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Original Article

C-reactive protein to albumin ratio as prognostic factors in lung cancer

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Abstract: Objective: The aims of this study is to evaluate the impact of C-reaction protein (CRP) to albumin ratio (CAR) on overall survival (OS) in lung cancer. Methods: Overall 210 patients with lung cancer were eligible for retrospective analysis between 2008 and 2014. The CAR of 197 patients were calculated. Univariate and multivariate Cox regression analysis were performed to determine the associations of CAR with OS. Results: Compared with low CAR (<0.43), high CAR (≥0.43) at diagnosis was associated with unfavorable tumor characteristics, including late tumor stage (III+IV in low vs high, 76.9% vs 89.2%, respectively, p=0.029), elevated LDH (p<0.001), PLR (p=0.001), NLR (p=0.001) and other tumor markers, such as NSE (p<0.001) and CEA (p=0.004). Furthermore, OS was also worse in high-CAR group at diagnosis (CAR<0.43 vs CAR≥0.43, median OS 27 vs 13 months, P<0.001). Inmultivariate cox analysis, CAR (adjusted Hazard Ratio (HR): 2.42, 95% confidence interval (CI): 1.35-3.7, p=0.002) and CEA at diagnosis (adjusted HR: 1.002, 95% CI: 1.000-1.004, P=0.040) were identified as independent prognostic factors for poor OS. Conclusion: CAR is an independent prognostic marker in lung cancer after adjusted by other confounding factors and the CAR could be a readily available biomarker in clinical setting.

Keywords: C-reactive protein, lung cancer, prognosis, inflammation

Introduction

Lung cancer is one of the most common cancers in the world and its mortalityranks first in all cancers [1]. With the development of earlier detection through screening with spiral computed tomography, the death rate of lung cancer was reduced 16%-20% in adults with smoking history [2]. Although the treatments and detections in lung cancer have made great progress and the 5 year survival rate has improved recent years, the ideal method to evaluate the prognosis of lung cancer remains unavailable.

Mounting evidence supported that system inflammation is associated with poor survival in patients with many cancers by promoting cancer cell proliferation and survival, angiogenesis, tumor metastasis [3, 4]. Inflammation-based prognostic scores, including neutrophil lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), Glasgow Prognostic Score (GPS) and modified Glasgow Prognostic Score (mGPS) have been reported to have prognosis effect on patients with cancers [5-9]. Recently, CAR showed its impact on a large variety of tumor types [10-18]. However, aside from our report, there was few studies regarding the effect of the CAR on prognosis in patients with lung cancer [19, 20].

Therefore, we investigated whether CAR has a prognostic value in patients with lung cancer in this study. We also evaluated the prognostic value of CAR adjusted by other inflammation factors and tumor markers.

Methods

Study population

Patients enrolled in this research were hospitalized in West China hospital between January 2008 and Dec 2014. Patients which met the following inclusion criteria were enrolled: 1) diagnosed lung cancer by biopsy: 2) including data about complete blood count, blood chemistries and other tumor markers. The exclusion criteria included: 1) current infection: 2) com-

Table 1. Baseline characteristics of patients

Variables	Number of patients (%)
Age, years (n=210)	
<60	73 (34.8)
≥60	137 (65.2)
Gender (n=210)	
Male	140 (66.7)
Female	70 (33.3)
Smoking status (n=210)	
Never smoking	86 (41.0)
Current or ex-smoker	124 (59.0)
Stage (n=200)	
I+II	37 (18.5)
III+IV	163 (81.5)
Lymph node metastasis (n=210)	
Yes	119 (56.7)
No	91 (43.3)
Histology (n=210)	
AC	125 (59.2)
SCC	53 (25.1)
SCLC	22 (10.4)
Other	10 (4.8)
Family history of cancer (n=143)	
Yes	26 (18.2)
No	117 (81.8)
Survival time (n=197)	
Median OS (range)	21.19

SCC: squamous cell carcinoma; AC: adenocarcinoma; SCLC: small cell lung cancer; OS: overall survival.

bined with other malignant tumor: 3) lacking of clinical pathological characteristics and related examinations. Our final study cohort included 210 patients.

