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Review Article

Detection of Antibody versus Antigen, Optimal Option of Different Serological Assays Based Tests for COVID-19 Diagnosis: A Meta-Analysis

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Abstract

Background: In this study, the diagnostic efficacy of antigen test and antibody test were assessed. Additionally, the difference of sensitivity, specificity, and diagnostic odds ratio were compared concerning efficacy of antibody test versus antigen test for Corona Virus Disease 2019 (COVID-19) diagnosis.

Methods: Online databases were searched for full-text publications and STATA software was used for data pooling and analysis before Sep 1st, 2022. Forrest plot was used to show the pooled sensitivity, specificity and diagnostic odds ratio. Combined receiver operating characteristic (ROC) curve was used to show the area of under curve of complex data.

Results: Overall, 25 studies were included. The sensitivity (0.68, 95% CI: 0.53-0.80) and specificity (0.99, 95% CI: 0.98-0.99) in antibody or antigen was calculated. The time point of test lead to heterogeneity. The area under curve (AUC) was 0.98 (95% CI: 0.96-0.99), and the diagnostic odds ratio (DOR) was 299.54 (95% CI: 135.61-661.64). Subgroup analysis indicated antibody test with sensitivity (0.59, 95% CI: 0.44-0.73) and specificity (0.98, 95% CI: 0.95-0.99) and antigen test with sensitivity of 0.77 (95% CI: 0.53-0.91) and specificity of 0.99 (95% CI: 0.98-1.00). Higher AUC and DOR were proved in antigen test.

Conclusion: The present study compared the efficacy of antibody test versus antigen test for COVID-19 diagnosis. Better diagnostic efficacy, lower heterogeneity, and less publication bias of rapid antigen testing was suggested in this study. This study would help us to make better strategy about choosing rapid and reliable testing method in diagnosis of the COVID-19 disease.

Keywords: SARS-CoV-2; COVID-19; Antibody test; Antigen test; Meta-analysis

Introduction

Global pandemics of Corona Virus Disease 2019 (COVID-19) impose great health crisis on our society. To timely recognize the suspected cases and confirmed cases, the role of diagnostic tool is accentuated. In order to perform a rapid and accurate diagnostic, real-time Reverse Transcription Polymerase Chain Reaction (RT-PCR) is still strongly recommended for RNA viruses such as

severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathogen of COVID-19, to date (1, 2). Effective method of SARS-CoV-2 testing could be used not only to instruct patient care and management, but also to guide establishment of public health strategy for epidemiological emergency. Real time RT-PCR has been found as the most reliable technique to diagnose COVID-19(2). Besides, the latest guideline and the most recent updates of series consensus on COVID-19 recommend real-time RT-PCR as the most reliable diagnostic method for COVID-19 all over the world (3-7). RT-PCR has been routinely used to confirm the diagnosis, however, whether RT-PCR should be considered as the only standard experimental test in the diagnosis of COVID-19 is still remaining controversial (8).

Unfortunately, several studies have pointed out the limitation and poor performance of this diagnostic technique, especially for its shortness of sensitivity. False negative rate of COVID-19 PCR testing should draw our attention, and negative results of real time RT-PCR should not be the only factor to exclude the diagnosis of COVID-19 (9). Besides, the sample collection for RT-PCR such as upper respiratory tract sample (nasal swab or pharyngeal swab) and lower respiratory tract sample requires experienced expertise from well-trained practitioner (10). Moreover, the long turnaround time for the availability of real-time RT-PCR test results also limited its application. In response to the need for diagnosing the disease among suspected cases quickly and accurately, multiple clinical laboratory methodology should be comprehensively applied. Accordingly, faster and easier point-of-care methods are necessary compared to the current routine test method of real-time RT-PCR. Recent studies designed to define the role of serological testing in COVID-19 diagnosis, as well as disclosing the potential correlation between serological response and prognosis. The testing of virus-specific antibody are important measurements to assess the population immunity against the COVID-19 disease (11). The serological response of SARS-CoV-2 specific antibody were well-maintained, and its relevance to the disease could assist COVID-19 diagnosis, prognosis and vaccine design (12). Notwithstanding RT-PCR remains the reference diagnostic test for SARS-CoV-2 infection, its sensitivity fluctuates based on the stage since initial infection (13-15). On the contrary, serological indexes represent relatively stable and valid response to SARS-CoV-2 infection, which might solve possible inconformity between a highly suspect clinical presentation with suggestive radiology image and negative real time RT-PCR test (7, 16). In addition, reliable and repeatable serological indexes could bridge the gap between contradictory results of real time RT-PCR assays and epidemiological spread.

