

# The prognostic role of Controlling Nutritional Status (CONUT) scores in patients with gastrointestinal stromal tumors

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## Research article

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# Abstract

**Background:** The Controlling Nutritional Status (CONUT) score is associated with the postoperative outcomes in various types of tumors. The relationship between the CONUT score and prognosis in patients with gastrointestinal stromal tumors (GISTs) needs to be clarified. **Methods:** Patients with completely resected primary GISTs in the absence of imatinib adjuvant therapy were included. Recurrence-free survival (RFS) was estimated with the Kaplan-Meier method and compared using log-rank test. Prognostic factors were compared using a Cox proportional hazards model. **Results:** A total of 455 patients were included. The median age was 57 years and 222 (48.8%) patients were male. The most common location was stomach (n= 219, 48.1%), the median tumor size was 4.5 cm (range 0.4-40.0) and the median mitotic index was 2/50 HPFs (range 0-200). Recurrence/metastasis developed in 92 (20.2%) patients. Patients were assigned to three groups: 219 (48.1%) were in normal nutrition group (CONUT=0-1), 196 (43.1%) were in light undernutrition group (CONUT=2-4) and 40 (8.8%) were in moderate-severe undernutrition group (CONUT $\geq$ 5). Primary tumor site, tumor size, mitotic index, tumor rupture and CONUT score were independent prognostic factors for RFS using multivariate analysis (p<0.05). **Conclusions:** The CONUT score was an independent prognostic factor for patients with completely resected GIST.

## Background

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors in the gastrointestinal tract[1]. Surgical resection is the main treatment for GISTs. However, recurrence/metastasis is common even after complete resection, and the 5-year recurrence-free survival (RFS) rate is only about 70% for all patients[2]. Adjuvant therapy with the tyrosine kinase inhibitor imatinib has dramatically improved RFS of patients with high-risk GISTs[3]. Risk stratification of patients diagnosed with GISTs is an essential part of postoperative treatment. Currently, primary tumor location, tumor size, mitotic index, and tumor rupture are recognized worldwide as parameters for stratifying the recurrence risk of GISTs. Several prognostic classification criteria have been established, based on these parameters, to assess the risk of recurrence [2, 4]. The prognostic role of some other parameters such as Ki-67 labeling index, p16 expression, age, and gender, are under investigation and remain controversial[5-9].

Preoperative conditions, particularly those affecting inflammatory or nutritional status, affect the clinical outcomes of patients with cancer[10-12]. Inflammatory markers, such as the neutrophil to lymphocyte ratio (NLR), the lymphocyte to monocyte ratio (LMR), and the platelet to lymphocyte ratio (PLR), have been introduced to predict the prognosis of various malignant tumors [11, 13-17]. Recently, immune-nutritional status measures, such as the prognostic nutritional index (PNI) and the Controlling Nutritional Status (CONUT) score, have been reported to be associated with postoperative prognoses in a number of cancer types [10-12, 18-21]. However, little research has addressed the association between immune-nutritional status parameters assessed by the CONUT score and outcomes for GIST patients. To our knowledge, this is the first study reporting the prognostic role of the CONUT score for patients with GISTs.

# Methods

## Patients inclusion

Patients with localized primary GISTs treated between January 2000 and December 2013 at the First Affiliated Hospital, Zhejiang University School of Medicine, were included. Diagnosis was based on a combination of histopathological evaluation and positive immunohistochemical staining for CD117 and/or DOG-1. Demographic and clinicopathologic information was collected, including patient age, gender, tumor location, tumor size, and mitoses. Tumor size was measured after 10% formalin fixation. Tumor mitoses were calculated as the number of mitoses per 50 high-power microscopic fields (HPFs). The risk of recurrence/metastasis was calculated using the modified NIH consensus criteria[4]. Preoperative blood samples were collected and assayed within 2 weeks prior to surgery.

