A Meta-Analysis of Accuracy and Sensitivity of CRISPR and Chest CT in COVID-19 Diagnosis

chun gao

Gansu University of Traditional Chinese Medicine

Jing-Jing Jiang

Gansu University of Traditional Chinese Medicine

Fu-Juan Feng

Gansu University of Traditional Chinese Medicine

Cai-Hong Wang

Gansu University of Traditional Chinese Medicine

Rong Wang

Gansu University of Traditional Chinese Medicine

Xiao-Wen Yao

Gansu University of Traditional Chinese Medicine

Yu-Xia Zhou

Gansu University of Traditional Chinese Medicine

Hui-Juan Shao

Gansu University of Traditional Chinese Medicine

Xue-Feng Ma

Gansu University of Traditional Chinese Medicine

Jun Huang

Gansu University of Traditional Chinese Medicine

Jiu-Cong Zhang (✉ zhangjiucong@163.com)

Department of Gastroenterology, The 940 Hospital of Joint Service Support Forces of PLA

Xiao-Hui Yu

Department of Gastroenterology, The 940 Hospital of Joint Service Support Forces of PLA

Research Article

Keywords: COVID-19, CRISPR, Chest CT, Diagnostic test, Meta-analysis

Posted Date: February 25th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1281697/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Objective To clarify the accuracy of clusters of regularly spaced short palindrome repeats (CRISPR) technology and chest CT in the diagnosis of Corona Virus Disease2019(COVID-19).

Methods The term "Corona Virus Disease " "clustered regularly spaced short palindromic repeats" "CRISPR", "chest CT", "sensitivity and specificity" as the subject words or keywords were searched in databases such as Pubmed, Embase, Cochrane Library, Wiley and Scopus and Chinese academic databases (such as CNKI, Wanfang and Chongqing VIP data) for relevant literature on the use of CRISPR technology and chest CT for the diagnosis of COVID-19. Meta-analysis was performed after literature screening, quality assessment and data extraction .

Results A total of 418 articles were retrieved, and 17 articles were finally included. The results showed that the combined sensitivity of CRISPR technology for diagnosing new coronary pneumonia infection was 0.96 [95% CI (0.93, 0.98)], and the combined specificity was 1.00 [95% CI (0.92, 1.00)], the combined positive likelihood ratio is 458.69 [95%CI (11.51, 18280.8)], the combined negative likelihood ratio is 0.04 [95% CI (0.02, 0.07)], the area under the SROC curve is 0.99 [95%CI(0.97,0.99)]. The combined sensitivity of chest CT in diagnosing new coronary pneumonia infection was 0.94 [95%CI (0.83, 0.98)], combined specificity was 0.55 [95% CI (0.22, 0.83)], combined diagnostic odds ratio was 19.90 [95% CI (7.88, 50.25)], the combined positive likelihood ratio is 2.08 [95%CI (1.00, 4.32)], the combined negative likelihood ratio is 0.10 [95% CI (0.05, 0.23)], the area under the SROC curve is 0.91 [95% CI (0.88, 0.93)]. The Deek funnel chart indicates that there is no potential publication bias among the included studies (PCRISPR = 0.03, P chest CT = 0.55).

Conclusion CRISPR technology has a better ability to detect infections in patients with COVID-19, and is better than chest CT in disease diagnosis. CRISPR technology, especially non-SHERLOCK type and multi-target gene detection, can be used to diagnose COVID-19 with higher accuracy ,and can be used for large-scale population screening.