Clinical data collections and following up

The clinical data were collected by physicians from the clinical charts and hospital discharge records, including age, gender, histological subtype, stage, smoking status. Stage and histological type were determined according to classification criteria lung tumors of the WHO [21, 22]. The CAR was defined as the value of serum CRP divided by the value of serum albumin and the NLR/PLR referred to absolute neutrophil count divided by the absolute lymphocyte count/absolute platelets divided by the absolute lymphocyte count. Values of CAR, NLR, PLR and other tumor markers were measured as the baseline values at diagnosis before treatment. Survival status was determined from the date of last follow-up in Dec, 2014. The overall survival time was defined as the time from confirmed diagnosis of lung cancer to the date of death, or to the date of last follow-up for patients who have not died before the censor date. All patients were followed up every 3-month by telephone until people died or lost to follow up. The contents of follow-up comprised recurrence, tumor progression and survival days.

Statistical methods

Student's t test or one-way ANOVA (Analysis of Variance) was used for continuous variables and Fisher's exact test or χ^2 test was used for comparison of categorical data. The ROC (Receive Operating Characteristic) curve analysis was carried out to assess the cut-off of CAR. The optimal cuto values were identified as the values that maximize the You den index (sensitivity + specificity - 1) [23]. Survival curves were estimated with the Kaplan-Meier method. The associations of CAR with survival were evaluated in univariable and multivariable cox regression models. Variables with a statistically significant univariate association were included in the multivariable model. Analysis was performed in SPSS 21.0 software. And the graphs were edited by Photoshop.

Result

Population characteristics

Overall 210 patients were eligible for this retrospective analysis. The median age of this study was 61.91 (28-89), most of them were older than 60 (n=137, 65.2%).

140 of all participations were male (65.2%), 70 were female (34.8%). The majority of patients were current or ex-smokers (n=124, 59.0%). According to classification criteria lung tumors of the WHO, 37 (18.5%) were in early stage (I+II) and 163 (81.5%) were in late stage (III+IV). Among all patients, 59.2% (n=125) were adenocarcinoma (AC), 25.1% (n=53) were squamous cell carcinoma (SCC), 10.4% (n=22) were small cell lung cancer (SCLC) and 4.8% (n=10) were others. The median overall survival time (OS) for all patients were 21.19 months. Other clinical characteristics at baseline are summarized in **Table 1**.

Table 2. Relationship between clinical characteristics and CAR in lung cancer using univariate logistic regression

Variables	CAR<0.43	CAR≥0.43	*P*-value
Age, years			0.591
<60	41 (36.9)	70 (57.9)	
≥60	35 (63.1)	51 (42.1)	
Gender			0.773
Male	74 (66.7)	59 (68.6)	
Female	37 (33.3)	27 (31.4)	
Smoking status			
Never smoking	48 (43.2)	32 (37.2)	0.392
Current or ex-smoker	63 (56.8)	54 (62.8)	
Stage			0.029*
I+II	24 (23.1)	9 (10.8)	
III+IV	80 (76.9)	74 (89.2)	
Lymph node metastasis			0.139
Yes	53 (47.7)	32 (37.2)	
No	58 (52.3)	54 (62.8)	
Histology			0.014*
AC	76 (68.5)	42 (48.8)	
SCC	19 (17.1)	31 (36.0)	
SCLC	6 (5.4)	3 (3.5)	
Other	10 (9.0)	10 (11.6)	
History			0.792
Yes	12 (17.9)	13 (19.7)	
No	55 (82.1)	53 (80.3)	
LDH at diagnosis, mean ± s.d	199.98 ± 80.21	270.71 ± 191.75	<0.001*
NSE at diagnosis, mean ± s.d	17.30 ± 18.29	34.01 ± 42.10	<0.001*
CEA at diagnosis, mean ± s.d	32.78 ± 86.57	58.75 ± 135.10	0.004*
CA199 at diagnosis, mean ± s.d	53.63 ± 132.89	49.50 ± 103.30	0.672
CA125 at diagnosis, mean ± s.d	115.94 ± 281.71	170.78 ± 345.26	0.566
PLR at diagnosis, mean ± s.d	136.52 ± 69.40	215.39 ± 105.73	0.001*
NLR at diagnosis, mean ± s.d	3.57 ± 2.46	6.03 ± 4.76	0.001*

*: p<0.05 is significant. SCC: squamous cell carcinoma; AC: adenocarcinoma; SCLC: small cell lung cancer; LDH: lactic dehydrogenase; NSE: neuron-specific enolase; CEA: carcinoembryonic antigen; CA199: carbohydrate antigen 19-9; CA125: carbohydrate antigen 125; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio.