The inclusion criteria were (1) age 18-80 years, (2) Eastern Cooperative Oncology Group (ECOG) performance status score 0-2, and (3) completely resected localized primary GIST. The exclusion criteria were (1) presence of hematological disorders, (2) history of any other malignancy or concurrent malignancy, (3) evidence of multiple/metastatic GISTs prior to or during surgery, (4) prescription of neoadjuvant or adjuvant therapy, (5) preoperative parenteral nutrition or blood transfusion treatment prior to blood sample collection, (6) survival <1 month postoperatively, and/or (7) incomplete clinical and laboratory data.

Preoperative CONUT scores were calculated based on serum albumin concentrations, peripheral lymphocyte counts, and total cholesterol concentrations. Albumin concentrations  $\geq 3.50$ , 3.00-3.49, 2.50-2.99, and  $< 2.50$  g/dL were scored as 0, 2, 4, and 6 points, respectively. Total lymphocyte counts  $\geq 1600$ , 1200-1599, 800-1199, and  $< 800/\text{mm}^3$  were scored as 0, 1, 2, and 3 points, respectively. Total cholesterol concentrations  $\geq 180$ , 140-179, 100-139, and  $< 100$  mg/dL were scored as 0, 1, 2, and 3 points, respectively. The CONUT score was defined as the sum of the albumin, lymphocyte, and cholesterol scores[22]. Degrees of undernutrition were classified as normal, light, moderate and severe, corresponding to CONUT scores of 0-1, 2-4, 5-8, and 9-12, respectively. [23](Table 1).

## Follow-up strategy

All patients were followed up every 3-6 months for the first 2 years, every 6-12 months for the next 3 years, and annually thereafter. Postoperative follow-up procedures included routine peripheral blood tests, abdominal enhanced computed tomography (CT), and endoscopy or abdominal magnetic resonance imaging (MRI), if necessary.

## Statistical analyses

Categorical data were analyzed using chi-square tests. Continuous data were analyzed using Kruskal-Wallis tests. RFS time was calculated from surgery to tumor recurrence/metastasis; patients alive at the time of last follow-up and those who died for any reason without GIST recurrence/metastasis were

censored. RFS were estimated using the Kaplan-Meier method and compared using log-rank tests. Prognostic factors were compared using Cox proportional hazards models. Only variables associated at  $p < 0.05$  in univariate analysis were entered into the multivariate model. All statistical analyses were performed using SPSS software ver. 19.0 (SPSS, Chicago, IL, USA). Two-sided  $p$ -values  $< 0.05$  were considered to reflect statistical significance.

## Results

### Clinicopathologic characteristics of patients

A total of 455 patients were enrolled. Overall, 222 (48.8%) patients were male and 233 (51.2%) patients were female. The median age of the patients was 57 y (range 20-80). The most common tumor location was stomach ( $n = 219$ , 48.1%), followed by jejunioileum ( $n = 127$ , 27.9%), duodenum ( $n = 52$ , 11.4%), colorectum ( $n = 43$ , 9.5%), and esophagus ( $n = 1$ , 0.2%). In addition, 13 patients (2.9%) had extra-gastrointestinal stromal tumors (E-GIST). Median tumor size was 4.5 cm (range 0.4-40.0), and the median mitotic index was 2/50 HPFs (range 0-200). Tumor rupture occurred in nine patients (2.0%). According to the modified NIH consensus criteria, 64 (14.1%), 201 (44.2%), 50 (11.0%), and 140 (30.8%) were categorized into the very low, low, intermediate, and high risk groups, respectively. Finally, 219 patients (48.1%) were in the normal nutrition group (CONUT=0-1), 196 (43.1%) in the light undernutrition group (CONUT=2-4), 36 (7.9%) in the moderate undernutrition group (CONUT=5-8), and four (0.9%) in the severe undernutrition group (CONUT=9-12). (Table 2).

### Correlation between CONUT scores and clinicopathologic characteristics

The relationships between CONUT scores and clinicopathologic characteristics are summarized in Table 2. Only four patients scored over 9, indicating severe undernutrition. We combined their data with those exhibiting moderate undernutrition to form a moderate-severe undernutrition group (CONUT  $\geq 5$ ) for analysis, as in a previous report[24].

