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Diagnostic value of circulating tumor cells in gastric cancer: A systematic review and Meta-analysis

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ADMINISTRATIVE INFORMATION

Support - Foshan City Health and Wellness Bureau (20230226).

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 February 2025 and was last updated on 7 February 2025.

INTRODUCTION

Review question / Objective P: patients with pathologic diagnosis of gastric cancer I: not applicable; C: healthy population and/or patients with benign gastric disease. o: overall sensitivity and specificity; S: studies included in the meta-analysis were diagnostic tests.

Rationale The overall accuracy of the various methods used to detect CTC in gastric cancer has not been described, and the use of CTC in the diagnosis of gastric cancer has been controversial. In detecting CTC in gastric cancer, some studies have suggested that CTC detection may be associated with detection method and disease stage, while others have failed to show such an association. Therefore, we conducted a meta-analysis to elucidate the relationship between CTC and gastric cancer.

Condition being studied Stomach cancer is the fifth most common type of cancer and the third leading cause of death worldwide. Gastric cancer incidence and mortality rates are increasing because most patients with gastric cancer are already in advanced stages of cancer at the time of diagnosis. A reliable screening test for gastric cancer is needed because of its poor prognosis, few treatment options, and susceptibility to metastasis, recurrence, and drug resistance. Currently, the initial diagnosis of gastric cancer still largely relies on endoscopy and pathologic biopsy, of which most patients require invasive procedures. Meanwhile, although many noninvasive biomarkers are being applied, their sensitivity and specificity are very limited. Therefore, there is an urgent need for a noninvasive, highly sensitive and specific diagnostic method to diagnose gastric cancer.

METHODS

Search strategy ((("Stomach Neoplasms"[Mesh]) OR ((((((((((((((((((Neoplasm, Stomach[Title/Abstract]) OR (Stomach Neoplasm[Title/Abstract])) OR (Gastric Neoplasms[Title/Abstract])) OR (Gastric Neoplasm[Title/Abstract])) OR (Neoplasm,

Gastric[Title/Abstract])) OR (Neoplasms, Gastric[Title/Abstract])) OR (Neoplasms, Stomach[Title/Abstract])) OR (Cancer of Stomach[Title/Abstract])) OR (Stomach Cancers[Title/Abstract])) OR (Cancer of the Stomach[Title/Abstract])) OR (Gastric Cancer[Title/Abstract])) OR (Cancer, Gastric[Title/Abstract])) OR (Cancers, Gastric[Title/Abstract])) OR (Gastric Cancers[Title/Abstract])) OR (Stomach Cancer[Title/Abstract])) OR (Cancers, Stomach[Title/Abstract])) OR (Cancer, Stomach[Title/Abstract])) OR (Gastric Cancer, Familial Diffuse[Title/Abstract]))) AND (("Neoplastic Cells, Circulating"[Mesh]) OR ((((((((((((((((((((((((CTC[Title/Abstract]) OR (Cells, Neoplasm Circulating[Title/Abstract])) OR (Cell, Neoplasm Circulating[Title/Abstract])) OR (Neoplasm Circulating Cell[Title/Abstract])) OR (Circulating Cells, Neoplasm[Title/Abstract])) OR (Circulating Neoplastic Cells[Title/Abstract])) OR (Cell, Circulating Neoplastic[Title/Abstract])) OR (Cells, Circulating Neoplastic[Title/Abstract])) OR (Circulating Neoplastic Cell[Title/Abstract])) OR (Neoplastic Cell, Circulating[Title/Abstract])) OR (Circulating Tumor Cells[Title/Abstract])) OR (Cell, Circulating Tumor[Title/Abstract])) OR (Cells, Circulating Tumor[Title/Abstract])) OR (Circulating Tumor Cell[Title/Abstract])) OR (Tumor Cell, Circulating[Title/Abstract])) OR (Tumor Cells, Circulating[Title/Abstract])) OR (Neoplasm Circulating Cells[Title/Abstract])) OR (Tumor Cells, Embolic[Title/Abstract])) OR (Cell, Embolic Tumor[Title/Abstract])) OR (Cells, Embolic Tumor[Title/Abstract])) OR (Embolic Tumor Cell[Title/Abstract])) OR (Tumor Cell, Embolic[Title/Abstract])) OR (Embolic Tumor Cells[Title/Abstract])) OR (Embolism, Tumor[Title/Abstract])) OR (Embolisms, Tumor[Title/Abstract])) OR (Tumor Embolism[Title/Abstract])) OR (Tumor Embolisms[Title/Abstract]))))) AND (sensitiv*[Title/Abstract] OR sensitivity and specificity[MeSH Terms] OR (predictive[Title/Abstract] AND value*[Title/Abstract]) OR predictive value of tests[MeSH Terms] OR accuracy*[Title/Abstract]).

