

Prognostic role of the pretreatment C-reactive protein/albumin ratio in gastric cancer

A systematic review and meta-analysis

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Abstract

Background: In recent years, several studies have investigated the prognostic role of the pretreatment C-reactive protein/albumin ratio (CAR) in gastric cancer and yielded conflicting results. Therefore, we performed a meta-analysis to assess the prognostic role of the pretreatment CAR in gastric cancer.

Methods: Studies assessing the prognostic role of the pretreatment CAR in patients with gastric cancer were searched from PubMed, Embase, and Cochrane Library up to June 6, 2019. Pooled hazard ratios (HRs) for overall survival (OS), recurrence-free survival (RFS), and cancer-specific survival (CSS) were estimated using a fixed-effects model.

Results: Eight observational studies including 3102 patients were enrolled in this meta-analysis. The pooled result showed that patients with a high CAR had worse OS (pooled HR=1.87; 95% confidence interval (CI)=1.55–2.26; $P < .001$). Results from subgroup analyses indicated that patient country, adjuvant chemotherapy rate, and CAR cut-off value could not affect the property of the correlation ($P < .001$). However, the intensity of the correlation was affected by these factors. In addition, patients with a high CAR had significantly worse RFS (pooled HR=2.11; 95% CI=1.41–3.15; $P < .001$) and CSS (HR=1.59; 95% CI=1.08–2.35; $P = .019$).

Conclusion: A high pretreatment CAR was significantly associated with poor survival for patients with gastric cancer. The prognostic significance of the pretreatment CAR in gastric cancer is need to be confirmed by clinical trials of large sample size.

Abbreviations: CAR = C-reactive protein/albumin ratio, CI = confidence interval, CSS = cancer-specific survival, HR = hazard ratio, MeSH = medical subject heading, NOS = Newcastle-Ottawa quality assessment scale, OS = overall survival, TNM = tumor-node-metastasis.

Keywords: C-reactive protein/albumin ratio, gastric cancer, meta-analysis, prognosis

1. Introduction

Gastric cancer is a major health issue worldwide due to high morbidity and mortality.^[1] In China, gastric cancer is the third highest cause of cancer death in men and the second in women.^[2] With the rise of targeted therapy and immunotherapy in recent years, the prognosis of gastric cancer has been greatly improved.

For example, the current 5-year survival rate for patients with early gastric cancer is 80% to 95%. However, patients with advanced gastric cancer have a five-year survival rate of only 2%.^[3] At present, the prognosis of patients with gastric cancer is mainly predicted according to traditional tumor-node-metastasis (TNM) stage. This prediction method has limited accuracy and cannot accurately stratify the patient's prognosis. Because of this, people have been working on exploring new biomarkers with high sensitivity and specificity that can accurately access the long-term prognosis of patients with gastric cancer.

C-reactive protein (CRP) is an important acute-phase response protein synthesized by liver cells and is one of the most sensitive indicators of inflammation.^[4] Tumor tissue can trigger the body's inflammatory response, so CRP of tumor patients is often elevated.^[4] Albumin (Alb) is synthesized by the liver and is the main component of human serum total protein.^[5] Albumin plays an important role in maintaining blood colloid osmotic pressure, transporting metabolites, and reflecting nutritional status.^[5] Because tumor patients have poor nutritional status, their serum albumin levels are often low. As an indicator that can reflect both inflammatory and nutritional status, CRP/Alb ratio (CAR) is elevated in most tumor patients.^[6] A higher CAR indicates a worse general condition for tumor patients.^[7]

The association between CAR and prognosis has been validated in a variety of tumors.^[8–10] Kudou et al^[11] and Liu et al^[12] found that patients with high pretreatment CAR levels had worse overall survival (OS), recurrence-free survival (RFS),

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and cancer-specific survival (CSS) in gastric cancer. However, the sample size contained in these studies was relatively small, and there were some differences in the results. To obtain an accurate result based on a larger sample size, we conducted this meta-analysis.

2. Methods

2.1. Search strategy

This meta-analysis was conducted in compliance with the Systematic Reviews and Meta-Analyses (PRISMA) guidelines.^[13] Literatures were searched from PubMed, Embase, and the Cochrane Library (last update by June 6, 2019) using the medical subject heading (MeSH) terms “C-reactive protein”, “albumins”, and “stomach neoplasms”. There were no language restrictions during the search.

2.2. Inclusion criteria

The inclusion criteria were as follows:

- (1) retrospective studies investigated the role of CAR in prognostic evaluation of gastric cancer;
- (2) the CAR was calculated with serum CRP and albumin levels before chemotherapy and surgery;
- (3) the hazard ratio (HR) and 95% confidence interval (CI) of CAR could be extracted.

2.3. Data extraction

Some important study characteristics were extracted, including the first author's surname, publication year, country, sample size, patients' ages, tumor location, proportion of patients receiving adjuvant chemotherapy, analysis method, CAR cut-off value, length of follow-up, TNM stage, and HRs and the corresponding 95% CIs of CAR. Because multivariate analysis considers the confounding factors, it is preferred to be adopted over univariate analysis.

