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Review Article

Diagnostic performance of circulating tumor cells in lung cancer: a systematic review and meta-analysis

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Abstract: *Background:* Previous studies have reported conflicting findings regarding the diagnostic value of circulating tumor cells (CTCs) for detecting lung cancer. In this study, we performed a meta-analysis to consolidate all the current evidence to assess the diagnostic value of CTCs in lung cancer. *Materials & methods:* We conducted a literature search of the PubMed, Embase, and Cochrane library databases from inception to June 2016 to identify relevant studies. The quality of the studies was assessed using the revised Quality Assessment for Studies of Diagnostic Accuracy tool. The sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio, and summary receiver operating characteristic (sROC) curve for CTC detection in individual studies were calculated and analyzed using a random effects model. Deek's funnel plots were used to evaluate publication bias. *Results:* Fifteen studies were included in the final meta-analysis. The pooled sensitivity of CTCs for lung cancer diagnosis was 0.63 (95% confidence interval [CI]: 0.60-0.65), and the pooled specificity was 0.94 (95% CI: 0.92-0.95). The pooled positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio were 15.62 (95% CI: 5.88-41.51), 0.39 (95% CI: 0.30-0.49), and 41.0 (95% CI: 16.6-101.3), respectively. The observed area under the sROC curve for CTCs and lung cancer was 0.9298. *Conclusion:* This systematic review suggests that CTCs detection alone cannot be recommended as a screening test for lung cancer. However, it might be used as a noninvasive method for the confirmation of the lung cancer diagnosis.

Keywords: Lung cancer, circulating tumor cells, diagnostic accuracy, meta-analysis

Introduction

Lung cancer is the most frequently diagnosed cancer globally and the leading cause of cancer-associated deaths [1]. It was estimated that 1.8 million new cases were diagnosed in 2013 and 1.6 million deaths occurred worldwide. Among these deaths, 62% occurred in developing countries, whereas 38% occurred in developed countries [2]. The 5-year survival rate for this disease still remains at only approximately 15%, and the majority of patients present with advanced disease at the time of diagnosis [3]. It is well known that early diagnosis and treatment are of great value in improving the survival rate and mortality. Low-dose computed tomography (LDCT) has been an effective screening tool for the early diagnosis of lung cancer, and its use has reduced the mortality of the disease by 20% [4]. However, these techniques require human interpretation and are thus prone to human error. Furthermore, the high rate of false positive detection of central tumors and small nodules has also raised concerns in the clinical settings [5].

Circulating tumor cells (CTCs) were first reported by Ashworth in 1869 [6] and were defined as tumor cells circulating in the peripheral blood that originated from the primary site of disease or metastatic neoplasms. Thus, it was hypothesized that the detection of CTCs in the peripheral blood may contribute to improved diagnosis and therapy in cancer patients. During the past decade, the detection of CTCs has been widely applied in the diagnosis of various cancers including lung cancer [7-10]. Many of the studies have shown that CTCs have potential value in assisting the diagnosis, evaluation of prognosis, and monitoring of the response to anticancer therapy [11-13]. Consistent with their obvious clinical relevance, CTCs have

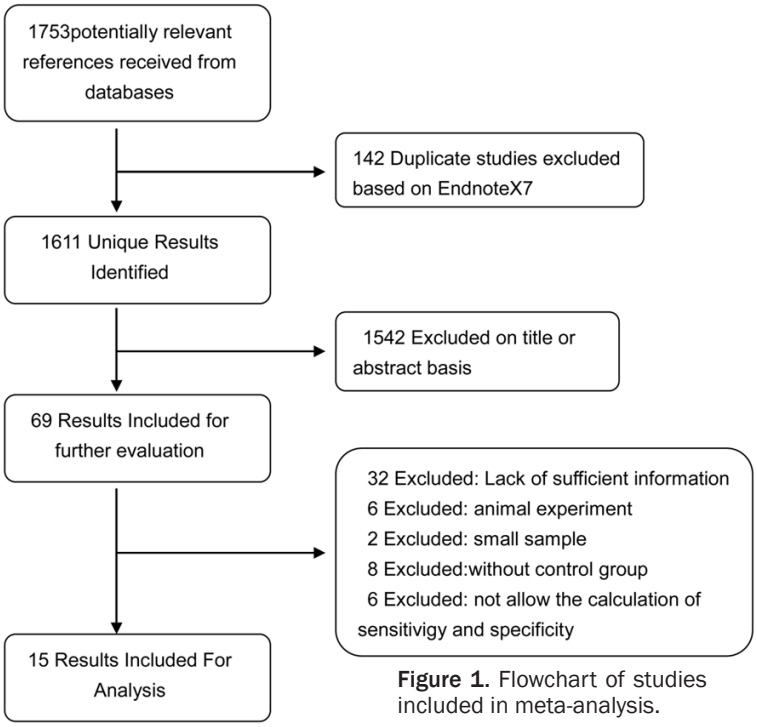

Figure 1. Flowchart of studies included in meta-analysis.

been recommended by the American Society of Clinical Oncology (ASCO) as acceptable novel tumor markers [14].