Introduction

Corona Virus Disease 2019 (COVID-19) that broke out at the end of December 2019 has been raging for more than 2 years, bringing unpredictable harm to the physical and mental health of all mankind and global economic development. As of January 6, 2021, more than 290 million confirmed SARS-CoV-2 cases have been reported globally, and more than 5.48 million COVID-19-related deaths have been reported. The World Health Organization has officially announced that due to the lack of effective antiviral drugs or vaccines, early detection of patients and immediate isolation of patients have played a mandatory role in the fight against COVID-19 [1]. In order to better control the epidemic, taking effective prevention and control measures, screening as many symptomatic and asymptomatic infections as possible, and tracking their contacts are the most effective ways to prevent the spread of the disease. At present, the detection methods of SARS-CoV-2 are mainly divided into three categories: nucleic acid detection, serological detection and chest CT. Nucleic acid testing is considered to be the "gold standard" for diagnosis [2], but it requires complex equipment and well-trained professional and technical personnel [3]. In the early stages of virus infection, due to the small number of viruses on nasopharyngeal swabs, False negative results may appear [4-5]. The irregular operation of the sampling personnel and the incorrect cooperation of the subject are all reasons for the false negative results. Similarly, the accuracy of serological testing is low, and it may take several days to several weeks for an infected person to develop a detectable antibody response after the onset of symptoms [6,26], and there may be poor sensitivity in the early stages of infection[7]. Therefore, serological testing is not suitable as an effective tool for early diagnosis. Chest computed tomography (CT) can detect lung lesions in patients in the developmental stage of COVID-19, but cannot accurately identify lung changes in mild or asymptomatic patients[8], and the specificity is not high, because other viruses or Diseases can cause similar phenomena. In addition, due to the risk of cross-infection with chest CT, and the potential harm of CT radiation to the patient's body, whether it can be used as the first choice for large-scale population screening remains to be discussed. Chest CT plays a central role in disease staging and treatment effects, but it is expensive, so it cannot be widely used in large-scale screening. This makes the COVID-19 pandemic have a strong demand for testing tools for the widely distributed SARS-CoV-2 genetic material. Recent studies have found that compared with chest CT, CRISPR technology has higher accuracy [9] and can be used for the diagnosis of the disease. The purpose of this systematic review and meta-analysis is to determine the diagnostic accuracy of CRISPR technology in COVID-19 patients through comparison with chest CT, and to provide a theoretical basis for rapid and large-scale screening of new coronary pneumonia infection.

Materials And Methods

1.1 Literature inclusion and exclusion criteria:

1.1.1Inclusioncriteria:

(1) Research type: prospective randomized controlled trial or reasonably designed retrospective study, whether blinded or not, but the two sets of data must be compared;(2) Research objects: suspected or confirmed COVID-19 cases, chest CT and CRISPR technology clearly report the number of positive cases;(3) Intervention measures: Two diagnostic methods are adopted, the application of chest CT and CRISPR technology in the diagnosis of COVID-19, and the two diagnostic methods are described in detail;(4) Outcome indicators: sensitivity, specificity, etc.

1.1.2 Exclusion criteria:

(1) The research object is other diagnostic methods for COVID-19, such as PCR; (2) Systematic review or meta-analysis; (3) There are no relevant outcome indicators of the study or incomplete reports in the literature; (4) The useful data cannot be extracted or cannot Obtain the full text; (5) Non-Chinese and English documents. The quality of the repeated report literature is poor, the research objects and intervention measures do not meet the inclusion criteria, the outcome measurement data is unreasonable, and the outcome measurement indicators cannot be provided or calculated.

1.2 Search strategy

Using a combination of subject terms and free words, computer search PubMed, The Cochrane Library, Web of Science and Wan-Fang database, VIP database, CNKI database, search the database until January 2022 publicly published comparative chest CT And related literature on the application of CRISPR technology in diagnosis of COVID-19. Chinese search terms: COVID-19, diagnosis, chest CT, CRISPR technology; English search terms: COVID-19, diagnosis, chest CT, X-Ray Computed Tomography, CRISPR.

1.3 Literature screening and data extraction

Two doctors will independently screen the retrieved documents. If there is any disagreement, please the third doctor to decide or resolve it through group discussion. The two doctors will screen the literature and extract the data according to the pre-set inclusion and exclusion criteria. After carefully reading the title and abstract of the literature, the literature that obviously does not meet the inclusion criteria is eliminated, and then by reading the full text Select the documents that may meet the inclusion criteria, then determine the final selected documents, and finally extract relevant materials. For those documents with incomplete information, contact the authors for help through emails, telephones, etc. The specific content of the data extraction includes: General information: author, title, study year and the number of cases in each group of the two methods; Outcome indicators: sensitivity, specificity, etc.

1.3 Data extraction and statistical analysis

Two doctors will independently screen the retrieved documents. If there is any disagreement, please the third doctor to decide or resolve it through group discussion. The two doctors will screen the literature and extract the data according to the pre-set inclusion and exclusion criteria. After carefully reading the title and abstract of the literature, the literature that obviously does not meet the inclusion criteria is eliminated, and then by reading the full text Select the documents that may meet the inclusion criteria, then determine the final selected documents, and finally extract relevant materials. For those documents with incomplete information, contact the authors for help through emails, telephones, etc. The specific content of the data extraction includes: (1)General information: author, title, study year and the number of cases in each group of the two methods;(2) Outcome indicators: sensitivity, specificity, etc.

