Turk J Gastroenterol *2017; 28: 439-45*

Gastrointestinal Tract

Preoperative albumin/globulin ratio is a potential prognosis predicting biomarker in patients with resectable gastric cancer

Fan Xue[1], Feng Lin[1], Min Yin[2], Ning Feng[1], Xu Zhang[1], You-Gang Cui[1], Yu-Peng Yi[1], Xiang-Yu Kong[1], Xi Chen[2], Wen-Zhi Liu[1]

[1]Department of Gastrointestinal Surgery, Affiliated Zhongshan Hospital of Dalian University, Dalian, China
[2]Department of Hepatobiliary Laparoscopic Surgery, Affiliated Zhongshan Hospital of Dalian University, Dalian, China

Cite this article as: Xue F, Lin F, Yin M, et al. Preoperative albumin/globulin ratio is a potential prognosis predicting biomarker in patients with resectable gastric cancer. Turk J Gastroenterol 2017; 28: 439-45.

ABSTRACT

Background/Aims: To investigate the prognostic significance of preoperative albumin to globulin ratio (AGR) in patients with resectable gastric cancer (GC).

Materials and Methods: According to the inclusion criteria, 269 GC patients (male:female=127:67; median age: 67 years) with a stage I through III who underwent gastrectomy with D2 lymphadenectomy and R0 resection were included. These patients were categorized into two groups, namely low AGR group and high AGR group, based on a cutoff point that was obtained using a receiver-operating characteristic curve. The correlations of preoperative AGR with the clinicopathological characteristics and overall survival were analyzed. Univariate and multivariate analysis were performed to assess the prognostic value of preoperative AGR.

Results: Age, gender, tumor size, T stage, and preoperative hemoglobin were significantly different between the low and high AGR groups ($p<0.05$). Moreover, using binary logistic regression analysis, female gender, older age, larger tumor size, and lower preoperative hemoglobin were found to be independent risk factors of low preoperative AGR. Kaplan-Meier curves showed a significantly lower overall survival for the low AGR group (13 months; 95% confidence interval (CI), 10.9-15.1) compared to the high AGR group (17 months; 95% CI, 13.8-20.2; $p=0.014$). The univariate analysis of all the variables showed that overall survival was significantly related to age; tumor size; differentiation degree; T stage; N stage; tumor, node, metastasis (TNM) stage; preoperative AGR; and hemoglobin ($p<0.05$). Results of multivariate analysis showed that low preoperative AGR (<1.36) was an independent risk factor for poorer overall survival in GC patients (odds ratio [OR]=1.5; 95% CI, 1.0-2.1; $p=0.041$).

Conclusion: Preoperative AGR was significantly associated with the prognosis of GC patients in our study. In addition, preoperative AGR is suggested to be a simple but efficient prognosis predicting biomarker in patients with GC.

Keywords: Gastric cancer, albumin to globulin ratio, prognosis, survival rate, inflammation

Original Article

INTRODUCTION

Globally, gastric cancer (GC) is the fifth most commonly diagnosed cancer and the third leading cause of cancer death (1). With the benefits from further improvements in diagnosis and treatment of GC, the five-year overall survival (OS) rate has increased to 28.0%-44.3% (2), but the prognosis still remains poor. The tumor, node, metastasis (TNM) staging system is recognized as the most important prognostic indicator of GC, however, it merely gives a partial prediction (3). Therefore, a simple and efficient biomarker is necessary to ensure comprehensive evaluation and accurate prediction.

Malnutrition and inflammation are frequent complications of gastrointestinal malignancies and have been associated with short- and long-term outcomes in cancers (4). Serum albumin and globulin are important laboratory indexes that are commonly used to assess the nutritional status and inflammatory response before surgery (5). The proinflammatory cytokines produced by tumors can stimulate the production of

Address for Correspondence: Wen-Zhi Liu E-mail: liuwenzhi1965@163.com
Received: March 28, 2017 **Accepted:** August 1, 2017 **Available Online Date:** October 25, 2017

acute-phase reaction proteins, which are calculated as part of the serum globulin, and suppress the synthesis of albumin (6). In addition, albumin plays a significant role in the distribution and pharmacological activities of anticancer drugs (7). As a consequence, low serum albumin and high serum globulin are two independent prognostic factors, as recently shown in various cancers (4,5,8). Therefore, we suppose that albumin to globulin ratio (AGR) is a potential preoperative biomarker for the assessment of the clinicopathological features and prognosis.

