

Pentraxin 3 as a promising biomarker for cancer detection: a systematic review and meta-analysis

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Abstract

Background Mounting studies reported that circulating pentraxin 3 (PTX3) expression level was significantly different between cancer patients and healthy groups, suggesting that PTX3 may be a potential biomarker for cancer detection. However, the results were inconsistent. In this paper, a systematic review and meta-analysis was performed to quantitatively assess the diagnostic value of PTX3 in cancer detection.

Methods A comprehensive computerized literature search was conducted in Embase, PubMed, Cochrane Library, Web of Science, Chinese National Knowledge Infrastructure (CNKI) from inception to July 31, 2019. Eligible studies were identified and raw data were extracted. Diagnostic estimates were synthesized using STATA (version 12.0) and MetaDisc (version 1.4) statistical software.

Results Overall, 9 studies from 8 citations with a total of 1408 cancer patients and 3116 controls were included in this meta-analysis. The global sensitivity was 0.70 (95% confidence interval (CI): 0.67 – 0.72), and the specificity was 0.77 (95% CI: 0.75 – 0.78). The pooled positive likelihood ratio (PLR), negative likelihood ratio (NLR), and the diagnostic odds ratio (DOR) were 2.86 (95% CI: 2.29 – 3.56), 0.40 (95% CI: 0.32 – 0.50) and 7.38 (95% CI: 5.05 – 10.78), respectively. The merged AUC was 0.80 (95% CI: 0.76 – 0.83).

Conclusion The serum PTX3 appears to be a reliable biomarker for cancer detection though large-scale multicenter studies are needed.

Background

Cancer is a significant public health problem. Over the past several decades, cancer is becoming one of the leading causes of death ranked only second to angiocardopathy worldwide though cancer management has advanced greatly. It is estimated, according to the World Health Organization, that the deaths from cancers will mount up to approximately 13.2 million in 2030[1]. In general, an early diagnosis and timely treatment are crucial in improving the overall survival rate among people suffering from cancer. The earlier the cancer is diagnosed, the easier the cancer is to treat and control. Whereas, most of the cancer patients are diagnosed at an advanced stage due to its aggression, early metastasis and the lack of characteristic early clinical features which may be useful in the early detection of the disease[2-4]. Meanwhile, the current reference gold standards for cancer diagnosis are mainly consist of biopsy, spiral computer tomography and magnetic resonance imaging. Though the biopsy show a good diagnostic performance in cancer screening, the invasiveness and uncomfortable experience for patients confine the broad application in clinic. Likewise, despite the good diagnostic accuracy in cancer detection, imaging techniques, like spiral computer tomography and magnetic resonance imaging, usually get patients under the risk of exposure to radiation and are associated with relatively high costs[5-7]. Therefore, it is urgent to develop new methods with high diagnostic accuracy and low invasiveness for the early detection of cancer.

Pentraxin 3 (PTX3), which is a member of the pentraxin superfamily, plays an important role in immune regulation, inflammation, cellular proliferation, and vascular remodeling[8-10]. PTX3 can be produced by several human cell types, for example, neutrophils, macrophages, fibroblasts, dendritic cells, smooth muscle cells, and endothelial cells[11]. Recently, a new wave of researches demonstrated that PTX3

might be a promising serological biomarker for various human malignancies, such as lung cancer, colorectal cancer, hepatocellular carcinoma, prostate cancer and pancreatic cancer[12-19]. Nevertheless, it is difficult to interpret the data because the results were inconsistent.

To summarize the currently available data, a systematic review and meta-analysis was conducted to evaluate the diagnostic performance of PTX3 in cancer screening based on several clinical trials.

Methods

This study was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) statement[20, 21].

Publication search strategy

A comprehensive literature search was carried out in PubMed, Embase, Cochrane Library, Web of Science, and China National Knowledge Infrastructure (CNKI) from inception up to July 31, 2019. The search words used for article identification included: i) "cancer" or "carcinoma" or "tumor" or "neoplasma"; ii) "pentraxin 3" or "PTX3"; iii) "diagnostic" or "diagnosis". Meanwhile, the literatures cited by all the suitable studies were scanned to acquire more relevant citations. Additionally, no language restrictions were applied in this systematic review and meta-analysis.

Study selection

Two researchers (Qindong Liang and Guangjie Zhang) carefully scanned all the searched papers and independently identified the articles suitable for the systematic review. The articles were considered eligible if they satisfied all the following criteria: 1) patients with cancer were confirmed by histopathological examination or endoscopy; 2) blood samples were collected before any operation; 3) level of pentraxin 3 was measured in serum, plasma or blood; 4) the study was a case-control, prospective or retrospective cohort design; 5) sufficient data to draw 2 by 2 contingency tables. On the contrary, letters, commentary, abstracts presented in conferences, case reports and reviews were excluded. For duplicate publications adopting the same population, we selected the most recent article or the one with most informative data.

Quality assessment

Study quality assessment was completed independently by the same two researchers according to the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) checklist[22]. Any disagreement was settled through thorough discussion, and when it was necessary, arbitration by a third researcher to reach an agreement.

Data extraction

Two investigators (Qindong Liang and Guangjie Zhang) meticulously scrutinized all the included articles and the relevant data of each enrolled studies was extracted. For each research, the following data were collected: 1) study characteristics (the first author's name, year of publication, country, assay method, the number of cases and control groups); 2) the diagnostic data (such as sensitivity, specificity, cutoff value, etc.). The exact number of 2 by 2 contingency tables (true positive (TP), false positive (FP), true negative (TN) and false negative (FN)) were obtained directly or by recalculation.

Statistic analysis

The global diagnostic variables with corresponding 95% confidence intervals (CIs), like sensitivity, specificity, PLR, NLR, and DOR were calculated using STATA (version 12.0) and Meta-Disc (version 1.4) software[23]. The SROC curve was drawn to evaluate the diagnostic performance and to calculate the area under curve (AUC). The pooled AUC was used to describe the overall accuracy as a potential summary of the SROC curve. Meanwhile, Spearman correlation test was performed to quantify the threshold effect. Heterogeneity induced by non-threshold effect between the included studies was measured by the Cochran Q method and the inconsistency index (I^2) test. P value < 0.1 and I^2 value > 50% indicated a significant heterogeneity existing in our systematic review. Moreover, meta-regression analysis was conducted to find out the sources of heterogeneity. At last, publication bias was determined by Deek' regression test. P value < 0.05 was considered to be statistically significant.