To our knowledge, the most popular test method of SARS-CoV-2 serological indexes are divided into two major classification: antibody test and antigen test (2, 16, 17). A combination of immunoglobulins (Ig)M testing and IgG testing could improve the sensitivity of COVID-19 diagnosis(18). Rapid antibody testing are indispensable for detecting a large scale population for its simplified operation, time saving process, and low cost, which made the antibody testing complementary to real time RT-PCR for fear of false negative cases(19). However, concerns about the efficacy of antibody testing in diagnosis of COVID-19 has also come up. The relevancy of positive antibody test to the diagnosis of COVID-19 are doubted (20, 21). In recent studies, several easy-to-perform rapid antigen detection tests were reported to play important role of the first line of test method in COVID-19 diagnosis (22, 23). Nonetheless, antigen detection rates were determined by viral loads, and unfortunately, the COVID-19 antigen test had unsatisfactory performance for its overall poor sensitivity (24).

Based on accumulated evidences, inconsistent results about antibody test or antigen test were attained. In the present meta-analysis, we aimed to testify the diagnostic efficacy of antigen test and antibody test, respectively. Additionally, the difference of sensitivity, specificity, and diagnostic odds ratio between different serological testing methods were compared. Rapid and reliable

testing method would obviously do well to effective management and better control of the world wide spread of the COVID-19 disease.

Methods

Database searching

This meta-analysis followed the instruction of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline. Electronic databases (PubMed, Embase, Web of Science, Google scholar, EBSCO, and the Cochrane library) was searched before Sep 1st, 2022. Terms used in publications retrieval were covid 19 antibody test, COVID 19 antigen test, SARS-CoV-2 antibody test, SARS-CoV-2 antigen test, or rapid SARS-CoV-2 test without language restriction.

Inclusion/exclusion criteria and data extraction

Two investigators searched the electronic database independently by the inclusion/exclusion criteria. In addition, a third investigator was added to make the final judgment if disagreement existed. The inclusion criteria included: diagnostic study design; subjects receiving SARS-CoV-2 pathogen test by ways of polymerase chain reaction (PCR), antibody test, or antigen test; PCR as golden standard; including case cohort and control cohort; full-text publication. The exclusion criteria included: animal or cell experiment based studies (basic research); cross-sectional study; case studies (case-reports or case-series); single-cohort study (without paralleled control); and review articles. The methodological quality of the studies included was assessed using an 11-item checklist recommended by Agency for Healthcare Research and Quality (AHRQ)(25).

Data synthesis and analysis

Endnote (Thomson Reuters EndNote X7.6) bibliographic software was used to create electronic citation. Two investigators independently extract data from each study, including last name of first author, publication year, publication region, number of study subjects, diagnostic method with golden standard, and experimental diagnostic method. The recommended method was used to assess the potential bias and heterogeneity for included studies.

Statistics

Data were analyzed using Stata version 12.0 (Stata Corporation, College Station, TX, USA). Before the data were synthesized, we first test the heterogeneity between the studies using Q Chi-square test. I^2 statistic was used to describe the percentage of the variability that attributed to heterogeneity across the studies rather than the chance. Studies with an I^2 statistic of <50% was considered to have no, low degree of heterogeneity. Pooled estimates were calculated to summarize the injury incidence rate. Forrest plot was used to show the pooled sensitivity, specificity and diagnostic odds ratio. Combined receiver operating characteristic (ROC) curve was used to show the area of under curve (AUC) of complex data. Subgroup analysis was performed to explore the potential sources of heterogeneity. Meta-regression analysis was applied to testify the changes of sports injury incidence in different session of Winter Paralympic Games. The assessment of publication bias was evaluated by using Deek's test. A 2-tailed *P*-value less than 0.05 was judged as statistically significant, except where otherwise specified.

Results

General description of study inclusion and characteristics of included studies

After searching electronic databases such as PubMed, Embase, Web of Science, Google Scholar, EBSCO, and the Cochrane library, recorded before Dec 1st, 2021 using terms of Covid 19 antibody test, Covid 19 antigen test, SARS-CoV-2 antibody test, SARS-CoV-2 antigen test, or rapid SARS-CoV-2 test, 26 (18, 23-47)studies were included for meta-analysis. The specific process of publication screening and filtration was shown in the flow diagram (Fig. 1). Characteristics of demographic data at baseline and the

overview of included studies were described in Table 1. The quality evaluation of included studies was depicted in Table 2, and all included studies attained the standard for meta-analysis.