2.4. Quality assessment

The Newcastle-Ottawa quality assessment scale (NOS)^[14] was used to assess the quality of each study. Quality assessment scores range from 0 (lowest) to 9 (highest), and a score of 6 or higher indicates high quality.

2.5. Statistical analysis

The optimal cut-off value obtained from the receiver operating characteristic (ROC) curve was used to distinguish the CAR level in all included studies. When HR and 95% CI were not reported, we estimated them based on data extracted from Kaplan–Meier survival curves.^[15] We assessed heterogeneity using the chi-square test (assessing the *P* value) and *I*² statistic.^[16,17] There was no heterogeneity only when the *P* value > .05 and the *I*² < 50%. If there was no heterogeneity, a fixed-effects model (the Mantel–Haenszel method) was used,^[18] otherwise a random effect model (DerSimonian–Laird method) was used.^[19] Begg and Egger tests (assessing the *P* value) and a funnel plot were used to estimate the publication bias. An asymmetric funnel plot and/or a *P*-value < .05 indicated publication bias. At this point, we adjusted

the publication bias using the “Trim and Fill” method.^[20] STATA version 12.0 (Stata Corporation, College Station, TX) was used to perform analyses or generate figures. A *P*-value < .05 indicated statistical significance.

All analyses were based on previous published studies; thus, no ethical approval or patient consent was required.

3. Results

3.1. Study characteristics

By searching the MeSH terms, 195 studies were retrieved from the databases. After preliminary screening, 185 studies were excluded. The full text of the remaining 10 studies was reviewed, and two were excluded due to lack of important data. Finally, a total of 3102 patients from eight studies were included in this meta-analysis (Fig. 1).^[11,12,21–26] The mean NOS score for the eight studies was 6.75, ranging from 5 to 9.

Table 1 shows the main characteristics of the included studies. The number of patients in each study varied between 114 and 688. All patients were from China or Japan. Seven studies reported the proportion of patients receiving adjuvant chemotherapy, which ranged from 14.1% to 100%. In most studies, the location of the gastric cancer included the upper, middle, and lower thirds of the stomach. The optimal CAR cut-off values determined according to their respective ROC curves were used in all studies. The HRs for OS were reported directly in five studies and were estimated indirectly in one study. The HRs for RFS in three studies were all reported directly. Only one study focused on patients' CSS. In addition, none of the patients in the included studies received preoperative or adjuvant radiotherapy.

3.2. Overall survival

The main results of the pooled analysis were showed in Table 2. Six studies including 2013 patients provided HRs and 95% CIs regarding the relationship between the CAR and OS in patients with gastric cancer. A fixed-effects model was used to pool the HRs of these studies because there was no significant heterogeneity (*I*² = 0%, *P* = .856). The pooled result showed that patients with a high CAR had worse OS (pooled HR = 1.87; 95% CI = 1.55–2.26; *P* < .001) (Fig. 2).

Subgroup analyses were subsequently performed to investigate the effects of different clinical characteristics on the pooled HR. The results showed that patient country, proportion of adjuvant chemotherapy, and CAR cut-off value could not affected the property of the association between the CAR and OS (*P* < .001, Table 2). However, the association between a high CAR and poor OS was stronger in Japanese patients than in Chinese patients (Table 2; Fig. 3A). In addition, the association between a high CAR and poor OS in the subgroup with a 100% adjuvant chemotherapy rate was comparatively lower (Table 2; Fig. 3B). When the CAR cut-off value was less than 0.1, the association between a high CAR and poor OS in patients with gastric cancer appeared comparatively higher (Table 2; Fig. 3C).

Because there was no significant heterogeneity, a fixed-effects model was also used for the sensitivity analysis. The results showed that the result pattern was not obviously affected by any single study (Fig. 4). In addition, the results from the meta-regression showed that patient country, proportion of adjuvant chemotherapy, and CAR cut-off value did not affected the pooled effect size (*P* = .254, *P* = .254, and *P* = .338, respectively).