Although earlier studies suggested that CTCs can be used as diagnostic and predictive markers in lung cancers patients [15-19], their diagnostic accuracy has been variable, with a sensitivity ranging from 30% to 91% and a specificity ranging from 67% to 100% [15-29]. Therefore, the objective of our study was to perform a comprehensive systematic review and meta-analysis of the published literature to systematically and quantitatively evaluate the accuracy of CTC evaluation for lung cancer screening.

Materials and methods

Search strategy

Our study was performed according to the guidelines for diagnostic meta-analyses [30, 31]. A systematic literature search was conducted in the PubMed, Embase, and Cochrane Library databases for relevant articles published before June 14, 2016. The electronic databases were searched using the following keywords: “lung cancer”, “lung neoplasm”, “lung carcinoma”, and “circulating tumor cells”. The MeSH terms used for searching included “neoplastic cells, circulating” and “lung neoplasms”. The references cited in all of the reviewed studies were also searched manually to identify additional eligible articles.

Selection criteria

Studies were included for analysis if they meet the following criteria: (1) studies regarding the diagnosis of lung cancer with CTCs; (2) studies with reference standards for lung cancer diagnosis; (3) the numbers of true positive (TP), false positive (FP), false negative (FN), and true negative (TN) cases were available or could be calculated to construct 2×2 contingency tables; (4) the number of enrolled patients was at least 30; and (5) papers were published in the English language literature. Moreover, for studies based on the same patient population, only the most informative study was included. The exclusion criteria were: (1) insufficient data to construct 2×2 contingency tables; (2) duplicate studies; and (3) commentaries, meeting abstracts, case-reports, review articles, or letters.

Data extraction and quality assessment

Information from each of the eligible studies was extracted by two investigators. Any disagreements were solved unanimously via discussion. The following information was extracted from each publication: name of the first author, year of publication, country of study, number of participants, tumor stage distribution of patients, markers used, methods to detect CTCs and diagnostic performance (TP, FP, FN, and TN). If the data were not directly reported, they were calculated based on the sensitivity (SEN) and specificity (SPE) data.

The quality of the studies was critically appraised independently by two reviewers. Quality assessment was conducted in each of the available studies according to the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) guidelines [32], which are consid-

Table 1. Summary of the selected studies included in meta-analysis

Study	Year	Country	Patients/ controls	Age (median)	Male%	Type of lung cancer	Tumor stage	Marker used	Detection method	TP	FP	FN	TN
Peck	1998	China	86/62	66	66.3	ADC 47 SQC 17 SMC 15 others 7	I-IV	CK-19	RT-PCR	32	1	54	61
Kurusu	1999	Japan	103/47	68	73.8	ADC 66 SQC 37	I-III	CEA	RT-PCR	62	0	41	47
De Luca	2000	Italy	30/38	-	-	-	IV	EGFR	RT-PCR	17	4	13	34
Huang	2007	China	51/40	58.6	52.9	ADC 21 SQC 30	I-IV	CK-19	ICC	26	0	25	40
Liu	2008	China	134/186	-	-	ADC 44 SQC 40 SMC 31 others 19	I-IV	BJ-TSA-9	RT-PCR	76	1	58	167
								Pre-proGRP		46	6	88	180
								SCC		32	12	102	174
								LUNX		25	8	109	178
								KRT-19		78	10	56	176
Tanaka	2009	Japan	125/25	-	-	ADC 85 SQC 22 SMC 9 others 9	I-IV	CEA	Cell Search	38	3	87	22
Wu	2009	China	47/31	-	-	ADC 27 SQC 7 SMC 13	I-IV	A594 cell	ICC	30	0	17	31
Devriese	2012	The Netherlands	46/46	58	63	ADC 30 SQC 8 others 8	III-IV	CK-7	RT-PCR	32	6	14	40
								CK-19		42	0	4	46
								EGP		32	2	14	44
								FN1		39	0	7	46
Chen	2013	China	42/10	62.2	-	14 SCC 19 ADC 9 others	I-IV	CK-19	ICC	20	0	22	10
Katseli	2013	Greece	125/71	65	72	37 SCC 58 ADC 23 SCLC 7 others	I-IV	CK-19	RT-PCR	57	5	68	66
								PTHrP		81	5	44	66
								LUNX		35	4	90	67
Lou	2013	China	72/44	58	66.7	18 SCC 42 ADC 12 others	I-IV	KB cells	LT-PCR	59	3	13	41
Yu	2013	China	153/113	59.4	64.8	51 SCC 102 ADC	I-IV	FR	q-PCR	112	37	41	76
Man	2014	China	254/126	64	51.2	154 ADC 100 others	I-IV	CLCA2	RT-PCR	195	6	59	120
								hTERT		144	0	110	126
								CK-7		195	0	59	126
								HMMR		178	6	76	120
Zhu	2014	China	74/40	63	68	25 SCC 41 ADC 8 others	I-IV	EpCAM	RT-PCR	34	2	40	38
								MUC1		32	1	42	39
Fiorelli	2015	Italy	60/17	69	83.3	18 SCC 29 ADC 13 others	I-IV	MF	ICC	54	1	6	16