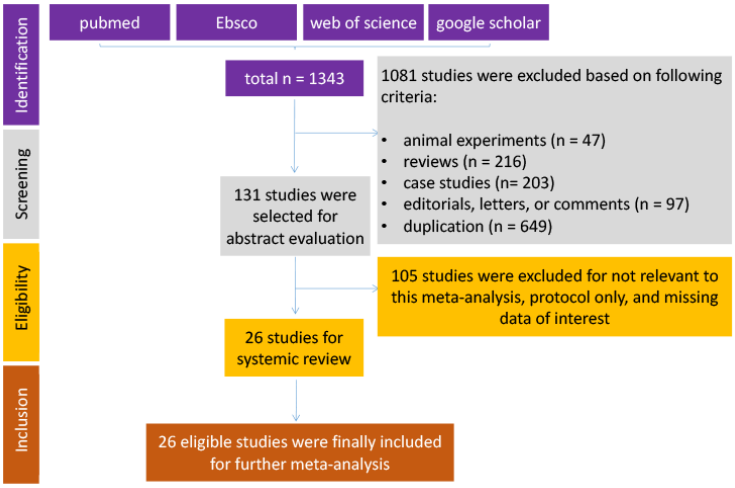

Fig. 1: Publication screening and filtration

Sensitivity and specificity of antibody test or antigen test in diagnosis of COVID-19

Pooled data indicated rapid testing of antibody or antigen had favorable sensitivity (0.68, 95% CI: 0.53 - 0.80) and great specificity (0.99, 95% CI: 0.98 - 0.99). The forest plot of combined sensitivity and specificity was shown in Fig.2A. However, the heterogeneity of pooled data was detected by using Q chi-square test (P<0.01). In order to detect the origin of heterogeneity in included studies, the univariable meta regression was applied (Fig. 2B). From the analysis, the testing method (antibody or antigen) contributed great heterogeneity (P<0.001). Besides, the time point of test (<7 d or >7 d) also lead to heterogeneity (P<0.05). However the study design (prospective or retrospective) didn't influence the heterogeneity (P>0.05). The integrative ROC curve suggested a good diagnostic efficacy with high AUC (0.98, 95% CI: 0.96 - 0.99), and the combined ROC curve was shown in Fig. 2C. Diagnostic odds ratio (DOR) of antibody test or antigen was depicted in forest plot (Fig. 2D), and DOR of rapid antibody/antigen testing was 299.54 (95% CI: 50.32– 234.73). No publication bias in included studies of antibody test or antigen test in diagnosis of COVID-19 was detected (P=0.06) by Deek's funnel plot (Fig. 2E).

Subgroup analysis of SARS-CoV-2 antibody test's efficacy in diagnosis of COVID-19

Pooled data indicated rapid testing of SARS-CoV-2 antibody had favorable sensitivity (0.59, 95% CI: 0.44-0.73) and great specificity (0.98, 95% CI: 0.95-0.99). The forest plot of combined sensitivity and specificity was shown in Fig. 3A. However, the heterogeneity of pooled data was detected by using Q chi-square test (P<0.01). In order to detect the origin of heterogeneity in included studies, the univariable meta regression was applied (Fig. 3B). From the analysis, the study design (prospective or retrospective) contributed to heterogeneity (P<0.05). However the time point of test (<7 d or >7 d) didn't influence the heterogeneity (P>0.05). The combined ROC curve shown in Fig. 3C indicated the diagnostic efficacy of antibody test by AUC (0.96, 95% CI: 0.94-0.97). DOR of antibody test shown in Fig. 3D was 43.76 (95% CI: 18.36-104.29). Publication bias in included studies of antibody test in diagnosis of COVID-19 was detected (P=0.01) by Deek's funnel plot which shown the asymmetric distribution of included studies (Fig. 3E).

