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Pretreatment Albumin/Globulin Ratio Predicts the Prognosis for Small-Cell Lung Cancer

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Abstract: The pretreatment albumin/globulin ratio (AGR) has been used as a prognostic factor in various cancers. This study aimed to evaluate the predictive value of AGR in small-cell lung cancer (SCLC).

We tested albumin and total proteins in plasma samples from 276 SCLC patients from our cancer center between January 2003 and December 2006. The AGR was defined by the formula: albumin/(total proteins−albumin). The correlation between AGR and overall survival (OS) was examined by Kaplan−Meier and Cox regression methods. For validation, AGR was used to evaluate the prognosis of SCLC in another independent group.

Total 276 patients (testing) and 379 patients (validation) were finally enrolled. The median OS was 15.31 months for testing patients and 15.06 months for validation patients, respectively. We determined 1.29 as the cutoff value by using the biostatistical tool (Cutoff Finder), then the patients in the testing group were classified into 2 groups. Kaplan–Meier curves showed high AGR group had significantly longer OS than low AGR group ($P = 0.026$). According to multivariate analyses, AGR was an independent prognostic factor for OS of SCLC patients in the testing group (HR, 1.35, 95% CI: 1.01–1.81, $P = 0.046$). In the validation group, AGR was also verified as a predictive factor for OS ($P < 0.001$), and the risk of SCLC in the low AGR group was 1.43 times higher than that in the high AGR group (HR, 1.43, 95% CI: 1.05–1.94, $P = 0.022$).

AGR is an independent prognostic marker in SCLC patients. Furthermore, it could be of great value in the management of SCLC patients.

(*Medicine* 95(12):e3097)

Abbreviations: AGR = albumin/globulin ratio, BMI = body mass index, ECOG-PS = Eastern Cooperation Oncology Group Performance Status, IL = interleukin, IQR = interquartile range, LDH = lactate dehydrogenase, OS = overall survival, PCI = prophylactic cranial irradiation, PS = performance status, SCLC = small-cell lung cancer, SYSUCC = Sun-Yat Sen University cancer center, TRT = thorax radiotherapy.

INTRODUCTION

Lung cancer is still the most common cause of cancer-related deaths.[1] Approximately 221,200 new lung cancer cases have been reported, and 158,400 died from this malignancy in the United Stated in 2015.[2] Small-cell lung cancer (SCLC) accounts for about 15% of lung cancer.[3,4] About 60% of SCLC patients appear extensive disease even with metastases into brain, bone, liver, and adrenal gland at diagnosis.[5] The National Comprehensive Cancer Network usually applied concurrent chemotherapy and radiotherapy as the standard treatments.[6] Especially for extensive-stage disease, etoposide-based chemotherapy is the appropriate treatment to ensure high response rate. However, the 2-year recurrence rate is 75% in patients with limited disease and almost 100% in patients with extensive disease, which is thought to be one of reasons for short survival of SCLC.[7,8] The 5-year overall survival (OS) rate in SCLC patients with limited and extensive diseases is 25% and 7.8%, respectively. Therefore, to improve the prognosis of SCLC in clinic, sensitive and specific factors for classifying cancer risk and predicting survival are extremely needed to help guide treatment.

Several laboratory and clinical markers have been identified as prognostic factors for SCLC in previous studies, including baseline serum CEA value, abnormally elevated lactate dehydrogenase (LDH), neuron-specific enolase, gender, performance status (PS), disease extent, age, and gender.[9–12] However, these factors have some limitations in clinical practice due to their high cost of testing, subjectivity, and instability. Therefore, to improve the accuracy and efficiency of prognostic factors, we need an optimal predictive factor that is closely linked to the OS in SCLC patients and can be easily detected.