1.4 Literature quality evaluation

Meta analysis is the collection and sorting of original research data and the second processing. The quality of the original research data included in the literature and the evaluation methods will affect the accuracy of the meta-analysis results, and even have a great impact on clinical practice. Misleading. This Meta-analysis uses QUADAS for quality evaluation. According to the QUADAS-2 evaluation items, the risk of bias is evaluated from the four aspects of "selection of cases", "tests to be evaluated", "gold standard", "case flow and progress", and at the same time the pre-assessment 3 parts of clinical applicability. From the results of the risk of bias evaluation, it can be found that the quality of the literature of all included studies is relatively good, and the high-risk items are mainly "case flow and progress" (Figure 2).

1.5 Statistical analysis

The RevMan5.4 software provided by the Cochrane Collaboration was used to conduct Meta analysis on the included research data. Each effect size is represented by a 95% confidence interval (CI). Due to the variability between different studies, there is heterogeneity, and I^2 is combined to determine the magnitude of heterogeneity quantitatively. If $I^2 < 50\%$, the fixed-effects model is used for meta-analysis; if $I^2 > 50\%$, the random-effects model is used for meta-analysis, and the difference is statistically significant with $P \leq 0.05$. Calculate the combined sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio and 95% confidence interval (CI) of each

document, and estimate the area under the comprehensive receiver operating characteristic (SROC) curve. The Deek funnel chart method was used to assess publication bias.

Results

2.1 Literature search results

A total of 418 articles were obtained through preliminary search of the database, 320 articles were included after deduplication, 268 articles were initially included after reading the title and abstract, and then the full text was read and 96 articles were excluded according to the established literature inclusion and exclusion criteria, and 18 articles were finally included. There are a total of 2668 patients in the literature (Figure 1). Among them, there are 13 articles evaluating the diagnostic value of CRISPR technology [10-22], and 4 articles on chest CT examination [23-26].

2.2 Basic information of the included studies

Table 1 and Table 2 are the basic information of all the included documents.

2.3 Meta analysis results

2.3.1 Threshold effect analysis

By drawing the SROC curve, there is no "shoulder-arm-like" distribution, which shows that there is no threshold effect in this study.

2.3.2 Non-threshold effect heterogeneity analysis

For all indicators $I^2 > 50\%$, a random effects model was used for Meta analysis. The results showed that the combined sensitivity of CRISPR technology for diagnosing new coronary pneumonia infection was 0.96 [95% CI (0.93, 0.98)], and the combined specificity was 1.00 [95% CI (0.92, 1.00)], the combined positive likelihood ratio is 458.69 [95% CI (11.51, 18280.8)], the combined negative likelihood ratio is 0.04 [95% CI (0.02, 0.07)], the area under the SROC curve is 0.99 [95% CI (0.97, 0.99)]. The combined sensitivity of chest CT in diagnosing new coronary pneumonia infection was 0.94 [95% CI (0.83, 0.98)], combined specificity was 0.55 [95% CI (0.22, 0.83)], combined diagnostic odds ratio was 19.90 [95% CI (7.88, 50.25)], the combined positive likelihood ratio is 2.08 [95% CI (1.00, 4.32)], the combined negative likelihood ratio is 0.10 [95% CI (0.05, 0.23)], and the area under the SROC curve is 0.91 [95% CI (0.88, 0.93)] See Figure 3~Figure 9.

2.3.3 Subgroup analysis

In view of the certain heterogeneity of this study, subgroup analysis was performed according to the publication year, country, inspection type, type of CRISPR involved, number of detected target genes, and number of included studies included in the literature study. In terms of CRISPR type, SHERLOCK and non- The pooled sensitivities of SHERLOCK were 0.89 (0.81, 0.95) and 0.97 (0.94, 0.98); pooled specificities were 1.00 (0.95, 1.00) and 1.00 (0.91, 1.00), respectively; pooled DOR was 651.44 (63.19, 6716.33), respectively And 10076 (339, 299372). The analysis found that the two subgroups did not overlap in specificity, sensitivity, and DOR 95% CI interval in the number of target genes detected, indicating that the difference between the two subgroups was statistically significant; SHERLOCK and non-SHERLOCK detection of AUC They were 0.5 and 0.98, respectively, and the difference in diagnostic accuracy was statistically significant. The results are shown in Table 3.