There were no significant differences in age, mitotic index, or rupture status among CONUT=0-1, CONUT=2-4 and CONUT  $\geq 5$  groups ( $p > 0.05$ ). However, fewer male patients than female patients had normal CONUT scores ( $p = 0.005$ ). There were significant differences in tumor site, size, serum albumin, total lymphocyte count, and total cholesterol among the three CONUT score groups ( $p < 0.05$ ). (Table 2).

### Survival analysis, univariate and multivariate analyses

The last patient follow-up was completed in June 2019. Median follow-up time was 110.0 months (range 7.0-232.0 months). Recurrence/metastasis developed in 92 patients (20.2%). Overall, the 5-year and 10-year RFS rates were 84.2% and 79.1%, respectively. The 5-year RFS rates were 88.0%, 83.1%, and 69.7% for CONUT=0-1, CONUT=2-4, and CONUT  $\geq 5$  groups, respectively. The higher CONUT score group had significantly shorter progression-free survival times ( $p = 0.001$ ). (Figure 1).

In the univariate analysis, sex (male vs. female, hazard ratio [HR] =2.155, 95% confidence interval [95% CI]: 1.403-3.310,  $p < 0.001$ ), age ( $\geq 57$  years vs.  $< 57$  years, HR =1.726, 95% CI: 1.132-2.629,  $p = 0.011$ ), primary tumor site (non-gastric vs. gastric, HR =2.584, 95% CI: 1.632-4.092,  $p < 0.001$ ), tumor size (5.1-10.0 cm vs.  $\leq 2.0$  cm, HR =7.462, 95% CI: 2.294-24.268,  $p = 0.001$ ;  $> 10.0$  cm vs.  $\leq 2.0$  cm, HR =22.759, 95% CI: 6.909-74.971,  $p < 0.001$ ), mitotic index (6-10/50HPFs vs. 0-5/50HPFs, HR =5.442, 95% CI: 3.189-9.284,  $p < 0.001$ ;  $> 10/50$ HPFs vs. 0-5/50HPFs, HR =16.853, 95% CI: 10.157-27.962,  $p < 0.001$ ), tumor rupture (present vs. absent, HR =4.363, 95% CI: 1.770-10.758,  $p = 0.001$ ), and CONUT score (CONUT=2-4 vs. CONUT=0-1, HR =1.699, 95% CI: 1.080-2.674,  $p = 0.022$ ; COUNT $\geq 5$  vs. CONUT=0-1, HR =3.023, 95% CI: 1.607-5.686,  $p = 0.001$ ) were found to be significant predictors for RFS. The multivariate analysis showed that primary tumor site (non-gastric vs. gastric, HR =2.385, 95% CI: 1.478-3.849,  $p < 0.001$ ), tumor size ( $> 10.0$  cm vs.  $\leq 2.0$  cm, HR =8.924, 95% CI: 2.558-31.130,  $p = 0.001$ ), mitotic index (6-10/50HPFs vs. 0-5/50HPFs, HR =5.964, 95% CI: 3.391-10.491,  $p < 0.001$ ;  $> 10/50$ HPFs vs. 0-5/50HPFs, HR =12.348, 95% CI: 7.108-21.451,  $p < 0.001$ ), tumor rupture (present vs. absent, HR =3.485, 95% CI: 1.302-9.324,  $p = 0.013$ ), and CONUT score (COUNT $\geq 5$  vs. CONUT=0-1, HR =2.835, 95% CI: 1.461-5.499,  $p = 0.002$ ) were independent prognostic factors for RFS. (Table 3)

## Discussion

Tumor progression has been shown to be affected not only by the malignant features of tumor cells themselves but also by the immunological and nutritional status of the patient[25]. Various types of blood sample-derived biomarkers that can simply and inexpensively predict postoperative survival in tumor patients have been introduced; these include systemic inflammatory response indicators, such as NLR and PLR, and, more recently, immune-nutritional status measure, such as PNI and CONUT[10-21].

