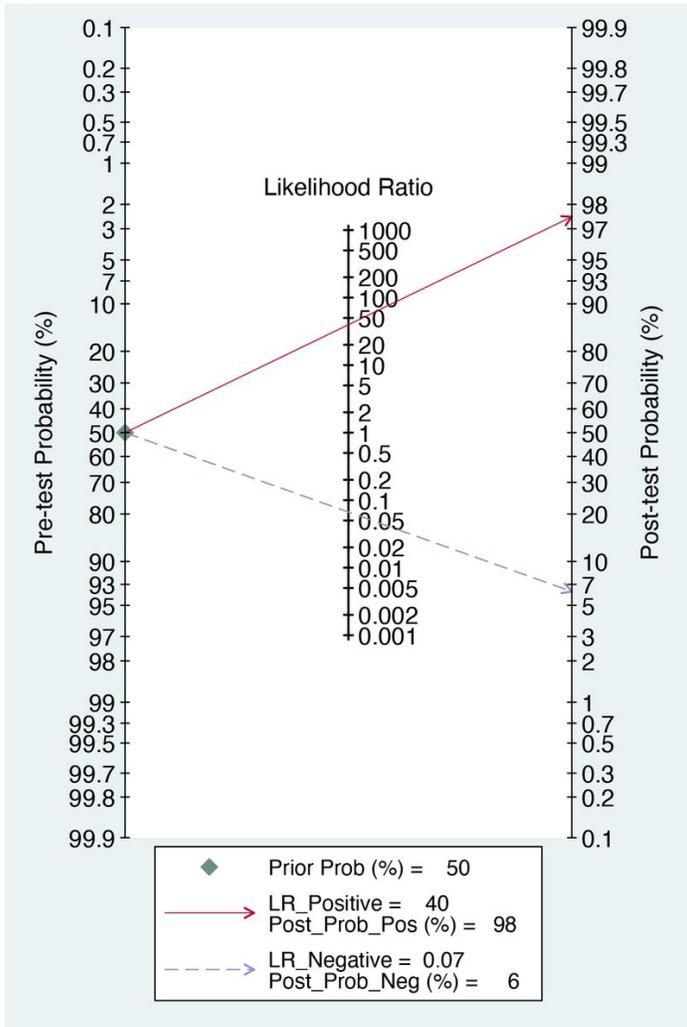


Figure 3

Figure 3

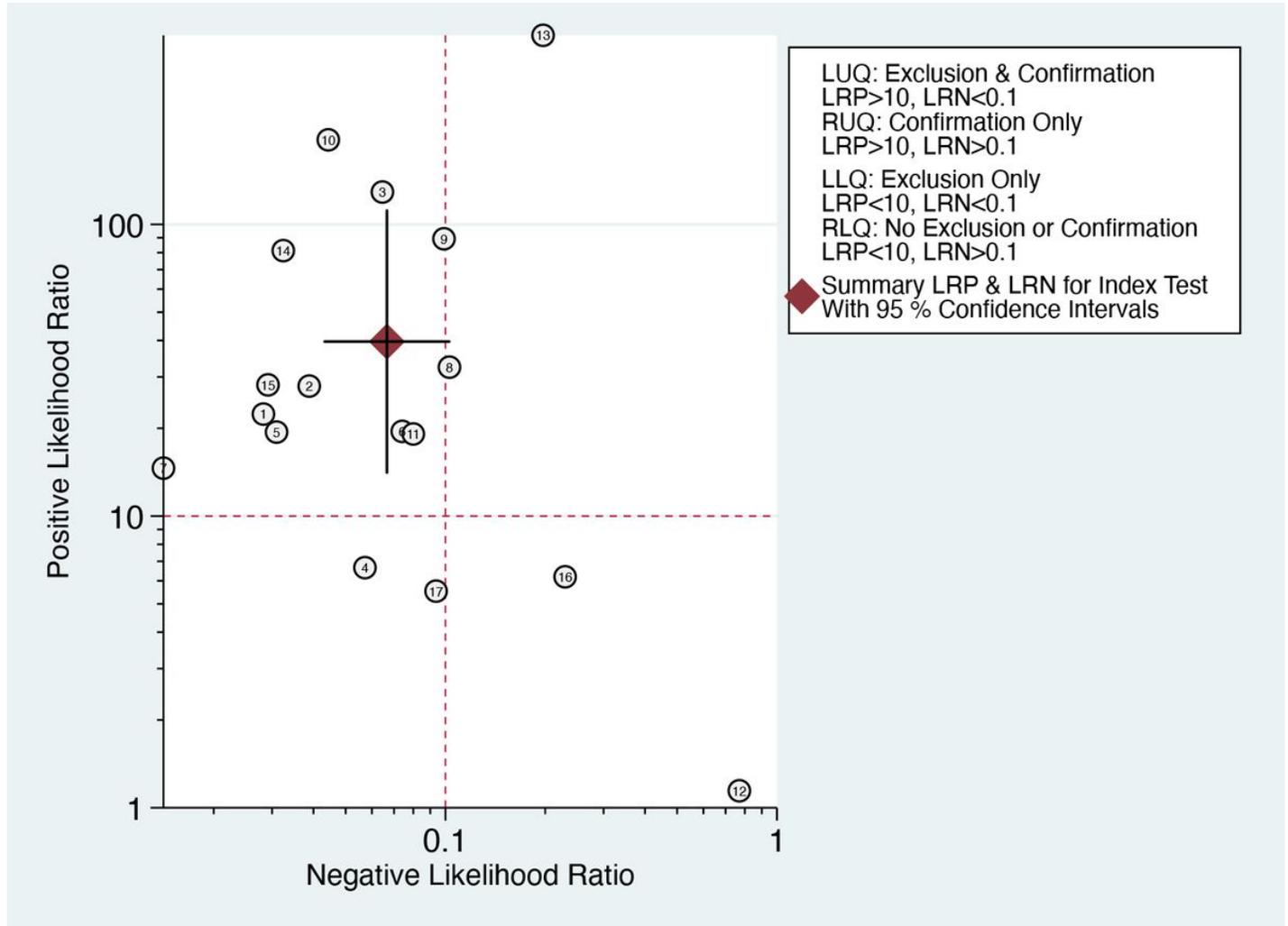


Figure 4

Figure 4

Supplementary Files

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