2.3.4 Meta regression analysis

In view of the certain heterogeneity of this study, subgroup analysis was performed according to the publication year, country, inspection type, type of CRISPR involved, number of detected target genes, and number of included studies included in the literature study. In terms of CRISPR type, SHERLOCK and non- The pooled sensitivities of SHERLOCK were 0.89 (0.81, 0.95) and 0.97 (0.94, 0.98); pooled specificities were 1.00 (0.95, 1.00) and 1.00 (0.91, 1.00), respectively; pooled DOR was 651.44 (63.19, 6716.33), respectively And 10076 (339, 299372). The analysis found that the two subgroups did not overlap in specificity, sensitivity, and DOR 95% CI interval in the number of target genes detected, indicating that the difference between the two subgroups was statistically significant; SHERLOCK and non-SHERLOCK detection of AUC They were 0.5 and 0.98, respectively, and the difference in diagnostic accuracy was statistically significant. The results are shown in Table 3.

2.4 Sensitivity analysis

This meta-analysis uses the sensitivity analysis method that comes with the RevMan5.4 software to analyze and exclude each group of indicators included in the study. First, single articles are eliminated one by one, and then the analysis is recalculated. Observing the I^2 , P value, and the combined effect size and 95% CI, after the single article was eliminated, and finally found that the results did not change much, we can see that the results of this study are reliable.

2.5 Publication bias

The Deek funnel chart was used to test the publication bias, suggesting that there is no potential publication bias among the included studies (P values are 0.03 and 0.55, respectively), as shown in Figure 10 and Figure 11.

Table 1 Basic information of the included literature related to the diagnosis of new coronary pneumonia by CRISPR

1st author	year	country	Published journals	TP	FP	FN	TN	type of CRISPR	Target gene
XiongErhu ^[10]	2021	China	Angew. Chem	34	0	1	29	CRISPR-cas9	ORF1ab, E
Zhu Xiong ^[11]	2021	China	ACS sensors	37	0	0	77	CRISPR-Cas12a	ORF1ab, N
ShreeyaAgrawal ^[12]	2020	United States	medRxiv	33	0	2	28	DISCoVER	N
ParinazFozouni ^[13]	2021	United States	Cell	5	0	0	5	CRISPR-cas13	N
Dan Xiong ^[14]	2020	China	medRxiv	11	0	0	11	CRISPR-Cas12a	ORF1ab, N
PattarapornNimsamer ^[15]	2020	Thailand	J Virol Methods	41	0	3	63	CRISPR-Cas12a	N1
Jon Arizti-Sanz ^[16]	2020	United States	bioRxiv	27	3	0	20	SHINE	ORF1a
Broughton JP ^[17]	2020	United States	Nature	38	0	2	42	DETECTRE	N, E
MaturadaPatchsung ^[18]	2020	Thailand	Nat Biomed Eng	71	0	10	73	SHERLOCK	S
Jennifer N. Rauch ^[19]	2020	United States	J Clin Microbiol	63	3	2	150	CREST	N
ZahirAli ^[20]	2020	Saudi Arabia	Virus Research	18	3	0	3	iSCAN	N, E
Ashwin Ramachandran ^[21]	2020	United States	Proc Natl Acad Sci U S A	30	0	2	32	CRISPR-Cas12a	N, E
Julia Joung ^[22]	2020	United States	medRxiv	12	0	0	5	SHERLOCK	N

Table 2 Basic information of the included literature related to the diagnosis of new coronary pneumonia by chest CT

1st author	year	country	Published journals	TP	FP	FN	TN	
Damiano Caruso ^[23]	2020	Italy	Radiology	60	42	2	54	chest CT
Wu J ^[24]	2020	China	Invest Radiol	76	14	4	6	chest CT
Yuki Himoto ^[25]	2020	Japan	Jpn J Radiol	4	1	2	14	chest CT
ZenghuiCheng ^[26]	2020	China	AJR Am J Roentgenol	11	17	0	5	chest CT