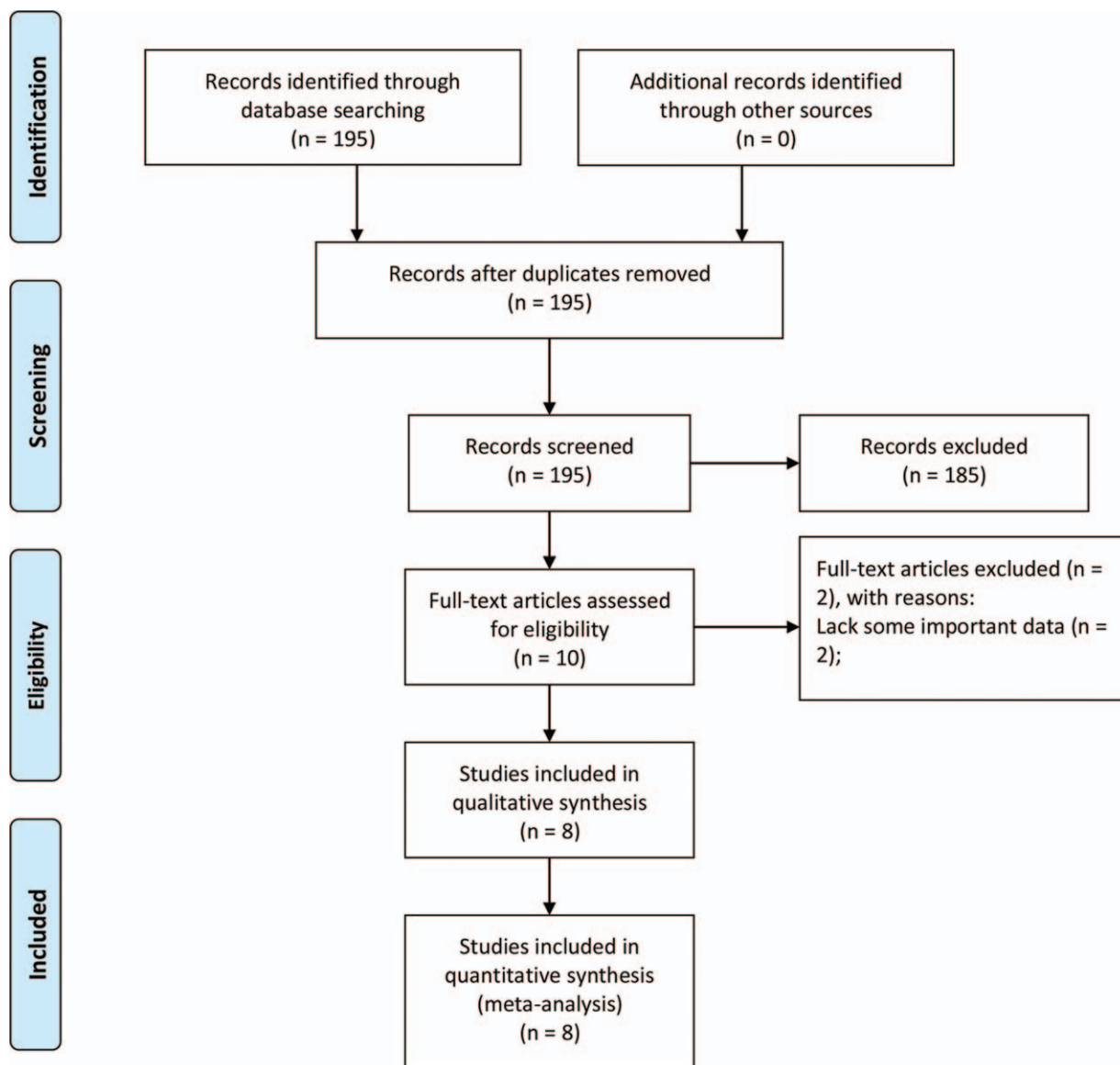


Figure 1. Flow diagram of the study selection process.

Table 1

Main characteristics of all studies included in the meta-analysis.

Study	Country	Case number	Age	Adjuvant chemotherapy (%)	Location	Tumor stage	Follow-up (months)	Cut-off value	Multivariate analysis	HRs provided from	Outcome
Kudou 2019 ^[11]	Japan	144	Median 65	47 (32.6)	Upper 144	I69/II41/III34	NR	0.1	Yes/No	Report/Report	OS/RFS
Liu 2018 ^[12]	China	688	Median 57	688 (100)	Lower 276/Upper + Middle 412	II193/III495	Median 36	0.2	Yes	Report	CSS
Liu 2015 ^[21]	China	455	Median 59	455 (100)	Upper 178/Middle 100/Lower 177	I60/II95/III300	Median 25	0.25	Yes	Report	OS
Mao 2017 ^[22]	China	337	Median 59	337 (100)	Proximal 166/Remote 84/Others 36	I40/II45/III126/IV71	NR	0.3778	Yes	Report	OS
Saito 2018 ^[23]	Japan	453	NR	64 (14.1)	NR	I-I1392/III-IV61	Median 61.9	0.0232	No	SC	OS
Toiyama 2016 ^[24]	Japan	384	Median 67	NR	NR	I223/II61/III58	Median 47.6	0.058	Yes/Yes	Report/Report	OS/RFS
Toyokawa 2018 ^[25]	Japan	240	Median 64.5	178 (74.2)	Upper 57/Middle 98/Lower 83/Whole 2	IIA111/IIIB129	Median 100.5	0.058	No	Report	OS
Xu 2019 ^[26]	China	401	Mean 58.6	256 (63.8)	Upper 117/Middle 69/Lower 191/Mix 24	I135/II84/III182	Median 29	0.131	Yes	Report	RFS

CSS=cancer-specific survival, HR=hazard ratio, NR=not reported, OS=overall survival, RFS=recurrence-free survival, SC=survival curve.