Table 1: Characteristics of demographic baseline

Author	*Region*	*Age*	*Female*	*HTN*	*DM*	*Case*	*Con-trol*	*Golden standard*	*Testing target*
Xie, et al.(18)	China	56.5 (49.25-64.75)	32 (57.1)	7 (12.5)	3 (5.4)	28	28	PCR	antibody
Canetti, et al.(35)	Italy	61 (54-74)	48 (57.8)	NG	NG	43	40	PCR	antibody
Fauziah, et al.(36)	Indonesia	46	15 (31.9)	NG	NG	27	20	PCR	antibody
Dohla et al.(38)	Germany	46 (28-72)	24 (49)	NG	NG	22	27	PCR	antibody
Hoffman et al.(37)	Sweden	NG	NG	NG	NG	29	124	PCR	antibody
Jin et al.(44)	China	47.0 (34.0–59.0)	26 (60.5)	10 (23.3)	3 (0.07)	27	33	PCR	antibody
Li et al.(25)	China	NG	NG	NG	NG	397	128	PCR	antibody
Shen et al.(27)	China	NG	61 (41)	25 (16.7)	8 (5.3)	97	53	PCR	antibody
Spicuzza et al.(26)	Italy	NG	NG	NG	NG	23	14	PCR	antibody
Xiang et al.(28)	China	51.0 (32.0-65)	85 (67.5)	NG	NG	66	60	PCR	antibody
Cassaniti et al.(45)	Italy	38.5 (25-69)	16 (32)	NG	NG	38	12	PCR	antibody
Agulló et al.(33)	Spain	38 (21–49.8)	372 (56.4)	46 (7)	21 (4.4)	132	520	PCR	antigen
Albert et al.(23)	Spain	36 (17-91)	239 (58)	NG	NG	54	358	PCR	antigen
Alemany et al.(39)	Spain	40.4 (24.5)	NG	NG	NG	951	455	PCR	antigen
Cerutti et al.(31)	Italy	35.9 (32.7–39.1)	NG	NG	NG	109	221	PCR	antigen
Chaimayo et al.(46)	Thailand	38.5 (21–72)	182 (40)	NG	NG	60	394	PCR	antigen
Gremmels et al.(44)	The Nether-lands	NG	844 (61.7)	NG	NG	139	1228	PCR	antigen
Gupta et al.(40)	India	34.1 (12.6)	99 (30.0)	NG	NG	77	253	PCR	antigen
Linares et al.(32)	Spain	39.0 (25.0–56.0)	131	NG	NG	84	235	PCR	antigen
Liotti et al.(30)	Italy	NG	NG	NG	NG	104	255	PCR	antigen
Nalumansi et al.(41)	Uganda	34 (32–35)	28 (11)	NG	NG	90	172	PCR	antigen
Porte et al.(29)	Chile	38 (29.5-44)	59 (46.5)	NG	NG	82	45	PCR	antigen
Scohy et al.(24)	Belgium	57.5 (0–94)	84 (56.8)	NG	NG	106	42	PCR	antigen
Toptan et al.(42)	Germany	NG	NG	NG	NG	58	9	PCR	antigen
Turcato et al.(34)	Italy	NG	NG	NG	NG	169	822	PCR	antigen
Akashi et al.(47)	Japan	36.0 (25.0–50.0)	341 (42.6)	NG	NG	110	690	PCR	antigen

NG: not given; PCR: Polymerase Chain Reaction; HTN: hypertension; DM: diabetes mellitus

Table 2: Quality assessment by AHRQ scale

Author	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*
Xie, et al.(18)	Yes	Unclear	Yes	Yes	No	Yes	Unclear	Yes	Unclear	Yes	Unclear
Canetti, et al.(35)	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes	Unclear	Yes	Unclear
Fauziah, et al.(36)	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes	Unclear	Yes	Unclear
Dohla et al.(38)	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes	Unclear	Yes	Unclear
Hoffman et al.(37)	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Jin et al.(44)	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Li et al.(25)	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Shen et al.(27)	Yes	Unclear	Yes	Yes	No	Yes	Yes	Unclear	Unclear	Yes	Unclear
Spicuzza et al.(26)	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Xiang et al.(28)	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Cassaniti et al.(45)	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Agulló et al.(33)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Albert et al.(23)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Alemany et al.(39)	Yes	Yes	Yes	Yes	No	Yes	Unclear	Yes	Yes	Yes	Unclear
Cerutti et al.(31)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Chaimayo et al.(46)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Gremmels et al.(43)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Gupta et al.(40)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Linares et al.(32)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Liotti et al.(30)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Nalumansi et al.(41)	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Unclear	Yes	Unclear
Porte et al.(29)	Yes	Yes	Yes	Yes	No	Yes	Unclear	Yes	Yes	Yes	Unclear
Scohy et al.(24)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Toptan et al.(42)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Turcato et al.(34)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Akashi et al.(47)	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Unclear	Yes	Unclear

Define the source of information (survey, record review) ; 2) List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications; 3) Indicate time period used for identifying patients; 4) Indicate whether or not subjects were consecutive if not population-based; 5) Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants; 6) Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements); 7) Explain any patient exclusions from analysis; 8) Describe how confounding was assessed and/or controlled; 9) If applicable, explain how missing data were handled in the analysis; 10) Summarize patient response rates and completeness of data collection; 11) Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained

Subgroup analysis of SARS-CoV-2 antigen test's efficacy in diagnosis of COVID-19

Pooled data suggested rapid testing of SARS-CoV-2 antigen had sensitivity of 0.77 and specificity of 0.99 (Fig. 4A). However, the heterogeneity of pooled data was detected using Q Chi-square test (P<0.01). In order to detect the origin of heterogeneity in included studies, the univariable meta regression was applied (Fig. 4B). From the analysis, the study design (prospective or retrospective) and the time point of test (<7 d or >7 d) did not contribute to the heterogeneity among included studies. The combined ROC curve shown in Fig. 4C indicated the diagnostic efficacy of antigen test by AUC. DOR of antigen test shown in Fig. 4D was 349.93. Deek's funnel plot shown the symmetric distribution of included studies (Fig. 4E), indicating no publication bias in included studies (P=0.21). In comparison with SARS-CoV-2 antibody test, higher AUC and DOR were proved in SARS-CoV-2 antigen test, indicating better diagnostic efficacy of rapid antigen testing. Besides, lower heterogeneity and publication bias detected in studies concerning rapid antigen testing suggested more reliable and stable results in those investigating set.