Table 3 CRISPR technology and chest CT diagnosis of new coronary pneumonia infection subgroup analysis results (point estimation and 95% CI)

type of detection	subgroup	Quantity included	sensitivity	specificity	Diagnostic odds ratio	Positive likelihood ratio	Negative likelihood ratio	SROC
CRISPR	2020	10	0.96	0.99	4452.91	183.64	0.04	0.99
			(0.91,0.98)	(0.90,1.00)	(259.99,76265.41)	(8.57,3934.04)	(0.02,0.09)	(0.97,0.99)
	2021	3	0.99	1	1308.57	44.51	0.04	0.99
			(0.93,1.00)	(0.97,1.00)	(119.59,14318.96)	(9, 220.01)	(0.01,0.13)	(0.96,0.99)
	China	3	0.96	1	1942.19	58.19	0.03	0.99
			(0.94,0.97)	(0.97,1.00)	(232.77,16205.42)	(11.94,283.51)	(0.01,0.11)	(0.98,1.00)
	Other countries	10	0.96	0.99	4150.83	175.11	0.04	0.99
			(0.91,0.98)	(0.89,1.00)	(246.07,70017.52)	(8.27, 3704.79)	(0.02,0.09)	(0.97,0.99)
	Single gene	7	0.96	0.26	2552	114.4	0.04	0.99
			(0.89,0.98)	(0.13,0.42)	(320, 20376)	(11.8, 1109.6)	(0.02,0.11)	(0.98,1.01)
	Multiple genes	6	0.97	1	767708	21110	0.03	0.98
			(0.93,0.99)	(0.03,1.00)	(1, 4.3e+11)	(10.0,1.4e+10)	(0.01,0.07)	(0.96,0.99)
Chest CT	SHERLOCK	2	0.89	1	651.44	37.58	0.12	0.5
			(0.81,0.95)	(0.95,1.00)	(63.19,6716.33)	(2.83,498.59)	(0.07,0.21)	
	Non-SHERLOCK	11	0.97	1	10076	316.1	0.03	0.98
			(0.94,0.98)	(0.91,1.00)	-339,299,372	(9.7,10265.5)	(0.02,0.06)	(0.97,0.99)
	China	2	0.96	0.26	7.79	1.3	0.17	0.8
			(0.89,0.99)	(0.15,0.41)	(2.26,28.07)	(1.07,1.58)	(0.06,0.49)	(0.76,0.83)
	Other countries	2	0.89	0.78	29.11	3.99	0.14	0.9
			(0.51,0.99)	(0.38,0.95)	(6.61,128.12)	(1.21,13.12)	(0.03,0.69)	(0.89,0.93)
	>50	2	0.96	0.26	7.97	1.3	0.17	0.94
			(0.89,0.99)	(0.14,0.42)	(2.26,28.07)	(1.07,1.58)	(0.06,0.49)	(0.92,0.98)
	<50	2	0.88	0.51	15.45	3.11	0.32	0.5
			(0.64,0.99)	(0.34,0.68)	(2.13,111.99)	(0.21,46.75)	(0.11,0.93)	

Discussion

The results of this study show that the combined sensitivity and combined specificity of CRISPR technology in diagnosing SARS-CoV-2 infection in COVID-19 patients are higher than the corresponding effect size of chest CT, indicating that CRISPR technology has a better detection of SARS in COVID-19 patients and the ability to identify and exclude patients with CoV-2 infection and the ability to exclude patients with non-SARS-CoV-2 infection, and the combined specificity of chest CT is 55%, less than 85%, and there is a high misdiagnosis rate, that is, for COVID-19 patients There is a certain false positive result in chest CT examination alone, which is consistent with the results of Varble et al. [28]. It may be because in patients with mild COVID-19, their chest CT gradually shows "ground glass density" as the disease progresses. It is caused by the evolution process of "shadow-paving stone sign-consolidation shadow". The combined positive likelihood ratios of CRISPR technology and chest CT are 458.69 and 2.08, respectively, and the combined negative likelihood ratios are 0.04 and 0.10, respectively. It is generally considered that the positive likelihood ratio is greater than 10, indicating that the pre-test probability and the post-test probability have a decisive change. The diagnosis can be confirmed. The greater the positive likelihood ratio, the greater the likelihood of the subject suffering from the disease, and the smaller the negative likelihood ratio, the higher the correct rate of the diagnosis of negative results [29]. The area under the SROC curve can judge the overall performance of the diagnostic test, and it is generally believed

that the area under the curve >0.9 has a higher accuracy. The AUC values of CRISPR technology and chest CT are 0.99 and 0.91, respectively. The SROC curve of the two tests can be drawn, and the two tests can be compared intuitively. From the above analysis, it is found that CRISPR technology has extremely high diagnostic value for the diagnosis of new coronary pneumonia infection, and is useful for disease diagnosis. The help is better than chest CT.