Results

Study selection

Running the systematic search, a total of 121 citations were found: 35 in PubMed, 61 in Embase, 0 in Cochrane Library, 11 in Web of Science, and 14 in CNKI, respectively. As depicted in the flowchart (**Figure 1**), 20 duplicate records were removed. Furthermore, after scanning the titles and abstracts, 83 records were discarded because they were irrelevant studies, abstracts, books, letters, meetings, or comments. Subsequently, 18 studies were identified for full-text reading. After reading the full-text of the 18 studies, 10 studies were excluded for the following reasons: two were not about cancer[24, 25], five did not refer to circulating PTX3[26-30], two articles did not report the diagnostic performance of circulating PTX3 in cancer detection[31, 32], one paper did not present sufficient data[33]. Finally, eight papers involving nine studies were included in this meta-analysis[12-16, 34-36].

Studies characteristics

The main features of the nine included studies, such as name of the first author, year of publication, country, cancer type, number of patients and controls, sensitivity and specificity, are presented in **Table 1** by descending order of publication year. The included studies enrolled a total of 1408 cancer patients and 3116 control individuals. Among these studies, six were conducted in China[12, 15, 34-36], two in Italy[13, 14], and one in USA[16]. Besides, six researches investigated the diagnostic value of PTX3 for lung cancer, and one for gastric cancer, colorectal cancer and prostate cancer, each. The publication date of the included studies rang from 2011 to 2019. All these studies used the method of enzyme linked immunosorbent assay (ELISA) to detect the serum level of PTX3.

Quality assessment

To assess the quality of these nine eligible studies, a graph of risk of bias and applicability concerns was drawn. As shown in **Figure 2**, only one study[13] conformed to all the quality assessment items, and the bias of the eligible studies was mainly focused on “patients selection” and “index test”. Specially, in the domain of patient selection, 5 studies[12, 14-16] did not state whether the study avoided inappropriate exclusions. Meanwhile, in the domain of index test, 6 studies[14, 15, 34-36] did not adopt blinded method and one study[12] was unclear if blinded method was used. Generally, all the included nine studies could be considered to be of upper quality.

Diagnostic accuracy analysis

Significant heterogeneity in sensitivity ($I^2 = 83\%$) and specificity ($I^2 = 87.4\%$) was observed. Therefore, a random effects model was adopted in this meta-analysis to assess the diagnostic accuracy of PTX3 in cancer screening. Shown in **Figure 3**, the global sensitivity (SE) was 0.70 (95% confidence interval (CI): 0.67 – 0.72), and the specificity (SP) was 0.77 (95% CI: 0.75 – 0.78). The pooled positive likelihood ratio (PLR), negative likelihood ratio (NLR), and the diagnostic odds ratio (DOR) were 2.86 (95% CI: 2.29 – 3.56), 0.40 (95% CI: 0.32 – 0.50) and 7.38 (95% CI: 5.05 – 10.78), respectively (**Figure 4 and Figure 5**). The area under the summary receiver operator characteristic (SROC) curve was 0.80 (95% CI: 0.76 – 0.83) (**Figure 6**).

Threshold effect analysis and Heterogeneity exploration

Spearman's rank correlation analysis was carried out to evaluate the heterogeneity caused by threshold effect between the included studies (run on MetaDisc, version 1.4). Spearman correlation coefficient was -0.233 and the *P*-value was 0.546 ($p > 0.05$), indicating that threshold effect was not the source of heterogeneity in this study. Nevertheless, heterogeneity indeed existed as the I^2 of SE and SP were 83% and 87.4%, separately. Thereupon, meta-regression analysis was conducted to explore the sources of heterogeneity (performed on MetaDisc, version 1.4). We considered ethnicity, assay kit, sample size, and cancer type as the most possible factors causing heterogeneity. However, no satisfactory clues were observed. The results of meta-regression analysis are listed in **Table 2**.

Publication bias

Deeks' funnel plot asymmetry analysis (tested with STATA, version 12.0) was run to assess the potential bias between the nine eligible studies. As shown in **Figure 7**, no indication of publication bias was observed ($t = 0.46$; $p > 0.05$).

Discussion

Though traditional surgical specimens or biopsy tissues and imaging techniques are used in the cancer diagnosis, limitations still exist mainly due to the invasive procedures and the delayed reflection of tumor dynamic changes. Besides, cancer patients are usually found at the relatively late stages and the outcome is generally poor. Therefore, it is urgent to develop new methods with high performance for cancer diagnosis using minimally invasive procedures. PTX3, also named TSG14, has been known as a candidate novel marker of inflammation[37], especially cancer-related inflammation[38, 39]. PTX3 involves in many crucial biological events, including cellular proliferation, angiogenesis, apoptosis, cancer

cell invasion and metastasis[8, 40]. Recent studies suggested PTX3 could be a potential serum biomarker for cancer screening[12-16]. However, to the best of our knowledge, there is no systematic evidence-based evaluation for PTX3 as a tumor marker in cancer detection. In this study, we performed a systematic review and meta-analysis to assess the diagnostic performance of circulating PTX3 in cancer diagnosis.

In this meta-analysis, a total of eight papers with 4524 individuals (1408 cancer patients and 3116 controls) were enrolled. Pooling the data from the included studies presented a combined SE of 0.70 (95% CI: 0.67 – 0.72) and a combined SP of 0.77 (95% CI: 0.75 – 0.78). Diagnostic odds ratio (DOR), a merged power of SE and SP, is a metric of overall diagnostic performance. A higher DOR, a better diagnostic accuracy. The global DOR of PTX3 in this study is 7.38 (95% CI: 5.05 – 10.78), implying that PTX3 was of good diagnostic performance in cancer screening. To further investigate the diagnostic performance, we drew the SROC curve and calculated the corresponding AUC. Generally speaking, an AUC value of 0.75 to 0.92 means a good overall diagnostic performance, 0.92 to 0.96 means very good, and 0.97 to 1 means excellent[41, 42]. The AUC of SROC curve for PTX3 was 0.8 (95% CI: 0.76 – 0.83), suggesting a good diagnostic accuracy. All of these results imply that PTX3 could be a novel promising diagnostic biomarker in cancer detection.