To date, increasing evidence supports that inflammation is associated with the initiation and progression of cancer.[13–16] As the major components in serum protein, albumin and globulin play important roles in the process of inflammation. Generally, serum albumin and globulin are used to assess the degree of nutrition status and severity of disease.[17] Interestingly, several studies demonstrated that serum albumin and globulin can be

Editor: Michael Masoomi.
Received: September 6, 2015; revised: November 17, 2015; accepted: February 25, 2016.
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This work was supported by Wu Jieping Medical Foundation Project (Grant No: 08-JC-003), Innovative Drug R&D Center (Grant No: 2013ZX09401003-002), National Natural Science Funds of China (Grant No: 81372502), Science and Technology Research Project of Guangdong Province (Grant No: 2012B031800371), and National High Technology Research and Development Program of China (Grant No: 2012AA02A502).
The authors have no conflicts of interest to disclose.
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ISSN: 0025-7974
DOI: 10.1097/MD.0000000000003097

used as biomarkers for recurrence and prognosis in many types of cancer including lung cancer.[11,18,19] High level of albumin or low globulin level is associated with better survival.[20–22] However, as a biochemical index, the testing of albumin or globulin alone can be influenced by many factors, which may limit their stability and application in clinic. Therefore, we assume that the assessment of albumin and globulin together might have better prognostic value. Previous studies demonstrated that serum albumin/globulin ratio (AGR) can predict the survival of cancer patients, including colorectal cancer and breast cancer.[23,24]

In this study, for the 1st time, we examined the prognostic value of AGR in SCLC patients. Moreover, we compared the prognostic value between clinical indexes (such as PS, cancer stage, and baseline characteristic) and AGR.

MATERIALS AND METHODS

Patients Selection

This retrospective study was carried out in 2 independent queues of SCLC patients: testing group and validation group.

The testing group included 276 consecutive patients who were histologically confirmed as SCLC at Sun-Yat Sen University cancer center (SYSUCC) between January 2003 and December 2006, while the validation group enrolled 379 consecutive patients diagnosed with SCLC at SYSUCC between January 2008 and December 2011. The inclusion criteria in both groups were as follows: cytologically or histologically diagnosed as primary SCLC, age of at least 18 years, staged according to the VALSG staging system, testing of pretreatment total proteins and albumin in serum, testing of normal liver functions, complete clinical data, and the assessment of PS and disease stage was performed at patient admission. Patients were excluded according to the following criteria: patients with detectable inflammatory disease and patients with liver disease. This study was approved by the Institutional Review Board of SYSUCC, and written informed consent was obtained from each patient.

Clinical Data Collection

We recorded the characteristics of all patients, including gender, age, smoking status, body mass index (BMI), disease stage, histology, treatment strategies, and the scale of Eastern Cooperation Oncology Group Performance Status (ECOG-PS). Smokers were defined as patients who had more than 100 cigarettes, and the stage of SCLC was determined according to the VALSG staging system. Etoposide-based chemotherapy was the combination of etoposide and platinum-based chemotherapy agent.

Definition of AGR

Blood samples were collected for the testing of albumin and total proteins before the initial treatment. All samples were analyzed at a central laboratory. AGR was calculated using the equation: AGR = albumin/(total proteins−albumin).

Follow-Up

All patients were carefully followed after initial treatment. The follow-up period was from the date of finishing the antitumor treatment to March 30, 2014 or death for any cause. The therapy response was evaluated by dynamic computed tomography scan after 2 cycles of treatment. All patients received computed tomography scan every 8 weeks after the completion of antitumor therapy. The response was assessed by the radiologist and treatment physician according to the Response Evaluation Criteria in Solid Tumors version 1.1. We compared the difference in the mean of OS that is defined as the interval from the date of diagnosis to the date of death for any cause or the last follow-up. Patients who did not die at the last follow-up were censored.

Statistical Analysis

The median value and range were calculated based on continuous variables, while the categorical variables were shown as numbers and percentages of subjects. All statistical analyses were performed by using SPSS 21.0 software (IBM, Armonk, NY). Continous variables were analyzed by 2-sample *t*-test, while the categorical variables were compared by the Chi-square or Fisher exact test. A web-based R software engineered and designed by Budczies et al[25] (http://molpath.charite.de/cutoff/) was used to define the optimal cutoff value of pretreatment AGR. Kaplan–Meier method was used to estimate the survival curve between OS and prognostic factors, which includes cancer stage, LDH, AGR, and ECOG-PS. The prognostic significance of variables was analyzed by using univariate log-rank test. Multivariate analysis by Cox proportional hazards model was performed to determine the independent prognostic factor. $P < 0.05$ was considered statistically significant for all analyses.

RESULTS

According to the inclusion and exclusion criteria of the present study, a total of 276 and 379 patients were enrolled in the testing and validation groups, respectively. The baseline characteristics of patients are presented in Table 1.