Association of CAR with baseline clinical characteristics in lung cancer

The cuto value of the CAR was determined to be 0.43 by ROC analysis. Correlation between CAR and clinical characteristics were shown in **Tables 2**, **3**. Then patients were divided into two groups based on the cutoff value (CAR<0.43, n=76; CAR≥0.43, n=121). Patients with high CAR were more likely to be classified as squamous cell carcinoma (SCC) and small cell lung cancer (SCLC). Moreover, higher CAR was also significantly associated with unfavorable tumor characteristics, including late tumor stage (III+IV in low vs high, 76.9% vs 89.2%, respectively, p=0.029), elevated LDH (p<0.001), PLR (p=0.001), NLR (p=0.001) and other tumor markers, such as NSE (p<0.001) and CEA (p=0.004). In multivariable logistic regression, CAR was only significantly related to stage, histology, elevated NSE and PLR (**Table 3**).

Association of CAR with prognosis in lung cancer

In total, median OS was 21.19 months among all patients. The patients with higher CAR at diagnosis have substantially shorter overall survival time (OS) compared with those with lower ones (CAR<0.43 vs CAR≥0.43, median OS 27 vs 13 months, P<0.001) (**Figure 1**). Stratified analysis was conducted according to stage. Patients with higher CAR of late tumor stage (III+IV) showed worse OS compared with those with lower ones (CAR<0.43 vs CAR≥0.43, median OS 24 vs 9 months, P<0.001) (**Figure 2B**). But there was no significant difference in patients with early tumor stage. Besides, the results of univariate and multivariate survival analysis in relation to OS in lung cancer were shown in **Table 4**. Stage, the elevated level of CAR, LDH, NSE, CEA, PLR and NLR at diagnosiswere independent prognostic factors for poor OS in univariate survival analysis. Moreover, CAR was identified as an significant prognostic factor for the overall survival (OS) when adjusted by clinicopathological factors, other inflammation-based factors and other tumor markers (adjusted Hazard Ratio (HR) 2.42, 95% confidence

Table 3. Relationship between clinical characteristics and CAR in lung cancer using multivariable logistic regression

Variables	CAR<0.43	CAR≥0.43	OR (95% CI)	*P*-value	B
Stage					
I+II	24 (23.1)	9 (10.8)	1.0		
III+IV	80 (76.9)	74 (89.2)	3.52 (1.05-11.78)	0.042*	1.257
Histology					
SCC	19 (17.1)	31 (36.0)	1.0		
AC	76 (68.5)	42 (48.8)	0.30 (0.12-0.75)	0.011*	-1.212
Other	6 (5.4)	3 (3.5)	0.66 (0.10-4.46)	0.669	-0.418
SCLC	10 (9.0)	10 (11.6)	0.18 (0.03-1.08)	0.061	-1.737
LDH at diagnosis, mean ± s.d	199.98 ± 80.21	270.71 ± 191.75	1.00 (0.99-1.01)	0.509	0.001
NSE at diagnosis, mean ± s.d	17.30 ± 18.29	34.01 ± 42.10	1.03 (1.00-1.06)	0.030*	0.029
PLR at diagnosis, mean ± s.d	136.52 ± 69.40	215.39 ± 105.73	1.01 (1.01-1.02)	<0.001*	0.010
NLR at diagnosis, mean ± s.d	3.57 ± 2.46	6.03 ± 4.76	1.12 (0.96-1.31)	0.160	0.113

*: p<0.05 is significant. SCC: squamous cell carcinoma; AC: adenocarcinoma; SCLC: small cell lung cancer; LDH: lactic dehydrogenase; NSE: neuron-specific enolase; CEA: carcino-embryonic antigen; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio.