PNI is calculated from serum albumin and total peripheral lymphocyte counts. Serum albumin concentration is known to be a reliable indicator of both nutritional status and systemic inflammation[26]. However, it has also been reported to be easily influenced by changes in body fluid volume, such as those due to dehydration/fluid retention status, as well as by inflammation caused by chronic disease[27, 28]. Total peripheral lymphocytes, which play an important role in the immune response to tumors, are known to indicate immunological and nutritional status[29]. A decrease in T-lymphocytes has been reported to correlate with poor prognosis, due to an inadequate immune response to cancer[30, 31].

Total cholesterol concentration is an indicator of a patient's caloric reserves[32]. Cholesterol, an essential component of the cell membrane, is involved in numerous biochemical pathways potentially correlated with cancer initiation and progression, as well as in immune responses. Low serum cholesterol levels were reported to be associated with poorer prognosis in patients with various cancers[27, 33-35]. A more accurate evaluation may be obtained by reducing the importance of serum albumin concentration in the evaluation criteria, and including the consideration of total cholesterol [23].

CONUT scoring is a nutritional evaluation system that is easy to calculate from serum albumin, total lymphocyte count, and total cholesterol. First reported by Ignacio et al., it is useful for evaluating the nutritional and immune status of patients[23]. Undernutrition is a complex state, and the CONUT score enables evaluation of its different aspects: the patient's protein reserve, calorie depletion, and immune defenses. The CONUT score can reflect immunological and nutritional status, and may serve as a good immuno-nutritional marker, calculated from inexpensive and objective laboratory assays.

CONUT has proven to be a promising scoring system for predicting outcomes in cancer patients undergoing surgery[18, 19, 21, 22]. However, no study has assessed the relationship between CONUT score and clinical outcome for GISTs. The present study has shown that recognized parameters such as primary tumor location, tumor size, mitotic index, and tumor rupture are effective for stratifying the recurrence risk of GISTs, and that the CONUT score is another independent scoring system that can predict outcomes in patients receiving complete GIST resection. Moderate-severe undernutrition (CONUT  $\geq 5$ ) was most likely to be seen in male patients, with non-gastric, larger GISTs. These patients suffered from hypoalbuminemia, lymphocytopenia, and hypocholesterolemia, preoperatively. CONUT  $\geq 5$  was significantly associated with poorer prognosis. Although these patients made up a relatively small fraction (8.8%) of the study cohort, they are worthy of attention. In clinical practice, patients with high CONUT scores should receive more effective adjuvant therapy, and a shortened follow-up interval. Furthermore, considering the promising results of targeted nutritional intervention, patients with high CONUT scores may benefit from preoperative nutritional interventions[36-38].

To our knowledge, this is the first study to show that the CONUT score is an independent prognostic factor for GIST patients receiving complete resection. Based on our findings, the preoperative CONUT score may be useful in the stratification of risk and in tailoring individualized treatments for GIST patients.

The present study has some limitations. First, this was a single-institution, retrospective study, and the number of cases was limited. Second, potential factors that affect inflammation-based and nutritional markers could not be excluded absolutely. Third, there is the potential for selection bias in the inclusion of patients in this study. With these limitations, the present study demonstrated that the CONUT score is a promising prognostic factor. Large-scale prospective validation studies are needed to confirm these findings.

## Conclusions

The CONUT score was independently associated with RFS in patients with GIST undergoing complete resection. The estimation of the CONUT score is inexpensive and easily performed using available laboratory data from daily clinical practice; it may be useful for treatment decision-making and improving follow-up performance.

## Declarations

**Ethics approval and consent to participate:** This study was approved by the institutional ethics committee of the First Affiliated Hospital, Zhejiang University School of Medicine (No. 2013-280). The consent obtained from the participants was verbal which was approved by the ethics committee.

**Availability of data and materials:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

**Competing interests:** Authors have no conflict of interest to declare.

**Funding:** None.

**Authors' contributions:** WLY: Conceptualization, formal analysis and writing - original draft. CHS: Formal analysis and methodology. JRY: Supervision and writing - review and editing. QZ Data curation. XSL: Data curation. HY: Investigation and validation. XKL: Investigation and validation.

