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Original Article

The sodium/D-dimer ratio predicts the effect of first-line chemotherapy and prognosis in patients with advanced gastric cancer

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Abstract: Background: Gastric cancer (GC) is one of the most common cancers worldwide. The survival time of patients with advanced gastric cancer (AGC) is shortened. We evaluated the role of the sodium/fibrinogen ratio (SFR) and sodium/D-dimer ratio (SDR) in predicting the first-line chemotherapy response, progression-free survival (PFS), and overall survival (OS) of patients with AGC. Methods: A total of 304 patients with AGC were retrospectively reviewed. SDR only was selected as a potential prognostic marker for the subsequent studies in this study. Based on the cut-off value of the SDR, the patients were divided into high-SDR and low-SDR groups and investigated for their clinicopathological features, first-line chemotherapy effects and clinical outcomes. Results: The cut-off value based on the SDR was 282.22, and the patients were divided into low-SDR (SDR ≤ 282.22) and high-SDR (SDR > 282.22) groups. The disease control rate was higher in the high-SDR group than in the low-SDR group (91.1% vs. 82.3%; $P = 0.036$). Patients with a high SDR had a longer median PFS and OS than those with a low SDR (PFS: 206.0 vs. 134.0 days, $P < 0.001$; OS: 435.0 vs. 295.5 days, $P < 0.001$). The SDR was an independent prognostic indicator in the multivariable analysis of PFS ($P < 0.001$) and OS ($P = 0.004$). In subgroup analyses, among the patients with normal sodium and D-dimer levels, SDR was still a reliable prognostic indicator of PFS and OS in patients with AGC (all $P \leq 0.001$). Conclusions: This study suggests that the SDR may serve as a prognostic indicator for chemotherapy outcome, PFS and OS for patients with AGC receiving first-line chemotherapy.

Keywords: Sodium/D-dimer ratio, gastric cancer, first-line chemotherapy, prognosis, progression-free survival, overall survival

Introduction

Gastric cancer (GC) is one of the most common malignant cancers in the world. Surgical resection is an essential treatment for patients with early GC, and the 5-year survival rate is 90% [1, 2]. However, the prognosis of most patients diagnosed with advanced gastric cancer (AGC) remains poor [3, 4]. Chemotherapy is still one of the most important treatment strategies for patients with AGC. Despite progress in oncologic therapies, the prognosis of patients with AGC is still poor, and overall survival (OS) rarely exceeds 12 months [5]. Therefore, it is crucial to identify inexpensive, readily available, easy to measure, and relatively accurate predictors of the prognosis of AGC. Reliable prognostic factors may help doctors make clinical decisions and tailor the treatment of individual patients that affect the prognosis of patients with cancer.

Electrolyte disturbance is a common symptom in tumour patients, and previous research revealed that it is associated with the poor clinical outcome of patients [6]. The decrease in sodium level (hyponatraemia) is a general electrolyte abnormality. Xu et al. found that hyponatraemia can predict postoperative complications and poor outcomes in patients with

GC [7]. Hypercoagulability state and systemic inflammation are also common in tumour patients and are associated with poor survival [8, 9]. Fibrinogen and D-dimer are critical components of the coagulation system [10, 11]. In addition, elevated levels of fibrinogen or D-dimer are useful markers of systemic inflammation [11, 12]. Cheng et al. revealed that an increase in plasma fibrinogen levels may be a predictor of poor survival in patients with GC and a risk factor related to invasive clinical characteristics in a meta-analysis [13]. Hara et al. demonstrated that a high D-dimer level might predict tumour recurrence and long-term survival in patients with AGC [14].

As mentioned above, sodium, fibrinogen and D-dimer alone may be prognostic markers for patients with GC. The sodium/fibrinogen ratio (SFR) or sodium/D-dimer ratio (SDR) is a combination of sodium and fibrinogen or D-dimer. Compared with sodium, fibrinogen and D-dimer alone, the SFR and SDR may be more efficient prognostic indicators. However, few studies have explored the value of the SFR and SDR in tumour prognosis. Therefore, we investigated the predictive value of the SFR and SDR in predicting the treatment effect and prognosis of patients with AGC who received first-line chemotherapy in this study.