To the best of our knowledge, several previous studies have demonstrated the correlation between the preoperative AGR and long-term survival of cancers (9-14), but GC has not been discussed. The purpose of this study was to find the cutoff value of AGR and to evaluate whether preoperative AGR has a prognostic value in patients with resectable GC.

MATERIALS AND METHODS

Patients

Ethics approval of our study was provided by the institutional review board of our hospital. We retrospectively reviewed patients who were diagnosed with GC and received gastrectomy with D2 lymphadenectomy and R0 resection from 2007 to 2012 at the Gastrointestinal Surgery Department. The inclusion criteria are as follows: pathological diagnosis is primary GC and absence of distant metastasis; no neoadjuvant chemotherapy; normal hepatic and renal function; and no history of chronic inflammatory disease or immunosuppressive therapy (1-4.). However, patients with a history of coronary heart disease, hypertension, chronic lung disease, cerebrovascular disease, and type II diabetes mellitus could be enrolled in the study. A total of 269 patients met the inclusion criteria and all these patients signed informed consent approved by the institutional review board.

Clinical and Laboratory Data

All the clinical and laboratory data were collected from the hospital database. Specific information includes gender, age, comorbidities, preoperative laboratory variables, and tumor characteristics. Data of cases that underwent the postoperative chemotherapy were also collected, and the postoperative chemotherapy protocol was designed after operations according to the tumor stage and individual characteristics. The stage of GC was in accordance with the American Joint Committee on Cancer classification system (seventh edition, 2010), and the preoperative laboratory variables analyzed in this study were measured before any treatment. All the patients were followed up periodically after the surgery until death or June 2015. The last date or deadline of follow-up was applied for the censored cases.

The value of AGR was calculated with the formula [AGR=serum albumin/serum globulin], and the appropriate cutoff point of preoperative AGR was obtained using a receiver-operating characteristic curve (Figure 1). As a result, the area under the curve was 0.657, and 1.36 was selected as the cutoff value, whereas sensitivity and specificity were 0.709 and 0.554, respectively. Thus, the patients were classified into a low (<1.36) or high (≥1.36) AGR group. Using the same method, the value of 108 g/L was selected as the optimal cutoff value of preoperative hemoglobin.

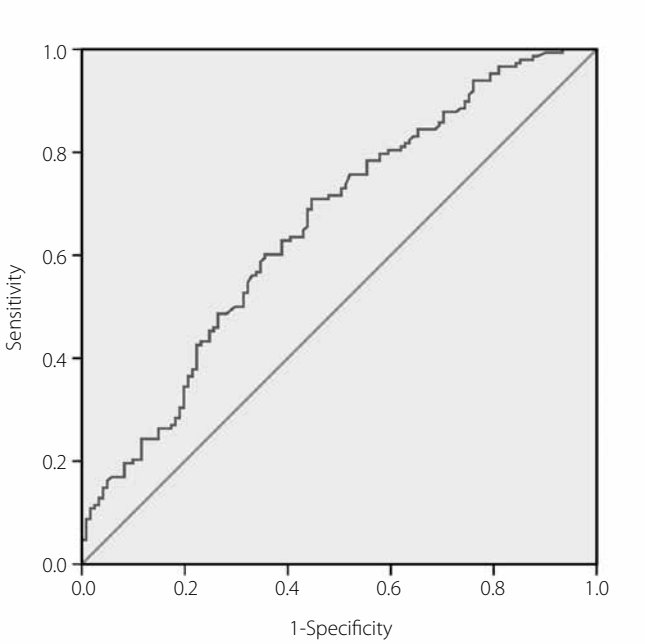

Figure 1. Receiver-operating characteristic curve of preoperative AGR (AGR cutoff value=1.36; sensitivity=0.709; specificity=0.554; area under curve=0.657; p<0.001)
AGR: albumin to globulin ratio