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## References

1. Joensuu H, Fletcher C, Dimitrijevic S et al. Management of malignant gastrointestinal stromal tumours. *Lancet Oncol* 2002; 3: 655-664.
2. Joensuu H, Vehtari A, Riihimaki J et al. Risk of recurrence of gastrointestinal stromal tumour after surgery: an analysis of pooled population-based cohorts. *Lancet Oncol* 2012; 13: 265-274.
3. DeMatteo RP, Ballman KV, Antonescu CR et al. Long-term results of adjuvant imatinib mesylate in localized, high-risk, primary gastrointestinal stromal tumor: ACOSOG Z9000 (Alliance) intergroup phase 2 trial. *Ann Surg* 2013; 258: 422-429.
4. Joensuu H. Risk stratification of patients diagnosed with gastrointestinal stromal tumor. *Hum Pathol* 2008; 39: 1411-1419.
5. Bischof DA, Kim Y, Behman R et al. A nomogram to predict disease-free survival after surgical resection of GIST. *J Gastrointest Surg* 2014; 18: 2123-2129.
6. Liu X, Qiu H, Zhang P et al. Ki-67 labeling index may be a promising indicator to identify "very high risk" gastrointestinal stromal tumor (GIST): a multicenter retrospective study of 1022 patients. *Hum Pathol* 2017.
7. Rossi S, Miceli R, Messerini L et al. Natural history of imatinib-naive GISTs: a retrospective analysis of 929 cases with long-term follow-up and development of a survival nomogram based on mitotic index and size as continuous variables. *Am J Surg Pathol* 2011; 35: 1646-1656.
8. Schmieder M, Wolf S, Danner B et al. p16 expression differentiates high-risk gastrointestinal stromal tumor and predicts poor outcome. *Neoplasia* 2008; 10: 1154-1162.

9. Zhao WY, Xu J, Wang M et al. Prognostic value of Ki67 index in gastrointestinal stromal tumors. *Int J Clin Exp Pathol* 2014; 7: 2298-2304.
10. Mohri Y, Inoue Y, Tanaka K et al. Prognostic nutritional index predicts postoperative outcome in colorectal cancer. *World J Surg* 2013; 37: 2688-2692.
11. Okamura Y, Ashida R, Ito T et al. Preoperative neutrophil to lymphocyte ratio and prognostic nutritional index predict overall survival after hepatectomy for hepatocellular carcinoma. *World J Surg* 2015; 39: 1501-1509.
12. Pinato DJ, North BV, Sharma R. A novel, externally validated inflammation-based prognostic algorithm in hepatocellular carcinoma: the prognostic nutritional index (PNI). *Br J Cancer* 2012; 106: 1439-1445.
13. Choi WJ, Cleghorn MC, Jiang H et al. Preoperative Neutrophil-to-Lymphocyte Ratio is a Better Prognostic Serum Biomarker than Platelet-to-Lymphocyte Ratio in Patients Undergoing Resection for Nonmetastatic Colorectal Cancer. *Ann Surg Oncol* 2015; 22 Suppl 3: S603-613.
14. Goto W, Kashiwagi S, Asano Y et al. Predictive value of lymphocyte-to-monocyte ratio in the preoperative setting for progression of patients with breast cancer. *BMC Cancer* 2018; 18: 1137.
15. Sharaiha RZ, Halazun KJ, Mirza F et al. Elevated preoperative neutrophil:lymphocyte ratio as a predictor of postoperative disease recurrence in esophageal cancer. *Ann Surg Oncol* 2011; 18: 3362-3369.
16. Stotz M, Pichler M, Absenger G et al. The preoperative lymphocyte to monocyte ratio predicts clinical outcome in patients with stage III colon cancer. *Br J Cancer* 2014; 110: 435-440.
17. Yodying H, Matsuda A, Miyashita M et al. Prognostic Significance of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio in Oncologic Outcomes of Esophageal Cancer: A Systematic Review and Meta-analysis. *Ann Surg Oncol* 2016; 23: 646-654.
18. Iseki Y, Shibutani M, Maeda K et al. Impact of the Preoperative Controlling Nutritional Status (CONUT) Score on the Survival after Curative Surgery for Colorectal Cancer. *PLoS One* 2015; 10: e0132488.
19. Liu X, Zhang D, Lin E et al. Preoperative controlling nutritional status (CONUT) score as a predictor of long-term outcome after curative resection followed by adjuvant chemotherapy in stage II-III gastric Cancer. *BMC Cancer* 2018; 18: 699.
20. Takagi K, Yagi T, Umeda Y et al. Preoperative Controlling Nutritional Status (CONUT) Score for Assessment of Prognosis Following Hepatectomy for Hepatocellular Carcinoma. *World J Surg* 2017; 41: 2353-2360.
21. Toyokawa G, Kozuma Y, Matsubara T et al. Prognostic impact of controlling nutritional status score in resected lung squamous cell carcinoma. *J Thorac Dis* 2017; 9: 2942-2951.
22. Harimoto N, Yoshizumi T, Inokuchi S et al. Prognostic Significance of Preoperative Controlling Nutritional Status (CONUT) Score in Patients Undergoing Hepatic Resection for Hepatocellular Carcinoma: A Multi-institutional Study. *Ann Surg Oncol* 2018; 25: 3316-3323.

