

INPLASY PROTOCOL

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None declared.

Monocyte chemoattractant protein-1 is a potential biomarker for sepsis diagnosis: a systematic review and meta-analysis

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Review question / Objective: With more than 30 million patients diagnosed with sepsis worldwide each year, finding suitable biomarkers for sepsis diagnosis is a top priority. This systematic evaluation is a diagnostic test for patients admitted to hospital with sepsis, and the test to be evaluated is MCP-1 concentration, with or without a diagnosis of having sepsis as a control, and the study method is an observational study.

Eligibility criteria: ① Observational Chinese and English literature on MCP-1 diagnosis of sepsis in adults published domestically and abroad; ② Patients aged ≥ 18 years; ③ True positive values (TP), false positive values (FP), false negative values (FN), and true negative values (TN) for MCP-1 diagnosis of sepsis can be directly extracted or indirectly calculated. 1.2.2. **Exclusion criteria** ① Non-clinical diagnostic studies; ② Literature that cannot extract data from the four-grid table or has obvious errors in the original research; ③ Animal experiments, dissertations, literature reviews, case reports, etc.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 March 2023 and was last updated on 27 March 2023 (registration number INPLASY202330110).

INTRODUCTION

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hospital with sepsis, and the test to be evaluated is MCP-1 concentration, with or without a diagnosis of having sepsis as a control, and the study method is an observational study.

Condition being studied: Sepsis is a life-threatening organ dysfunction caused by a

host response to infection and is the leading cause of death in patients with severe infection, burns, and ICU patients. Over 30 million people are diagnosed with sepsis worldwide each year, with a death rate of 15%-25%. The inflammatory cytokine storm caused by excessive activation of the immune system is a key step in the treatment of sepsis and is the main cause of rapid progression and multiple organ dysfunction. Early diagnosis of sepsis is of great significance for early goal-directed bundle therapy, improving sepsis treatment capabilities, and improving patient prognosis. In some cases, it is still difficult to distinguish sepsis from non-bacterial SIRS, such as surgery, trauma, and pancreatitis without infection. Therefore, finding sepsis-related biomarkers has become one of the research directions for early diagnosis. As early as the 1980s, a series of studies on tumor necrosis factor (TNF), interleukin-1 β (IL-1 β), and interleukin-6 (IL-6) as biomarkers showed that their plasma levels were related to the severity and outcome of sepsis. Elevated levels of IL-6 and IL-8 can predict the occurrence of neonatal sepsis. In 2003, C-reactive protein (CRP) and procalcitonin (PCT) were also included in the sepsis-2 guidelines. However, CRP has low specificity and lag time. Plasma PCT levels rise after 4 hours of infection and peak after 8-24 hours. Although it peaks earlier than CRP, it is still too late for the 6-hour bundle therapy for sepsis treatment. Currently, the main basis for diagnosing sepsis is the Sequential Organ Failure Assessment (SOFA) score, which contains many indicators and has the same lag time in detection, making early diagnosis difficult. Therefore, finding and applying biomarkers for sepsis diagnosis with high sensitivity and specificity in clinical practice is an urgent task. Monocyte chemoattractant protein-1 (MCP-1), also known as chemokine (CC-motif) ligand 2 (CCL2), is a member of the CC chemokine family that interacts with the CCR2 chemokine receptor on the cell surface and induces or promotes the expression of other inflammatory factors/cells. It mediates the migration and infiltration mechanism of inflammatory cells (such as

monocytes/macrophages and other cytokines) at the site of inflammation, and plays a role in the inflammatory immune response, infection, and tumor occurrence. Multiple studies have shown that MCP-1 levels are significantly elevated in sepsis and are associated with the occurrence of MODS, and play a role in the cell apoptosis mechanism of various diseases, which may be a more "direct" marker of infection.

METHODS

Search strategy: Computer searches were conducted in PubMed, Cochrane Library, Embase, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), Web of Science, Scopus, and Wanfang Data for literature containing MCP-1 detection for sepsis diagnosis. The research was searched in Chinese and English databases using the subject words and free words of "sepsis", "monocyte chemoattractant factor-1", "bloodstream infection", "predictive", and "MCP-1", combined with MeSH subject terms, from the establishment of the database to February 20, 2023. Language restrictions were set to Chinese and English. Relevant materials and conference papers in Chinese and English were manually searched, and the attached references were consulted. (((((((((((((((sepsis[Title/Abstract]) OR (Bloodstream Infections[Title/Abstract])) OR (Infection, Bloodstream[Title/Abstract])) OR (Pyemia[Title/Abstract])) OR (Pyemias[Title/Abstract])) OR (Pyohemia[Title/Abstract])) OR (Pyohemias[Title/Abstract])) OR (Pyaemia[Title/Abstract])) OR (Septicemia[Title/Abstract])) OR (Septicemias[Title/Abstract])) OR (Poisoning, Blood[Title/Abstract])) OR (Blood Poisoning[Title/Abstract])) OR (Blood Poisonings[Title/Abstract])) OR (Poisonings, Blood[Title/Abstract])) OR (Severe Sepsis[Title/Abstract])) OR (Sepsis, Severe[Title/Abstract])) OR ("Sepsis"[Mesh])) AND ((pla2[Title/Abstract]) OR (Phospholipase A2[Title/Abstract]) OR (PLA-2[Title/Abstract])) AND (sensitive*[Title/Abstract] OR sensitivity and specificity[MeSH] OR (predictive[Title/