Our study has several advantages. Firstly, the computerised search did not involve any language restriction on the publications in order to enroll more suitable studies besides English version. Secondly, our study is the first systematic review to verify the overall diagnostic accuracy of circulating PTX3 in cancer screening. Thirdly, PTX3 could be a potential biomarker for cancer with minimal invasiveness comparing to bioscopy and pathological examination.

However, our study also has some weaknesses. At first, though meticulous comprehensive search was carried out in PubMed, Embase, Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), only nine eligible studies were included in this meta-analysis. Besides, substantial heterogeneity in sensitivity ($I^2 = 83\%$) and specificity ($I^2 = 87.4\%$) exists between the included studies. According to the results of Spearman's rank correlation analysis (Spearman coefficient = -0.233, p value = 0.546), threshold effect was not the source of heterogeneity. Furthermore, we conducted meta-regression analysis to identify the factor(s) causing heterogeneity. Several covariates, like ethnicity, assay kit, sample size, and cancer type were adopted as the most possible source(s) of heterogeneity. Unfortunately, no statistical significant evidence was obtained. What's more, although there was no significant publication bias among the studies presented by Deeks' funnel plot asymmetry analysis (**Figure 7**), some latent bias may still exist because positive results are likely to be reported.

Conclusions

In conclusion, this systematic review and meta-analysis provide convincing evidence that PTX3 is of considerable diagnostic accuracy and may be a potential biomarker in cancer detection. However, as the current diagnostic data are limited, more multicenter, well-designed high quality trials with large sample size should be done to strengthen the theory of PTX3 in cancer diagnosis.

Abbreviations

PTX3: pentraxin 3; GC: gastric cancer; CRC: colorectal cancer; LC: lung cancer; PC: prostate cancer; N: number; NR: not report; CNKI: Chinese National Knowledge Infrastructure; SE: sensitivity; SP: specificity; PLR: positive likelihood ratio; NLR: negative likelihood ratio; DOR: diagnostic odds ratio; SROC: summary receiver operator characteristic; AUC: area under curve; TP: true positive; FP: false positive; TN: true negative; FN: false negative; ELISA: enzyme linked immunosorbent assay; PRISMA: preferred reporting items for systematic reviews and meta-analysis; QUADAS-2: quality assessment of diagnostic accuracy studies 2.

Declarations

Acknowledgement

NA

Authors' contributions

Changguo Gu designed this systematic review and meta-analysis; Qindong Liang and Guangjie Zhang carried out the literature search and drafted the manuscript; Qindong Liang, Guangjie Zhang and Huaan Huang analyzed the data; Nai Xing, Shangchun Sheng and Changguo Gu were involved in revising the manuscript; all the authors read and approved the final manuscript.

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Availability of data and materials

Data and materials are available upon request.

Ethics approval and consent to participate

This study was approved by the Ethics committee of Affiliated Hospital & Clinical Medical College of Chengdu University. The patients enrolled

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. McGuire S: **World Cancer Report 2014. Geneva, Switzerland: World Health Organization, International Agency for Research on Cancer, WHO Press, 2015.** *Advances in Nutrition* 2016, **7**(2):418-419.
2. Gupta AK, Brenner DE, Turgeon DK: **Early detection of colon cancer: new tests on the horizon.** *Molecular diagnosis & therapy* 2008, **12**(2):77-85.
3. Kelsen DP, Ginsberg R, Pajak TF, Sheahan DG, Gunderson L, Mortimer J, Estes N, Haller DG, Ajani J, Kocha W *et al.*: **Chemotherapy followed by surgery compared with surgery alone for localized esophageal cancer.** *The New England journal of medicine* 1998, **339**(27):1979-1984.
4. Portenoy RK, Thaler HT, Kornblith AB, Lepore JM, Friedlander-Klar H, Coyle N, Smart-Curley T, Kemeny N, Norton L, Hoskins W *et al.*: **Symptom prevalence, characteristics and distress in a cancer population.** *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation* 1994, **3**(3):183-189.
5. Mahadevia PJ, Fleisher LA, Frick KD, Eng J, Goodman SN, Powe NR: **Lung cancer screening with helical computed tomography in older adult smokers: a decision and cost-effectiveness analysis.** *Jama* 2003, **289**(3):313-322.
6. Ganti AK, Mulshine JL: **Lung cancer screening.** *The oncologist* 2006, **11**(5):481-487.
7. Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, Gareen IF, Gatsonis C, Marcus PM, Sicks JD: **Reduced lung-cancer mortality with low-dose computed tomographic screening.** *The New England journal of medicine* 2011, **365**(5):395-409.