Methods and patients

Patients

This was a retrospective study. Between June 2014 and March 2019, we analysed 304 patients diagnosed with AGC at Liaoning Cancer Hospital & Institute (Liaoning, China). The exclusion criteria of this study were as follows: (1) patients who had pre-existing liver and kidney disease, thrombosis, or inflammatory disease including autoimmune disorder and infection; (2) those who were receiving anti-inflammatory and anticoagulant drugs; and (3) patients with human epidermal growth factor receptor 2 amplification or overexpression. Patients must meet all the eligibility criteria to be enrolled in the study. Eligible patients (1) were confirmed histologically as having gastric adenocarcinoma; (2) were diagnosed with stage III-IV disease based on the 8th International Union Against Cancer (UICC) criteria of tumour-node-metastasis (TNM) classification for GC; (3) received at least two courses of first-line chemotherapy; and (4) had an Eastern Cooperative Oncology Group Scale of Performance Status ≤ 2.

The first-line chemotherapy regimen in this study was as follows: CapeOX (oxaliplatin + capecitabine), SOX (oxaliplatin + S1), DOF (docetaxel + oxaliplatin + 5-fluorouracil) and DCF (docetaxel + cisplatin + 5-fluorouracil). We collected the data before first-line chemotherapy regarding patient demographic characteristics, laboratory variables, tumour differentiation degree, presence of distant metastasis and peritoneal dissemination. The first-line chemotherapy response was evaluated after every two courses of chemotherapy by computed tomography (CT) based on the Response Evaluation Criteria in Solid Tumours (RECIST 1.1). Assessment of first-line chemotherapy response consisted of complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). The disease control rate (DCR) was defined as the proportion of patients whose best response was a CR, a PR or SD. The objective response rate (ORR) was defined as the proportion of patients whose best response was a CR or PR among all patients. After the failure of first-line chemotherapy, the patients were followed up until they died or the end of the follow-up. The endpoint of the follow-up period was 1 June 2020. Progression-free survival (PFS) was defined as the interval from initiation of first-line chemotherapy to the occurrence of PD or death without evidence of progression. Overall survival (OS) was defined as the interval from initiation of first-line chemotherapy to death or last follow-up.

The SFR and SDR were calculated [SFR = sodium (mmol/L)/fibrinogen (g/L) ratio]; [SDR = sodium (mmol/L)/D-dimer (mg/L) ratio]. The primary endpoints of the study were PFS and OS; the secondary endpoints were DCR and ORR.

Statistical analysis

The receiver operating characteristic (ROC) curve was used to verify the efficacy of SDR and SFR for predicting OS and to calculate the area under the curve (AUC), sensitivity, and specificity. Categorical variables were presented as numbers with percentages and compared using Fisher's exact test or χ^2 test. We

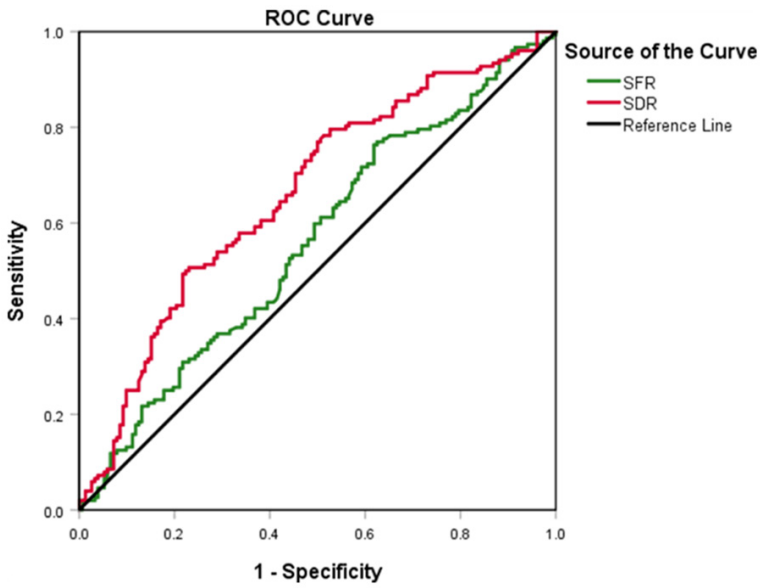

Figure 1. ROC curves for the ability of pre-treatment SDR and SFR to predict OS for patients with AGC. ROC, receiver operating characteristic; SFR, sodium/fibrinogen ratio; SDR, sodium/D-dimer ratio; AGC, advanced gastric cancer.

used Prism 8 in R to produce violin plots. The PFS and OS curves were calculated using the Kaplan-Meier method, and the log-rank test determined prognostic differences. A univariate screen of potential predictors of PFS and OS using the Cox proportional hazard model for each variable was performed. Those variables that were clinically and statistically significant in the univariate analysis were included in multivariate Cox regression models. *P*-values < 0.05 was considered significant. All data were analysed by Prism 8 (GraphPad) and SPSS software (SPSS Inc., Chicago, IL, USA).