Statistical Analysis

All statistical analyses were performed using Statistical Package for Social Sciences version 22.0 (IBM Corp.; Armonk, NY, USA). A chi-square or Fisher's exact test was used to evaluate the categorical variables, while an independent t-test was used for continuous variables between the high and low AGR groups. Moreover, binary logistic regression analysis was performed to identify any clinicopathological correlations with the low preoperative AGR value. The analysis of OS was performed using the Kaplan-Meier method and then compared using log-rank test. Univariate analyses were performed for all the variables, and those variables that were confirmed to be statistically significant were further analyzed by a multivariate Cox regression model. A p<0.05 is considered statistically significant in the analyses.

RESULTS

Preoperative AGR and Clinicopathological Characteristics

Statistical analysis divided 269 eligible GC patients into two groups by the cutoff point of preoperative AGR; 114 pa-

Table 1. Comparison of variables between low and high AGR ratio group

Variable	Total (n=269)	Low AGR group (n=114)	High AGR group (n=155)	p
Gender				0.006
Male	202 (75.1%)	76 (37.6%)	126 (62.4%)	
Female	67 (24.9%)	38 (56.7%)	29 (43.3%)	
Age, years	65.77 (64.42-67.12)	68.27 (66.10-70.44)	63.93 (62.25-65.61)	
<70	153 (56.9%)	50 (32.7%)	103 (67.3%)	0.000
≥70	116 (43.1%)	64 (55.2%)	52 (44.8%)	
Cardiopulmonary disease				0.705
Yes	63 (23.4%)	28 (44.4%)	35 (55.6%)	
No	206 (76.6%)	86 (41.7%)	120 (58.6%)	
Diabetes mellitus				0.096
Yes	26 (9.7%)	15 (57.7%)	11 (42.3%)	
No	243 (90.3%)	99 (40.7%)	144 (59.3%)	
Tumor size	4.80 (4.48-5.12)	5.55 (5.01-6.09)	4.21 (3.84-4.58)	0.000
<5 cm	147 (54.6%)	43 (29.3%)	104 (70.7%)	0.000
≥5 cm	122 (45.4%)	71 (58.2%)	51 (41.8%)	
Differentiation degree				0.070
Well-moderate	140 (52.0%)	52 (37.1%)	88 (62.9%)	
Poor undifferentiation	129 (48.0%)	62 (48.1%)	67 (51.9%)	
T stage				0.022
T1	30 (11.2%)	8 (26.7%)	22 (73.3%)	
T2	88 (32.7%)	30 (34.1%)	58 (65.9%)	
T3	42 (15.6%)	20 (47.6%)	22 (52.4%)	
T4	109 (40.5%)	56 (51.4%)	53 (48.6%)	
N stage				0.145
N0	115 (42.8%)	48 (41.7%)	67 (58.3%)	
N1	38 (14.1%)	12 (31.6%)	26 (68.4%)	
N2	39 (14.5%)	14 (35.9%)	25 (64.1%)	
N3	77 (28.6%)	40 (51.9%)	37 (48.1%)	
TNM stage				0.308
Stage I	85 (31.6%)	31 (36.5%)	54 (63.5%)	
Stage II	63 (23.4%)	26 (41.3%)	37 (58.7%)	
Stage III	121 (45.0%)	57 (47.1%)	64 (52.9%)	
Preoperative HGB	119.25 (102.53-114.47)	108.50 (102.53-114.47)	127.15 (122.72-131.58)	0.000
<108 g/L	84 (31.2%)	49 (58.3%)	35 (41.7%)	0.000
≥108 g/L	185 (68.8%)	65 (35.1%)	120 (64.9%)	
Postoperative chemotherapy				0.062
Yes	124 (46.1%)	45 (36.3%)	79 (63.7%)	
No	145 (53.9%)	69 (47.6%)	76 (52.4%)	

