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Yang, S¹; Zhang, ZX²; Shen, LL³.**ADMINISTRATIVE INFORMATION****Support** - This study was supported by Huzhou Science and Technology Plan Project (Grant No. 2022GY45).**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202360074**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 June 2023 and was last updated on 25 June 2023.**INTRODUCTION**

Review question / Objective Numerous articles explore significance of pretreatment C-reactive protein (CRP) in predicting prognosis of cervical cancer (CC) cases. But there are no consistent results. The present meta-analysis focused on identifying exact role of CRP in predicting CC prognosis.

Condition being studied This work thoroughly searched PubMed, Web of Science, Embase, and Cochrane Library databases from inception till April 18, 2023. The significance of CRP level in predicting CC prognostic outcome was estimated according to the combined hazard ratios (HRs) along with relevant 95% confidence intervals (CIs).

METHODS

Search strategy In this work, we thoroughly searched PubMed, Web of Science, Embase, and Cochrane Library databases from inception till

April 18, 2023. The following key words and search terms were used: (C-reactive protein OR CRP OR c-reactive protein) AND (cervical cancer OR cervical carcinoma OR uterine cervix cancer OR cervical neoplasm OR cervix cancer). Only English studies were considered.

Participant or population The diagnosis of CC was made based on pathology for patients.

Intervention Studies explored association of serum CRP levels with any survival outcomes of CC patients and a cut-off value to determine low/high CRP level was identified.

Comparator CC patients with low CRP levels.

Study designs to be included Cohort studies, including prospective and retrospective cohorts published in English.

Eligibility criteria Studies were included according to criteria below: (i) the diagnosis of CC was made

based on pathology; (ii) studies explored association of serum CRP levels with any survival outcomes of CC patients; (iii) available hazard ratios (HRs) together with associated 95% confidence intervals (CIs) in prognosis from studies or calculable data based on the information in articles; (iv) a cut-off value to determine low/high CRP level was identified; and (v) studies published in English. Studies below were eliminated: (i) reviews, meeting abstracts, case reports, comments, letters; (ii) animal studies; and (iii) duplicates.

Information sources In this work, we thoroughly searched PubMed, Web of Science, Embase, and Cochrane Library databases from inception till April 18, 2023.

Main outcome(s) We selected overall survival (OS) as primary outcome, whereas progression-free survival (PFS) as secondary outcome.

Quality assessment / Risk of bias analysis

Subgroup analyses of OS and PFS were conducted to detect possible heterogeneity source. This work also conducted sensitivity analysis by removing one article each time in sequence for evaluating whether the combined results were robust. Funnel plots and Begg's test were employed for assessing publication bias.

Strategy of data synthesis The pooled HRs and 95% CIs were calculated for estimating significance of CRP levels in predicting CC prognosis. In general, a combined HR > 1 with 95% CI not overlapping 1 is considered to indicate a significant association with poor prognosis, and a combined HR < 1 95% CI not overlapping 1 indicates a better prognosis. The inter-study heterogeneities were evaluated through Cochran's Q-test along with the I² statistics. The I² statistic was used to quantify the degree of heterogeneity among studies, with I² < 25%, 25%–75%, and >75% representing low, moderate, and high degrees of inconsistency, respectively. In the analysis of pooled data, we used two different computational models according to the traits of the included studies. And the cutoff point for significant heterogeneity was set as I²>50%. With high heterogeneity being determined based on I²>50% and Q-test p<0.10, so a random-effects model (REM) (DerSimonian-Laird method)[40] should be used; otherwise, a fixed-effects model (FEM) (Mantel-Haenszel method) is utilized.

Subgroup analysis Subgroup analyses of OS and PFS were conducted to detect possible heterogeneity source.

Sensitivity analysis This work also conducted sensitivity analysis by removing one article each time in sequence for evaluating whether the combined results were robust.

Language restriction English.

Country(ies) involved China.

Keywords C-reactive protein; cervical cancer; meta-analysis; prognosis; evidence-based medicine.

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