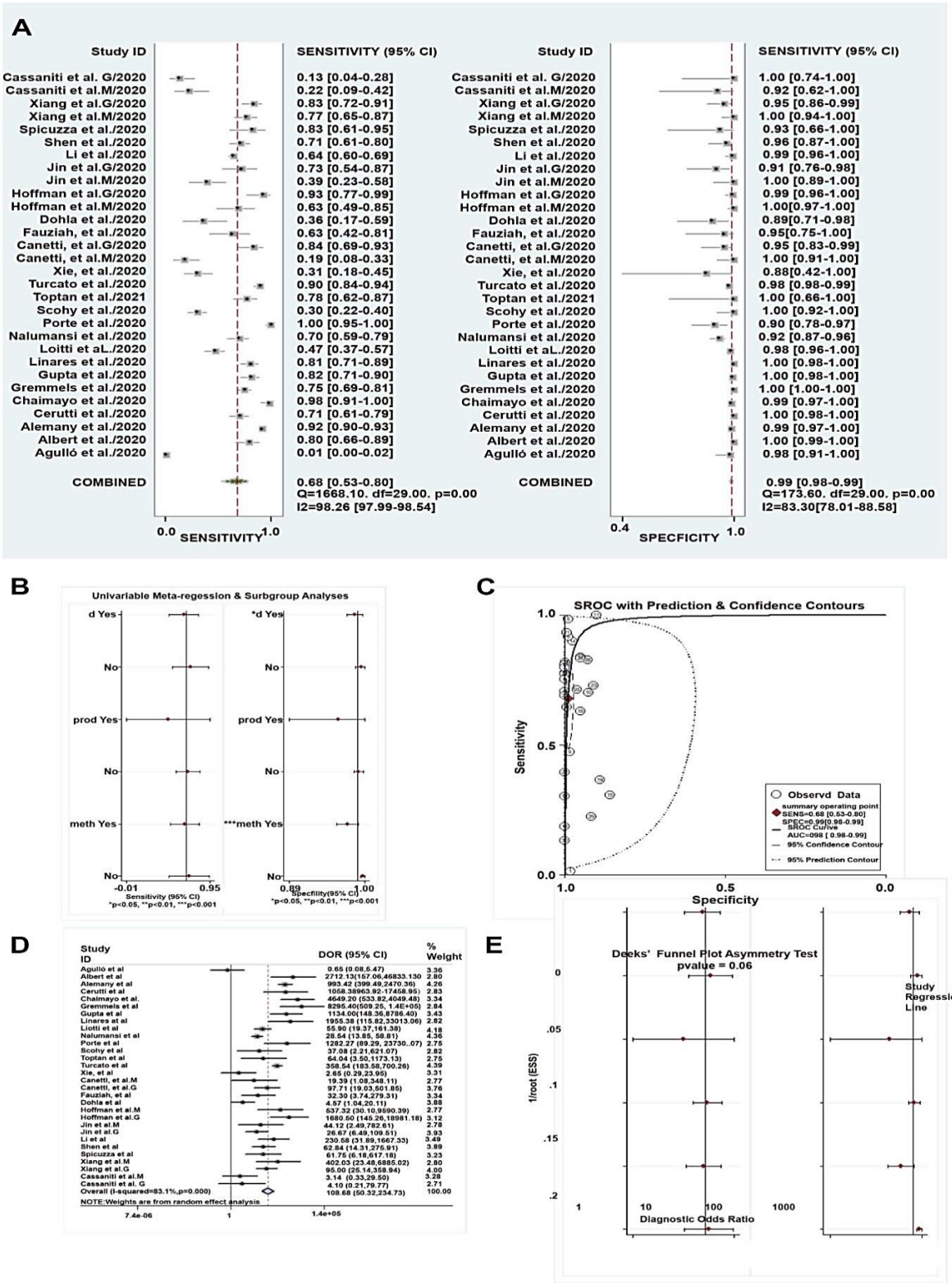

Fig. 2: Sensitivity and specificity of antibody test or antigen test in diagnosis of COVID-19: the forest plot of combined sensitivity and specificity (A);meta regression to detect the heterogeneity of pooled data (B); combined ROC curve to show the AUC (C); forest plot to show the DOR (D); publication bias analysis (E)