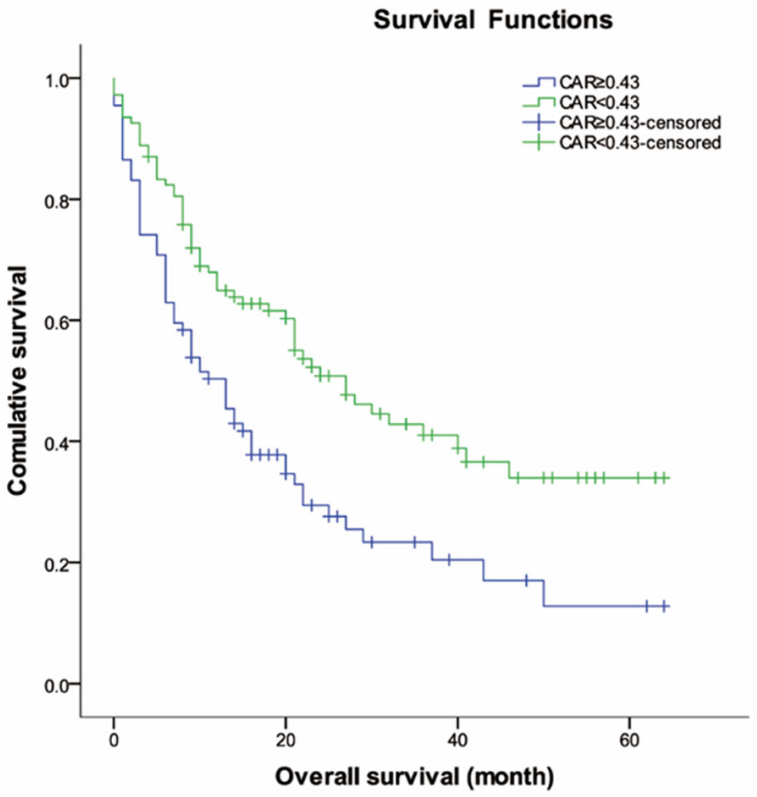

Figure 1. Kaplan-Meier curves for overall survivalaccording to CAR at diagnosis. OS stratified by CAR at diagnosis (CAR<0.43 vs CAR≥0.43, median OS 27 vs 13 months, P<0.001). Abbreviations: CAR: C-reaction protein to albumin ratio; OS: overall survival.

interval (CI) 1.35-3.7, p=0.002). Furthermore, multivariate Cox analysis identified CEA at diagnosis (adjusted HR: 1.002; 95% CI: 1.000-1.004, P=0.040) also as an independent prognostic factor for OS.

Discussion

In this study, we investigated utility of CAR as prognostic factors in lung cancer by retrospective analysis of 197 patients with lung cancer. We found that CAR was significantly correlated with stage, histology, NSE and PLR at diagnosis. Moreover, CAR was independently associated with poor prognosis in lung cancer.

It is increasingly recognized that the host systemic inflammatory response plays a critical role in the development and progression of many cancers [24, 25]. The emerging studies of several cancer-related inflammatory prognostic scores were reported in recent years, such as NLR, PLR, mGPS and CAR. However, the mechanism by which these inflammatory factors may impact prognosis remains unclear. Also as a biomarker of system inflammation, C-reaction protein (CRP) is a kind