Abbreviations: CK, Cytokeratin; CEA, carcinoembryonic antigen; EGFR, epidermal growthfactorreceptor; TSA-9, tumorspecificantigen9; Pre-proGRP, pre-progastrin releasing peptide; SCC, squamous cell carcinoma antigen; LUNX, lung-specific X protein; KRT-19, Keratin 19; A594 cell, Alexa Flora 594 cell; EGP, human epithelial glycoprotein; FN1, fibronectin 1; PTHrP, parathyroid hormone-related protein; FR, folate receptor; CLCA2, Ca^{2+}-activated chloride channel-2; hTERT, human telomerase catalytic subunit; HMMR, hyaluronanmediated motility receptor; EpCAM, epithelial cell adhesion molecule; MF, malignant features; RT-PCR, reverse transcriptionpolymerase chain reaction; LT-PCR, ligand-targeted polymerase chain reaction; ADC, adenocarcinoma; SQC, squamous cell carcinoma; ICC, immunocytochemistry.

ered to have a more precise rating of bias and applicability of primary studies than the original tool.

Statistical methods

We used a bivariate regression approach to estimate the pooled SEN, SPE, positive likelihood ratio (PLR), negative LR (NLR), diagnostic odds ratio (DOR), and summary receiver operating characteristic (sROC) curves with their corresponding 95% confidence intervals (CIs) to summarize the results. If a particular study included several markers for CTC detection, the marker with the best SPE or the best SEN was used for the analysis of the pooled diagnostic accuracy. The Q test and I-square (I^2) statistics were used to evaluate heterogeneity, where $I^2 \geq 50\%$ or $P \leq 0.05$ suggested substantial heterogeneity across studies. During these circumstances, a random effects model (DerSimonian Laird method) was used for analysis;

Table 2. Overall quality assessment of the selected studies (based on QUADAS-2 questionnaire)

Studies	Risk of bias			Flow and timing	Applicability		
	Patient selection	Index test	Reference standard		Patient selection	Index test	Reference standard
Peck	H	L	L	L	H	L	L
Kurusu	L	L	U	L	L	L	U
De Luca	L	L	L	L	L	L	L
Huang	H	L	L	L	H	L	L
Liu	L	L	L	U	L	L	L
Tanaka	H	L	U	L	H	L	U
Wu	H	L	L	L	H	L	L
Devriese	L	L	L	L	L	L	L
Chen	L	L	H	L	L	L	H
Katseli	H	L	U	L	H	L	U
Lou	L	L	L	U	L	L	L
Yu	L	L	L	L	L	L	L
Man	L	L	H	U	L	L	H
Zhu	L	H	L	H	L	H	L
Fiorelli	L	L	L	L	L	L	L

H = High risk; L = Low risk; U = Unclear.