Baseline Demographics in the Testing Group

In the testing group, the median age was 59 years (interquartile range [IQR] 52–66 years) and 239 enrolled patients were male (86.6%). The majority of enrollers were smokers (n = 238, 86.2%) and presented an ECOG-PS of 0–1 (n = 249, 90.2%). The median value of BMI was 22.5 (IQR 20.3–24.8). Among them, 161 patients were in limited stage (58.3%) and the other patients were in extensive stage (41.7%). The majority (n = 244, 88.4%) of patients received etoposide-based chemotherapy as 1st-line treatment and 49 (17.8%) patients underwent prophylactic cranial irradiation (PCI) after chemotherapy. Moreover, 87 (31.5%) patients received thorax radiotherapy (TRT) after or together with chemotherapy.

Using the biostatistical tool and Cutoff Finder, we found that the range of cutoff value for AGR was wide. The optimal cutoff value of 1.29 was determined for assessing OS (Figure 1).[26] All patients were divided into 2 groups: AGR $\geqq$ 1.29 (n = 197, 71.4%) and AGR < 1.29 (n = 79, 28.6%), the clinicopathological characteristics in each subgroup are described in Table 2. Patients with a higher AGR ($\geqq$1.29) were presented with a significantly lower LDH level ($P = 0.003$) and a significantly higher BMI ($P = 0.024$) compared with the patients with lower AGR. However, gender ($P = 0.583$), age ($P = 0.605$), PS ($P = 0.940$), cancer stage ($P = 0.771$), chemotherapy regimen ($P = 0.111$), and smoking status ($P = 0.736$) of patients were similar between 2 subgroups.

Baseline Demographics in Validation Group

In the validation group, the median age of the patients was 60 years (IQR 54–66 years) and 326 enrolled patients

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TABLE 1. The Characteristics of all Patients and Univariate Survival Analysis

Variables	Testing Group (n = 276)			Validation Group (n = 379)		
	Cases, N, %	Median OS, months (95% CI)	*P* Value*	Cases, *N* (%)	Median OS, months (95% CI)	*P* Value*
Age, years	59 (52–66)†		0.971	60 (54–66)†		0.090
Gender			0.264			0.262
Male	236 (86.6)	17.0 (14.75–19.32)		326 (86)	19.8 (16.70–22.90)	
Female	37 (13.4)	16.9 (10.69–23.04)		53 (14)	20.6 (7.37–33.90)	
Smoking status			0.178			0.606
Smoker	238 (86.2)	17.1 (14.85–19.35)		298 (78.6)	20.0 (16.38–23.69)	
Never-smoker	38 (13.8)	16.9 (11.41–22.32)		81 (21.4)	18.7 (13.06–24.34)	
BMI, kg/m^2			0.375			0.854
<22.5	135 (50.0)	16.2 (12.91–19.49)		204 (53.8)	20.0 (15.88–24.19)	
≥22.5	141 (50.0)	17.3 (14.50–20.17)		175 (46.2)	19.6 (16.20–23.07)	
Disease stage			<0.001			<0.001
Limited stage	161 (58.3)	19.9 (16.82–22.90)		201 (53.0)	33.9 (23.60–44.20)	
Extensive stage	155 (41.7)	12.6 (10.05–15.15)		178 (47.0)	14.7 (11.91–17.49)	
ECOG-PS			0.006			<0.001
0	98 (35.5)	17.1 (14.83–19.38)		228 (60.2)	21.3 (15.69–26.91)	
1	151 (54.7)	17.3 (14.51–20.16)		127 (33.5)	19.6 (13.73–23.47)	
2	27 (9.8)	7.0 (3.52–10.42)		24 (6.3)	10.8 (8.44–13.10)	
AGR			0.026			<0.001
≥1.29	197 (71.4)	17.1 (14.84–19.37)		288 (76.0)	23.0 (17.86–28.20)	
<1.29	79 (28.6)	16.2 (11.77–20.63)		91 (24.0)	13.2 (10.76–15.71)	
LDH, U/L			0.001			<0.001
Normal range	170 (61.6)	18.7 (16.81–20.66)		231 (60.9)	26.5 (20.18–32.75)	
Abnormally range	106 (38.4)	11.5 (8.79–14.28)		148 (39.1)	14.4 (11.71–17.02)	
Chemotherapy regime			0.097			0.287
Etoposide-based	244 (88.4)	17.3 (15.43–19.24)		341 (90.0)	19.6 (16.94–22.33)	
Others	32 (11.6)	13.6 (14.91–19.15)		38 (10.0)	23.3 (10.81–35.86)	
Prophylactic cranial irradiation			0.078			<0.001
Yes	49 (17.8)	18.2 (14.63–21.71)		104 (27.4)	29.1 (23.49–34.72)	
No	227 (82.2)	16.2 (13.67–18.73)		275 (72.6)	17.0 (14.57–19.50)	
Thorax radiotherapy			<0.001			<0.001
Yes	87 (31.5)	20.9 (13.93–27.94)		150 (39.6)	30.8 (20.38–41.15)	
No	189 (68.5)	14.1 (11.83–16.44)		229 (60.4)	16.2 (14.15–18.18)	

