



# High albumin-bilirubin grade predicts worse short-term complications in gastric cancer patients with metabolic syndrome: a retrospective study

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**Background:** Preoperative albumin-bilirubin (ALBI) grade has been proposed and applied in recent years to evaluate the prognosis of liver cancer, but its role in gastric cancer (GC) is still unclear. This research aimed to examine the prognostic value of ALBI grade after gastrectomy among patients with GC complicated with metabolic syndrome (MetS).

**Methods:** There were 628 patients who received radical resection for GC. Laboratory data and short-term results were collected prospectively, and preoperative ALBI grades were calculated from the albumin and bilirubin levels. The appropriate ALBI cutoff value was calculated by receiver operating characteristic (ROC) curve analysis, which we used to put patients into high ( $>-2.54$ ) and low ( $\leq-2.54$ ) ALBI grade groups. The differences between the short-term complication rates of the two groups were analyzed with the chi-square test.

**Results:** Of the included patients, 133 (21.2%) and 495 (78.8%) had high and low ALBI grades, respectively. A high ALBI grade ( $P=0.001$ ), body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> ( $P=0.001$ ), and hypertension ( $P=0.018$ ) were independent risk factors for postoperative complications. In GC patients with and without MetS, the high ALBI subgroup showed more overall complications than the low ALBI subgroup ( $P=0.028$  and  $P=0.001$ ). Among GC patients with MetS, those with a high ALBI grade showed a higher incidence of serious complications than those with a low ALBI grade ( $P=0.001$ ); a similar, nonsignificant trend occurred in non-MetS patients ( $P=0.153$ ).

**Conclusions:** The preoperative ALBI grade is important in the prognosis of GC patients with MetS after gastrectomy. GC patients with MetS can lower their incidence of serious complications by adjusting their preoperative ALBI grade.

**Keywords:** Albumin-bilirubin (ALBI); gastric cancer (GC); metabolic syndrome (MetS); prognosis; complications

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## Introduction

As the fifth most common cancer worldwide, gastric cancer (GC) has the fourth highest global mortality rate (1). Thanks to advances in chemotherapy, radiotherapy, immunotherapy and targeted drugs, the survival and cure rate of GC have improved significantly (2,3). Surgical resection remains the curative treatment for GC, but the high complication rate after GC resection is a great concern for clinicians and needs to be evaluated and improved (4,5). In the past, there was no simple, objective index to forecast the long-term prognosis and postoperative complications after GC surgery. The albumin-bilirubin (ALBI) grade, as a new scoring tool, was proposed by scholars in 2015. It can evaluate liver reserve function based on serum albumin and bilirubin levels. In recent years, researchers have found that ALBI grade can predict the prognosis of tumor patients, especially liver cancer patients (6). In the prognostic evaluation of GC patients, ALBI grade also plays an increasingly important role (7). Preoperative ALBI grading can forecast postoperative complications and total survival in GC patients, especially those with a tumor, nodes, and metastases (TNM) stage of II–III (8). Thus, ALBI grading can be a simple and reliable indicator for the prognosis of GC patients.

GC, as a metabolically depleting malignant tumor, may be complicated by metabolic syndrome (MetS) (9). As a group of co-occurring metabolic disorders, MetS includes

obesity, hypertension, hyperlipidemia, and diabetes (10). A growing number of studies have confirmed the negative impact of preoperative MetS on the prognosis of patients after radical resection of GC (9,11). It could likely be due to negative impact MetS has on cardiovascular system. A previous study has reported that low high density lipoprotein-cholesterol (HDL-C) levels tend to be accompanied by advanced lymph node stages of cancer, which leads to poor prognosis (12). In addition, hypertension and diabetes may lead to intimal hyperplasia of blood vessels, resulting in poor tissue healing, and to some extent, leading to the occurrence of anastomotic leakage (13). However, we still need a robust model to demonstrate the differences between patients with GC with MetS and patients with non-MetS GC. Using the ALBI grading system, the short-term clinical prognosis of GC patients with MetS might be predicted, providing a basis for early interventions for postoperative complications.

This research aimed to determine whether the preoperative ALBI grade can be used for the prognostic evaluation of GC patients with MetS. We present this article in accordance with the STARD reporting checklist (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-23-599/rc>).