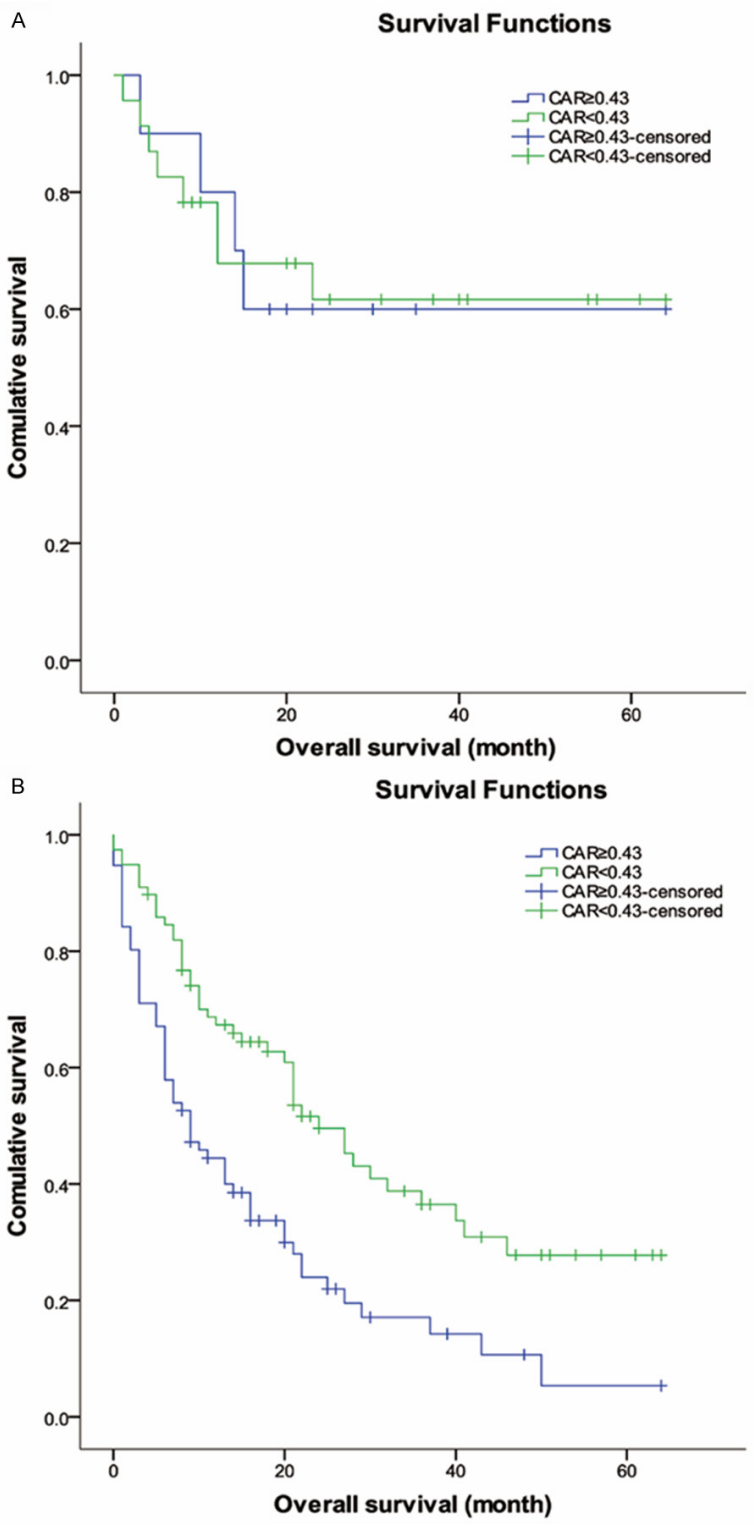

Figure 2. Kaplan-Meier curves for overall survival according to CAR and stage. OS stratified according to the CAR at diagnosis in (A) stage I+II (CAR<0.43 vs CAR≥0.43, 60% vs 65.2% *, P=0.944) (B) stage III+IV (CAR<0.43 vs CAR≥0.43, median OS 24 vs 9 months, P<0.001). Abbreviations: CAR: C-reaction protein to albumin ratio; OS: overall survival; *, Mortality in patients with early tumor stage was less than 50%, so median survival time could not be calculated. Five survival rates were compared in two groups.

of acute reactive protein synthesized by liver cells, which is caused by microbial invasion or tissue injury [26]. And its prognostic value in patients with various types of cancer was investigated in many researches [27-33]. Albumin can reflect the nutritional status of patients with cancers and malnutrition is correlated with worse survival. The CAR was primarily used to predict 90-day mortality in sepsis by Ranzani OT et al [34]. Then its prognostic value was explored in varies of cancers [10-16, 18, 20]. More recently, Kinoshita A et al and Chen Z et al found that CAR has better performance than other inflammation-based factors [10, 35]. Therefore, CAR that not only indicate the inflammatory status but also the nutritional status may be a potential prognostic predictor for lung cancer and we assessed this in our study.

As shown in **Table 2**, we found that higher CAR was associated with different clinical factors, such as late tumor stage, elevated tumor markers and other inflammation-based markers in lung cancer, which was consistent with previous studies [19, 20]. After adjusted, we also found that patients with an elevated CAR were more likely to be SCC with late tumor stage. Moreover, NSE in patients with CAR≥0.43 was almost 2 times higher than those with lower CAR in the multivariable analysis. This may also lead to poor prognosis in patients with high CAR.

The previous researches had demonstrated that CAR was a prognostic factor in gastrointestinal cancer [11-13, 17]. However, the cutoff value and

Table 4. Univariate and multivariate survival analyses in relation to OS in lung cancer