AGR = albumin/globulin ratio, BMI = body mass index, CI = confidence interval, ECOG-PS = Eastern Cooperation Oncology Group Performance Status, LDH = lactate dehydrogenase, OS = overall survival.

* Log-rank test.

† Median (interquartile range).

were males (86.0%). The majority of enrollers were smokers (n = 298, 78.6%) and showed an ECOG-PS of 0–1 (n = 355, 93.7%). The median value of BMI was 22.1 (IQR 20.0–24.7). Among them, 201 and 178 patients were in the limited (53.0%) and extensive (47.0%) stages, respectively. Most of patients received etoposide-based chemotherapy as 1st-line treatment (n = 341, 90.0%) and 104 patients (27.4%) underwent PCI after chemotherapy. Moreover, 150 (39.6%) patients received TRT after or together with chemotherapy. According to the cutoff value of AGR score, the baseline characteristics of patients are shown in Table 2. Compared with the patients with lower AGR, the patients with a higher AGR (≧ 1.29) were presented a significantly lower LDH level ($P = 0.005$), better ECOG-PS score ($P = 0.002$), and with limited stage ($P = 0.001$). However, the gender ratio ($P = 0.051$) and age ($P = 0.094$) were not significantly different between 2 subgroups.

AGR and OS in the Testing Group

In the testing group, 63 patients were still alive and 213 patients died at the last follow-up. The median OS of the 276 eligible patients was 15.31 months (IQR 8.20–28.31 months). According to the univariate analysis, AGR ($P = 0.026$), disease stage ($P < 0.001$), LDH level ($P = 0.001$), having TRT ($P < 0.001$), and ECOG-PS score ($P = 0.006$) were significantly associated with OS (Table 1, Figure 2). However, there were no significant correlation between OS and age ($P = 0.971$), gender ($P = 0.264$), BMI ($P = 0.375$), chemotherapy regime ($P = 0.097$), smoking status ($P = 0.178$), and PCI ($P = 0.078$) (Table 1). According to the multivariate analysis, we verified the significant factors of univariate survival analysis by testing the independent indexes. The analyses indicated that AGR ($P = 0.046$), ECOG-PS ($P = 0.044$), and disease stage ($P < 0.001$) were the independent predictive factors for OS (Table 3). Patients with lower AGR (<1.29) were estimated

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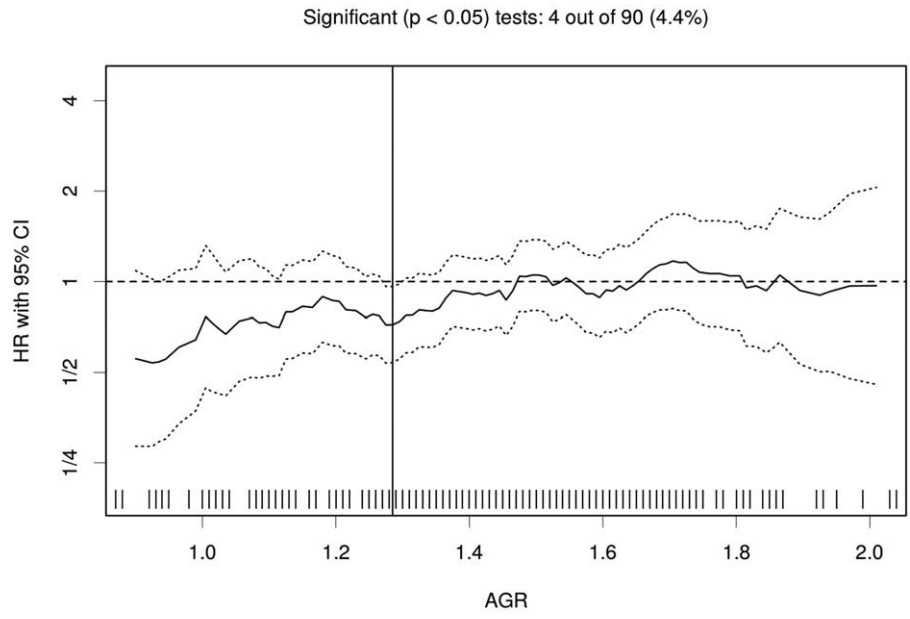