Abstract] AND value*[Title/Abstract]) OR predictive value of tests[MeSH] OR accuracy*[Title/Abstract]) Computer searches were conducted in PubMed, Cochrane Library, Embase, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), Web of Science, Scopus, and Wanfang Data for literature containing MCP-1 detection for sepsis diagnosis. The research was searched in Chinese and English databases using the subject words and free words of "sepsis", "monocyte chemoattractant factor-1", "bloodstream infection", "predictive", and "MCP-1", combined with MeSH subject terms, from the establishment of the database to February 20, 2023. Language restrictions were set to Chinese and English. Relevant materials and conference papers in Chinese and English were manually searched, and the attached references were consulted. Two researchers searched Chinese databases (CNKI, CBM, Wanfang Data) and English databases (PubMed, Cochrane Library, Embase, Web of Science, Scopus).

Participant or population: Adult patients with sepsis without other severe diseases.

Intervention: MCP-1 level in plasma criteria for sepsis.(sepsis-3/2/1).

Comparator: Non-septic patients or healthy people.

Study designs to be included: Observational studies.

Eligibility criteria: ① Observational Chinese and English literature on MCP-1 diagnosis of sepsis in adults published domestically and abroad; ② Patients aged ≥ 18 years; ③ True positive values (TP), false positive values (FP), false negative values (FN), and true negative values (TN) for MCP-1 diagnosis of sepsis can be directly extracted or indirectly calculated. 1.2.2. Exclusion criteria ① Non-clinical diagnostic studies; ② Literature that cannot extract data from the four-grid table or has obvious

errors in the original research; ③ Animal experiments, dissertations, literature reviews, case reports, etc.

Information sources: Chinese databases (CNKI, CBM, Wanfang Data) and English databases (PubMed, Cochrane Library, Embase, Web of Science, Scopus).

Main outcome(s): Sensitivity, specificity, AUC, TP, PF, TN, PN.

Additional outcome(s): Average age, cut-off point, sex ratio, test method.

Data management: EndNote 9.

Quality assessment / Risk of bias analysis: The QUADAS-2 tool in Review Manager 5.4 was used to evaluate the quality of the studies. The four aspects of case selection, trials to be evaluated, gold standard, case flow, and clinical applicability were judged as "yes", "no", or "unclear", and the corresponding risk levels were defined as "low risk", "high risk", and "uncertain", i.e., when the answer for a particular item is "yes", the risk of bias is considered low. If the answer is "no", the possibility of bias is considered, and if the answer is "unclear", it means that there are not enough data to judge the risk of bias. Deek's funnel plot was drawn to evaluate publication bias.

Strategy of data synthesis: MetaDisc V1.4 and STATA 16.0 software were used to analyze and merge sensitivity, specificity, and their corresponding 95% confidence intervals, combined positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR), and to draw a summary receiver operating characteristic (sROC) curve. The area under the curve (AUC) and Q^* index were calculated to determine the diagnostic value of MCP-1 for sepsis. Spearman's coefficient was used to determine whether there was heterogeneity caused by the threshold effect, and Cochrane-Q value of DOR was calculated to test for non-threshold effects. The I^2 statistic was used to test for heterogeneity in the included studies. $I^2 < 50\%$ indicates non-significant

heterogeneity, and a fixed-effect model is used. When $I^2 > 50\%$, significant heterogeneity is present, and a random-effect model is used.

Subgroup analysis: The I^2 statistic was used to test the heterogeneity of the included studies, with $I^2 < 50\%$ indicating insignificant heterogeneity and a fixed-effects model; when $I^2 > 50\%$ indicating significant heterogeneity, a random-effects model was used and subgroup analysis was performed to determine the source of heterogeneity. A sensitivity analysis was also performed to assess the stability of the results, the subgroup analysis is performed to determine the source of heterogeneity. Sensitivity analysis was performed to evaluate the stability of the results.

Sensitivity analysis: After deleting any one of them, the combined results of the remaining papers are not significantly different from those without deletion, which means that the sensitivity analysis is passed.

Country(ies) involved: China.

Keywords: sepsis, MCP-1, meta-analysis, diagnostic.

Contributions of each author:

Author 1 - Zhuo Chen - Zhuo,C contributed to study design, search strategy, screening of studies, data extraction, and statistical analysis, as well as writing the manuscript.
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