8. Baruah P, Dumitriu IE, Peri G, Russo V, Mantovani A, Manfredi AA, Rovere-Querini P: **The tissue pentraxin PTX3 limits C1q-mediated complement activation and phagocytosis of apoptotic cells by dendritic cells.** *Journal of leukocyte biology* 2006, **80**(1):87-95.
9. Mantovani A, Garlanda C, Bottazzi B: **Pentraxin 3, a non-redundant soluble pattern recognition receptor involved in innate immunity.** *Vaccine* 2003, **21** Suppl 2:S43-47.
10. Garlanda C, Bottazzi B, Bastone A, Mantovani A: **Pentraxins at the crossroads between innate immunity, inflammation, matrix deposition, and female fertility.** *Annual review of immunology* 2005, **23**:337-366.
11. Lin Q, Fu F, Shen L, Zhu B: **Pentraxin 3 in the assessment of ventilator-associated pneumonia: an early marker of severity.** *Heart & lung : the journal of critical care* 2013, **42**(2):139-145.
12. Liu B, Zhao Y, Guo L: **Increased serum pentraxin-3 level predicts poor prognosis in patients with colorectal cancer after curative surgery, a cohort study.** *Medicine* 2018, **97**(40):e11780.
13. Infante M, Allavena P, Garlanda C, Nebuloni M, Morengi E, Rahal D, Roncalli M, Cavuto S, Pesce S, Monari M *et al*: **Prognostic and diagnostic potential of local and circulating levels of pentraxin 3 in lung cancer patients.** *International journal of cancer* 2016, **138**(4):983-991.
14. Stallone G, Cormio L, Netti GS, Infante B, Selvaggio O, Fino GD, Ranieri E, Bruno F, Prattichizzo C, Sanguedolce F *et al*: **Pentraxin 3: a novel biomarker for predicting progression from prostatic inflammation to prostate cancer.** *Cancer research* 2014, **74**(16):4230-4238.
15. Zhang D, Ren WH, Gao Y, Wang NY, Wu WJ: **Clinical significance and prognostic value of pentraxin-3 as serologic biomarker for lung cancer.** *Asian Pacific journal of cancer prevention : APJCP* 2013, **14**(7):4215-4221.
16. Diamandis EP, Goodglick L, Planque C, Thornquist MD: **Pentraxin-3 is a novel biomarker of lung carcinoma.** *Clinical cancer research : an official journal of the American Association for Cancer Research* 2011, **17**(8):2395-2399.
17. Di Caro G, Carvello M, Pesce S, Erreni M, Marchesi F, Todoric J, Sacchi M, Montorsi M, Allavena P, Spinelli A: **Circulating Inflammatory Mediators as Potential Prognostic Markers of Human Colorectal Cancer.** *PloS one* 2016, **11**(2):e0148186.
18. Song T, Wang C, Guo C, Liu Q, Zheng X: **Pentraxin 3 overexpression accelerated tumor metastasis and indicated poor prognosis in hepatocellular carcinoma via driving epithelial-mesenchymal transition.** *Journal of Cancer* 2018, **9**(15):2650-2658.
19. Kondo S, Ueno H, Hosoi H, Hashimoto J, Morizane C, Koizumi F, Tamura K, Okusaka T: **Clinical impact of pentraxin family expression on prognosis of pancreatic carcinoma.** *British journal of cancer* 2013, **109**(3):739-746.
20. Moher D, Liberati A, Tetzlaff J, Altman DG: **Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement.** *Ann Intern Med* 2009, **151**(4):264-269, W264.
21. Page MJ, Moher D: **Evaluations of the uptake and impact of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) Statement and extensions: a scoping review.** *Syst Rev* 2017, **6**(1):263.

22. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MM, Sterne JA, Bossuyt PM: **QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies.** *Ann Intern Med* 2011, **155**(8):529-536.
23. Zamora J, Abaira V, Muriel A, Khan K, Coomarasamy A: **Meta-DiSc: a software for meta-analysis of test accuracy data.** *BMC Med Res Methodol* 2006, **6**:31.
24. Ozsu S, Abul Y, Mentese A, Bektas H, Uzun A, Ozlu T: **Pentraxin-3: A novel biomarker for the differentiation of parapneumonic effusion and malignant pleural effusion.** *European Respiratory Journal* 2012, **40**((Ozsu S.; Abul Y.; Mentese A.; Bektas H.; Uzun A.; Ozlu T.)).
25. Zhou X, Kang F, Wang S, Wang J: **Diagnosis efficacy of plasma PTX3 under the guidance of 18F-FDG PET/CT in patients with Takayasu's arteritis.** *Journal of Nuclear Medicine* 2017, **58**((Kang F.) Xi'An, China).
26. Liu C, Yao Y, Wang W: **Pentraxin-3 as a prognostic marker in patients with small-cell lung cancer.** *Med Oncol* 2014, **31**(10):014-0207.
27. Locatelli M, Ferrero S, Martinelli Boneschi F, Boiocchi L, Zavanone M, Maria Gaini S, Bello L, Valentino S, Barbati E, Nebuloni M *et al.*: **The long pentraxin PTX3 as a correlate of cancer-related inflammation and prognosis of malignancy in gliomas.** *Journal of neuroimmunology* 2013, **260**(1-2):99-106.
28. Miyake M, Goodison S, Chang M, Dai Y, Urquidi V, Rosser CJ: **A multi-analyte assay for the noninvasive detection of bladder cancer.** *Journal of Clinical Oncology* 2013, **31**(6).
29. Peng X, Xue H, Lü L, Shi P, Wang J: **Accumulated promoter methylation as a potential biomarker for esophageal cancer.** *Oncotarget* 2017, **8**(1):679-691.
30. Urquidi V, Goodison S, Ross S, Chang M, Dai Y, Rosser CJ: **Diagnostic potential of urinary α 1-antitrypsin and apolipoprotein e in the detection of bladder cancer.** *Journal of Urology* 2012, **188**(6):2377-2383.
31. Takeda N, Asai K, Ijiri N, Yamamoto N, Watanabe T, Kamoi H, Kanazawa H, Hirata K: **Pentraxin-3 as a Biomarker for Febrile Neutropenia in Patients with Lung Cancer.** *Osaka city medical journal* 2015, **61**(1):43-52.
32. Zhang J, Wang TY, Niu XC: **Increased Plasma Levels of Pentraxin 3 Are Associated with Poor Prognosis of Colorectal Carcinoma Patients.** *The Tohoku journal of experimental medicine* 2016, **240**(1):39-46.
33. Goodison S, Chang M, Dai Y, Urquidi V, Rosser CJ: **A Multi-Analyte Assay for the Non-Invasive Detection of Bladder Cancer.** *PloS one* 2012, **7**(10).
34. Chen L: **Application value of serum Pentraxin-3 in diagnosis of gastric cancer.** *Laboratory Medicine and Clinic* 2019(03):343-346.
35. Lu K: **The diagnostic value of the levels of CYFRA21-1, Pentraxin-3, ProGRP for non-small cell lung cancer.** *China Journal of Laboratory Diagnosis* 2016(03):378-380.
36. Xu JZ, H: **The value of serum pentraxin-3 combined with HE4 in NSCLC diagnosis and prognosis** *Chinese Journal of Clinical Laboratory Science* 2015, **33**(04):282-284.