Variables	Univariate				Multivariate				
	HR	95% CI lower	95% CI upper	P	HR	95% CI lower	95% CI upper	*p*-value	B
Age, years									
<60	1.0				-	-	-	-	
≥60	1.27	0.88	1.83	0.212	-	-	-	-	
Gender									
Male	1.0				-	-	-	-	
Female	1.05	0.72	1.54	0.784	-	-	-	-	
Smoking status									
Never smoking	1.0				-	-	-	-	
Current or ex-smoker	1.22	0.84	1.76	0.294	-	-	-	-	
Stage									
I+II	1.0				1.0				
III+IV	2.58	1.42	4.71	0.002*	1.50	0.81	2.81	0.199	0.408
Lymph node metastasis									
Yes	1.0				-	-	-	-	
No	1.37	0.95	1.98	0.093	-	-	-	-	
Histology									
SCC	1.0				-	-	-	-	
AC	0.74	0.49	1.12	0.156	-	-	-	-	
Other	0.84	0.35	1.99	0.685	-	-	-	-	
SCLC	0.77	0.40	1.48	0.432	-	-	-	-	
History									
Yes	1.0				-	-	-	-	
No	0.78	0.44	1.38	0.391	-	-	-	-	
CAR									
<0.43	1.0				1.0				
≥0.43	2.00	1.39	2.88	<0.001*	2.24	1.35	3.70	0.002*	0.805
LDH at diagnosis, mean ± s.d	1.002	1.001	1.003	<0.001*	1.000	0.998	1.001	0.931	<0.001
NSE at diagnosis, mean ± s.d	1.007	1.002	1.012	0.004*	1.004	0.998	1.011	0.202	0.004
CEA at diagnosis, mean ± s.d	1.002	1.000	1.003	0.009*	1.002	1.000	1.004	0.040*	0.002
CA199 at diagnosis, mean ± s.d	1.001	0.999	1.002	0.288	-	-	-	-	
CA125 at diagnosis, mean ± s.d	1.000	1.000	1.001	0.119	-	-	-	-	
PLR at diagnosis, mean ± s.d	1.002	1.001	1.004	0.007*	0.999	0.996	1.001	0.251	-0.001
NLR at diagnosis, mean ± s.d	1.08	1.04	1.13	<0.001*	1.05	0.98	1.11	0.159	0.044

*: p<0.05 is significant. OS: overall survival; SCC: squamous cell carcinoma; AC: adenocarcinoma; SCLC: small cell lung cancer; CAR: C-reaction protein-to-albumin ration; LDH: lactic dehydrogenase; NSE: neuron-specific enolase; CEA: carcino-embryonic antigen; CA199: carbohydrate antigen 19-9; CA125: carbohydrate antigen 125; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio.

the prognosis of CAR remain unclear. It was suggested that optimal cutoff value for prognostic indicator could better choose from other studies. Here, we analyzed optimal cutoff by ROC curve, then we performed sensitivity analyses to determine the cutoff value as 0.43. The cutoff value 0.43 for the CAR were determined to distinguish between those with a higher risk of adverse outcome and those with a lower risk. Then we analyze the association of CAR with prognosis according to different cofounding factors based on this value. Our study confirms the previous conclusion that CAR is an independent prognostic factor after adjusted by other cofounding factors in lung cancer [19, 20]. Although the clinical stage is not the main factor in multivariable Cox regression model, the patients with high CAR in late tumor stage

have shorter survival time than those with low CAR. It's reasonable that patients with late tumor stage may bear more tumor burden, which result in shorter survival time.

Our research was the first to assess the prognostic effect of CAR based on all other subtypes of lung cancer. Meanwhile, another advantage of our research is that detailed information on tumor characteristic and other tumor markers were recorded to analyze their impact on CAR.

As a retrospective study, there are several limitations inherent to its design, including the retrospective data collection. Moreover, the prognostic value of CAR was found in many type of tumor, which indicated that CAR might not be a tumor-specific marker. Besides, there still are several confounding factors which were not included in this study. Therefore, it remains to be validated in large-scale prospective researches.

In conclusion, our results suggested that CAR is an independent prognostic marker in lung cancer. The CAR could be a readily available biomarker in clinical setting.

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Disclosure of conflict of interest

None.

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References

[1] Siegel RL, Miller KD and Jemal A. Cancer statistics, 2015. CA Cancer J Clin 2015; 65: 5-29.

[2] National Lung Screening Trial Research Team, Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, Gareen IF, Gatsonis C, Marcus PM and Sicks JD. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 2011; 365: 395-409.

[3] Roxburgh CS and Mcmillan DC. Role of systemic inflammatory response in predicting survival in patients with primary operable cancer. Future Oncology 2010; 6: 149-163.

[4] Bambury RM, Teo MY, Power DG, Yusuf A, Murray S, Battley JE, Drake C, O'Dea P, Bermingham N and Keohane C. The association of pre-treatment neutrophil to lymphocyte ratio with overall survival in patients with glioblastoma multiforme. J Neurooncol 2013; 114: 149-154.