Results

ROC curves predicting OS

The ROC curves are shown in **Figure 1**. We used ROC analysis to determine the cut-off values for SDR and SFR. The AUC and optimal cut-off value of the SDR were 0.661 ($P < 0.001$) and 282.22, with a sensitivity of 50.7% and specificity of 77.0%. The AUC of the SFR was 0.560 ($P = 0.073$). Because the *P*-value of the AUC for the SFR is greater than 0.05, the SFR may not be a potential predictor of prognosis in patients with AGC. We next used the SDR only to investigate the relationship between the SDR and first-line chemotherapy response and the prognosis of patients with AGC. We regrouped patients into the high-SDR group (SDR > 282.22) and low-SDR (SDR ≤ 282.22) group based on the cut-off value of SDR.

Clinicopathological features of patients

The numbers of patients in the low-SDR group and high-SDR group were 192 and 112, respectively. The median age of the patients was 60 years, and most of them were male. Younger age ($P = 0.010$), worse pathological differentiation ($P = 0.006$), more multiple organ metastases ($P = 0.030$), worse tumour stages ($P = 0.008$) and higher serum CA72-4 ($P = 0.001$) were more frequently observed in the low-SDR group than in the high-SDR group (**Table 1**).

Tumour response to first-line chemotherapy

As shown in **Figure 2**, patients who achieved DCR had higher levels of SDR than those who progressed ($P = 0.002$). The DCR was higher in patients with a high SDR (91.1%) than in patients with a low SDR (82.3%; $P = 0.036$). The ORR in the high-SDR group (13.4%) was slightly higher than that in the low-SDR group (12.5%), but there was no statistical significance ($P = 0.822$).

Survival

The median PFS and OS for all patients were 158.5 and 338.5 days, respectively. As shown in **Figure 3**, patients with a low SDR had a shorter PFS than those with a high SDR (median PFS: 134.0 vs. 206.0 days, $P < 0.001$). The median OS for patients with a low SDR and high SDR was 295.5 days and 435.0 days, respectively, and the OS difference was significant ($P < 0.001$).

In the multivariable analysis of PFS, the SDR ($P < 0.001$) was an independent prognos-

Table 1. Baseline clinicopathological features

Features	Total	Low-SDR	High-SDR	*P-value*
No. of patients	304	192	112	
Sex				
Male	200	124 (64.6%)	76 (67.9%)	0.562
Female	104	68 (35.4%)	36 (32.1%)	
Age (years)				
< 60	146	103 (53.6%)	43 (38.4%)	0.010
≥ 60	158	89 (46.4%)	69 (61.6%)	
Performance status				
= 0-1	255	163 (84.9%)	92 (82.1%)	0.529
= 2	49	29 (15.1%)	20 (17.9%)	
Body mass index (kg/m^2)				
< 18.5	40	24 (12.5%)	16 (14.3%)	0.657
≥ 18.5	264	168 (87.5%)	96 (85.7%)	
Pathological differentiation				
Moderately, Well	81	41 (21.4%)	40 (35.7%)	0.006
Mucinous, Poorly	223	151 (78.6%)	72 (64.3%)	
The number of organs affected by metastasis				
< 2	199	117 (60.9%)	82 (73.2%)	0.030
≥ 2	105	75 (39.1%)	30 (26.8%)	
TNM stage				
III	60	29 (15.1%)	31 (27.7%)	0.008
IV	244	163 (84.9%)	81 (72.3%)	
Haemoglobin (g/L)				
< 115	116	81 (42.2%)	35 (31.3%)	0.058
≥ 115	188	111 (57.8%)	77 (68.8%)	
Platelet count (×10^9/L)				
≤ 300	207	124 (64.6%)	83 (74.1%)	0.086
> 300	97	68 (35.4%)	29 (25.9%)	
CEA (ng/mL)				
≤ 5	174	104 (54.2%)	70 (62.5%)	0.157
> 5	130	88 (45.8%)	42 (37.5%)	
CA72-4 (U/mL)				
≤ 6	130	68 (35.4%)	62 (55.4%)	0.001
> 6	174	124 (64.6%)	50 (44.6%)	

SDR, sodium/D-dimer ratio; TNM, tumour-node-metastasis; CEA, carcinoembryonic antigen; CA72-4, carbohydrate antigen 72-4.

tic factor (**Table 2**). The SDR (P = 0.004) remained an independent prognostic factor in the multivariable analysis of OS (**Table 3**).