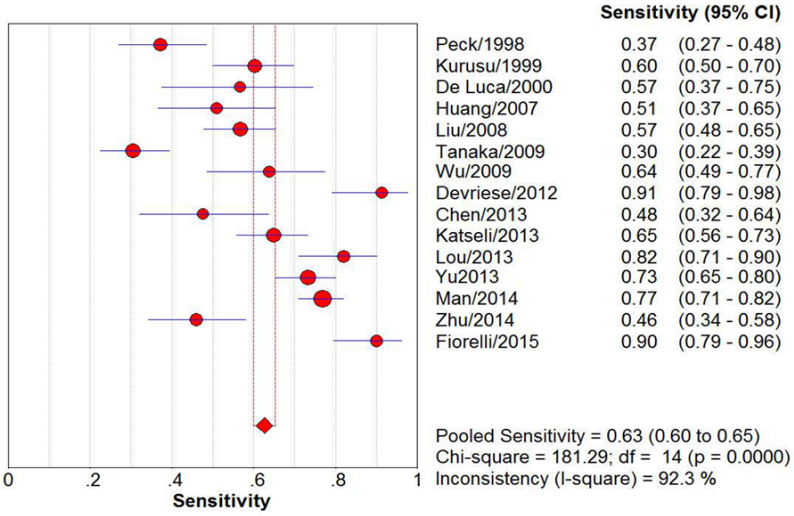

Figure 2. Forest plot showing the estimated sensitivity of CTCs in the included studies. The size of each dot is proportional to sample size. The center of each dot and the horizontal line show the sensitivity and corresponding 95% confidence intervals (CI), respectively. The center of the diamond indicates overall sensitivity and the ends correspond to 95% CI.

otherwise, a fixed effects model (Mantel-Haenszel method) was applied [33, 34]. Additionally, we calculated the Spearman correlation coefficient to analyze the diagnostic threshold effects.

To explore the possible sources of heterogeneity among the eligible studies, a meta-regression analysis was performed according to the characteristics of the included studies. Furthermore, studies were stratified by marker type, country of study origin, detection method, and sample size to perform subgroup analyses.

Evidence of publication bias was evaluated by Deek's funnel plot analysis (a regression of diagnostic log odds ratio against 1/sqn't). A non-zero slope coefficient suggested significant small study bias [34]. All calculations were performed using Stata software (version 12.0, College Station, TX) and Meta-Disc 1.4 (XI Cochrane Colloquium, Barcelona, Spain).

Results

Search results

A total of 1753 articles were identified based on the electronic searches of the databases. We excluded 142 papers describing duplicate studies using Endnote X7 software. Upon further review of the abstracts, 1542 articles were excluded. Thereafter, based on the inclusion criteria, an additional 54 articles were excluded, and thus, 15 studies [15-29] including 2298 patients were finally selected for the analysis. A detailed description of the search strategy is illustrated in **Figure 1**.

Characteristics of the eligible studies and quality assessment

The characteristics of the individual studies are provided in **Table 1**. Among the 15 total studies

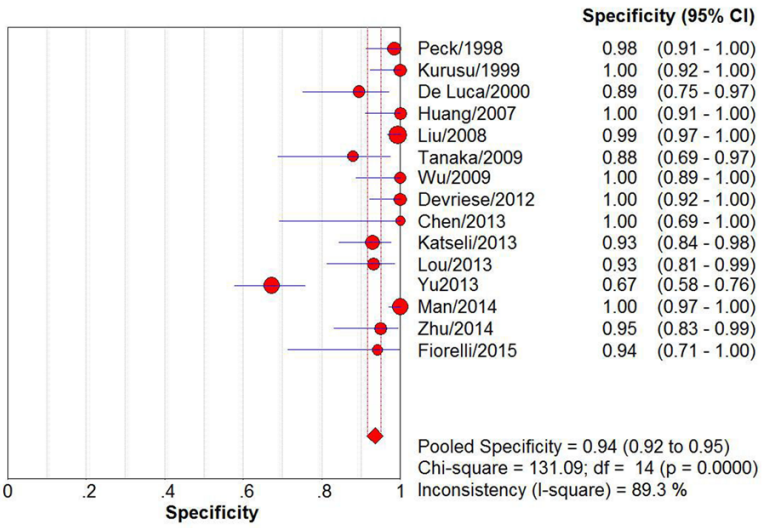

Figure 3. Forest plot showing the estimated specificity of CTCs in the included studies. The size of each dot is proportional to sample size. The center of each dot and the horizontal line show the specificity and corresponding 95% confidence intervals (CI), respectively. The center of the diamond indicates overall specificity and the ends correspond to 95% CI.