37. Ozsu S, Abul Y, Mentese A, Bektas H, Uzun A, Ozlu T, Porcel JM: **Pentraxin-3: A novel biomarker for discriminating parapneumonic from other exudative effusions.** *Respirology* 2013, **18**(4):657-662.
38. Germano G, Frapolli R, Simone M, Tavecchio M, Erba E, Pesce S, Pasqualini F, Grosso F, Sanfilippo R, Casali PG *et al*: **Antitumor and anti-inflammatory effects of trabectedin on human myxoid liposarcoma cells.** *Cancer research* 2010, **70**(6):2235-2244.
39. Lai CS, Li S, Chai CY, Lo CY, Dushenkov S, Ho CT, Pan MH, Wang YJ: **Anti-inflammatory and antitumor promotional effects of a novel urinary metabolite, 3',4'-didemethylnobiletin, derived from nobiletin.** *Carcinogenesis* 2008, **29**(12):2415-2424.
40. Rutkowski MJ, Sughrue ME, Kane AJ, Mills SA, Parsa AT: **Cancer and the complement cascade.** *Molecular cancer research : MCR* 2010, **8**(11):1453-1465.
41. Swets JA: **Measuring the accuracy of diagnostic systems.** *Science* 1988, **240**(4857):1285-1293.
42. Jones CM, Athanasiou T: **Summary receiver operating characteristic curve analysis techniques in the evaluation of diagnostic tests.** *The Annals of thoracic surgery* 2005, **79**(1):16-20.

Figures

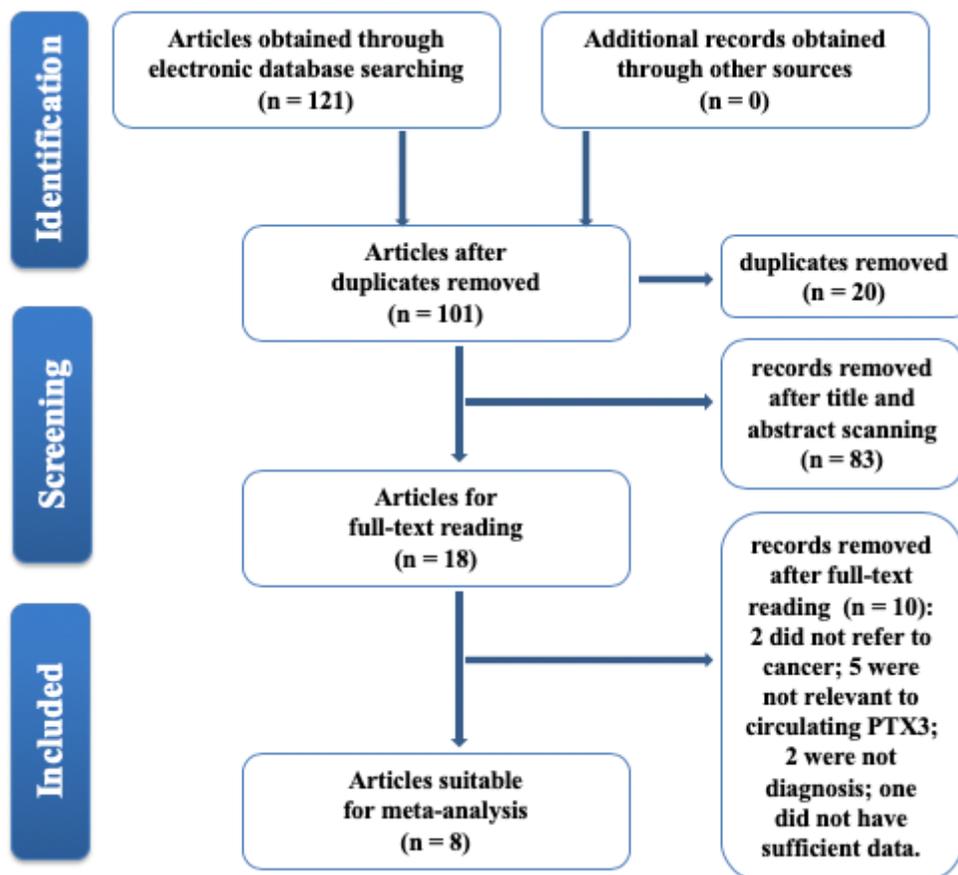


Figure 1

Flowchart of eligible studies selection.