Additional survival analyses

Further subgroup analysis was conducted to determine if the above association between the SDR and PFS and OS was merely secondary to hyponatraemia (serum sodium level < 135 mmol/L) or an increased D-dimer level (serum D-dimer level > 0.55 mg/L). In subgroup analyses, among those patients with normal sodium levels (serum sodium level ≥ 135 mmol/L, n = 285), patients with a high SDR had a longer PFS (median PFS: 205.0 vs. 135.0 days, P < 0.001) and OS (median OS: 415.0 vs. 293.0 days, P < 0.001) than those with a low SDR. Additionally, in the patient subgroup with normal D-dimer levels (serum D-dimer level ≤ 0.55 mg/L, n = 123), patients with a high SDR were associated with pro-

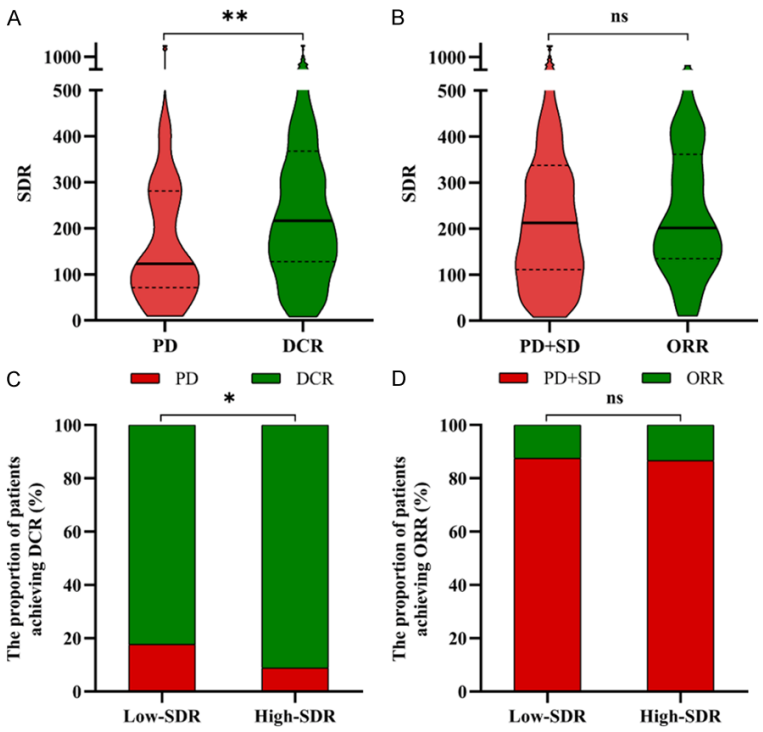

Figure 2. Relationship between the (A) DCR and (B) ORR and the SDR value. The proportion of patients achieving (C) DCR and (D) ORR in the low-SDR group and high-SDR group. In the violin plots, the horizontal dotted lines indicate Q1 and Q3, and the horizontal bars within the violin indicate the median. *, $P < 0.05$; **, $P < 0.01$; ns, $P > 0.05$; SDR, sodium/D-dimer ratio; PD, progressive disease; SD, stable disease; DCR, disease control rate; ORR, objective response rate; Q1, first quartile; Q3, third quartile.

longed PFS (median PFS: 206.0 vs. 112.0 days, $P = 0.001$) and OS (median OS: 435.0 vs. 267.0 days, $P < 0.001$) (**Figure 4**).