Values are presented as number (%) or mean (95% CI)
AGR: albumin to globulin ratio; HGB: hemoglobin; TNM: tumor, node metastasis; CI: confidence interval

tients were in the low AGR group (<1.36) and 155 in the high AGR group (≥1.36). As summarized in Table 1, significant differences existed between the low and high AGR group in terms of age, gender, tumor size, T stage, and preoperative hemoglobin. It could indicate that the patients in the low AGR group were older in age, had more number of females, a larger tumor size, more advanced T stage, and lower preoperative hemoglobin levels compared to

Table 2. Binary logistic regression analysis of low AGR associated risk factors

Variable	OR (95% CI)	p
Gender (referent: male)		0.018
Female	2.161 (1.140-4.099)	
Age (referent: <70), years		0.001
≥70	2.676 (1.523-4.703)	
Cardiopulmonary disease (referent: no)		0.952
Yes	1.020 (0.531-1.959)	
Diabetes mellitus (referent: no)		0.279
Yes	1.697 (0.651-4.425)	
Tumor size (referent: <5 cm)		0.007
≥5 cm	2.357 (1.263-4.399)	
Differentiation degree (referent: well-moderate)		0.075
Poor undifferentiation	1.692 (0.949-3.015)	
T stage (referent: T1)		0.399
T2	1.563 (0.539-4.536)	0.411
T3	3.489 (0.646-18,828)	0.146
T4	4.605 (0.781-27,141)	0.092
N stage (referent: N0)		0.238
N1	0.832 (0.198-3.504)	0.803
N2	0.970 (0.166-5.666)	0.973
N3	2.241 (0.342-14,690)	0.400
TNM stage (referent: Stage I)		0.370
Stage II	0.315 (0.063-1.572)	0.159
Stage III	0.182 (0.012-2.679)	0.241
Preoperative HGB (referent: ≥108 g/L)		0.032
<108 g/L	2.002 (1.062-3.772)	

AGR: albumin to globulin ratio; CI: confidence interval; HGB: hemoglobin; OR: odd ratio; TNM: tumor, node metastasis

the high AGR group. Furthermore, with progression in the depth of tumor infiltration and TNM stage, the percentage of patients with low preoperative AGR increased accordingly.

The outcome of binary logistic regression analysis in Table 2 showed that four covariates were found to be independent risk factors of low preoperative AGR value; these include female gender, older age, larger tumor size, and lower preoperative hemoglobin level. This indicated that the individuals who were females (odds ratio [OR], 2.2; 95% confidence interval [CI], 1.1-4.1; p=0.018), were aged >70 years (OR=2.7; 95% CI, 1.5-4.7; p=0.001), or whose preoperative hemoglobin was <108 g/L (OR=2.0; 95% CI, 1.1-3.8; p=0.032), and those whose tumors were larger than 5 cm (OR=2.4; 95% CI, 1.3-4.4; p=0.007) had a higher incidence of low preoperative AGR value compared to others.

Table 3. Results of univariate and multivariate survival analysis

Variable	Univariate analysis	Multivariate analysis	
	p	p	OR (95% CI)
Gender	0.195		
Male			
Female			
Age, years	0.009	0.001	
<70			Referent
≥70			1.841 (1.284-2.641)
Cardiopulmonary disease	0.070		
Yes			
No			
Diabetes mellitus	0.149		
Yes			
No			
Tumor size	0.000	0.152	
<5 cm			Referent
≥5 cm			0.748 (0.502-1.113)
Differentiation degree	0.008	0.914	
Well-moderate			Referent
Poor undifferentiation			0.981 (0.686-1.402)
T stage	0.000	0.105	
T1			Referent
T2		0.068	3.981 (0.902-17.564)
T3		0.057	4.934 (0.951-25.616)
T4		0.023	6.809 (1.304-35.541)
N stage	0.000	0.003	
N0			Referent
N1		0.657	0.817 (0.336-1.989)
N2		0.821	1.128 (0.397-3.205)
N3		0.120	2.358 (0.800-6.948)
TNM stage	0.000	0.373	
Stage I			Referent
Stage II		0.330	1.622 (0.613-4.289)
Stage III		0.172	2.877 (0.632-13.105)
Preoperative HGB	0.033	0.939	
≥108 g/L			Referent
<108 g/L			1.016 (0.675-1.530)
Preoperative AGR	0.000	0.041	
≥1.36			Referent
<1.36			1.470 (1.016-2.127)
Postoperative chemotherapy	0.140		
Yes			
No			