23. Ignacio de Ulibarri J, Gonzalez-Madrono A, de Villar NG et al. CONUT: a tool for controlling nutritional status. First validation in a hospital population. *Nutr Hosp* 2005; 20: 38-45.
24. Daitoku N, Miyamoto Y, Tokunaga R et al. Controlling Nutritional Status (CONUT) Score Is a Prognostic Marker in Metastatic Colorectal Cancer Patients Receiving First-line Chemotherapy. *Anticancer Res* 2018; 38: 4883-4888.
25. Elinav E, Nowarski R, Thaiss CA et al. Inflammation-induced cancer: crosstalk between tumours, immune cells and microorganisms. *Nat Rev Cancer* 2013; 13: 759-771.
26. McMillan DC, Elahi MM, Sattar N et al. Measurement of the systemic inflammatory response predicts cancer-specific and non-cancer survival in patients with cancer. *Nutr Cancer* 2001; 41: 64-69.
27. Cengiz O, Kocer B, Surmeli S et al. Are pretreatment serum albumin and cholesterol levels prognostic tools in patients with colorectal carcinoma? *Med Sci Monit* 2006; 12: CR240-247.
28. de Ulibarri Perez JI, Fernandez G, Rodriguez Salvanes F, Diaz Lopez AM. Nutritional screening; control of clinical undernutrition with analytical parameters. *Nutr Hosp* 2014; 29: 797-811.
29. Walsh SR, Cook EJ, Goulder F et al. Neutrophil-lymphocyte ratio as a prognostic factor in colorectal cancer. *J Surg Oncol* 2005; 91: 181-184.
30. Dolcetti R, Viel A, Doglioni C et al. High prevalence of activated intraepithelial cytotoxic T lymphocytes and increased neoplastic cell apoptosis in colorectal carcinomas with microsatellite instability. *Am J Pathol* 1999; 154: 1805-1813.
31. Ropponen KM, Eskelinen MJ, Lipponen PK et al. Prognostic value of tumour-infiltrating lymphocytes (TILs) in colorectal cancer. *J Pathol* 1997; 182: 318-324.
32. Gadgil MD, Anderson CA, Kandula NR, Kanaya AM. Dietary patterns are associated with metabolic risk factors in South Asians living in the United States. *J Nutr* 2015; 145: 1211-1217.
33. Kitahara CM, Berrington de Gonzalez A, Freedman ND et al. Total cholesterol and cancer risk in a large prospective study in Korea. *J Clin Oncol* 2011; 29: 1592-1598.
34. Ko K, Park YH, Lee JW et al. Influence of nutritional deficiency on prognosis of renal cell carcinoma (RCC). *BJU Int* 2013; 112: 775-780.
35. Windler E, Ewers-Grabow U, Thiery J et al. The prognostic value of hypocholesterolemia in hospitalized patients. *Clin Investig* 1994; 72: 939-943.
36. Marin Caro MM, Laviano A, Pichard C. Nutritional intervention and quality of life in adult oncology patients. *Clin Nutr* 2007; 26: 289-301.
37. Nikniaz Z, Somi MH, Nagashi S, Nikniaz L. Impact of Early Enteral Nutrition on Nutritional and Immunological Outcomes of Gastric Cancer Patients Undergoing Gastrostomy: A Systematic Review and Meta-Analysis. *Nutr Cancer* 2017; 69: 693-701.
38. Xu J, Zhong Y, Jing D, Wu Z. Preoperative enteral immunonutrition improves postoperative outcome in patients with gastrointestinal cancer. *World J Surg* 2006; 30: 1284-1289.