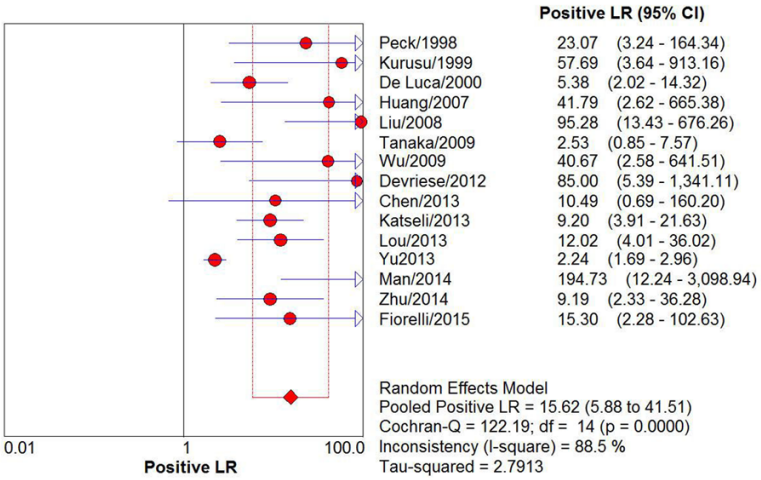

Figure 4. Forest plot showing the pooled positive likelihood ratio (PLR) for lung cancer diagnosis based on CTC evaluation. The size of each dot is proportional to sample size. The center of each dot and the horizontal line show the PLR and corresponding 95% confidence intervals (CI), respectively. The center of the diamond indicates overall PLR and the ends correspond to 95% CI.

identified based on the search strategy, 11 studies were performed in Asia [15, 16, 18, 20, 22-24, 26-29] and 4 in Europe [17, 19, 21, 25]. All but three studies [17, 20, 21] included lung cancer patients with stage I-IV disease. A total of five studies [17, 23, 25, 27, 28] used several markers for CTC detection, and the other 10 studies [15, 16, 18-22, 24, 26, 29] used only one marker for detection. The polymerase chain reaction (PCR)-based method for detection was used in 10 studies [15, 17, 18, 20, 21, 23, 25-28], whereas an immunological method was used in the other five studies [16, 19, 22, 24, 29].

In addition, we applied the QUADAS-2 questionnaire to assess the quality of the included studies, and the details are listed in **Table 2**. Overall, the study quality was satisfactory.

Diagnostic assessment

The pooled SEN of CTCs for lung cancer diagnosis was 0.63 (95% CI: 0.60-0.65) as seen in **Figure 2**, and the pooled SPE was 0.94 (95% CI: 0.92-0.95) as seen in **Figure 3**. In addition, the pooled PLR, NLR, and DOR were 15.62 (95% CI: 5.88-41.51) (**Figure 4**), 0.39 (95% CI: 0.30-0.49) (**Figure 5**), and 41.0 (95% CI: 16.6-101.3) (**Figure 6**), respectively. The sROC curve analysis illustrated the relationship between SEN and SPE (**Figure 7**). The area under the curve (AUC) for CTCs and lung cancer was 0.9298, indicating that CTCs are a useful biomarker for lung cancer diagnosis.

Univariate meta-regression and subgroup analysis

The heterogeneity I^2 values for SEN, SPE, PLR, NLR, and DOR were 92.3%, 89.3%, 88.5%, 91.2%, and 79.3%, respectively, indicating the presence of significant heterogeneity among the included studies. The Spearman correlation coefficient value was 0.136 (P = 0.630), which indicated that heterogeneity was not likely due to the threshold effect. Thus, we performed meta-regression and subgroup analyses to explore

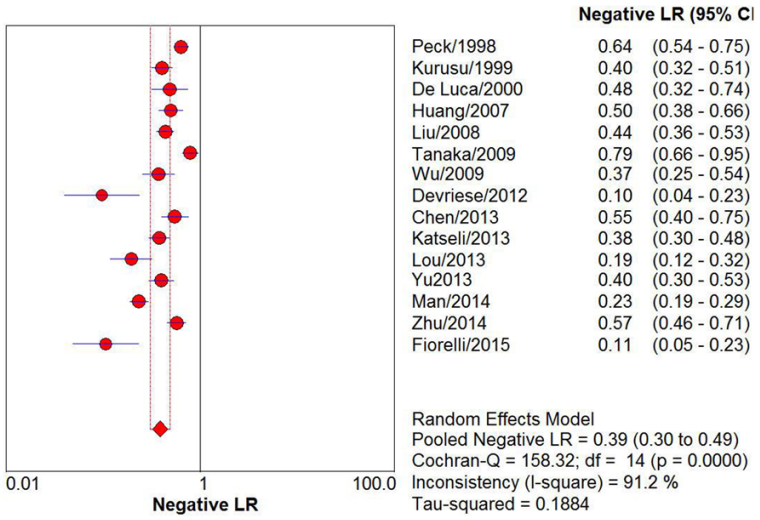

Figure 5. Forest plot showing the pooled negative likelihood ratio (NLR) for lung cancer diagnosis based on CTC evaluation. The size of each dot is proportional to sample size. The center of each dot and the horizontal line show the NLR and corresponding 95% confidence intervals (CI), respectively. The center of the diamond indicates overall NLR and the ends correspond to 95% CI.