FIGURE 1. HR for OS independent of cutoff point for AGR in small-cell lung cancer patients. The vertical line designates the optimal cutoff point with the most significant (log-rank test) split. The plots were generated using the biostatistical tool Cutoff Finder. AGR = albumin/globulin ratio, HR = hazard ratio, OS = overall survival.

TABLE 2. Clinicopathological Characteristics of Patients Stratified by AGR

	Test Group (n = 276)			Validation Group (n = 379)		
Variables	**AGR ≧ 1.29, n, %**	**AGR < 1.29, n, %**	***P* Value**	**AGR ≧ 1.29, n, %**	**AGR < 1.29, n, %**	***P* Value**
Age, years			0.605			0.094
Gender			0.583			0.051
Male	172 (87.3)	67 (84.8)		253 (87.8)	73 (80.2)	
Female	25 (12.7)	12 (15.2)		35 (12.2)	18 (19.8)	
Smoking status			0.736			0.002
Smoker	169 (85.8)	69 (87.3)		237 (82.3)	61 (67.0)	
Never-smoker	28 (14.2)	10 (12.7)		51 (17.7)	30 (33.0)	
BMI, kg/m^2			0.002			0.062
<22.5	85 (43.1)	50 (63.3)		150 (52.1)	54 (59.3)	
≥22.5	112 (56.9)	29 (36.7)		138 (47.9)	37 (40.7)	
Disease stage			0.771			0.001
Limited stage	116 (58.9)	45 (57.0)		167 (58.0)	34 (37.4)	
Extensive stage	81 (41.1)	37 (43.0)		121 (42.0)	57 (62.6)	
ECOG-PS			0.940			0.002
0	68 (34.5)	30 (38.0)		188 (65.3)	40 (44.0)	
1	112 (56.9)	39 (49.4)		84 (29.2)	43 (47.3)	
2	17 (8.6)	10 (12.7)		16 (5.6)	8 (8.8)	
LDH, U/L			0.003			0.005
Normal range	128 (65.0)	42 (53.2)		184 (63.9)	47 (51.6)	
Abnormally range	69 (35.0)	37 (46.8)		104 (36.1)	44 (48.4)	
Chemotherapy regime			0.111			0.04
Etoposide-based	178 (90.4)	66 (83.5)		254 (88.2)	87 (95.6)	
Others	19 (9.6)	13 (16.5)		34 (11.8)	4 (4.4)	

AGR = albumin/globulin ratio, BMI = body mass index, CI = confidence interval, ECOG-PS = Eastern Cooperation Oncology Group Performance Status, LDH = lactate dehydrogenase, OS = overall survival.