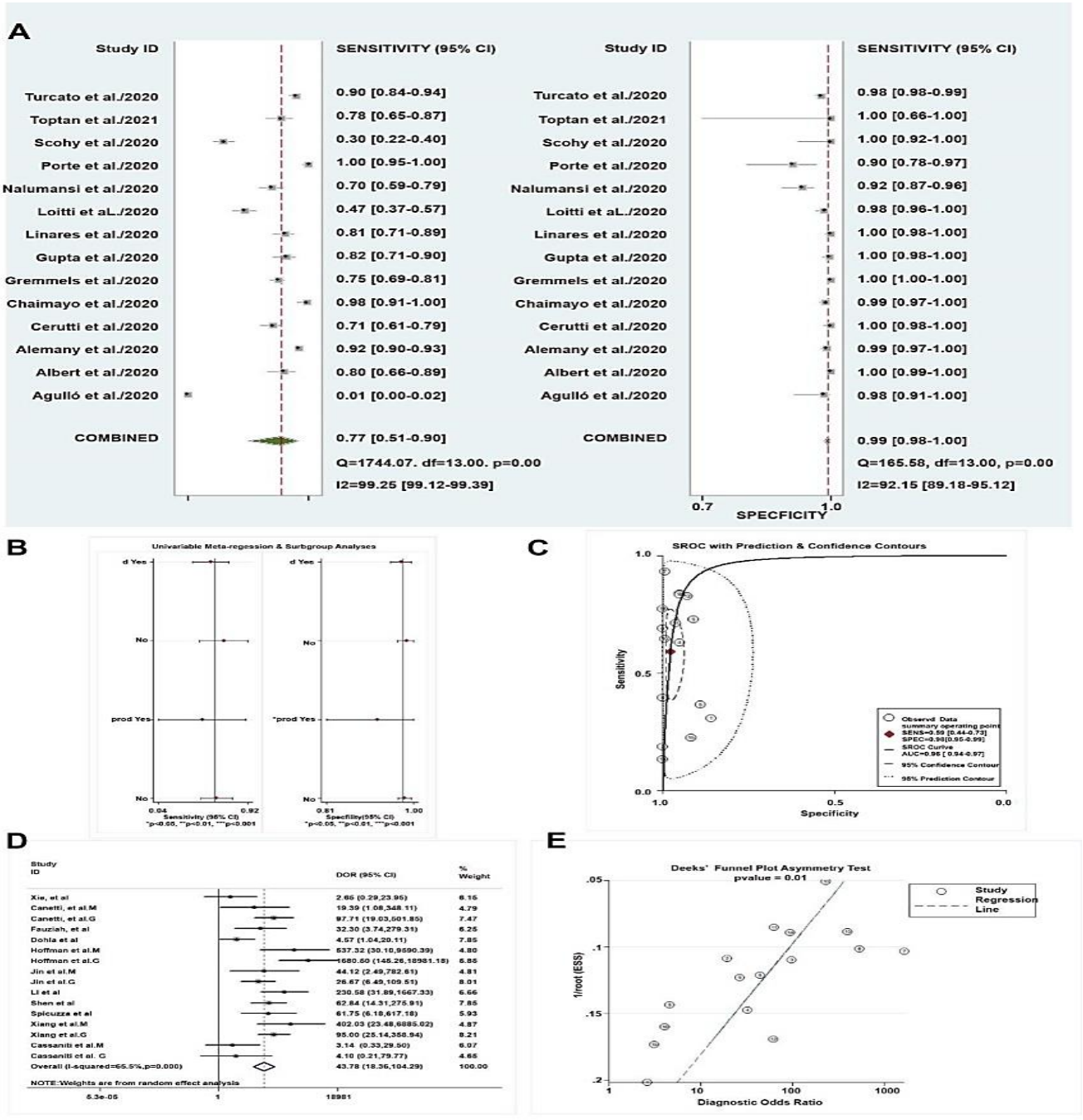

Fig. 3: Subgroup analysis of SARS-CoV-2 antibody test's efficacy in diagnosis of COVID-19: the forest plot of combined sensitivity and specificity (A); meta regression to detect the heterogeneity of pooled data (B); combined ROC curve to show the AUC (C); forest plot to show the DOR (D); publication bias analysis (E)