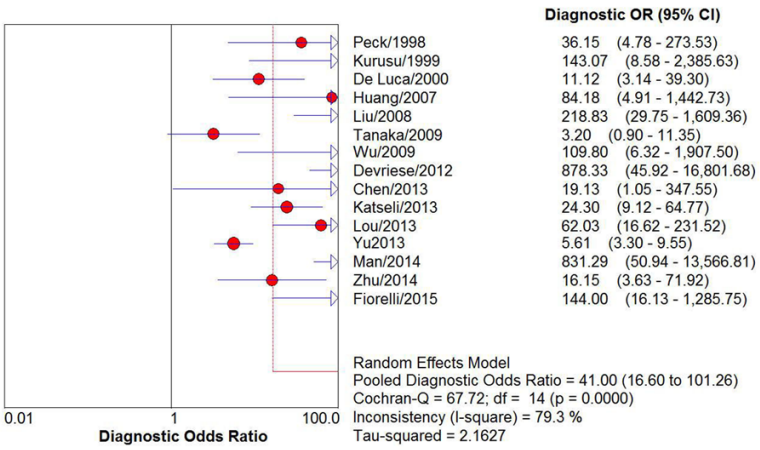

Figure 6. Forest plot showing the diagnostic odds ratio (DOR) for lung cancer diagnosis based on CTC evaluation. The size of each dot is proportional to sample size. The center of each dot and the horizontal line show the DOR and corresponding 95% confidence intervals (CI), respectively. The center of the diamond indicates overall DOR and the ends correspond to 95% CI.

the potential sources of heterogeneity. Meta-regression analysis showed that the sample size, type of marker used for CTC detection, and ethnicity of the patients may have contributed to the significant heterogeneity. As shown in **Table 3**, the subgroup analysis of studies with smaller sample size (100 subjects) yielded a SEN value of 0.68, a SPE of 0.97, and an AUC value of 0.9519. In contrast, the studies with a larger sample size had significantly decreased SEN, SPE, and AUC values. After carefully reading the original articles, we observed that the studies with smaller sample size groups enrolled more advanced patients, which indicated that the value of CTCs in the diagnosis of lung cancer may differ between tumor stages. In the subgroup analysis based on ethnicity, we observed a SEN value of 0.60 (95% CI: 0.57-0.63), a SPE value of 0.93 (95% CI: 0.91-0.95), and an AUC value of 0.788 for the Asian group. However, the European group displayed higher SEN, SPE, and AUC values of 0.74 (95% CI: 0.69-0.80), 0.94 (95% CI: 0.90-0.97), and 0.9574, respectively. Moreover, the subgroup analyses based on the markers showed that the CTCs detected by the marker cytokeratin 19 (CK19) had a SEN value of 0.57 (95% CI: 0.52-0.63) and a SPE value of 0.97 (95% CI: 0.94-0.99), whereas CTCs detected by carcinoembryonic antigen (CEA) had SEN and SPE values of 0.44 (95% CI: 0.37-0.51) and 0.96 (95% CI: 0.88-0.99), respectively. This data set suggested that there were no significant differences based on the use of these two for CTC detection. A similar pattern was observed in the subgroup analysis based on the CTCs detection methods. All these data are shown in **Table 3**. Thus, factors like markers and detection methods did not substantially affect the diagnostic accuracy of CTCs, and the influencing factors are complex.

Assessment of publication bias

Finally, we also assessed the publication bias in the studies included in the present meta-