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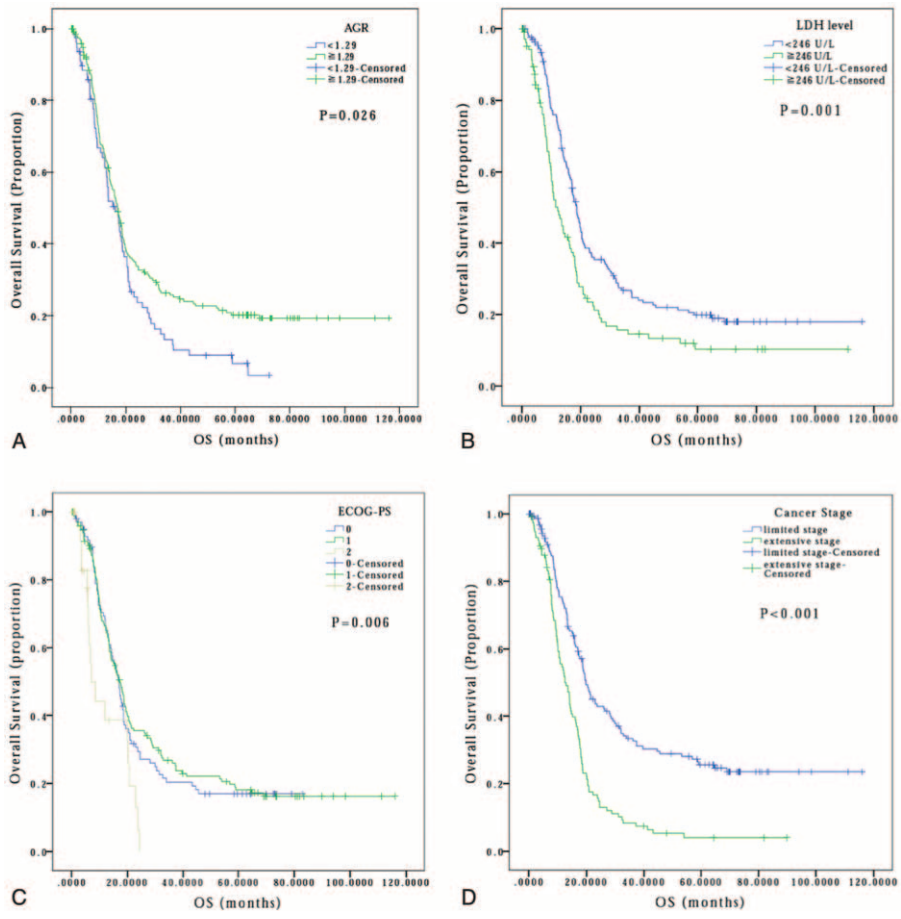

FIGURE 2. OS curves comparing patients in the testing group with (A) high AGR level versus low AGR level, (B) high LDH versus low LDH, (C) good PS versus bad PS, and (D) limited disease versus extensive disease. AGR = albumin/globulin ratio, LDH = lactate dehydrogenase, OS = overall survival, PS = performance status.

TABLE 3. Results From Cox Regression Model (Adjusted for Age, Sex, Disease stage, PS, and AGR)

	Testing Group (276)				Validation Group (379)			
Variables	**Hazard Ratio**	**95% LL**	**CI UL**	***P* Value**	**Hazard Ratio**	**95% LL**	**CI UL**	***P* Value**
ECOG-PS				0.044				<0.001
0	–	–	–		–	–	–	
1	1.01	0.76	1.36		1.09	0.81	1.46	
2	1.90	1.12	3.20		4.31	2.47	7.50	
AGR				0.046				0.022
≧1.29	–	–	–		–	–	–	
<1.29	1.35	1.61	1.81		1.43	1.05	1.95	
Disease stage				<0.001				<0.001
Limited stage	–	–	–		–	–	–	
Extensive stage	2.00	1.49	2.71		2.50	1.87	3.45	
LDH (per 100 U/L increment)				0.231				0.004
Normal range	–	–	–		–	–	–	
Abnormally elevated	1.20	0.89	1.63		1.52	1.14	2.01	

AGR = albumin/globulin ratio, CI = confidence interval, ECOG-PS = Eastern Cooperation Oncology Group Performance Status, LDH = lactate dehydrogenase, LL = lower limit, UL = upper limit.

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to have 1.35 times higher risk of death than those with higher AGR (≥1.29) (HR, 1.35; 95% CI, 1.01–1.81, $P = 0.046$).

AGR and OS in the Validation Group

In the validation group, 205 (54.1%) patients died at the last follow-up. The median OS of 379 patients was 15.06 months (IQR 8.67–27.17 months). According to the univariate analysis, the OS was significantly associated with AGR ($P < 0.001$), ECOG-PS ($P < 0.001$), cancer stage ($P < 0.001$), TRT ($P < 0.001$), LDH level ($P < 0.001$), and PCI ($P < 0.001$) (Table 1, Figure 3). However, other variables including gender ($P = 0.262$), smoking statue ($P = 0.606$), chemotherapy regime ($P = 0.287$), and age ($P = 0.090$) were not associated with OS. According to the multivariate analysis, the significant prognostic factors were AGR ($P = 0.022$), ECOG-PS ($P < 0.001$), cancer stage ($P < 0.001$), and LDH level ($P = 0.004$) (Table 3). Moreover, the patients with lower AGR (<1.29) were associated with poorer OS and had 1.43 times higher risk of death than those with higher AGR (≥1.29) (HR, 1.43; 95% CI, 1.05–1.94; $P = 0.022$).