## Tables

Table 1. Assessment of the patient's nutritional status according to the CONUT score

Variables	Degree of undernutrition			
	Normal	Light	Moderate	Severe
Serum albumin				
Concentration (g/dL)	≥3.50	3.00-3.49	2.50-2.99	<2.50
Score	0	2	4	6
Total lymphocyte				
Count (/mm <sup>3</sup> )	≥1600	1200-1599	800-1199	<800
Score	0	1	2	3
Total cholesterol				
Concentration (mg/dL)	≥180	140-179	100-139	<100
Score	0	1	2	3
CONUT score (total)	0-1	2-4	5-8	9-12

CONUT: Controlling Nutritional Status

Table 2. Clinical characteristics of the three groups according to the degree of undernutrition

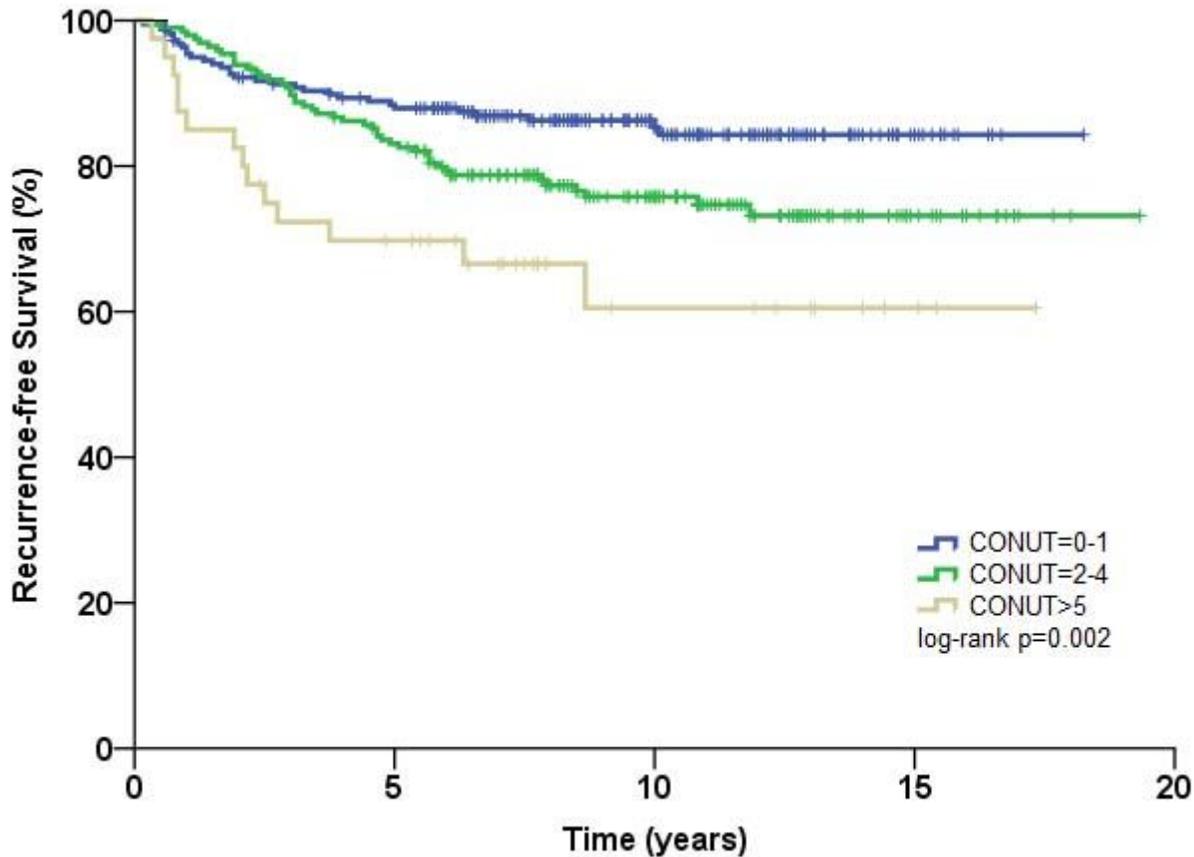
Characteristics	Normal nutrition group (CONUT=0-1) (median/range)	Light undernutrition group (CONUT=2-4) (median/range)	Moderate-severe undernutrition group (COUNT≥5) (median/range)	p-value
Number of patients	219	196	40	
Age, years	57/20-80	57/23-79	56/38-79	0.953
Gender, (male/female)	91/128	105/91	26/14	0.005
Tumor site:				<0.001
Stomach	129	78	12	
Duodenum	19	26	7	
Jejunoleum	36	73	18	
Colorectum	26	15	2	
Esophagus	1	0	0	
E-GIST	8	4	1	
Tumor size, cm	4.0/0.4-19.0	4.5/0.7-40.0	5.0/0.6-20.0	0.002
Mitotic index, /50HPFs	2/0-100	2/0-200	2/0-30	0.638
Tumor rupture, (present/absent)	5/214	3/193	1/39	0.834
Serum albumin, g/dl	4.4/3.0-6.8	4.1/2.9-5.9	3.3/2.4-4.8	<0.001
Total lymphocyte count, /mm <sup>3</sup>	1800/300-3200	1300/500-2300	900/400-3500	<0.001
Total cholesterol, mg/dl	188/94-330	149/48-248	111/78-174	<0.001