After the analysis of the diagnostic threshold effect, the SROC curve does not show a typical "shoulder-arm shape", indicating that there is no threshold effect. For the included studies, the combined effect size was calculated, showing sensitivity, specificity and positive likelihood ratio $P < 0.05$. Therefore, there is heterogeneity among the studies. In order to explore and find the source of heterogeneity, subgroup analysis and Meta regression were carried out according to the publication year of the included literature research, the country, the type of research involving CRISPR, and the number of detected target genes, etc., both of which indicate the type of CRISPR research. It may be the source of the heterogeneity of the included literature research. Both subgroup analysis and Meta regression indicate that the type of research used to detect CRISPR is statistically significant, and that non-SHERLOCK detection has higher specificity, sensitivity and diagnostic odds ratio than SHERLOCK.

Another major source of heterogeneity is the "detection of the number of target genes". The genes of the new coronavirus are mainly composed of 16 non-structural proteins at one end of the open reading frame (ORF) and genes such as S protein, N protein, and E protein [30]. Subgroup analysis and Meta regression found that the number of target genes to be detected has a certain statistical significance. Multi-gene detection has higher sensitivity, specificity and diagnostic odds ratio than single-gene detection. The larger the DOR value, the better the diagnosis effect [31]. Combining the above analysis shows that compared to chest CT, CRISPR technology has better value for the diagnosis of COVID-19.

This study has the following advantages: on the basis of fully incorporating relevant Chinese and English literature, Meta regression and subgroup analysis methods are used to assess the source of heterogeneity, and at the same time, two diagnostic tests are indirectly compared, and two diagnostic tests are used to achieve diagnostics. Test network Meta analysis method, namely multi-test SROC curve diagram method and adjusted indirect comparison method. The limitations of this study: (1) The sample size of the included literature is small, which is prone to bias; (2) The included patients do not necessarily conform to the principle of randomness, and selection bias is inevitable, and a larger sample of randomized research is required. Verification; (3) In the included literature, there are few studies on the accuracy of the series and parallel use of different diagnostic tests, so the best combination of the series and parallel use of different diagnostic tests cannot be optimally obtained, and the feasibility and cost-effectiveness of the combinations cannot be evaluated. Despite these limitations, our research provides new insights for the detection of SARS-CoV-2 infection.

In summary, the results of this systematic review and meta-analysis are that for the detection of SARS-CoV-2 infection in COVID-19 patients, CRISPR technology and chest CT have high clinical diagnostic value. Meta analysis shows that the use of CRISPR technology is superior to chest CT, and it has a lower misdiagnosis rate, which provides new ideas for the effectiveness of COVID-19 patients' diagnosis. Because the diagnostic sensitivity of chest CT scans is lower than CRISPR technology, CRISPR technology is necessary for any individual with suspicious symptoms. Therefore, the application of CRISPR technology can be used for rapid diagnosis of COVID-19, and large-scale population screening is essential. CRISPR technology has become an extremely attractive diagnostic tool and has shown great potential in the development of a new generation of molecular diagnostic methods. In the future, more large-scale, multi-center prospective studies are needed to explore the relevance of CRISPR technology in diagnosing SARS-CoV-2 infection, so as to help control the development of the epidemic.

Declarations

Data availability

All data generated or analyzed during this study are included in this published article.

Author contributions

Jiu-Cong Zhang was the principal investigator and supervisor of the project. Jing-Jing Jiang, Fu-Juan Feng, Xiao-Wen Yao, Rong Wang and Cai-Hong Wang individually screened the data and make the data extraction sheet and tables of the article. Chun Gao had designed the search strategy and wrote the manuscript. Yu-Xia Zhou, Hui-Juan Shao, Xue-Feng Ma, Jun-Huang and Xiao-Hui Yu co-supervised the project and data curation.

Competing interests

The authors declare no competing interests.