Discussion

In clinical studies, electrolyte disorders are a relatively frequent finding in patients with cancer, and electrolyte disorders signal the presence of paraneoplastic processes and portend a poor prognosis [6]. Hyponatraemia is a common electrolyte disorder. It has been well documented that there is a relationship between hyponatraemia and the prognosis of patients with cancer, including GC [7, 15]. In addition, a hypercoagulable state and systemic inflammation are commonly encountered in patients with cancer, and several previous studies have identified that the clinical outcomes of patients with hypercoagulability and inflammation are unsatisfactory [8, 9]. Fibrinogen and D-dimer are vital components of the coagulation system. Some studies have shown that fibrinogen and D-dimer are not only indicators of blood coagulation but also markers of inflammation [11, 12]. Some reports support the relationship between fibrinogen and D-dimer alone and clinical outcome in patients with GC [13, 14, 16]. SFR or SDR is a combination of sodium and fibrinogen or D-dimer, which may be more accurate in predicting the prognosis and chemotherapy response of patients with AGC than sodium, fibrinogen and D-dimer alone. However, there are few studies on the relationship between SFR, SDR and tumour prognosis.

To our knowledge, this is the first report to investigate the prognostic value of pre-treatment SFR and SDR in patients with AGC who received first-line chemotherapy. In the present study, because the AUC of ROC curve analysis revealed that the SDR (AUC = 0.661, $P < 0.001$) was higher than the SFR (AUC = 0.560), and the *P*-value of the SFR was not statistically significant ($P = 0.073$), the SDR may be a more powerful prognostic factor than the SFR. We found that young age ($P = 0.010$), poorly differentiated histology ($P = 0.006$), more multiple organ metastases ($P = 0.030$), high tumour stages ($P = 0.008$) and elevated serum CA72-4 ($P = 0.001$) were associated with pre-treatment low SDR. In a subsequent study regarding the role of the SDR on the effect of first-line chemotherapy and the prognosis of patients with AGC, the results revealed that patients with a high SDR had a higher DCR than patients with a low SDR (91.1% vs. 82.3%; $P = 0.036$). A high SDR predicted longer PFS (206.0 vs. 134.0 days, $P < 0.001$) and OS (435.0 vs. 295.5 days, $P < 0.001$) than a low SDR in AGC. Furthermore, only the SDR was an independent prognostic factor for PFS ($P < 0.001$) and OS ($P = 0.004$) in patients with AGC in the multivariate analysis. Patients with GC with normal levels of sodium and D-dimer may have a better prognosis than

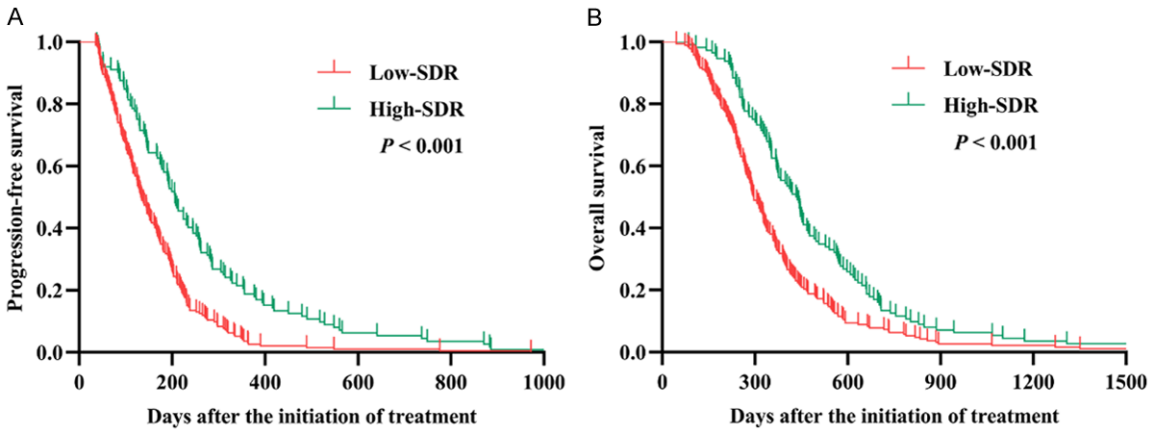

Figure 3. Kaplan-Meier estimates of (A) PFS and (B) OS in patients with low SDR and high SDR. SDR, sodium/D-dimer ratio; PFS, progression-free survival; OS, overall survival.