## Methods

### Patients

Participants were continuously recruited at the First Affiliated Hospital of Wenzhou Medical University (Wenzhou, China) from 2010 to 2015. Inclusion criteria: (I) age >18 years; (II) preoperative pathological diagnosis of gastric adenocarcinoma; (III) surgical methods for subtotal gastrectomy; (IV) complete medical records; and (V) follow-up for 1 year without loss to follow-up. Exclusion criteria: (I) patients who underwent palliative or emergency operation; (II) patients who underwent presurgical chemotherapy or radiotherapy; (III) patients whose medical records lacked laboratory tests, such as bilirubin and albumin; (IV) presence of severe organic liver disease or other malignant tumors; and (V) an American Society of Anesthesiologists (ASA) classification greater than ASA III (i.e., not medically suitable for surgery). According to the above criteria, 56 patients were excluded from the study. Finally, 628 patients were included, and each patient provided written informed consent to participate in the study. The research was approved by the Ethics Committee of the First

### Highlight box

#### Key findings

- Gastric cancer (GC) patients with an albumin-bilirubin (ALBI) value greater than  $-2.54$  had a significantly higher incidence of complications. GC patients who also had MetS had a significantly increased risk of serious complications.

#### What is known and what is new?

- Preoperative ALBI grading can forecast postoperative complications and the total survival in GC patients, especially those with a tumor, node, metastasis stage of II–III.
- Using the ALBI grading system, the short-term clinical prognosis of GC patients with MetS may be predicted, providing a basis for early interventions for postoperative complications.

#### What is the implication, and what should change now?

- We identified a potent preoperative tool to assess the risk of postoperative complications in patients with GC with MetS. We need more research to confirm the long-term significance of preoperative ALBI grading for these patients.

Affiliated Hospital of Wenzhou Medical University (No. 2022202). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

### Data collection

Preoperative demographic and disease features of patients were collected, including the following: (I) age, sex, history of hypertension, body mass index (BMI), and history of diabetes; (II) blood indicators, including albumin (ALB) and total bilirubin (TB); and (III) pathological information from surgical specimens examined by the pathology department, including the pathological kind, tumor size, tumor location, extent of differentiation, and TNM stage, in accordance with the American Joint Committee on Cancer (AJCC), 8<sup>th</sup> edition. Data on short-term postoperative complications, including surgical and medical complications, were collected. To decrease the risk of data bias, all assessments were performed by two trained scholars blinded to each other's ratings and to the other patient data.

### Preoperative ALBI grade

Venous blood was collected from all patients recruited within 7 days before surgery. The analysis of TB and ALB was conducted in a medical laboratory that met national testing standards. The formula for the ALBI score is shown below (14):

$$ALBI \text{ score} = (0.66 \times \log_{10} TB) + (-0.085 \times ALB) \quad [1]$$

where TB is in  $\mu\text{mol/L}$  and ALB is in  $\text{g/L}$ .

### Assessment of MetS

The screening indicators used to identify patients with MetS were the fasting blood glucose level, blood pressure, waist circumference, circulating degrees of triglycerides, and high-density lipoprotein (HDL) cholesterol levels (15). Since Chinese obesity is characterized by abdominal obesity, it was unreasonable to use only the waist circumference to represent the obesity of the patients (16). Therefore, we adopted the MetS standard put forward by the Chinese Diabetes Association in 2004, which is more suitable to the Chinese population. Under this standard, MetS is defined by having at least three of the following four components: (I) obesity:  $\text{BMI} \geq 25 \text{ kg/m}^2$ ; (II) hypertension: systolic/diastolic blood pressure  $\geq 140/90 \text{ mmHg}$  or a diagnosis of hypertension that is being actively treated; (III)

hyperglycemia: fasting blood glucose  $\geq 6.1 \text{ mmol/L}$ , 2-hour plasma glucose  $\geq 7.8 \text{ mmol/L}$ , or previously diagnosed diabetes; and (IV) dyslipidemia: triglycerides  $\geq 1.7 \text{ mmol/L}$  or HDL cholesterol  $< 0.9 \text{ mmol/L}$  in males and  $< 1.0 \text{ mmol/L}$  in females (17).

