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.

Participants 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.

**Contributions of each author**
Author 1 - Sheng Yang.
Email: ysh20200116@126.com
Author 2 - Zongxin Zhang.
Email: zhongxin1006@126.com
Author 3 - Linglong Shen.
Email: chaoren5121132023@163.com