Table 2
Pooled hazard ratios for patients' survival according to subgroup analyses.

Outcome subgroup	Study number	Case number	HR (95%CI) – model	P value	Heterogeneity	
					I ² (%)	P
OS	6	2013	1.87 (1.55–2.26) – fixed	<.001	0	.856
Country						
Japan	4	1221	2.19 (1.62–2.95) – fixed	<.001	0	.996
China	2	792	1.68 (1.32–2.15) – fixed	<.001	0	.725
Proportion of AC						
100%	2	792	1.68 (1.32–2.15) – fixed	<.001	0	.725
Others	4	1221	2.19 (1.62–2.95) – fixed	<.001	0	.996
Cut-off value						
<0.1	3	1077	2.16 (1.57–2.97) – fixed	<.001	0	.685
≥0.1	3	936	1.73 (1.37–2.19) – fixed	<.001	0	.994
RFS	3	929	2.11 (1.41–3.15) – fixed	<.001	0	.614
CSS	1	688	1.59 (1.08–2.35)	.019	–	–

AC=adjuvant chemotherapy, CI=confidence interval, CSS=cancer-specific survival, HR= hazard ratio, OS=overall survival, RFS=recurrence-free survival.

Because the funnel plot was asymmetrical (Fig. 5), and the *P* value for the Egger test was .007, there was a publication bias in this meta-analysis. Therefore, a “Trim and Fill” method under a fixed-effects model was used. The adjusted pooled HR for OS was 1.74 (95% CI=1.47–2.05; *P* < .001).

3.3. Recurrence-free survival

Three studies including 929 patients provided the HR and 95% CI regarding the correlation between the CAR and RFS in patients with gastric cancer. We used a fixed-effects model to pool