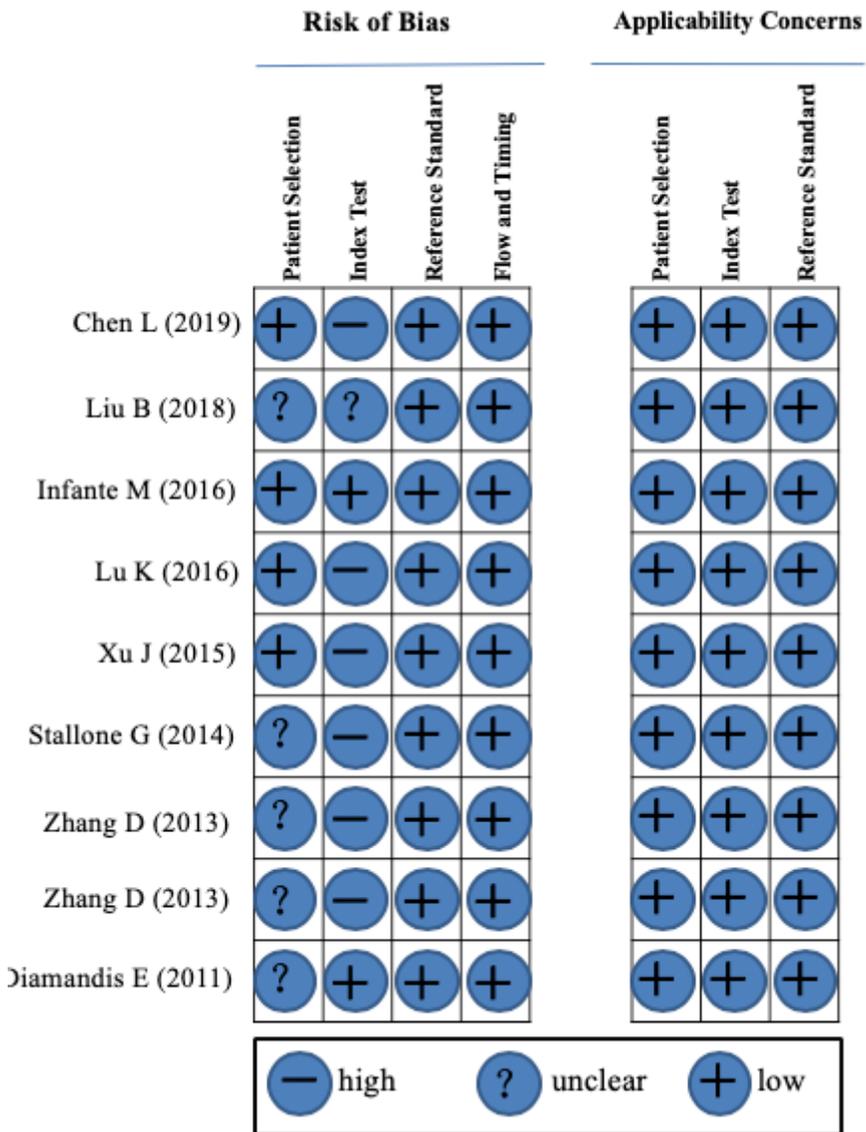


Figure 2

Quality assessment of the nine included studies.

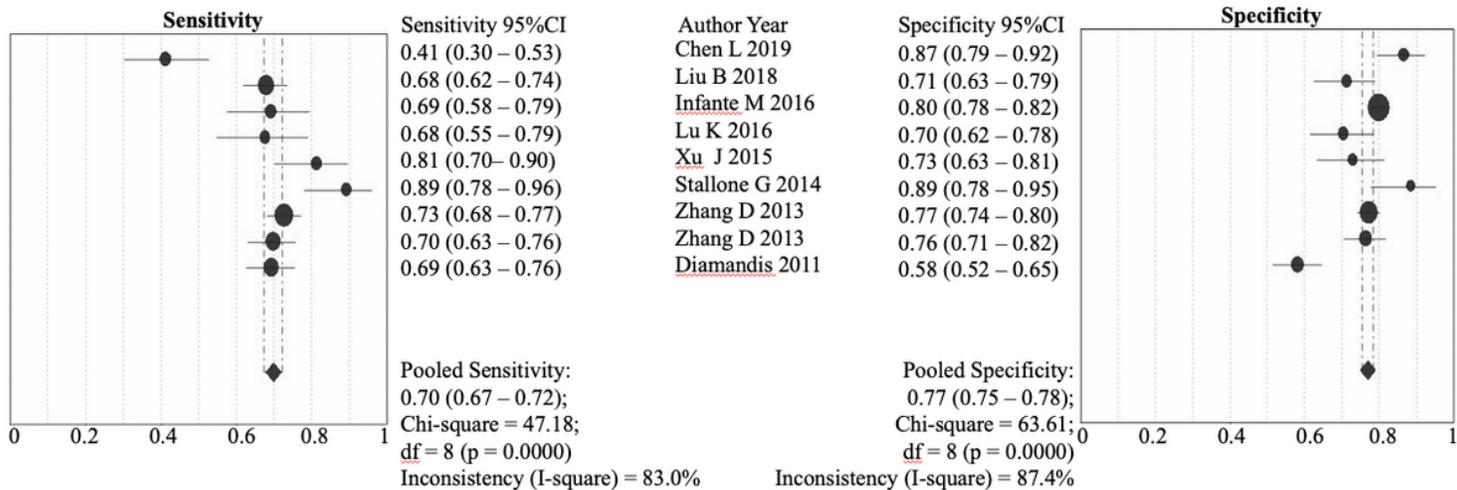


Figure 3

Forest plots of sensitivity and specificity of PTX3 in cancer diagnosis.

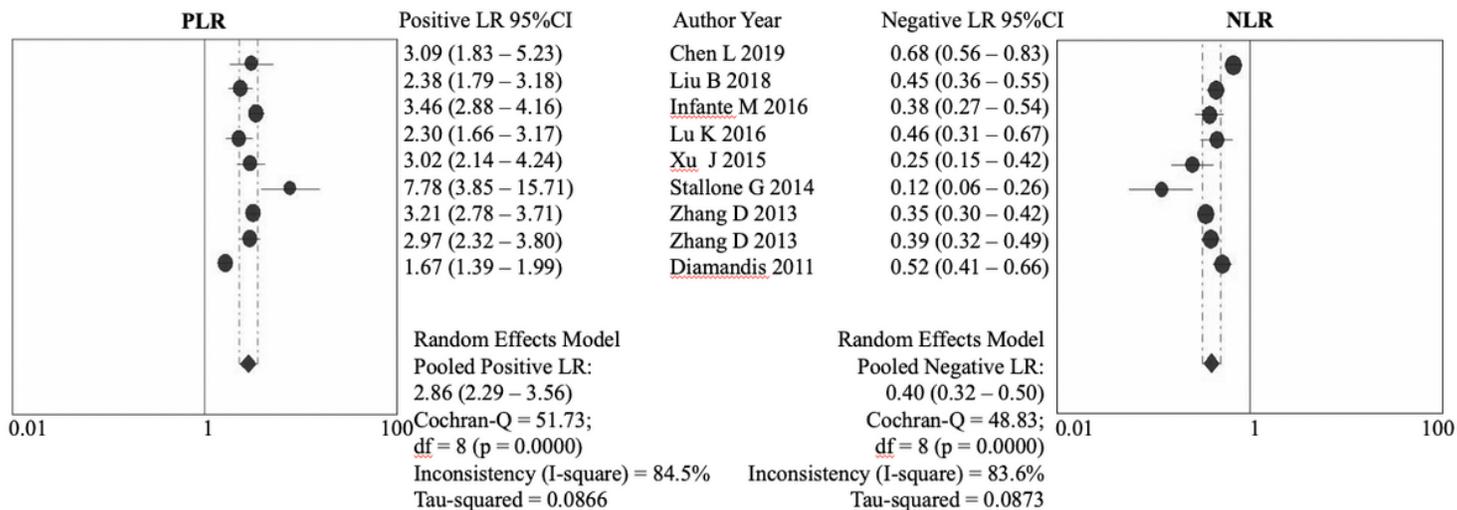


Figure 4

Forest plots for Positive Likelihood Ratio and Negative Likelihood Ratio of PTX3 in cancer diagnosis.