Table 2. Univariable and multivariable analysis for PFS

	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% *CI*	*p*-value	Hazard ratio	95% *CI*	*p*-value
Sex (male)	1.173	0.923-1.491	0.192			
Age (≥ 60 years)	0.907	0.723-1.138	0.399			
Performance status (= 2)	1.157	0.851-1.571	0.352			
Body mass index (< 18.5 kg/m^2)	0.775	0.555-1.083	0.135	0.847	0.603-1.189	0.337
Pathological differentiation (Mucinous, Poorly)	1.248	0.967-1.612	0.089	1.198	0.926-1.550	0.169
The number of organs affected by metastasis (≥ 2)	1.390	1.096-1.764	0.007	1.272	0.985-1.642	0.065
TNM stage (IV)	1.331	1.000-1.771	0.050	1.088	0.797-1.485	0.595
Haemoglobin (< 115 g/L)	0.864	0.683-1.092	0.221			
Platelet count (> 300×10^9/L)	1.006	0.789-1.282	0.961			
CEA (> 5 ng/mL)	1.071	0.851-1.349	0.558			
CA72-4 (> 6 U/mL)	1.357	1.077-1.711	0.010	1.138	0.892-1.452	0.298
SDR > 282.22	0.529	0.415-0.673	<0.001	0.583	0.451-0.753	<0.001

PFS, progression-free survival; CI, confidence interval; TNM, tumour-node-metastasis; CEA, carcinoembryonic antigen; CA72-4, carbohydrate antigen 72-4; SDR, sodium/D-dimer ratio.

Table 3. Univariable and multivariable analysis for OS

	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% *CI*	*p*-value	Hazard ratio	95% *CI*	*p*-value
Sex (male)	1.120	0.883-1.421	0.352			
Age (≥ 60 years)	0.770	0.613-0.967	0.025	0.828	0.655-1.046	0.113
Performance status (= 2)	1.159	0.853-1.575	0.345			
Body mass index (< 18.5 kg/m^2)	0.979	0.701-1.366	0.900			
Pathological differentiation (Mucinous, Poorly)	1.342	1.040-1.731	0.024	1.280	0.988-1.658	0.061
The number of organs affected by metastasis (≥ 2)	1.353	1.063-1.722	0.014	1.269	0.978-1.646	0.073
TNM stage (IV)	1.301	0.980-1.728	0.069	1.160	0.853-1.579	0.344
Haemoglobin (< 115 g/L)	0.909	0.720-1.147	0.423			
Platelets count (> 300×10^9/L)	0.989	0.777-1.259	0.928			
CEA (> 5 ng/mL)	1.175	0.934-1.478	0.168	1.116	0.872-1.427	0.384
CA72-4 (> 6 U/mL)	1.222	0.973-1.535	0.085	1.099	0.857-1.410	0.456
SDR > 282.22	0.609	0.481-0.771	<0.001	0.692	0.541-0.886	0.004

OS, overall survival; CI, confidence interval; TNM, tumour-node-metastasis; CEA, carcinoembryonic antigen; CA72-4, carbohydrate antigen 72-4; SDR, sodium/D-dimer ratio.