### Assessment of short-term complications

According to Clavien Dindo classification, short-term complications were classified and included in statistical analysis. Severe complications are defined as complications of level three or higher. Short term complications include surgical and medical complications. Surgical complications can be divided into Gastrointestinal dysfunction, Bleeding, Intraperitoneal effusion, Anastomotic leakage and Intestinal obstruction. Medical complications can be divided into Pulmonary infection, Pleural effusion, Venous thrombosis and Unexplained high fever. Among them, unexplained high fever is defined as a condition where the body temperature exceeds  $39 \text{ }^\circ\text{C}$  without identifying the cause.

### Statistical methods

Normally distributed constant variables are presented as average ( $\bar{x}$ ) and standard deviation (SD), while nonnormally distributed constant variables are presented as median (M) and interquartile range (IQR). Categorical variables are shown as numbers and percentages and were compared with Pearson's chi-square test or Fisher's exact test. Proper cutoff values for ALBI were calculated by receiver operating characteristic (ROC) curve analysis. The cutoff value was the ALBI value that optimized the sensitivity and specificity by maximizing the Youden index, where:

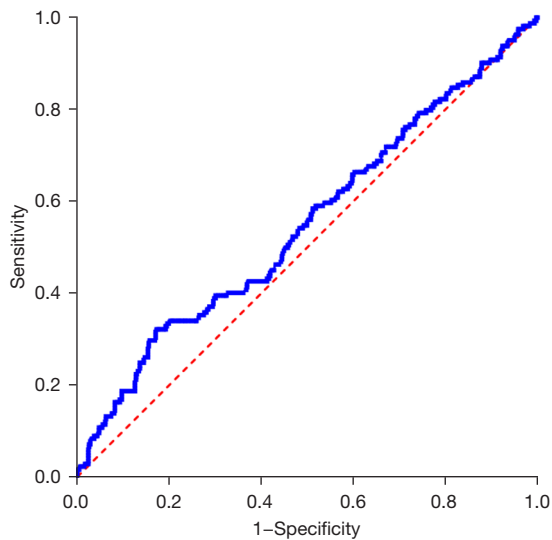
$$\text{Youden index} = (\text{sensitivity}) + (\text{specificity}) - 1 \quad [2]$$

Statistical significance was accepted with a two-sided  $P < 0.05$ . The statistical calculations were done with SPSS software (25.0 IBM, Armonk, NY, USA).

## Results

### Clinical characteristics of patients

The ROC curve of preoperative ALBI grade is shown in *Figure 1*. Using the Youden index, the ALBI grade cutoff was calculated as  $-2.54$ . The area under the curve (AUC) is 0.551. Patients were divided into two groups around the ALBI grade cutoff: the group with low ALBI grade ( $\leq -2.54$ )



**Figure 1** ROC curve of ALBI grade. ROC, receiver operating characteristic; ALBI, albumin-bilirubin.

and the group with high ALBI grade ( $>-2.54$ ). Among 628 patients, 133 (21.2%) showed a high ALBI grade and 495 (78.8%) had a low ALBI grade. *Table 1* shows the clinicopathological characteristics of these GC patients.

The group with high ALBI grade was older ( $P=0.001$ ) and their mean tumor size was greater than that of the low ALBI grade group ( $P=0.001$ ). TNM stage differed significantly between the high ALBI grade group and the low ALBI grade group ( $P=0.004$ ), but no difference in sex, history of hypertension or diabetes, or tumor location was observed. Notably, in line with the definition of ALBI, the high ALBI subgroup had a greater TB value ( $P=0.001$ ) and a lower ALB value ( $P=0.001$ ) than the low ALBI subgroup.

### *ALBI and short-term complications*

Postoperative complications had an overall incidence of 26.1% (*Table 2*). Complications occurred in 53 and 111 cases in the high and low ALBI subgroups, respectively, with incidence rates of 39.8% and 22.4% ( $P=0.001$ ). The high ALBI subgroup showed a higher incidence of serious complications of grade 3 than the low ALBI subgroup (7.5% *vs.* 4.4%,  $P=0.152$ ), but the difference was not statistically significant. In addition, the ALBI subgroup showed a higher incidence of both surgical complications (26.3% *vs.* 14.3%,  $P=0.001$ ) and medical complications (12.8% *vs.* 6.7%,  $P=0.021$ ) than the low ALBI subgroup.