AGR: albumin to globulin ratio; CI: confidence interval; HGB: hemoglobin; OR: odd ratio

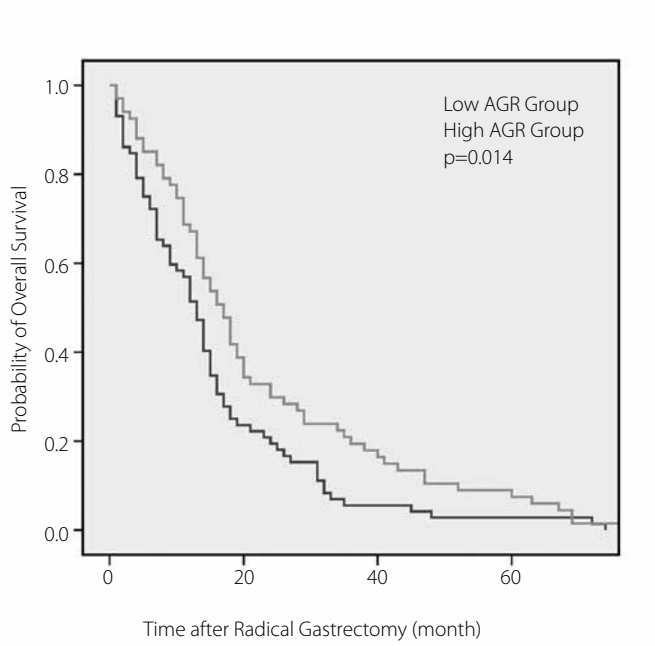

Figure 2. Kaplan-Meier curve of patients with GC after radical gastrectomy (AGR<1.36 vs ≥1.36)
AGR: albumin to globulin ratio; GC: gastric cancer

Preoperative AGR and Prognosis of GC Patients

The median follow-up time was 40 months (range, 1-108 months). There were 130 surviving patients on the deadline of follow-up and 139 cases were confirmed to have died. In particular, 24 patients who were lost to follow-up were excluded in our study. The median OS of the low and high AGR groups was 13 months (95% CI, 10.9-15.1) and 17 months (95% CI, 13.8-20.2), respectively, (p=0.014). The Kaplan-Meier curve showed a significantly lower OS in the low AGR group compared to the high AGR group (Figure 2). The univariate analysis of all the variables showed that age, tumor size, differentiation degree, T stage, N stage, TNM stage, preoperative AGR, and hemoglobin have significant influences on the prognosis of GC patients (Table 3). The statistically significant parameters in univariate analysis were then enrolled in a multivariate analysis. Eventually, older age (≥70), worse N stage, and low preoperative AGR (<1.36) were confirmed the independent risk factors for the lower OS time of GC patients (Table 3).

DISCUSSION

Our major finding is that preoperative AGR is significantly associated with the OS of GC patients. Preoperative AGR has been demonstrated as a prognostic predictor in various cancers (9-14), but there was no literature discussing the predictive value of preoperative AGR in GC patients when we were accomplishing this study. Interestingly, a similar research was recently published whose results indicated that AGR was just an independent disease-free survival marker and not the OS marker (15). However, as the results showed, low preoperative AGR (<1.36) remained an independent prognostic factor for OS after controlling the irrelevant variables in a multivariable analysis. Therefore, more studies are needed to discuss the predictive value of preoperative AGR on the prognosis of GC patients.