References

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA*. 2020 Apr 7;323(13):1239-1242. doi: 10.1001/jama.2020.2648. PMID: 32091533.
2. Patchsung M, Jantarug K, Pattama A, et al. Clinical validation of a Cas13-based assay for the detection of SARS-CoV-2 RNA. *Nat Biomed Eng*. 2020;4(12):1140-1149. doi:10.1038/s41551-020-00603-x
3. Zhang K, et al. Routine saliva testing for the identification of silent coronavirus disease 2019 (COVID-19) in healthcare workers. *Infect Control Hosp Epidemiol*. 2021;42(10):1189-1193. doi:10.1017/ice.2020.1413
4. You Y, et al. Asymptomatic COVID-19 infection: diagnosis, transmission, population characteristics [published online ahead of print, 2021 Jul 30]. *BMJ Support Palliat Care*. 2021;bmj.spcare-2020-002813. doi:10.1136/bmj.spcare-2020-002813
5. Schuit E, Veldhuijzen IK, Venekamp RP, et al. Diagnostic accuracy of rapid antigen tests in asymptomatic and presymptomatic close contacts of individuals with confirmed SARS-CoV-2 infection: cross sectional study. *BMJ*. 2021;374:n1676. Published 2021 Jul 27. doi:10.1136/bmj.n1676
6. Mathew BJ, Vyas AK, Khare P, et al. Laboratory diagnosis of COVID-19: current status and challenges. *Iran J Microbiol*. 2021;13(1):1-7. doi:10.18502/ijm.v13i1.5485
7. Chen Y, Chan KH, Hong C, et al. A highly specific rapid antigen detection assay for on-site diagnosis of MERS. *J Infect*. 2016;73(1):82-84. doi:10.1016/j.jinf.2016.04.014
8. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study [published correction appears in Lancet. 2020 Feb 4;]. *Lancet*. 2020;395(10225):689-697. doi:10.1016/S0140-6736(20)30260-9
9. Chen JS, Ma E, Harrington LB, et al. CRISPR-Cas12a target binding unleashes indiscriminate single-stranded DNase activity [published correction appears in Science. 2021 Feb 19;371(6531):]. *Science*. 2018;360(6387):436-439. doi:10.1126/science.aar6245
10. Xiong E, Jiang L, Tian T, et al. Simultaneous Dual-Gene Diagnosis of SARS-CoV-2 Based on CRISPR/Cas9-Mediated Lateral Flow Assay. *Angew Chem Int Ed Engl*. 2021;60(10):5307-5315. doi:10.1002/anie.202014506
11. Zhu X, Wang X, Li S, et al. Rapid, Ultrasensitive, and Highly Specific Diagnosis of COVID-19 by CRISPR-Based Detection. *ACS Sens*. 2021;6(3):881-888. doi:10.1021/acssensors.0c01984
12. Agrawal S, et al. Rapid, point-of-care molecular diagnostics with Cas13. Preprint. *medRxiv*. 2021;2020.12.14.20247874. Published 2021 Apr 5. doi:10.1101/2020.12.14.20247874
13. Fozouni P, et al. Amplification-free detection of SARS-CoV-2 with CRISPR-Cas13a and mobile phone microscopy. *Cell*. 2021;184(2):323-333.e9. doi:10.1016/j.cell.2020.12.001
14. Xiong D, et al. Rapid detection of SARS-CoV-2 with CRISPR-Cas12a. *PLoS Biol*. 2020;18(12):e3000978. Published 2020 Dec 15. doi:10.1371/journal.pbio.3000978
15. Nimsamer P, et al. Comparative performance of CRISPR-Cas12a assays for SARS-CoV-2 detection tested with RNA extracted from clinical specimens. *J Virol Methods*. 2021;290:114092. doi:10.1016/j.jviromet.2021.114092
16. Arizti-Sanz J, et al. Streamlined inactivation, amplification, and Cas13-based detection of SARS-CoV-2. *Nat Commun*. 2020;11(1):5921. Published 2020 Nov 20. doi:10.1038/s41467-020-19097-x
17. Broughton James P, et al. CRISPR-Cas12-based detection of SARS-CoV-2. *Nat Biotechnol*. 2020;38(7):870-874. doi:10.1038/s41587-020-0513-4
18. Patchsung M, et al. Clinical validation of a Cas13-based assay for the detection of SARS-CoV-2 RNA. *Nat Biomed Eng*. 2020;4(12):1140-1149. doi:10.1038/s41551-020-00603-x
19. Rauch JN, et al. A Scalable, Easy-to-Deploy Protocol for Cas13-Based Detection of SARS-CoV-2 Genetic Material. *J Clin Microbiol*. 2021;59(4):e02402-20. Published 2021 Mar 19. doi:10.1128/JCM.02402-20
20. Ali Z, et al. iSCAN: An RT-LAMP-coupled CRISPR-Cas12 module for rapid, sensitive detection of SARS-CoV-2. *Virus Res*. 2020;288:198129. doi:10.1016/j.virusres.2020.198129
21. Ramachandran A, et al. Electric field-driven microfluidics for rapid CRISPR-based diagnostics and its application to detection of SARS-CoV-2. *Proc Natl Acad Sci U S A*. 2020;117(47):29518-29525. doi:10.1073/pnas.2010254117
22. Joung J, et al. Point-of-care testing for COVID-19 using SHERLOCK diagnostics. Preprint. *medRxiv*. 2020;2020.05.04.20091231. Published 2020 May 8. doi:10.1101/2020.05.04.20091231