[5] Gu X, Sun S, Gao XS, Xiong W, Qin S, Qi X, Ma M, Li X, Zhou D, Wang W and Yu H. Prognostic value of platelet to lymphocyte ratio in non-small cell lung cancer: evidence from 3,430 patients. Sci Rep 2016; 6: 23893.

[6] Nikolić I, Kukulj S, Samaržija M, Jeleč V, Žarak M, Orehovec B, Taradi I, Romić D, Kolak T and Patrlj L. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio help identify patients with lung cancer, but do not differentiate between lung cancer subtypes. Croat Med J 2016; 57: 287-292.

[7] Sanchez-Salcedo P, de-Torres JP, Martinez-Urbistondo D, Gonzalez-Gutierrez J, Berto J, Campo A, Alcaide AB and Zulueta JJ. The neutrophil to lymphocyte and platelet to lymphocyte ratios as biomarkers for lung cancer development. Lung Cancer 2016; 97: 28-34.

[8] Wang X, Teng F, Kong L and Yu J. Pretreatment neutrophil-to-lymphocyte ratio as a survival predictor for small-cell lung cancer. Onco Targets Ther 2016; 9: 5761-5770.

[9] Fan H, Shao ZY, Xiao YY, Xie ZH, Chen W, Xie H, Qin GY and Zhao NQ. Comparison of the glasgow prognostic score (GPS) and the modified glasgow prognostic score (mGPS) in evaluating the prognosis of patients with operable and inoperable non-small cell lung cancer. J Cancer Res Clin Oncol 2016; 142: 1285-1297.

[10] Chen Z, Shao Y, Fan M, Zhuang Q, Wang K, Cao W, Xu X and He X. Prognostic significance of preoperative C-reactive protein: albumin ratio in patients with clear cell renal cell carcinoma. Int J Clin Exp Pathol 2014; 8: 14893-900.

[11] Haruki K, Shiba H, Shirai Y, Horiuchi T, Iwase R, Fujiwara Y, Furukawa K, Misawa T and Yanaga K. The C-reactive protein to albumin ratio predicts long-term outcomes in patients with pancreatic cancer after pancreatic resection. World J Surg 2016; 40: 2254-2260.

[12] Liu X, Sun X, Liu J, Kong P, Chen S, Zhan Y and Xu D. Preoperative C-reactive protein/albumin ratio predicts prognosis of patients after curative resection for gastric cancer. Transl Oncol 2015; 8: 339-345.

[13] Liu Z, Jin K, Guo M, Long J, Liu L, Liu C, Xu J, Ni Q, Luo G and Yu X. Prognostic value of the CRP/Alb ratio, a novel inflammation-based score in pancreatic cancer. Ann Surg Oncol 2017; 24: 561-568.