Participant or population Patients with pathologic diagnosis of gastric cancer.

Intervention Diagnostic accuracy of ctc in patients with gastric cancer.

Comparator Healthy population and/or patients with benign gastric disease.

Study designs to be included Studies included in the meta-analysis were diagnostic tests.

Eligibility criteria Inclusion criteria: (1) the type of literature collected had to be based on diagnostic tests; (2) patients with a pathologic diagnosis of gastric cancer; (3) patients with a clear negative control group (healthy population and/or patients with benign gastric diseases) (4) the study samples were peripheral blood; and (5) the study language was Chinese and/or English.
Exclusion criteria: (1) inability to present valid outcome data from the literature; (2) duplication; and (3) unavailability of full text.

Information sources A literature search was conducted in Pubmed, Cochrane, Embase, Web of science, Ovid MEDLINE, and Scopus Chinese databases, and in the Chinese databases of China Knowledge, Wanfang, Wipro, China Biomedical, and Yanshou databases, to identify studies published from the time of library construction to January 30, 2025, investigating the presence or absence of CTCs in the peripheral blood of patients with gastric cancer. the presence of CTCs in the peripheral blood of gastric cancer patients.

Main outcome(s) Overall sensitivity and specificity of CTC for detecting gastriccancer.

Additional outcome(s) None.

Data management The database was searched for the proposed literature using EndNote software to manage, check, exclude review/systematic evaluation/meta-analysis literature, exclude animal testing, further screen the literature by reading the abstracts, and finally download the full text the following data were extracted independently by two researchers the following data were extracted according to the inclusion and exclusion criteria: first author author's name, year of publication, country, language, number of cases and number of controls stage of cancer in the patient, diagnostic accuracy, CTC isolation and enrichment methods, CTC identification and detection methods spirit, sensitivity, specificity, time of blood collection, diagnostic threshold, gold standard diagnostic methods, and the extracted literature was evaluated for quality of literature using QUADAS-2 tool.

Quality assessment / Risk of bias analysis The methodological quality of all included studies was assessed by 2 authors using the QUADAS-2 Scale.

Strategy of data synthesis The Cochran's Q statistic and I^2 statistic were used to assess the heterogeneity between all eligible studies, and influence analysis would be performed If high heterogeneity(I^2>50) was found. We also used

meta-regression to explore the source of heterogeneity. The Deeks' funnel plot was used to evaluate the publication bias in meta-analysis about diagnostic accuracy, and there is no publication bias if the p value obtained by Deeks' test is greaterthan 0.1 ($p > 0.1$). A 2-sided $P < 0.05$ was considered statistically significant for all statisticalanalyses.

Subgroup analysis Meta regression was performed if the heterogeneity of total sensitivity and specificity was significant, and regression analysis was performed based on the followingparameters: 1. CTC isolation and enrichment methods, CTC identification and detection methods; 2. blood collection time; 3. tumor clinical staging.

Sensitivity analysis Sensitivity analysis will be performed by excluding studies with outlier values (e.g., very low or very high procedural costs compared to other studies from the same country and comparable patient setting, outcomes, and procedure) and repeating the primary analysis.

Language restriction English and/or Chinese.

Country(ies) involved China/Japan/Korea.

Keywords circulating tumor cells; gastric cancer; diagnosis; meta-analysis.

Dissemination plans The results of this study will be summarized in English and disseminated by submission for publication in a peer-review journal.

Contributions of each author

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