DISCUSSION

In this study, we examined the predictive value of AGR in SCLC patients from our cancer center. To our knowledge, this is the 1st report to analyze the correlation between AGR and OS in SCLC patients. Patients with high AGR (≥1.29) had longer OS than those with low AGR (<1.29). The results of multivariate analysis demonstrated that AGR was an independent prognostic factor after adjusting cancer stage, gender, smoke status, ECOG PS, LDH, and BMI in SCLC patients. Moreover, these findings were validated in an independent population.

SCLC is an extremely aggressive malignancy with early recurrence and metastasis.[3,26] Although SCLC is sensitive to cytotoxic agents and radiotherapy, the 5-year survival rate in SCLC patients is extremely low.[27] Over the years, the prognosis of SCLC patients has been slightly improved. Therefore, it is necessary to further explore the prognostic factors of OS to better stratify those who are likely to benefit from treatment, which may optimally and reasonably utilize the limited medical resource.

Previous studies have demonstrated that ECOG PS, TNM stage, neuron-specific enolase, and LDH can predict the prognosis of SCLC patients.[28,29] Consistent with previous findings, we found that limited staging, better ECOG PS, and normal LDH level significantly correlated with longer survival, compared with poor PS, extensive staging, and elevated LDH levels. However, the prognostic value of these factors is inconsistent in various studies.

Serum albumin helps to balance blood PH and maintain the intravascular pressure. Albumin is often regarded as a marker

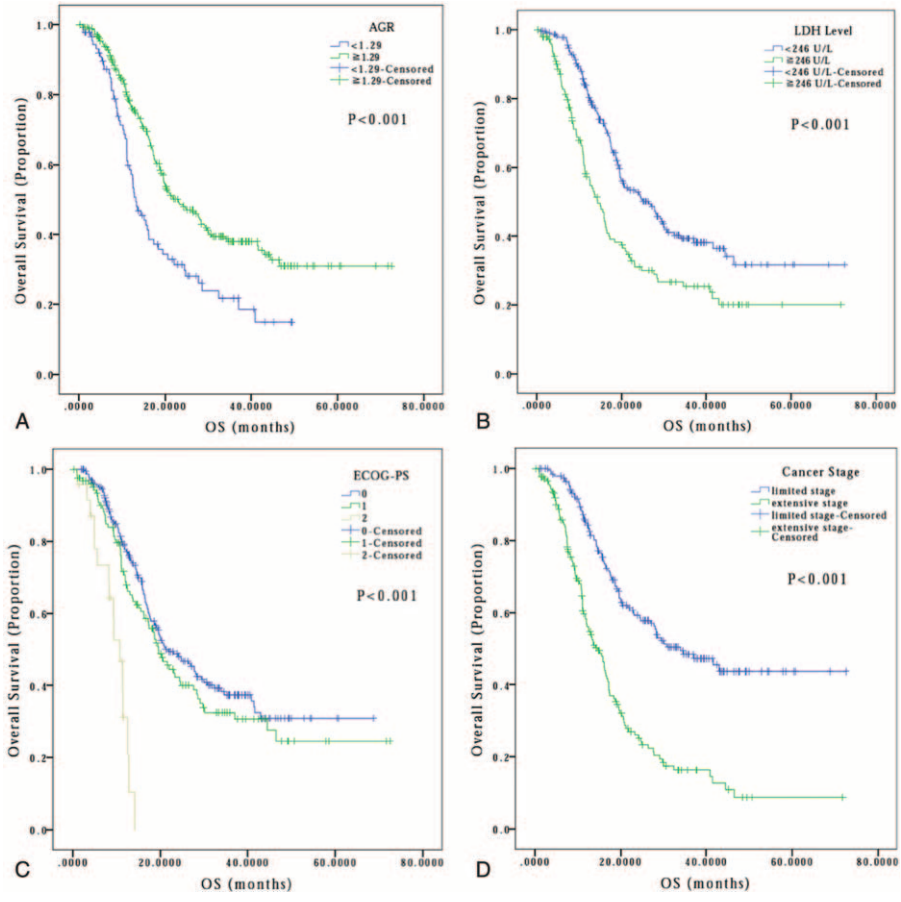

FIGURE 3. OS curves comparing patients in the validation group with (A) high AGR level versus low AGR level, (B) high LDH versus low LDH, (C) good PS versus bad PS, and (D) limited disease versus extensive disease. AGR = albumin/globulin ratio, LDH = lactate dehydrogenase, OS = overall survival, PS = performance status.