**Table 1** Clinical data by ALBI grade

ALBI grade	High ALBI group (n=133)	Low ALBI group (n=495)	P value
Sex			0.423
Female	34 (25.6)	144 (29.1)	
Male	99 (74.4)	351 (70.9)	
Age			0.001*
<65 years	44 (33.1)	287 (58.0)	
$\geq 65$ years	89 (66.9)	208 (42.0)	
Hypertension			0.819
Yes	27 (20.3)	105 (21.2)	
No	106 (79.7)	390 (78.8)	
Diabetes			0.963
Yes	29 (21.8)	107 (21.6)	
No	104 (78.2)	388 (78.4)	
TNM stage			0.004*
I	26 (19.5)	160 (32.3)	
II	18 (13.5)	83 (16.8)	
III	77 (57.9)	201 (40.6)	
IV	12 (9.0)	51 (10.3)	
TB, $\mu\text{mol/L}$	10.3 $\pm$ 9.7	7.5 $\pm$ 4.6	0.001*
ALB, g/L	33.2 $\pm$ 3.9	41.5 $\pm$ 3.9	0.001*
Tumor size, cm	4.3 $\pm$ 1.9	3.3 $\pm$ 1.9	0.001*
Tumor location			0.600
Cardiac	6 (4.5)	18 (3.6)	
Noncardiac	66 (49.6)	263 (53.1)	

Results in the table are presented as mean  $\pm$  SD or number (%). \*,  $P<0.05$ . Count variables were compared by the chi-square test, except those with a theoretical number less than 5 were compared by Fisher's exact probability test; ALBI, albumin-bilirubin; TB, bilirubin; TNM stage, according to American Cancer Joint Committee 8<sup>th</sup> edition TNM stage; ALB, albumin.

### *MetS and short-term complications*

In accordance with the MetS criteria proposed by the Chinese Diabetes Association in 2004, 84 of the 628 patients met the criteria for MetS group and 544 were in the non-METs group. Compared with the non-MetS group, the MetS group displayed a higher risk of complications (41.7% *vs.* 23.7%,  $P=0.001$ ).

**Table 2** Postoperative outcome

Factors	Total (n=628)	High ALBI group (n=133)	Low ALBI group (n=495)	P value
Total complications	164 (26.1)	53 (39.8)	111 (22.4)	0.001*
Complications of grade 3 or higher	32 (5.1)	10 (7.5)	22 (4.4)	0.152
Classification of complications surgical complications	106 (16.9)	35 (26.3)	71 (14.3)	0.001*
Gastrointestinal dysfunction	38 (6.1)	12 (9.0)	26 (5.3)	
Bleeding	17 (2.7)	2 (1.5)	15 (3.0)	
Intraperitoneal effusion	10 (1.6)	2 (1.5)	8 (1.6)	
Anastomotic leakage	18 (2.9)	8 (6.0)	10 (2.0)	
Intestinal obstruction	30 (4.8)	8 (6.0)	22 (4.4)	
Medical complications	50 (8.0)	17 (12.8)	33 (6.7)	0.021*
Pulmonary infection	39 (6.2)	15 (11.3)	24 (4.8)	
Pleural effusion	12 (1.9)	4 (3.0)	8 (1.6)	
Venous thrombosis	2 (0.3)	1 (0.8)	1 (0.2)	
Unexplained high fever	6 (1.0)	1 (0.8)	5 (1.0)	

Results in the table are presented as number (%). \*,  $P < 0.05$ . Count variables were compared by the chi-square test, except those with a theoretical number less than 5 were compared by Fisher's exact probability test. ALBI, albumin-bilirubin.