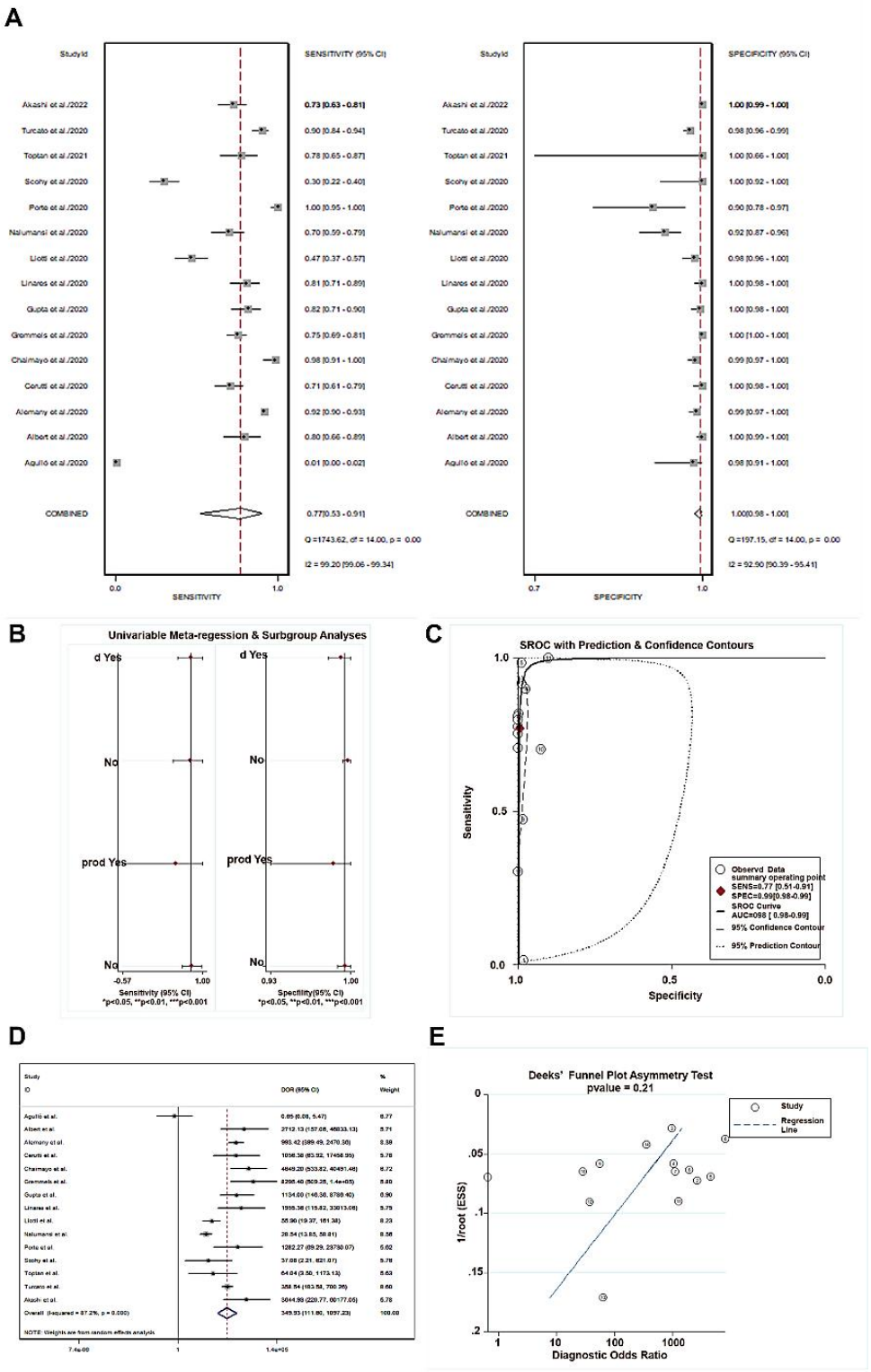

Fig. 4: Subgroup analysis of SARS-CoV-2 antigen test's efficacy in diagnosis of COVID-19: the forest plot of combined sensitivity and specificity (A); meta regression to detect the heterogeneity of pooled data (B); combined ROC curve to show the AUC (C); forest plot to show the DOR (D); publication bias analysis (E)

Discussion

In this study, the diagnostic efficacy of antigen test and antibody test were evaluated. Additionally, the difference of sensitivity, specificity, and diagnostic odds ratio were compared. Finally, 25 studies were included. The sensitivity (0.68, 95% CI: 0.53-0.80) and specificity (0.99, 95% CI: 0.98-0.99) in antibody or antigen test was calculated. In term of antibody or antigen test, the AUC was 0.98 (95% CI: 0.96-0.99), and the DOR was 299.54 (95% CI: 135.61-661.64). Subgroup analysis indicated antibody test with sensitivity of 0.59 (95% CI: 0.44-0.73) and specificity of 0.98 (95% CI: 0.95 - 0.99). However, the antigen test seemed to have better sensitivity of 0.77 (95% CI: 0.51-0.91) and specificity of 0.99 (95% CI: 0.98-1.00). Higher AUC and DOR were proved in antigen test (AUC: 0.99, 95% CI: 0.98-1.00; DOR: 302.68, 95% CI: 93.90-975.71) in comparison with antibody test (AUC: 0.96, 95% CI: 0.94-0.97; DOR: 43.76, 95% CI: 18.36-104.29), indicating better diagnostic efficacy of rapid antigen testing. Besides, it suggested that more reliable and stable results in those investigation set concerning rapid antigen testing for lower heterogeneity and publication bias detected in those studies.