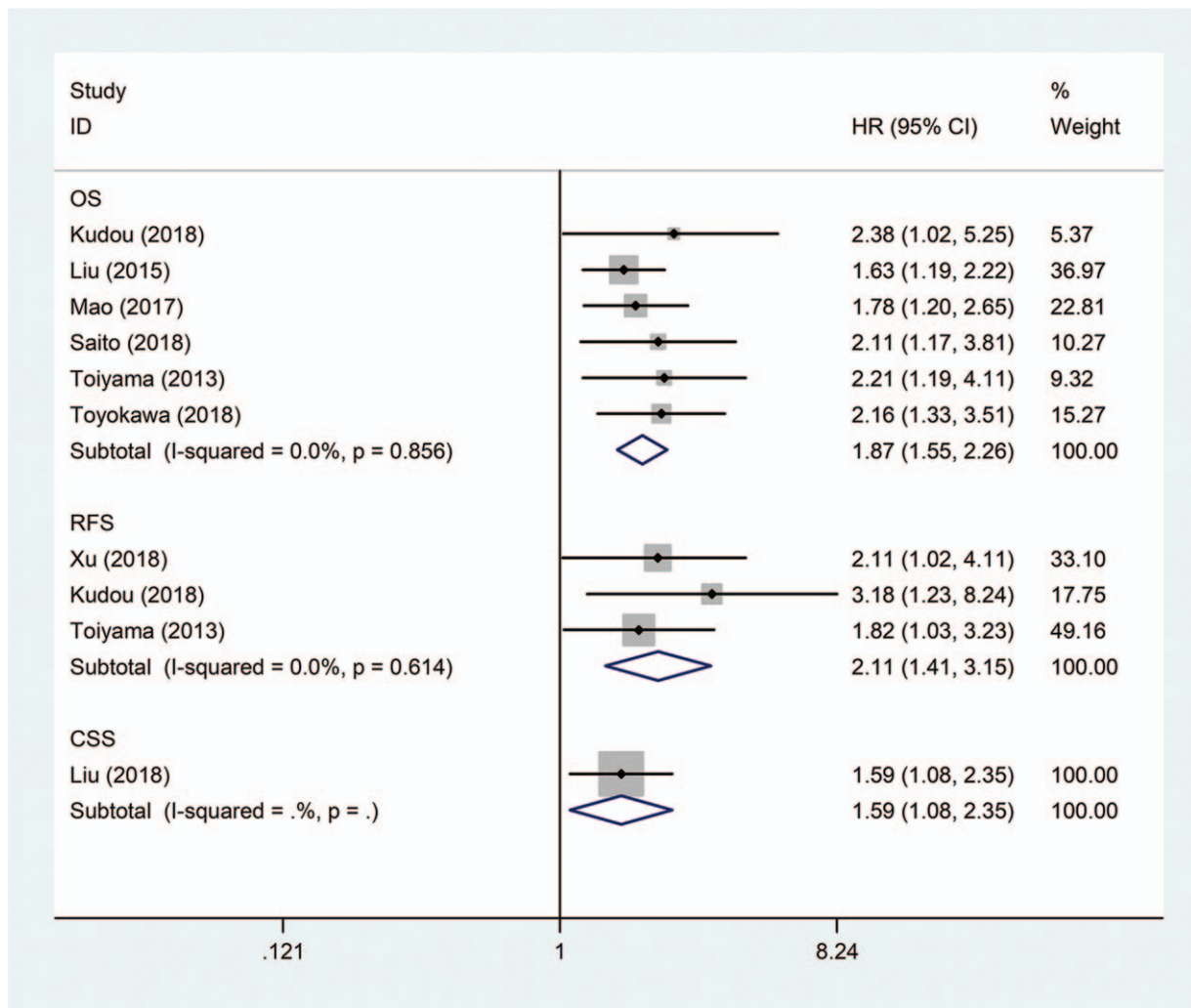


Figure 2. Forest plots of studies evaluating the hazard ratio for the survival of gastric cancer patients with a high C-reactive protein/albumin.

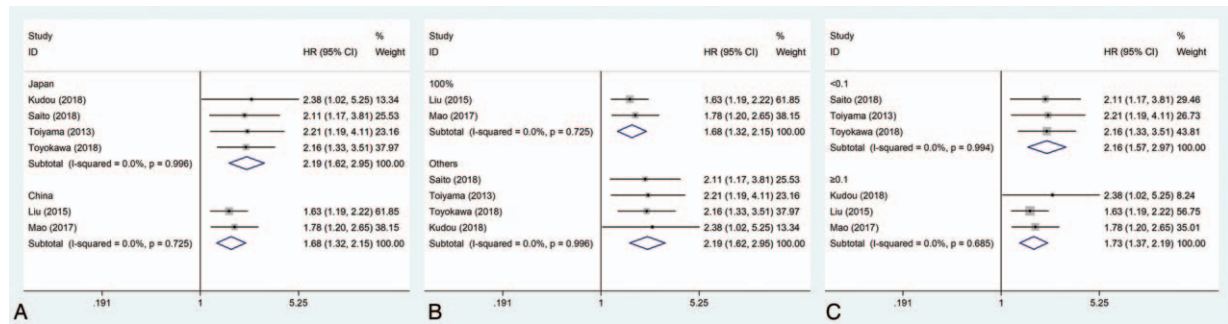


Figure 3. Forest plots of studies evaluating the hazard ratio for the overall survival of gastric cancer patients with a high C-reactive protein/albumin ratio divided by country (A), adjuvant chemotherapy rate (B), or cut-off value (C).

the HRs because there was no significant heterogeneity in these studies (

3.4. Cancer-specific survival

Only one study, which including 688 patients and was carried out by Liu et al,^[12] provided data regarding the association between the CAR and patients’ CSS in gastric cancer. They demonstrated through multivariate analysis that patients with a high CAR had worse CSS (HR = 1.59; 95% CI= 1.08–2.35;

4. Discussion

In recent years, several biological indicators reflecting the systemic inflammatory response have shown an important role in the prognostic evaluation of many types of tumor.^[27–30] The CAR is the ratio of serum CRP level to serum albumin level.

The serum CRP level is related to the activity of tumors because specific antigens on the surface of tumor cells can induce the anti-tumor immune response, and tumor cells also produce inflammatory proteins to promote the secretion of CRP.^[31–33] Low-serum albumin level indicating that the body is in a state of malnutrition, which has been shown to be associated with poor outcomes in gastric cancer.^[34,35] Gastric cancer often causes difficulty in eating and/or digestive dysfunction, so the proportions of malnutrition and cachexia in patients with gastric cancer are comparatively high. In addition, patients with gastric cancer usually receive multiple treatments, including surgery, radiation therapy, and chemotherapy. These treatments can cause inappetence and abnormal protein metabolism, leading to intensified malnutrition. Therefore, the CAR that can comprehensively reflect inflammation and nutritional status is very suitable for predicting the prognosis of gastric cancer.

Although no study has clearly shown that CAR has an impact on tumorigenesis and metastasis, it may indirectly affect tumorigenesis and metastasis through serum CRP and albumin. A high CAR represents elevated serum CRP concentration and/or