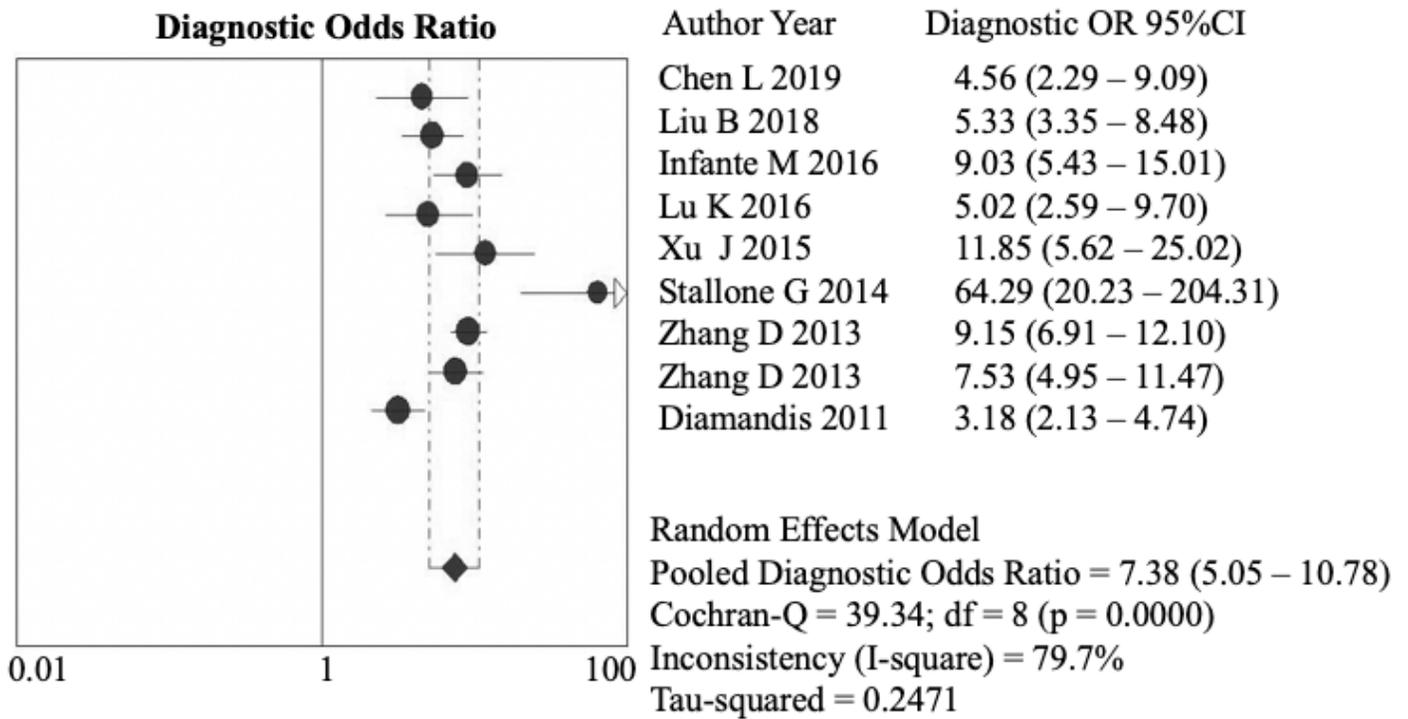


Figure 5

Diagnostic Odds Ratio of PTX3 in cancer diagnosis.