The value of AGR is calculated with albumin and globulin, which are not only the two main constituents of serum protein that maintain osmotic pressure but also are affected by the nutritional status and systemic inflammation. There exists close interactions between serum albumin and tumors, with the results that the serum albumin level provides potential prognostic significance in cancer (5). Firstly, because of anepithymia and malabsorption, patients with gastrointestinal cancers have a higher risk of hypoalbuminemia compared to others (16). Secondly, the tumor can induce systemic inflammation, which in turn, may be a stimulus for tumor and immune cells to produce cytokines, such as interleukin (IL)-1β, IL-6, and tumor necrosis factor. These cytokines have an effect on suppressing the synthesis of albumin and increasing the permeability of capillaries, which can promote the loss of albumin (5). Thirdly, as the major target of oxidant stress, albumin has an antioxidant function and prevents damage in lipids, nucleic acids, and other proteins (17). Therefore, serum albumin plays an important role in stabilizing DNA replication and inhibiting carcinogenesis (18). Lastly, serum albumin, a multifunctional protein in plasma, can influence the therapeutic efficacy of anticancer treatment. Recent studies have demonstrated that albumin has a great impact on the distribution and pharmacological activities of anticancer drugs as a transporter in plasma (7). Gupta et al. (5) reviewed 53 reports on the relation between serum albumin level and prognosis of different cancers, including GC, most of which concluded that lower albumin levels predicted a poorer survival. Similarly, our additional analysis showed that preoperative albumin was a significant predictor and protective factor of OS (OR=0.9; 95% CI, 0.9-1.0; p<0.001).

In contrast, serum globulin, also known as nonalbumin proinflammatory protein, has complex components, including acute phase proteins, immunoglobulins, interleukins, and tumor markers (19). Prior studies have reported that some of these inflammation markers play an important role in the carcinogenesis, progression, metastasis, and recurrence of tumors (20). In the study by Chen et al. (8), low pretreatment serum globulin predicts a better prognosis for GC patients. Moreover, increases of some nonalbumin proinflammatory proteins, such as C-reactive protein, alpha and gamma globulin, complement C3, and IgA were also shown to have a negative impact on the survival of various cancer patients (21-23). However, the univariate analysis of our data showed that preoperative globulin was not significantly correlated with OS (OR=1.0; 95% CI, 1.0-1.1; p=0.123). We presumed that the reasons for the negative result are that the actual value of globulin can be altered by hemodilution or hemoconcentration, and redundant components of globulin may cause errors in the outcome.

Above all, both preoperative albumin and globulin are candidates for a prognostic indicator of GC, but the preoperative serum globulin in our study was not significantly correlated with survival. We assume that prognostic indicators based on the ratio of albumin to globulin are more accurate considering the following advantages. Firstly, AGR can take into account two identified predictors, which makes it more powerful than each alone. We observed that low preoperative AGR (<1.36) could still identify patients who had a poorer prognosis, even if their serum albumin levels were normal (≥35 g/L; OR=1.7; 95% CI, 1.2-2.6; p=0.008). Secondly, AGR is calculated in the form of two values, which can avoid the influences of hemodilution or hemoconcentration (14). However, we cannot also evade the disadvantages of AGR. Obviously, AGR still cannot eliminate the interference of unwanted components of globulin in the analysis results. Furthermore, serum albumin has a relatively stable value because of its half-life of about 20 days, while components of serum globulin have various half-lives, ranging from hours to several days. The level of serum albumin and globulin measured at the same time may reflect different periods of status (24). In addition, Alkan (16) recognized that AGR was not a predictor but a misleader because AGR can be affected by multiple factors. It is similar to our finding that the level of preoperative AGR can be significantly influenced by gender, age, preoperative hemoglobin, and tumor size. However, in our opinion, this is exactly why AGR can make a comprehensive assessment on both physical condition and tumor status for predicting prognosis. It is true that preoperative AGR perhaps is not the most precise prognostic indicator, but it is a simple and efficient prognosis predicting biomarker that is shown in an increasing number of studies.

More interestingly, AGR may also be a potential risk factor for cancer incidence more than a predictor for cancer survival. A study involving 26,974 healthy individuals has demonstrated that low AGR was a risk factor for nine malignancies and significantly correlated with the morbidity of liver and hematologic malignancies (25). From a genetic perspective, AGR was reported the target phenotype of the *TNFRSF13B* and *FADS1* genes, but neither of these was associated with tumors (26). Exploring the genetic basis of AGR for predicting cancer incidence may be the direction for our future research.