The real time RT-PCR has been routinely treated as golden standard method of COVID-19 diagnosis. Nevertheless, this method is criticized for its low sensitivity and high false negative rate. Accordingly, it is important to explore other effective and economical testing method to improve the detection rate of COVID-19. A study enrolled 56 subjects was designed to detect SARS-CoV-2 infection by using both IgM/IgG antibody and nucleic acid tests, indicating IgM/IgG antibody testing could serve as complement to real time RT-PCR testing to attain better sensitivity (18). Another study aimed to analyze the proportion of those who developed a positive IgM/IgG response for SARS-CoV-2 suggested that the role of IgG/IgM testing assay could be used as a point-of-care test which may gain particular relevance to shorten duration of decision make to refer patients to a COVID-19 designated hospital or not (35). However, the performance of combined IgM and IgG antibody test has a high specificity without false-positive result, while the sensitivity of the test was as low as 65.5% (95% CI: 45.7-82.1) (36). In addition to IgM test or IgG test, determination of the secretory antibody IgA specific to SARS-CoV-2 (IgA) in saliva and serum could help to refine the diagnosis of COVID-19 (48). The sensitivity and specificity of antibody test attained inconsistent results, however, the pooled data suggested a low sensitivity of 0.59 and high specificity of 0.98 in our study.

In comparison with difference to antibody test whose sensitivity was a little disappointing, sensitivity of antigen test method was significantly elevated to 0.77 in this study. Additionally, the antigen test also achieved high specificity of 0.99, which lead to low false positive rate of SARS-CoV-2 infection. Results of our study was consistent with the PROSPERO study (48), which reported that specificity and sensitivity of antigen test were detected as 99.4% (95% CI: 99.1-99.8) and 68.4% (95% CI: 60.8-75.9), respectively. Besides, the PROSPERO study also reported that antigen test showed better performance in the European and American populations which could be owing to its extensive application in these areas. Regardless of not bad diagnostic efficacy of antigen test or antibody test in this meta-analysis, significant heterogeneity among included studies should draw our attention. From Meta regression, heterogeneity across the studies mainly originated from the discordance of the time point of test (<7 d or >7 d). Torres et al reported that different time point of sample acquisition could influence the sensitivity of antigen test, and they proposed that establishing the optimal sampling time point for upper respiratory tract seemed imperative to pinpoint test sensitivity (49). Besides, sensitivity of antibody test was also

reported to correlate with timing of detection. IgG-antibody test carried out from 0-6 d, 7-14 d and >14 d after the SARS-CoV-2 RT-PCR test displayed 30%, 73% and 100% positivity rates in different COVID-19 group. In cases with samples taken >14 d after RT-PCR diagnosis, both negative prediction value and positive prediction value significantly increased (50). Therefore, the time point of test should be optimized, on the other hand, repeatedly applied test should be done to prudently avoid causing false negative results.

Antigen test or antibody test could be an alternative in places lack of professional laboratory settings. Besides, the negative samples of antigen test or antibody test can be re-tested by using real time RT-PCR to reduce false negative results, if some case with high degree of suspicion is met. Considering the high specificity of antigen test and high sensitivity of antibody test, the efficacy of alliance of antibody test and antigen test, rarely reported before in Covid-19 diagnosis, is worthy of being investigated in future.

The included studies were major of retrospective design, and this might dampen the evidence intensity of our study. Well-designed prospective clinical trial of diagnostic test should be carried out.

Conclusion

The present study summarized the comparison between SARS-CoV-2 antigen/antibody test. Higher AUC and DOR were proved in SARS-CoV-2 antigen test, indicating better diagnostic efficacy of rapid antigen testing. Besides, lower heterogeneity and publication bias detected in studies concerning rapid antigen testing suggested more reliable and stable results in those investigating sets. This study compared the efficacy of antibody test versus antigen test for Covid-19 diagnosis, and better diagnostic efficacy, lower heterogeneity, and less publication bias of rapid antigen testing was suggested. This study would help us to make better strategy about choosing rapid and reliable testing method in diagnosis of the Covid-19 disease.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

All the authors declare that they have no conflict of interest.

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