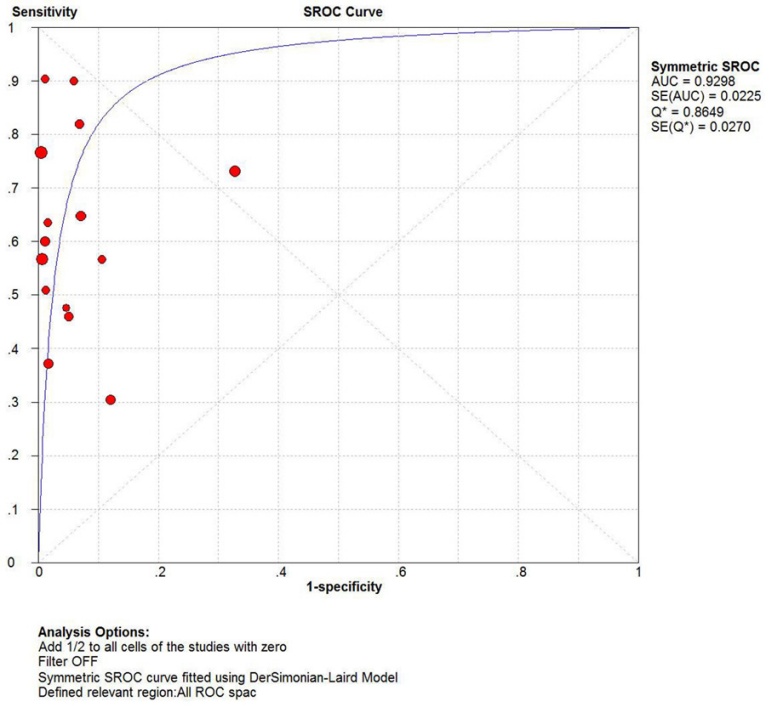

Figure 7. Summary receiver operating characteristic (sROC) curve showing the diagnostic performance of CTCs for lung cancer.

analysis. As seen in **Figure 8**, there was no obvious asymmetry in the funnel plot. The results of the Deeks test showed that there was no significant publication bias (P = 0.307) among the 15 studies investigating the diagnostic accuracy of CTCs for lung cancer.

Discussion

There is growing enthusiasm for the use of CTCs in the diagnosis of lung cancer due to several limitations of the conventional screening tests and their more invasive nature that pose logistic difficulties for tumor sampling [35]. However, the reporting of variable data on the diagnostic efficacy of CTC-based molecular detection methods [17, 25, 36] poses a big question. There have been different meta-analyses about the use of CTCs in the detection of other cancers, including a meta-analysis conducted by Liang *et al.* [37] that reported pooled SEN and SPE values for CTC detection in patients with ovarian cancer of 0.67 and 0.78, respectively. Tang *et al.* [38] reported that the pooled SEN and SPE for CTC detection in patients with gastric cancer were 0.42 and 0.99, respectively. However, in patients with bladder and urothelial cancer, the overall SEN and SPE of CTC detection were 0.35 and 0.89, respectively [39]. The present study is the first meta-analysis to estimate the pooled diagnostic accuracy of CTC detection protocols in lung cancer.

Our results suggested that CTC detection assays in patients with lung cancer had relatively limited diagnostic value, because it failed to identify more than two-thirds of the patients (SEN was only 0.63). However, the SPE was quite high (0.94) as observed in gastric, bladder, and urothelial cancers. The likelihood ratios described the discriminatory properties of positive and negative test results. A PLR greater than 10 and a NLR less than 0.1 have been noted as providing convincing diagnostic evidence, whereas those above 5 and below 0.2 give strong diagnostic evidence [40]. In our study, the PLR value of 15.62 suggested that few patients in whom CTCs were detected would be falsely diagnosed with lung cancer as compared with healthy controls. However, there is still a possibility of patients having lung cancer even though the CTC assay results are negative, because the NLR value was only 0.39, which meant that the probability of someone in whom CTCs were not detected having lung cancer was 39%. Similarly, the high AUC (0.9298) value reflected the overall high diagnostic accuracy of CTC detection. These data suggested that CTC detection can not be suitable as a first-line screening test, but may be useful for the confirmation of lung cancer diagnosis.

Numerous serum tumor markers have been employed for the diagnosis of lung cancer, such as CK19, CK7, CEA, human epithelial glycoprotein/EpCAM, squamous cell carcinoma antigen, fibronectin 1, and tissue inhibitor of metalloproteinase 1, and the levels of all these markers are obviously higher in lung cancer patients than in controls [17, 41, 42]. Although rare studies have compared the diagnostic performance of these tumor markers directly, the present meta-analysis has shown that the mean SEN and SPE of CTCs detected using CK19 is higher