Adjuvant chemotherapy can improve the outcomes of the patients with resectable GC, which has been demonstrated by accumulating evidence (27). The univariate analysis of postoperative chemotherapy in the previous statistics showed no significant influence on the prognosis (p=0.140), but the result turned out to be positive in the patients with Stage III GC (p=0.036) when cases were grouped according to the TNM stage. Furthermore, when the patients with Stage III GC were divided into two groups based on preoperative AGR, we found that postoperative chemotherapy can improve OS only in the high AGR group (20 months; 95% CI, 12.7-27.4 vs 13 months; 95% CI, 6.5-19.5; p=0.027), while postoperative chemotherapy had no significant influence on OS in the low AGR group (14 months; 95% CI, 11.0-17.0 vs 12 months; 95% CI, 1.7-22.3; p=0.304). The reason for this has been previously detailed; the patients with malnutrition and inflammation would only experience the severe side effects from adjuvant chemotherapy instead of benefiting from it. Therefore, further studies are needed to confirm the hypothesis that AGR is one of the initial evaluation indexes for postoperative chemotherapy effect.

The limitations of our study are the retrospective design, a small sample from a single center, and the lack of specific nonalbumin proinflammatory protein levels. In spite of these limitations, to the best of our knowledge, our study is the first to discuss the relationship between preoperative AGR and the prognosis of GC patients. Further improved analyses to examine the prognostic value of preoperative AGR in GC patients are needed.

In summary, preoperative AGR was significantly associated with the OS of GC patients and low preoperative AGR was an independent risk factor for GC patients. Furthermore, preoperative AGR might be a reflection of both physical condition and tumor status, since age, gender, preoperative hemoglobin, and tumor size all had a significant impact on the level of preoperative AGR in our study. These findings suggest that preoperative AGR is a simple but efficient prognosis predicting biomarker in patients with GC. Further clinical and fundamental studies are needed to validate our demonstration.

Ethics Committee Approval: Ethics committee approval was received for this study from the Institutional Review Board of Affiliated Zhongshan Hospital of Dalian University (Decision Date: 03.07.2011/Decision No: 20110094).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - W.Z.L., F.X.; Design - W.Z.L., F.X.; Supervision - F.L.; Resource - M.Y., N.F.; Materials - X.Z., Y.G.C., Y.P.Y., X.Y.K.; Data Collection and/or Processing - X.C.; Analysis and/or Interpretation - F.X.; Literature Search - F.X.; Writing - W.Z.L., F.X.; Critical Reviews - F.L.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: This study was supported by Scientific Reseaerch Funding Project of Liaoning Provincial Department of Education (Project No: L2015022).