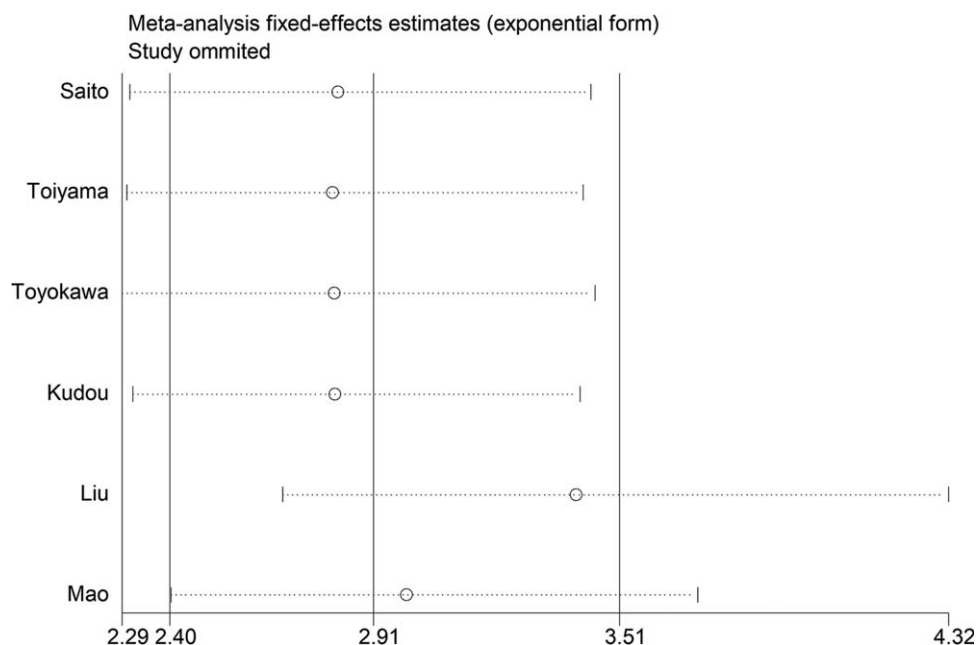


Figure 4. Sensitivity analysis of studies evaluating the relationship between the C-reactive protein/albumin ratio and overall survival in patients with gastric cancer.

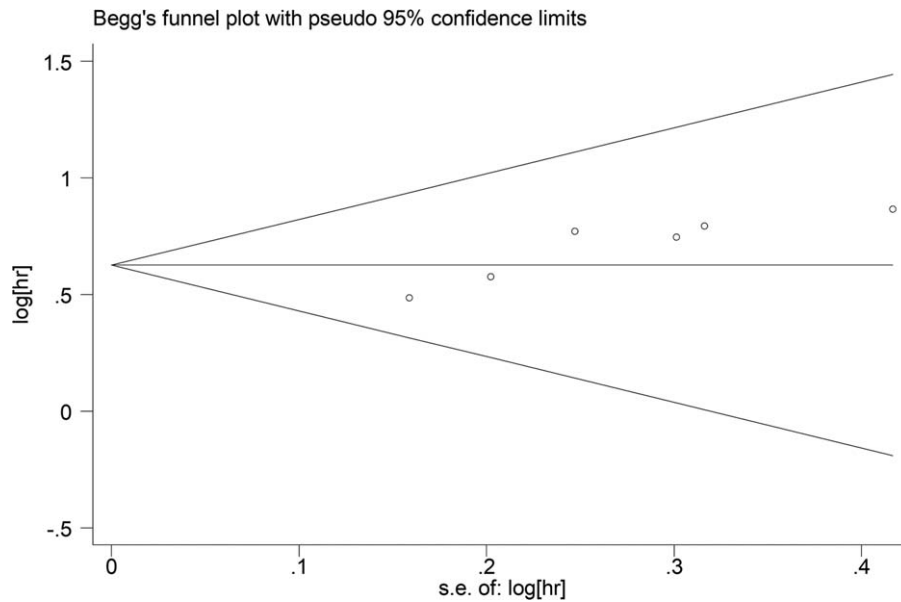


Figure 5. Funnel plot to examine publication bias among studies evaluating the relationship between the C-reactive protein/albumin ratio and overall survival in patients with gastric cancer.

low-serum albumin level. Elevated serum CRP concentrations are often accompanied by increased serum concentrations of vascular endothelial growth factor, contributing to tumor formation and progression.^[36] Albumin is the most commonly used indicator in the clinical evaluation of patients' nutritional status.^[37] Low-serum albumin levels suggest malnutrition, which can alter the tumor cell biology in the tumor microenvironment and damage the immune system to promote tumor growth and metastasis.^[38,39] Therefore, a high CAR indicates that the body is in a favorable state for tumorigenesis and metastasis, which should be given more attention in clinical practice. The Glasgow Prognostic Score (GPS) and modified GPS (mGPS) are two other biological indicators calculated according to serum CRP and albumin concentrations, which can also be used for predicting the prognosis of gastric cancer.^[40,41] However, compared to CAR, GPS, and mGPS applications are more complicated because they are based on scores converted from serum CRP and albumin concentrations. In addition, a previous study used a stepwise regression method to find main factors affecting prognosis, and the results showed that CAR is more suitable for building the best-fit prediction model than GPS or mGPS.^[42] Another previous study compared the area under the curve (AUC) of CAR, GPS, and mGPS.^[21] The results show that the AUC of CAR is the largest, suggesting that CAR is more suitable for prognostic evaluation.^[21]

This meta-analysis, including the data of 3102 patients enrolled in eight studies, strongly suggested that patients with a high pretreatment CAR have poor outcomes in gastric cancer. Results from subgroup analyses indicated that patient country, adjuvant chemotherapy rate, and CAR cut-off value affected the intensity of the association between pretreatment CAR and OS but did not affect the property of the association. For example, the association between a high CAR and poor OS was comparatively lower in the Chinese or the 100% adjuvant chemotherapy rate subgroups. Remarkably, the two studies in the Chinese subgroup were the same as the two studies in the 100% adjuvant chemotherapy rate subgroup. Therefore, it is still not clear whether the difference between the subgroups is caused

by nationality or by chemotherapy. A randomized controlled trial may be needed to find the answer.