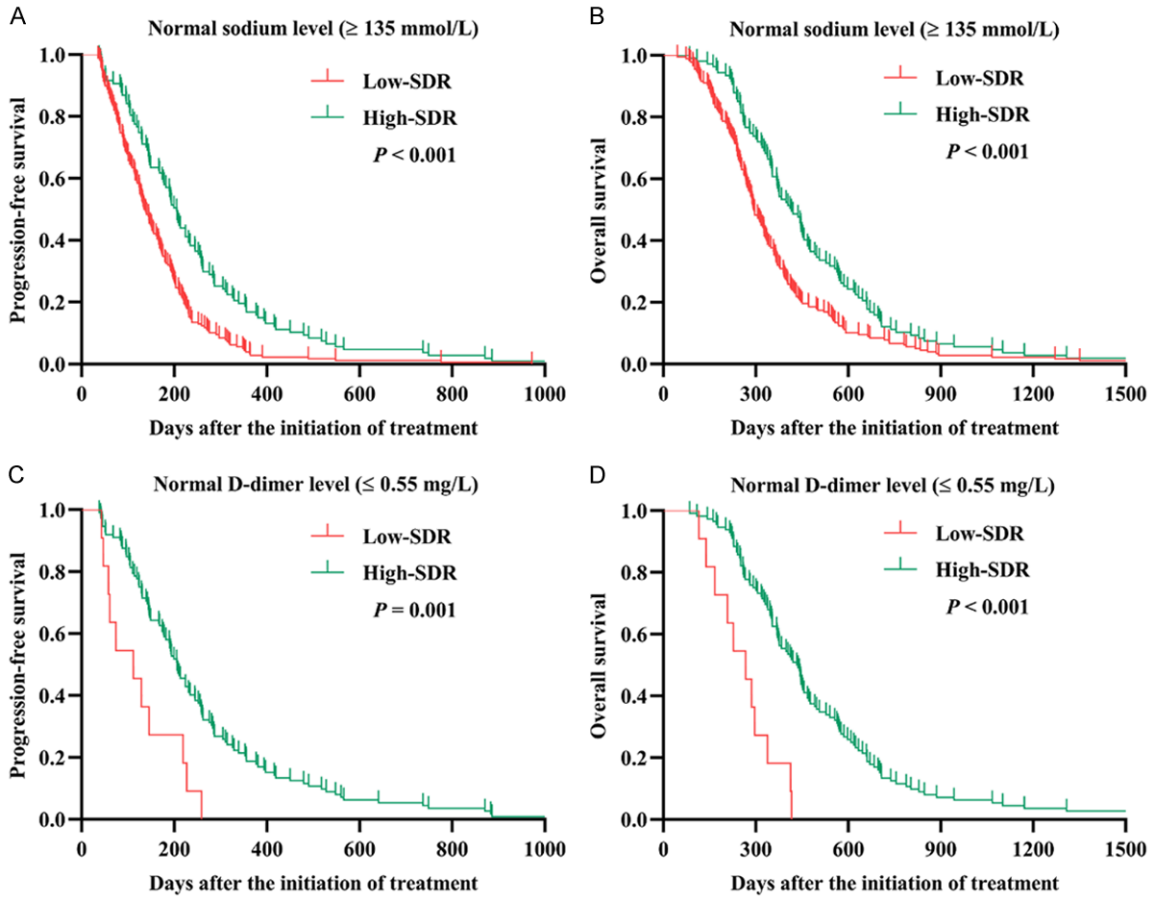

Figure 4. Subgroup analysis for the association between the SDR and PFS and OS in the subgroups stratified by (A and B) normal sodium level and (C and D) normal D-dimer level. SDR, sodium/D-dimer ratio; PFS, progression-free survival; OS, overall survival.

those with hyponatraemia and high levels of D-dimer [7, 17]. Interestingly, in this study, the subgroup analysis found that SDR was still a reliable prognostic indicator of PFS and OS in patients with normal levels of sodium and D-dimer. The results suggested that the SDR might be a robust independent prognostic marker and is superior to sodium and D-dimer alone.

In this study, we found that compared with the SDR (sodium/D-dimer ratio), the SFR (sodium/fibrinogen ratio) could not predict OS ($P > 0.05$), which may be due to the different abilities of D-dimer and fibrinogen alone in predicting the prognosis of patients with different stages. There were 304 cases in this research, most of which were patients with multiple metastases in stage IV (n = 244). Lin et al. found that D-dimer showed the best prediction ability in metastasized digestive cancer, while the fibrinogen level had a stronger correlation with prognosis in patients with local cancer [18]. Diao et al. also claimed that plasma D-dimer levels were increased in patients with GC with distant metastasis, especially patients with haematogenous metastasis [19]. These results are consistent with our observations: more multiple organ metastases ($P = 0.030$) and TNM stage IV ($P = 0.008$) were associated with low SDR. These results suggest that D-dimer may be involved in tumour metastasis. In terms of fibrinogen, the development of tumours may be related to it. However, the different predictive effects of D-dimer and fibrinogen in metastatic and local tumours need to be further studied.

We revealed the role of the SDR as a prognostic factor to predict the prognosis and response to first-line chemotherapy in patients with AGC in this study. However, the exact

mechanism by which the SDR is a predictor of prognosis for AGC is still not entirely clear. Hyponatraemia, a hypercoagulable state, and systemic inflammation may be related to it.