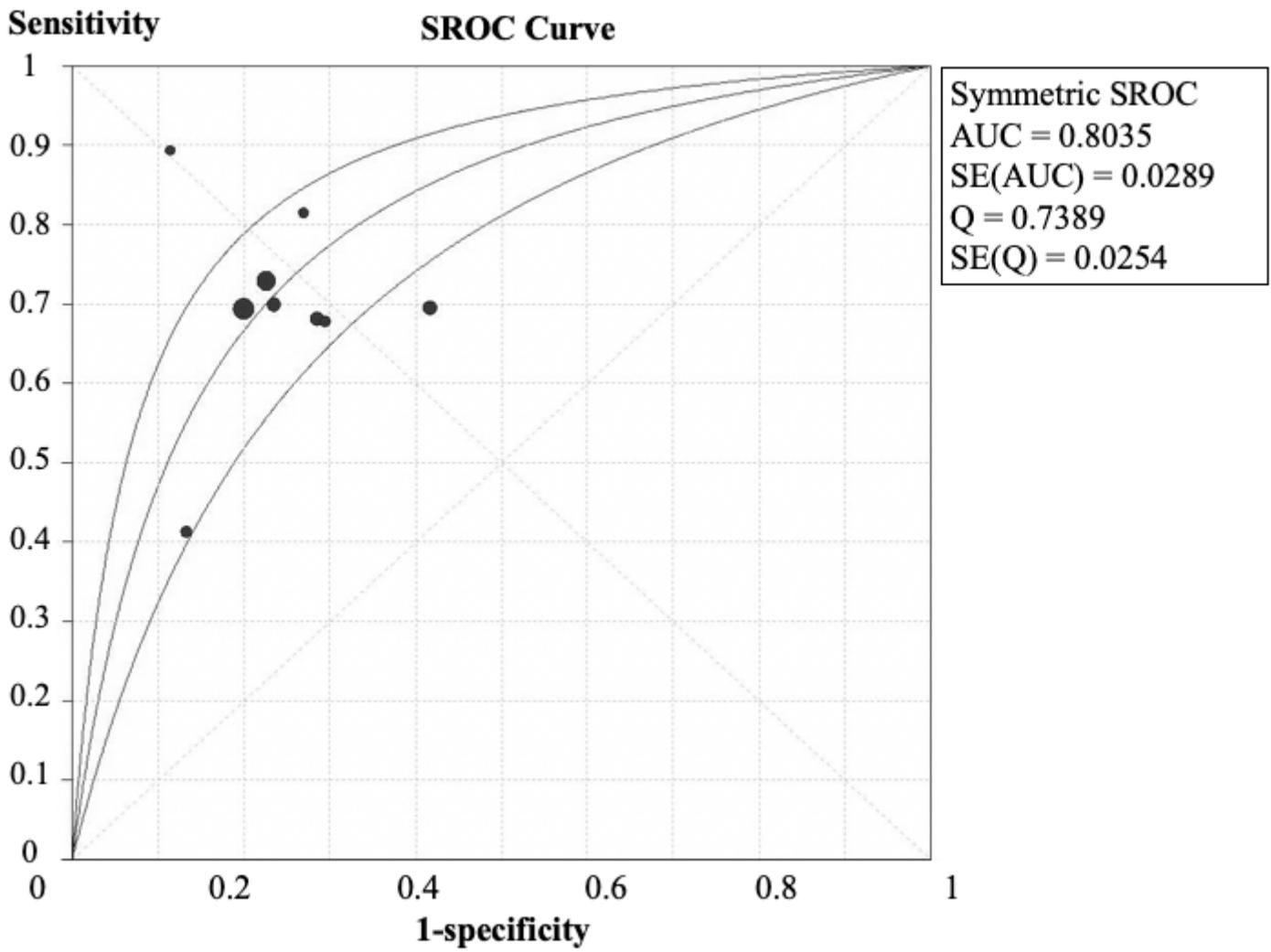


Figure 6

Summary receiver operating characteristic curve.

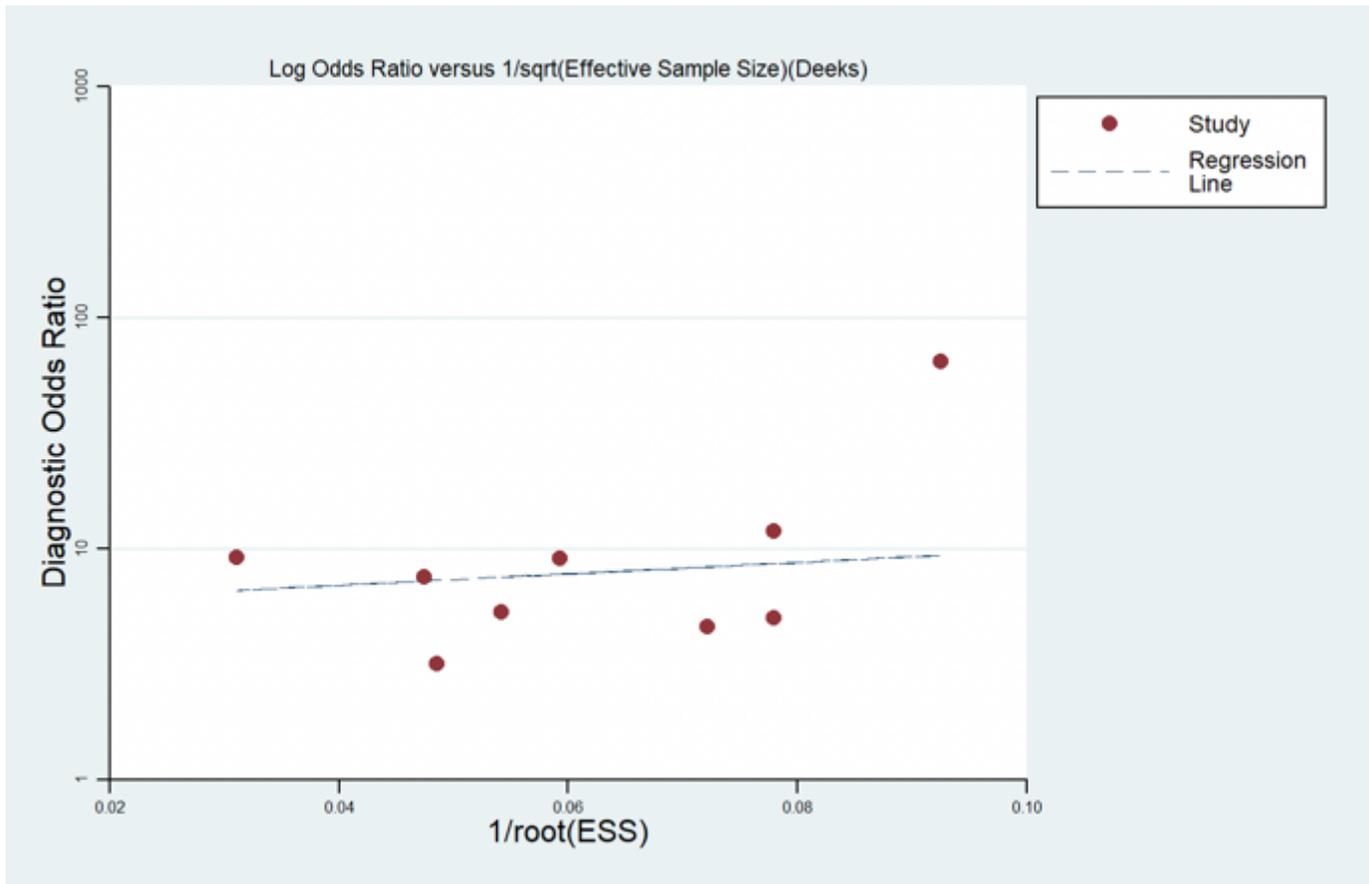


Figure 7

Deeks' funnel plot of publication bias.

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