This meta-analysis is the first study to systematically review and analyze the prognostic role of the CAR in gastric cancer. There are still some deficiencies in this meta-analysis. First, this study included only eight eligible studies, which resulted in relatively insufficiency data in the subgroup analyses. For example, we failed to perform a subgroup analysis of pathological types. Second, all included patients were from China or Japan, so the findings of this may be more suitable for Asian patients. For Caucasian gastric cancer patients, the prognostic role of the CAR remains unknown, but the prognostic role of serum CRP and albumin has been clarified.^[43,44] Ilhan et al^[43] reported that the level of serum CRP in Caucasian gastric cancer patients was significantly higher than that in healthy persons. Palaj et al^[44] found that high-serum albumin levels were associated with more lymph node involvement and worse OS in Caucasian gastric cancer patients. Similar findings have been observed in Asian patients,^[45,46] suggesting that serum CRP and albumin play a similar role in Asian patients as they do in Caucasian patients. Therefore, we speculate that a high CAR is also associated with poor prognosis in Caucasian gastric cancer patients. Third, some included studies provided only the HRs from univariate analysis, so the effect size may be overestimated. Finally, several HRs were estimated according to the data extracted from the survival curves, whereas there is error between estimated HRs and actual HRs.

In conclusion, the pretreatment CAR is convenient and precise for predicting the prognosis of patients with gastric cancer. The pretreatment CAR may also be of guiding significance to nutritional support and anti-inflammatory treatment for patients with gastric cancer. The findings of this study are still need to be confirmed by clinical trials of large sample size.

Author contributions

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Supervision: Changping Wu.

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Writing – review & editing: Changping Wu.