E-GIST: extra-gastrointestinal stromal tumor; HPFs: high-power microscopic fields

Table 3. Univariate and multivariate analyses of prognostic factor for RFS

Variables	Univariate analyses			Multivariate analyses		
	HR	95%CI	p-value	HR	95%CI	p-value
Age ( $\geq 57$ years vs. $< 57$ years)	1.726	1.132-2.629	0.011	1.277	0.814-2.002	0.287
Gender (male vs. female)	2.155	1.403-3.310	$< 0.001$	1.089	0.681-1.739	0.722
Tumor site (non-gastric vs. gastric)	2.584	1.632-4.092	$< 0.001$	2.385	1.478-3.849	$< 0.001$
Tumor size (cm)			$< 0.001$			$< 0.001$
$\leq 2.0$	1			1		
2.1-5.0	2.611	0.790-8.626	0.116	1.406	0.415-4.761	0.584
5.1-10.0	7.462	2.294-24.268	0.001	3.243	0.965-10.904	0.057
$> 10.0$	22.759	6.909-74.971	$< 0.001$	8.924	2.558-31.130	0.001
Mitotic index (/50HPFs)			$< 0.001$			$< 0.001$
0-5	1			1		
6-10	5.442	3.189-9.284	$< 0.001$	5.964	3.391-10.491	$< 0.001$
$> 10$	16.853	10.157-27.962	$< 0.001$	12.348	7.108-21.451	$< 0.001$
Tumor rupture (present vs. absent)	4.363	1.770-10.758	0.001	3.485	1.302-9.324	0.013
CONUT score			0.002			0.005
CONUT=0-1	1			1		
CONUT=2-4	1.699	1.080-2.674	0.022	1.115	0.688-1.809	0.658
CONUT $\geq 5$	3.023	1.607-5.686	0.001	2.835	1.461-5.499	0.002

## Figures



## Figure 1

Recurrence-free survival by CONUT scores from univariable analysis. CONUT: Controlling Nutritional Status