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for nutritional status of patients in clinical practice.[17] Recent studies revealed a potential relationship between chronic inflammation and cancer. Inflammatory mediators from cells, such as nuclear factor-kappa B, ribonuclease L, scavenger receptor 1, 5-hydroxytryptamine, anaphlatoxin, interleukin (IL)-1, and IL-6, may alter the tumor microenvironment and promote tumorigenesis by increasing the proliferation, metastasis, and immune escape of tumor cells.[30,31] These findings support chronic inflammation is associated with poor OS in patients with different cancers, including SCLC.[16,32,33] Albumin constitutes the major classes of chronic inflammation. The production of albumin would decrease owing to the inflammation cytokines, such as IL-1 and IL-6. Previous researches have also discovered it had a strong association with several types of cancers, including lung cancer.[21,34–38] Those findings demonstrated that low baseline level of serum albumin could predict poor OS in cancer patients, especially at advanced stage.[39] Globulin as another major protein also plays a part in chronic inflammation. Some components of globulin would increase under the condition of inflammation. The high level of globulin is considered to be a marker of activation of inflammation. Moreover, several studies indicated that globulin is associated with the OS of cancer patients.[20,22]

Since the level of albumin is related to many factors, such as stress, illness, hepatic insufficiency, and changes in the volume of body fluids, albumin cannot be widely used in clinic to predict OS in cancer patients. To avoid the limitation of albumin, we hypothesized that the combination of serum albumin and globulin into a new index may better predict the OS of cancer patients. Recently, the concept of AGR has been proposed, which means albumin/(total proteins−albumin) AGR would not be affected by the factors above. Moreover, AGR was able to identify those who may have poor prognosis even they had normal level of albumin. Therefore, we considered the AGR as a more appropriate and accurate prognostic marker for cancer patients than serum albumin or globulin alone. A number of studies indicated that the AGR can predict the OS of cancer patients.[23,40] In non-SCLC, Duran et al[41] and Yao et al[42] indicated that lower AGR value was significantly associated with longer OS. So, we proposed that the AGR could also be a prognostic factor for SCLC patients.

Our present study demonstrated the strong prognostic value of the AGR in SCLC patients. In our study, a 1.29 cutoff value for the AGR was used for predicting OS in SCLC patients. Based on this cutoff value, the univariate analysis revealed that the AGR is associated with poor prognosis in both testing and validation groups. The patients who had AGR < 1.29 showed 1.35 times higher risk of death than those with AGR $\geqq 1.29$ in the testing group, which value was as high as 1.43 times in the validation cohort. According to multivariate analyses, when adjusted for other variables such as cancer stage, CRP/Alb ratio, independently predicted the OS of SCLC patients. Our results validate the excellent prognostic value of the AGR in SCLC patients. Moreover, the AGR is featured with the characteristics of inexpensive, easy to test, and standardized evaluation criteria worldwide. However, there are a few limitations in our study.

(1) No other inflammatory prognostic factors were used to analyze the insufficient part of AGR.
(2) This is a single-center retrospective study at our cancer center, so our findings need to be validated in a large-scale prospective validation study.

In summary, this study first demonstrated that the AGR is an independent factor for predicting the OS in SCLC patients. The AGR would be a better prognostic marker for SCLC patients in clinic.

ACKNOWLEDGEMENT

The authors thank Wu Jieping Medical Foundation Project (Grant No: 08-JC-003), Innovative Drug R&D Center (Grant No: 2013ZX09401003-002), National Natural Science Funds of China (Grant No: 81372502), Science and Technology Research Project of Guangdong Province (Grant No: 2012B031800371), and National High Technology Research and Development Program of China (Grant No: 2012AA02A502) for the support.

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