References

- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. *CA Cancer J Clin* 2017;67:7–30.
- Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2015. *CA Cancer J Clin* 2016;66:115–32.
- Fock KM. Review article: the epidemiology and prevention of gastric cancer. *Aliment Pharmacol Ther* 2014;40:250–60.
- Weinhold B, Ruther U. Interleukin-6-dependent and -independent regulation of the human C-reactive protein gene. *Biochem J* 1997;327 (Pt 2):425–9.
- Fuhrman MP, Charney P, Mueller CM. Hepatic proteins and nutrition assessment. *J Am Diet Assoc* 2004;104:1258–64.
- Ren Y, Fan X, Chen G, et al. Preoperative C-reactive protein/albumin ratio to predict mortality and recurrence of patients after curative resection with hepatocellular carcinoma. *Med Clin (Barc)* 2018; 153:183–90.
- Miyamoto T, Fujitani M, Fukuyama H, et al. The C-reactive protein/albumin ratio is useful for predicting short-term survival in cancer and noncancer patients. *J Palliat Med* 2018;22:532–7.
- He X, Li JP, Liu XH, et al. Prognostic value of C-reactive protein/albumin ratio in predicting overall survival of Chinese cervical cancer patients overall survival: comparison among various inflammation based factors. *J Cancer* 2018;9:1877–84.
- Haruki K, Shiba H, Horiuchi T, et al. Impact of the C-reactive protein to albumin ratio on long-term outcomes after hepatic resection for colorectal liver metastases. *Am J Surg* 2017;214:752–6.
- Wu M, Guo J, Guo L, et al. The C-reactive protein/albumin ratio predicts overall survival of patients with advanced pancreatic cancer. *Tumour Biol* 2016;37:12525–33.
- Kudou K, Saeki H, Nakashima Y, et al. C-reactive protein/albumin ratio is a poor prognostic factor of esophagogastric junction and upper gastric cancer. *J Gastroenterol Hepatol* 2019;34:355–63.
- Liu X, Wu Z, Lin E, et al. Systemic prognostic score and nomogram based on inflammatory, nutritional and tumor markers predict cancer-specific survival in stage II-III gastric cancer patients with adjuvant chemotherapy. *Clin Nutr* 2019;38:1853–60.
- Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009;62:e1–34.
- Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;25:603–5.
- Tierney JF, Stewart LA, Ghersi D, et al. Practical methods for incorporating summary time-to-event data into meta-analysis. *Trials* 2007;8:16.
- Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539–58.
- Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.
- Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* 1959;22:719–48.
- DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177–88.
- Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000;56:455–63.
- Liu X, Sun X, Liu J, et al. Preoperative C-reactive protein/albumin ratio predicts prognosis of patients after curative resection for gastric cancer. *Transl Oncol* 2015;8:339–45.
- Mao M, Wei X, Sheng H, et al. C-reactive protein/albumin and neutrophil/lymphocyte ratios and their combination predict overall survival in patients with gastric cancer. *Oncol Lett* 2017;14:7417–24.
- Saito H, Kono Y, Murakami Y, et al. Prognostic significance of the preoperative ratio of C-reactive protein to albumin and neutrophil-lymphocyte ratio in gastric cancer patients. *World J Surg* 2018; 42:1819–25.
- Toiyama Y, Shimura T, Yasuda H, et al. Clinical burden of C-reactive protein/albumin ratio before curative surgery for patients with gastric cancer. *Anticancer Res* 2016;36:6491–8.
- Toyokawa T, Muguruma K, Tamura T, et al. Comparison of the prognostic impact and combination of preoperative inflammation-based and/or nutritional markers in patients with stage II gastric cancer. *Oncotarget* 2018;9:29351–64.
- Xu BB, Lu J, Zheng ZF, et al. The predictive value of the preoperative C-reactive protein-albumin ratio for early recurrence and chemotherapy benefit in patients with gastric cancer after radical gastrectomy: using randomized phase III trial data. *Gastric Cancer* 2019;22:1016–28.
- Zhou X, Du Y, Huang Z, et al. Prognostic value of PLR in various cancers: a meta-analysis. *PLoS One* 2014;9:e101119.
- Kawashima M, Murakawa T, Shinozaki T, et al. Significance of the Glasgow Prognostic Score as a prognostic indicator for lung cancer surgery. *Interact Cardiovasc Thorac Surg* 2015;21:637–43.
- Templeton AJ, McNamara MG, Seruga B, et al. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. *J Natl Cancer Inst* 2014;106:dju124.
- Powell A, Parkinson D, Patel N, et al. Prognostic significance of serum inflammatory markers in gastric cancer. *J Gastrointest Surg* 2018;22: 595–605.
- Mroczo B, Groblewska M, Gryko M, et al. Diagnostic usefulness of serum interleukin 6 (IL-6) and C-reactive protein (CRP) in the differentiation between pancreatic cancer and chronic pancreatitis. *J Clin Lab Anal* 2010;24:256–61.
- Balkwill F, Mantovani A. Inflammation and cancer: back to Virchow? *Lancet* 2001;357:539–45.
- Nozoe T, Korenaga D, Futatsugi M, et al. Immunohistochemical expression of C-reactive protein in squamous cell carcinoma of the esophagus – significance as a tumor marker. *Cancer Lett* 2003;192: 89–95.
- Lin JX, Lin JP, Xie JW, et al. Prognostic importance of the preoperative modified systemic inflammation score for patients with gastric cancer. *Gastric Cancer* 2019;22:403–12.
- Saito H, Kono Y, Murakami Y, et al. Postoperative serum albumin is a potential prognostic factor for older patients with gastric cancer. *Yonago Acta Med* 2018;61:72–8.
- Xavier P, Belo L, Beires J, et al. Serum levels of VEGF and TNF-alpha and their association with C-reactive protein in patients with endometriosis. *Arch Gynecol Obstet* 2006;273:227–31.
- Hu JY, Yi W, Xia YF, et al. [Impact of pretherapy body mass index on prognosis of nasopharyngeal carcinoma]. *Ai Zheng* 2009;28:1043–8.
- McMillan DC. Systemic inflammation, nutritional status and survival in patients with cancer. *Curr Opin Clin Nutr Metab Care* 2009;12:223–6.
- Aoyagi T, Terracina KP, Raza A, et al. Cancer cachexia, mechanism and treatment. *World J Gastrointest Oncol* 2015;7:17–29.
- Zhang CX, Wang SY, Chen SQ, et al. Association between pretreatment Glasgow prognostic score and gastric cancer survival and clinicopathological features: a meta-analysis. *Onco Targets Ther* 2016;9:3883–91.
- Hirashima K, Watanabe M, Shigaki H, et al. Prognostic significance of the modified Glasgow prognostic score in elderly patients with gastric cancer. *J Gastroenterol* 2014;49:1040–6.
- Shao Y, Ning Z, Chen J, et al. Prognostic nomogram integrated systemic inflammation score for patients with esophageal squamous cell carcinoma undergoing radical esophagectomy. *Sci Rep* 2015;5:18811.
- Ilhan N, Ilhan N, Ilhan Y, et al. C-reactive protein, procalcitonin, interleukin-6, vascular endothelial growth factor and oxidative metabolites in diagnosis of infection and staging in patients with gastric cancer. *World J Gastroenterol* 2004;10:1115–20.
- Palaj J, Keckes S, Marek V, et al. Fibrinogen levels are associated with lymph node involvement and overall survival in gastric cancer patients. *Anticancer Res* 2018;38:1097–104.
- Migita K, Matsumoto S, Wakatsuki K, et al. Postoperative serum C-reactive protein level predicts long-term outcomes in stage I gastric cancer. *J Surg Res* 2019;242:323–31.
- Kang SC, Kim HI, Kim MG. Low serum albumin level, male sex, and total gastrectomy are risk factors of severe postoperative complications in elderly gastric cancer patients. *J Gastric Cancer* 2016;16:43–50.