23. Caruso D, et al. Chest CT Features of COVID-19 in Rome, Italy. 2020;296(2):E79-E85. doi:10.1148/radiol.2020201237
24. Wu J, et al. Chest CT Findings in Patients With Coronavirus Disease 2019 and Its Relationship With Clinical Features. *Invest Radiol.* 2020;55(5):257-261. doi:10.1097/RLI.0000000000000670
25. Himoto Y, et al. Diagnostic performance of chest CT to differentiate COVID-19 pneumonia in non-high-epidemic area in Japan. *Jpn J Radiol.* 2020;38(5):400-406. doi:10.1007/s11604-020-00958-w
26. Cheng Z, et al. Clinical Features and Chest CT Manifestations of Coronavirus Disease 2019 (COVID-19) in a Single-Center Study in Shanghai, China. *AJR Am J Roentgenol.* 2020;215(1):121-126. doi:10.2214/AJR.20.22959
27. Jiang JJ, et al. Research progress on detection of asymptomatic infection of novel coronavirus pneumonia. *Journal of Hainan Medical University.* doi:10.13210/j.cnki.jhmu.20211221.001.
28. Varble Net al. CT and clinical assessment in asymptomatic and pre-symptomatic patients with early SARS-CoV-2 in outbreak settings [published correction appears in *Eur Radiol.* 2020 Dec 8;]. *Eur Radiol.* 2021;31(5):3165-3176. doi:10.1007/s00330-020-07401-8
29. Tian JH, Chen JF. Guidebook for systematic reviews/meta-analyses of diagnostic tests. China Medical Science and Technology Press, 2015.
30. Graham RL, Baric RS. Recombination, reservoirs, and the modular spike: mechanisms of coronavirus cross-species transmission. *J Virol.* 2010;84(7):3134-3146. doi:10.1128/JVI.01394-09
31. Glas AS, Lijmer JG, Prins MH, et al. The diagnostic odds ratio: a single indicator of test performance. *J Clin Epidemiol.* 2003;56(11):1129-1135. doi:10.1016/s0895-4356(03)00177-x

Figures

Figure 1

The number of articles during several steps based on the PRISMA flow diagram

Figure 2

Quality evaluation results of the included literature based on the QUADAS-2 standard

0.60

Figure 3

Forest plot of combined sensitivity and combined specificity of CRISPR in diagnosing new coronary pneumonia infection

0.60

Figure 4

Forest plot of combined diagnostic odds ratio for CRISPR diagnosis of new coronary pneumonia infection

0.60

Figure 5

Forest plot of combined likelihood ratio for CRISPR diagnosis of new coronary pneumonia infection

0.60

Figure 6

Forest plot of combined sensitivity and specificity of chest CT diagnosis of new coronary pneumonia infection

0.60

Figure 7

Forest plot of combined diagnostic odds ratio of chest CT diagnosis of new coronary pneumonia infection

0.60

Figure 8

Forest plot of combined likelihood ratio of chest CT diagnosis of new coronary pneumonia infection

Figure 9

Comprehensive receiver operating characteristic curve of CRISPR technology and chest CT diagnosis of new coronary pneumonia infection

Figure 10

The Deeks' funnel plot curve for assessment of publication bias by CRISPR technology

Figure 11

The Deeks' funnel plot curve for assessment of publication bias by chest CT

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [PRISMA2020checklist.docx](#)