REFERENCES

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015; 65: 87-108. [CrossRef]
2. Lepage C, Sant M, Verdecchia A, et al. Operative mortality after gastric cancer resection and long-term survival differences across Europe. Br J Surg 2010; 97: 235-9. [CrossRef]
3. Edge SB, 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: 1471-4. [CrossRef]
4. Nazha B, Moussaly E, Zaarour M, Weerasinghe C, Azab B. Hypoalbuminemia in colorectal cancer prognosis: Nutritional marker or inflammatory surrogate? World J Gastrointest Surg 2015; 7: 370-7. [CrossRef]
5. Gupta D, Lis CG. Pretreatment serum albumin as a predictor of cancer survival: a systematic review of the epidemiological literature. Nutr J 2010; 9: 69. [CrossRef]
6. Bugada D, Allegri M, Lavand'homme P, De Kock M, Fanelli G. Inflammation-based scores: a new method for patient-targeted strategies and improved perioperative outcome in cancer patients. Biomed Res Int 2014; 2014: 142425. [CrossRef]
7. Rehman MT, Khan AU. Understanding the interaction between human serum albumin and anti-bacterial/ anti-cancer compounds. Curr Pharm Des 2015; 21: 1785-99. [CrossRef]
8. Chen J, Zhou Y, Xu Y, Zhu HY, Shi YQ. Low pretreatment serum globulin may predict favorable prognosis for gastric cancer patients. Tumour Biol 2016; 37: 3905-11. [CrossRef]
9. Zhang B, Yu W, Zhou LQ, et al. Prognostic significance of preoperative albumin-globulin ratio in patients with upper tract urothelial carcinoma. PLoS One 2015; 10: e0144961. [CrossRef]
10. Azab B, Kedia S, Shah N, et al. The value of the pretreatment albumin/globulin ratio in predicting the long-term survival in colorectal cancer. Int J Colorectal Dis 2013; 28: 1629-36. [CrossRef]
11. Yao Y, Zhao M, Yuan D, Gu X, Liu H, Song Y. Elevated pretreatment serum globulin albumin ratio predicts poor prognosis for advanced non-small cell lung cancer patients. J Thorac Dis 2014; 6: 1261-70.
12. Duran AO, Inanc M, Karaca H, et al. Albumin-globulin ratio for prediction of long-term mortality in lung adenocarcinoma patients. Asian Pac J Cancer Prev 2014; 15: 6449-53. [CrossRef]
13. Du XJ, Tang LL, Mao YP, et al. The pretreatment albumin to globulin ratio has predictive value for long-term mortality in nasopharyngeal carcinoma. PLoS One 2014; 9: e94473. [CrossRef]
14. Azab BN, Bhatt VR, Vonfrolio S, et al. Value of the pretreatment albumin to globulin ratio in predicting long-term mortality in breast cancer patients. Am J Surg 2013; 206: 764-70. [CrossRef]
15. Toiyama Y, Yasuda H, Ohi M, et al. Clinical impact of preoperative albumin to globulin ratio in gastric cancer patients with curative intent. Am J Surg 2017; 213: 120-6. [CrossRef]
16. Alkan A, Köksoy EB, Utkan G. Albumin to globulin ratio, a predictor or a misleader? Ann Oncol 2015; 26: 443-4. [CrossRef]
17. Roche M, Rondeau P, Singh NR, Tarnus E, Bourdon E. The antioxidant properties of serum albumin. FEBS Lett 2008; 582: 1783-7. [CrossRef]
18. Anraku M, Shintomo R, Taguchi K, et al. Amino acids of importance for the antioxidant activity of human serum albumin as revealed by recombinant mutants and genetic variants. Life Sci 2015; 134: 36-41. [CrossRef]
19. Chang WJ, Du Y, Zhao X, Ma LY, Cao GW. Inflammation-related factors predicting prognosis of gastric cancer. World J Gastroenterol 2014; 20: 4586-96. [CrossRef]
20. Solinas G, Marchesi F, Garlanda C, Mantovani A, Allavena P. Inflammation-mediated promotion of invasion and metastasis. Cancer Metastasis Rev 2010; 29: 243-8. [CrossRef]
21. Obata J, Kikuchi E, Tanaka N, et al. C-reactive protein: a biomarker of survival in patients with localized upper tract urothelial carcinoma treated with radical nephroureterectomy. Urol Oncol 2013; 31: 1725-30. [CrossRef]
22. Codina Cazador A, Salvá Lacombe JA, Fernández-Llamazares Rodríguez J, Ruiz Feliu B, Codina Barreras A, Moreno Aguado V. Immunoglobulins and the complement system in colorectal cancer. Rev Esp Enferm Apar Dig 1989; 75: 143-8.
23. Cohen MH, Makuch R, Johnston-Early A, et al. Laboratory parameters as an alternative to performance status in prognostic stratification of patients with small cell lung cancer. Cancer Treat Rep 1981; 65: 187-95.
24. Deng Q, He B, Liu X, et al. Prognostic value of pre-operative inflammatory response biomarkers in gastric cancer patients and the construction of a predictive model. J Transl Med 2015; 13: 66. [CrossRef]
25. Suh B, Park S, Shin DW, et al. Low albumin-to-globulin ratio associated with cancer incidence and mortality in generally healthy adults. Ann Oncol 2014; 25: 2260-6. [CrossRef]
26. Hong KW, Jin HS, Song D, Kwak HK, Kim SS, Kim Y. Genome-wide association study of serum albumin: globulin ratio in Korean populations. J Hum Genet 2013; 58: 174-7. [CrossRef]
27. Zhao JH, Gao P, Song YX, et al. Which is better for gastric cancer patients, perioperative or adjuvant chemotherapy: a meta-analysis. BMC Cancer 2016; 16:631. [CrossRef]