### Short-term postoperative complications

Table 3 displays the outcomes of the univariate and multivariate analyses of postoperative complications. In univariate analysis, a high ALBI grade [odds ratio (OR) = 2.292,  $P = 0.001$ ], MetS (OR = 2.298,  $P = 0.001$ ), age  $\geq 65$  years (OR = 1.669,  $P = 0.005$ ), BMI  $\geq 25$  kg/m<sup>2</sup> (OR = 2.377,  $P = 0.001$ ), hypertension (OR = 1.713,  $P = 0.010$ ), and hyperglycemia (OR = 1.550,  $P = 0.036$ ) were all correlated with postoperative complications. In multivariate analysis, a high ALBI grade [OR = 2.544, 95% confidence interval (CI): 1.676–3.862,  $P = 0.001$ ], BMI  $\geq 25$  kg/m<sup>2</sup> (OR = 2.568, 95% CI: 1.557–4.235,  $P = 0.001$ ), and hypertension (OR = 1.675, 95% CI: 1.093–2.567,  $P = 0.018$ ) were independent risk factors for postoperative complications.

### GC patients with MetS vs. GC patients without MetS

Table 4 shows that among GC patients with MetS, those in the high ALBI subgroup were prone to more complications ( $P = 0.028$ ). Similarly, in GC patients without MetS, those in the high ALBI subgroup had more complications ( $P = 0.001$ ). In GC patients with MetS, those in the high ALBI subgroup were more prone to serious complications ( $P = 0.001$ ), while this was not significant in patients without MetS.

### Discussion

As a means of liver function evaluation, the ALBI grade has increasingly attracted the attention of researchers. Many studies have shown that ALBI grade influences the prognosis of patients with liver cancer (18,19). In terms of mortality related to nonmalignant tumors, the ALBI score also has a predictive role (20). The ALBI grade has been shown to have predictive value for the prognosis of patients with advanced GC (8). Due to their consumptive characteristics, malignant tumors, especially GC, are easily complicated by MetS (21). MetS has a negative impact on the prognosis of GC, mainly by increasing the incidence rate of complications and prolonging the duration of the hospital stay (22). However, there is no research on whether different ALBI levels indicate the prognosis of patients with GC complicated by MetS.

We used ROC curve analysis to calculate the appropriate cutoff value of the ALBI grade. When the Youden index reaches a maximum value, the values of the sensitivity and specificity are optimal. Thus, we divided patients into high ALBI (21.2%) and low ALBI (78.8%) groups around a cutoff value of  $-2.54$ . First, we evaluated the role of the preoperative ALBI grade and confirmed that it can forecast the short-term complications of patients with GC. However, the ability to forecast severe complications in

**Table 3** Univariate and multivariate analyses of factors associated with postoperative complications

Factors	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
ALBI grade (high ALBI vs. low ALBI)	2.292 (1.527–3.441)	0.001*	2.544 (1.676–3.862)	0.001*
MetS (yes/no)	2.298 (1.427–3.701)	0.001*		
Age ( $\geq 65$ / $< 65$ years)	1.669 (1.166–2.391)	0.005*		
Sex (male/female)	1.155 (0.773–1.725)	0.482	–	–
BMI ( $\geq 25$ / $< 25$ kg/m <sup>2</sup> )	2.377 (1.463–3.860)	0.001*	2.568 (1.557–4.235)	0.001*
Hypertension (yes/no)	1.713 (1.133–2.591)	0.010*	1.675 (1.093–2.567)	0.018*
Diabetes (yes/no)	1.550 (1.026–2.341)	0.036*		
Laparoscopic surgery (yes/no)	1.749 (0.750–4.078)	0.190		
TNM stage (III, IV/I, II)	1.220 (0.852–1.748)	0.278	–	–
Preoperative low albumin (yes/no)	1.278 (0.807–2.022)	0.295	–	–
Anemia before surgery (yes/no)	0.892 (0.554–1.434)	0.636		
Differentiation of tumor (low/median or high)	0.991 (0.659–1.490)	0.964	–	–
Tissue typing (ulcerative/nonulcerative)	1.108 (0.747–1.644)	0.609		

\*,  $P < 0.05$ . OR, odds ratio; CI, confidence interval; ALBI, albumin-bilirubin; MetS, metabolic syndrome; BMI, body mass index; TNM, tumor-node-metastasis.