Table 3. Subgroup analysis for the diagnostic accuracy of CTCs in lung cancer

Analysis scenario	Sensitivity (95% CI)	Specificity (95% CI)	PLR (95% CI)	NLR (95% CI)	DOR (95% CI)	AUC
Overall	0.63 (0.60, 0.65)	0.94 (0.92, 0.95)	16 (6, 42)	0.39 (0.30, 0.49)	41 (17, 101)	0.9298
Marker						
CK19	0.57 (0.52, 0.63)	0.97 (0.94, 0.99)	13 (7, 27)	0.42 (0.29, 0.63)	45 (15, 139)	0.8981
CEA	0.44 (0.37, 0.51)	0.96 (0.88, 0.99)	10 (0.2, 514)	0.57 (0.28, 1.15)	18 (0.3, 1265)	Unavailable
Ethnicity						
Asian	0.60 (0.57, 0.63)	0.93 (0.91, 0.95)	18 (5, 71)	0.44 (0.34, 0.56)	39 (12, 127)	0.788
European	0.74 (0.69, 0.80)	0.94 (0.90, 0.97)	10 (4, 24)	0.23 (0.12, 0.46)	48 (11, 210)	0.9574
Detection method						
PCR	0.66 (0.63, 0.69)	0.93 (0.91, 0.95)	18 (5, 63)	0.37 (0.28, 0.48)	47 (15, 144)	0.8194
Immunological	0.52 (0.46, 0.57)	0.97 (0.92, 0.99)	11 (3, 44)	0.42 (0.26, 0.68)	33 (5, 212)	0.9437
Sample size						
≥100	0.61 (0.58, 0.64)	0.93 (0.90, 0.94)	14 (4, 52)	0.42 (0.31, 0.57)	32 (10, 102)	0.7942
<100	0.68 (0.63, 0.74)	0.97 (0.94, 0.99)	16 (5, 49)	0.32 (0.20, 0.51)	64 (15, 267)	0.9519

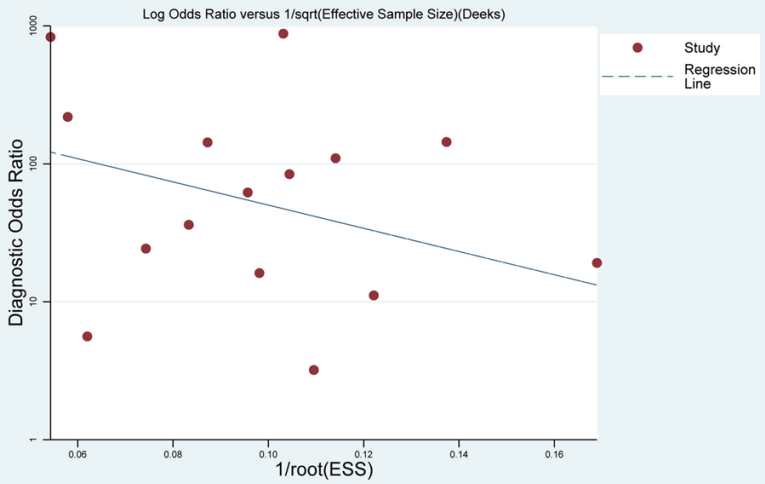

Figure 8. Funnel plot for the assessment of publication bias.

than that of CTCs detected using CEA as the marker. More studies are required to directly compare the diagnostic accuracy of these markers and decide which is better as a potential diagnostic biomarker for CTCs in lung cancer.

It should be noted that we observed significant heterogeneity among the selected studies by the Q-test and I^2 statistical analysis. The threshold effect is a primary cause of heterogeneity in test accuracy studies, but the Spearman correlation coefficient of our test suggested that the threshold effect was not a source of heterogeneity in our meta-analysis. Subgroup analysis further showed that the diagnostic performance of CTCs in the European population was better than that in the Asian population. This indicated that the value of CTCs in the diagnosis of lung cancer may differ among different races. Furthermore, to exclude technique-based bias, we divided our studies into subgroups according to the use of PCR-based and immunological-based CTC detection methods. Interestingly, although only the CellSearch system, which is an immunological-based method, has been approved by the US Food and Drug Administration for the determination of CTCs [43], we found that use of the PCR-based methods was associated with a higher SEN but lower SPE compared to those with the immunological method. These results indicated that both PCR-based and immunological-based methods are promising techniques for the detection of CTCs in lung cancer patients.

Our study had several limitations to consider. First, this study was based on the findings of observational studies, which tend to have more potential confounding factors than randomized controlled trials. Second, the control population included in our study was quite heterogeneous. Different studies used different controls, such as healthy individuals and those with benign disease. Uniform control groups must be established so that the diagnostic

accuracy of CTCs will not be overestimated. Third, Because of the lack of original data, we can not carry out subgroup analysis by pathological types to prove whether there exists difference between small cell lung cancer and non-small cell lung cancer. Furthermore, our analysis was based on published studies, and the fact that positive results are easier to publish than negative data can lead to publication bias. However, we did not find significant publication bias among the included studies based on Deek's funnel plots analysis.

In conclusion, our study has highlighted the potential clinical role of CTC detection as an indicator of lung cancer. Our results suggested that CTC evaluation may not be suitable as a first-line screening test. However, the high overall SPE and PLR values indicated the potential value of CTC detection as a quick and noninvasive method for confirming the lung cancer diagnosis. Further high-quality, well-designed, large-scale multicenter studies are required to determine the optimal tumor markers and molecular methods for CTC detection in lung cancer patients.

Disclosure of conflict of interest

None.

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