Previous studies have shown that hyponatraemia is related to poor survival and therapeutic effects in patients with cancer [20-23], suggesting that it may have a direct impact on cancer progression and treatment resistance. Some studies have found that low sodium levels stabilize and enhance glucocorticoid-induced protein kinase 1 transcription through hypotonic stress, which is associated with cancer cell metastasis [24, 25]. Hyponatraemia may influence the activity and regulation of sodium ion pumps and sodium channels. Their abnormal function in many types of cancer can lead to the deterioration of cancer [26-28]. Hyponatraemia can also activate the renin-angiotensin-aldosterone system [29]. In the renin-angiotensin-aldosterone system, angiotensin-I converting enzyme (ACE) and aldosterone are the most important determinants. Alvarenga et al. reported that ACE activation can promote melanoma cell proliferation and metastasis [30]. Additionally, Queisser et al. found that high aldosterone levels can accelerate tumour cell proliferation and survival. Aldosterone can also cause DNA damage and lead to the transformation of normal cells into malignant cells [31].

Hypercoagulability states are a severe clinical problem in patients with cancer. A study found that the risk of thrombosis in tumour patients is six times higher than that in normal people [32], which may be due to the interaction between endothelial cells and cancer cells mediated by cancer procoagulants and cytokines derived from cancer cells [33, 34]. Previous studies have shown that these coagulation factors play an important role in tumour initiation, development, and metastasis [33, 35]. Moreover, coagulation abnormalities are related to the poor prognosis of patients with cancer [36]. It has also been reported that the fibrinolytic system promotes tumour growth through a series of mechanisms, including tumour cell proliferation, inhibition of apoptosis, angiogenesis, and extracellular matrix degradation [37]. As a product of fibrin degradation, D-dimer is produced when cross-linked fibrin is broken down by plasmin-induced fibrinolysis. Therefore, D-dimer as a predictor can reflect the degradation of cross-linked fibrin polymers by plasmin and is widely used as an evaluation means for thrombosis [11]. Many studies have revealed the role of elevated D-dimer levels as an adverse prognostic factor in patients with different tumours, including lung cancer, digestive cancer, and breast cancer [18, 38-43].

It is now becoming clear that inflammation is closely related to tumours [44]. Inflammation is related to the initiation, promotion, progression, invasion, and metastasis of tumours [45]. Inflammation promotes the development of tumours through a series of chemical mediators and inflammatory cells [46, 47]. Chronic inflammation increases the chance of DNA damage and mutation by inducing a high cell renewal rate and high oxidative microenvironment, leading to carcinogenesis [48]. Furthermore, cytokines and inflammatory cells establish a tumour inflammatory microenvironment, which is a crucial element of all tumours and participates in tumour progression by promoting immune evasion, migration, proliferation, and survival [49, 50]. When patients with cancer are on medication, chemotherapy-induced inflammation is common, chemotherapeutic drugs are linked to nuclear factor-kappa B activation, and proinflammatory cytokines increase, which can lead to tumour-acquired resistance resulting in treatment failure and subsequent metastasis [51]. What is promising and exciting is that it has been reported that anti-inflammatory therapy is efficacious in tumour prevention and suppression to a certain extent [44]. Recently, many studies have shown that the level of serum D-dimer is a useful marker of inflammation with advantages for the detection of inflammation [52-54]. Clinically, not only is D-dimer significantly increased in inflammatory diseases, but its level is also negatively correlated with favourable prognosis [55, 56].

The advantages of this study are as follows. This is the first study to describe a role for SDR in cancer. Our research shows that the SDR as a prognostic indicator can predict the therapeutic effect, PFS and OS of patients with AGC receiving first-line chemotherapy and may be superior to the SFR, sodium, and D-dimer alone. In the subgroup with a good

prognosis, that is, the subgroup with normal levels of sodium and D-dimer, the SDR was still a powerful prognostic predictor of PFS and OS. As a non-invasive, readily available, and inexpensive detection method, the SDR is suitable for preliminary screening of patients with AGC before receiving first-line chemotherapy and might help clinicians adjust treatment regimens for patients with different prognoses.

Despite the above efforts and advantages of this study, some limitations in the present study still need to be addressed. First, this study is retrospective in nature. Second, a small number of patients were included in this study. Therefore, in the future, large-scale and well-designed prospective trials are needed to verify the results. Third, the SDR changed dynamically regardless of solidum or D-dimer during treatment. Thus, the SDR change could also reflect survival. We plan to pursue these questions in subsequent studies.

In conclusion, our study confirmed the prognostic role of the SDR and weighed its impact on the efficacy of first-line chemotherapy, PFS and OS of patients with AGC. Based on our findings, the SDR can be used as a prognostic tool, at least for patients with AGC.

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Disclosure of conflict of interest

None.

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