**Table 4** GC patients with MetS vs. GC patients without MetS

Factors	GC with MetS, n (%)			GC without MetS, n (%)		
	High ALBI group (n=13)	Low ALBI group (n=71)	P	High ALBI group (n=120)	Low ALBI group (n=424)	P
Total complications	9 (69.2)	26 (36.6)	0.028*	44 (36.7)	85 (20.0)	0.001*
Complications of grade 3 or higher	2 (15.4)	4 (5.6)	0.001*	8 (6.7%)	18 (4.2)	0.153

\*,  $P < 0.05$ . MetS, metabolic syndrome; GC, gastric cancer; ALBI, albumin-bilirubin.

patients with grade 3 and greater GC was not significant. Surprisingly, the preoperative ALBI grade could forecast the prognosis of surgical and medical complications of GC. The surgical and medical complications greatly increased in patients with a high ALBI grade, which can provide significant guidance for preoperative interventions.

Through multivariate analysis, we found that a high ALBI grade was an independent risk factor for complications. One possible mechanism is that poor preoperative liver function affects the nutritional and metabolic status of patients, worsening their poor prognosis (23). As obesity worsens, the proportion of fat cells in the body increases, and metabolic function decreases with the increase in the proportion of functional fat, resulting

in possible postsurgical malnutrition and worsening the prognosis (24,25). This may explain why BMI  $\geq 25$  kg/m<sup>2</sup> was an independent risk factor for postoperative complications. In addition, the blood vessels of patients with high blood pressure are often very fragile, especially those who are relatively overweight, and their blood vessels contain high levels of cholesterol and fat. Compared with healthy people, the postoperative metabolism and anti-inflammatory activity of hypertensive patients are poor (26,27). Therefore, hypertension may be an independent risk factor for complications.

In our view, MetS not only includes the patient's BMI, but also other metabolic indicators in the human body, which reflects the overall metabolic status of the patient from one

side, rather than just changes in body size. Compared to using BMI alone, MetS is more representative in terms of validating ALBI values from a holistic perspective. Unlike previous studies, we evaluated MetS and GC separately and found that in GC patients with and without MetS, the high ALBI subgroup showed higher overall complications than the low ALBI subgroup. However, for GC patients with MetS, those with a high ALBI grade had a higher incidence of serious complications than those with a low ALBI grade, which difference was not significant in non-MetS patients. In patients with a preoperative diagnosis of MetS, the regulation of TB and ALB has a positive effect of preventing serious complications. In non-MetS patients, the preoperative adjustment of the ALBI grade may prevent overall complications.

Compared with some nonobjective factors such as ascites and hepatic encephalopathy that are part of the assessment of liver function by Child-Pugh grading, the assessment of ALBI grade is more objective (28). It has only two components, albumin and bilirubin, making the assessment simple and inexpensive, and these two indicators are routinely tested when patients are admitted to the hospital, which provides a stable environment for the assessment. The effect of albumin on the prognosis of GC has been relatively clear (29). Many studies have tried to develop tools made up of albumin combined with other factors to predict the prognosis of GC, such as D-dimer and hemoglobin (30,31). Compared with the functions of these models, ALBI grade is more focused on the evaluation of liver function. Patients with GC often need to adjust their liver function before surgery. If liver function is damaged, it will affect hemostasis during the operation and recovery after the operation.

This research has several limitations that cannot be ignored. First, this was a single-center study in Chinese people. Although it was done in a large tertiary hospital in southern Zhejiang Province, larger, multicenter trials and clinical data are still needed to verify our conclusions. Second, this study focused on the short-term outcomes of the patients and did not address long-term follow-up. We are conducting longer studies to determine the long-term significance of the ALBI grade for GC patients with MetS.

## Conclusions

In conclusion, preoperative ALBI grading can predict the prognosis of GC patients with MetS. A high ALBI grade, BMI  $\geq 25$  kg/m<sup>2</sup>, and hypertension are independent risk

elements for postoperative complications. By adjusting the preoperative ALBI grade, the incidence of postoperative complications, particularly the incidence of serious complications, in GC patients with MetS can be improved.

The preoperative ALBI grade is important in the prognosis of GC patients with MetS after gastrectomy. GC patients with MetS can lower their incidence of serious complications by adjusting their preoperative ALBI grade.

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## Footnote

*Reporting Checklist:* The authors have completed the STARD reporting checklist. Available at <https://jgo.amegroups.com/article/view/10.21037/jgo-23-599/rc>

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Each patient provided written informed consent to participate in the study. The research was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical

University (No. 2022202). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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