[14] Park HC, Kim MY and Kim CH. C-reactive protein/albumin ratio as prognostic score in oral squamous cell carcinoma. J Korean Assoc Oral Maxillofac Surg 2016; 42: 243-250.
[15] Wei XL, Wang FH, Zhang DS, Qiu MZ, Ren C, Jin Y, Zhou YX, Wang DS, He MM, Bai L, Wang F, Luo HY, Li YH and Xu RH. A novel inflammation-based prognostic score in esophageal squamous cell carcinoma: the C-reactive protein/albumin ratio. BMC Cancer 2015; 15: 350.
[16] Wong TC, Su HY, Chen YT, Wu PY, Chen HH, Chen TH, Hsu YH and Yang SH. Ratio of C-reactive protein to albumin predicts muscle mass in adult patients undergoing hemodialysis. PLoS One 2016; 11: e0165403.
[17] Wu M, Guo J, Guo L and Zuo Q. The C-reactive protein/albumin ratio predicts overall survival of patients with advanced pancreatic cancer. Tumour Biol 2016; 37: 12525-12533.
[18] Zhang Y, Zhou GQ, Liu X, Chen L, Li WF, Tang LL, Liu Q, Sun Y and Ma J. Exploration and Validation of C-reactive protein/albumin ratio as a novel inflammation-based prognostic marker in nasopharyngeal carcinoma. J Cancer 2016; 7: 1406-1412.
[19] Zhang F, Ying L, Jin J, Chen K, Zhang N, Wu J, Zhang Y and Su D. The C-reactive protein/albumin ratio predicts long-term outcomes of patients with operable non-small cell lung cancer. Oncotarget 2017; 8: 8835-8842.
[20] Zhou T, Zhan J, Hong S, Hu Z, Fang W, Qin T, Ma Y, Yang Y, He X, Zhao Y, Huang Y, Zhao H and Zhang L. Ratio of C-reactive protein/albumin is an inflammatory prognostic score for predicting overall survival of patients with small-cell lung cancer. Sci Rep 2015; 5: 10481.
[21] Edge SB and Compton CC. The American joint committee on cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol 2010; 17: 1471-1474.
[22] Travis WD, Brambilla E and Riely GJ. New pathologic classification of lung cancer: relevance for clinical practice and clinical trials. J Clin Oncol 2013; 31: 992-1001.
[23] Lai CY, Tian L and Schisterman EF. Exact confidence interval estimation for the Youden index and its corresponding optimal cut-point. Comput Stat Data Anal 2012; 56: 1103-1114.
[24] Gioulbasanis I, Pallis A, Vlachostergios PJ, Xyrafas A, Giannousi Z, Perdikouri IE, Makridou M, Kakalou D and Georgoulias V. The glasgow prognostic score (GPS) predicts toxicity and efficacy in platinum-based treated patients with metastatic lung cancer. Lung Cancer 2012; 77: 383-388.
[25] McMillan DC. The systemic inflammation-based glasgow prognostic score: a decade of experience in patients with cancer. Cancer Treat Rev 2013; 39: 534-540.
[26] Morris-Stiff G, Gomez D and Prasad KR. C-reactive protein in liver cancer surgery. Eur J Surg Oncol 2008; 34: 727-729.
[27] Alifano M, Falcoz PE, Seegers V, Roche N, Schussler O, Younes M, Antonacci F, Forgez P, Dechartres A, Massard G, Damotte D and Regnard JF. Preresection serum C-reactive protein measurement and survival among patients with resectable non-small cell lung cancer. J Thorac Cardiovasc Surg 2011; 142: 1161-1167.
[28] Eggers H, Seidel C, Schrader AJ, Lehmann R, Wegener G, Kuczyk MA and Steffens S. Serum C-reactive protein: a prognostic factor in metastatic urothelial cancer of the bladder. Med Oncol 2013; 30: 705.
[29] Kinoshita A, Onoda H, Takano K, Imai N, Saeki C, Fushiya N, Miyakawa Y, Nishino H and Tajiri H. Pretreatment serum C-reactive protein level predicts poor prognosis in patients with hepatocellular carcinoma. Med Oncol 2012; 29: 2800-2808.
[30] Li YJ, Li ZM, Xia Y, Huang JJ, Huang HQ, Xia ZJ, Lin TY, Li S, Cai XY, Wu-Xiao ZJ and Jiang WQ. Serum C-reactive protein (CRP) as a simple and independent prognostic factor in extranodal natural killer/T-cell lymphoma, nasal type. PLoS One 2013; 8: e64158.
[31] Oh BS, Jang JW, Kwon JH, You CR, Chung KW, Kay CS, Jung HS and Lee S. Prognostic value of C-reactive protein and neutrophil-to-lymphocyte ratio in patients with hepatocellular carcinoma. BMC Cancer 2013; 13: 1-9.
[32] Shao N and Cai Q. High pretreatment serum C-reactive protein level predicts a poor prognosis for combined small-cell lung cancer. Tumor Biology 2015; 36: 1-6.
[33] Tomita M, Shimizu T, Ayabe T, Nakamura K and Onitsuka T. Elevated preoperative inflammatory markers based on neutrophil-to-lymphocyte ratio and C-reactive protein predict poor survival in resected non-small cell lung cancer. Anticancer Res 2012; 32: 3535-3538.
[34] Ranzani OT, Zampieri FG, Forte DN, Azevedo LC and Park M. C-reactive protein/albumin ratio predicts 90-day mortality of septic patients. PLoS One 2013; 8: e59321.
[35] Kinoshita A, Onoda H, Imai N, Iwaku A, Oishi M, Tanaka K, Fushiya N, Koike K, Nishino H and Matsushima M. The C-reactive protein/albumin ratio, a novel inflammation-based prognostic score, predicts outcomes in patients with hepatocellular carcinoma. Ann Surg Oncol 2015; 22: 803-810.