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# The Preoperative Geriatric Nutritional Risk Index Predicts Postoperative Complications in Elderly Patients with Gastric Cancer Undergoing Gastrectomy

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**Abstract.** *Background/Aim: The relationship between the preoperative Geriatric Nutritional Risk Index (GNRI) and morbidity of patients with gastric cancer (GC) undergoing gastrectomy has not yet been reported. Our study aimed to investigate whether preoperative GNRI is associated with short-term outcomes in elderly patients with GC. Patients and Methods: This study enrolled 348 elderly patients with GC who were more than 75 years old and underwent curative gastrectomy for GC at our Institution between January 2006 and December 2015. GNRI was invoked to stratify patients as high (GNRI≥92; n=190) or low (GNRI<92; n=158) GNRI nutritional status. The clinicopathologic features and short-term outcomes were compared. Results: In multivariate analysis, low GNRI emerged as an independent predictor of postoperative complications (Clavien Dindo classification grade II≤). Low GNRI demonstrated significantly more frequent extra-surgical complications than high GNRI. Significantly more patients with low GNRI suffered from postoperative pneumoniae than patients with high GNRI (p=0.013). On the other hand, the incidence of surgical field complications such as leakage, pancreatic fistula and intraabdominal abscess did not differ significantly between the groups. Conclusion: GNRI is useful in predicting postoperative complications of elderly patients with GC undergoing gastrectomy. Preoperative GNRI has merit as a gauge of postoperative complications in the extra-surgical field, especially pneumonia. There was no relationship between preoperative GNRI and surgical field complications in this setting.*

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The average age of patients with gastric cancer (GC) undergoing gastrectomy is rising with increased life expectancy. Elderly patients usually have various comorbidities such as cardiovascular diseases, decreased respiratory function, and renal dysfunction (1, 2). It has been reported that the rate of morbidity and mortality is higher in elderly patients than in younger adults, and when postoperative complications occur in elderly patients, their daily life activity decreases due to delay in wound healing, decrease of muscular mass, and long-term hospitalization (3, 4).

Malnutrition is one of the reasons that elderly patients are recognized as patients at high risk. It has been reported that many elderly patients lack nourishment and disease-related malnutrition is associated with higher mortality and morbidity, delay in recovery from illness, and length of postoperative stay in hospital. Patients with GC often suffer from malnutrition because of digestive symptoms like stomach ache or protein leakage from ulceration of the tumor (5-7). Thus, evaluation of nutritional status before operation in elderly patients is important for surgical risk assessment. As nutritional parameters, body mass index (BMI), prognostic nutritional index (PNI), controlling nutritional status (CONUT), serum albumin or skeletal muscle mass have been reported (8-11). However, the optimal cut-off value of these indexes is different for each report. Therefore, as for now, there is no gold standard parameter in nutrition evaluation.

The Geriatric Nutritional Risk Index (GNRI) devised by Bouillanne *et al.* is a prognostic nutritional index of nutrition-related risk associated with severity of malnutrition and mortality of hospitalized elderly patients (12). GNRI is calculated by taking into consideration serum albumin level, ideal body weight (IBW), and present body weight (PBW). Patients are assigned into four groups by this index as follows: no risk (GNRI: >98), low risk (GNRI: 92 to 98), moderate risk (GNRI: 82 to <92), and major risk (GNRI: <82) (12). Yamada *et al.* reported that low GNRI (<91.2) was the most accurate cutoff to identify hemodialysis patients at nutritional risk (13). Kinugasa Y *et al.* reported that low GNRI (<92) predicted increased mortality independent of age and gender in patients with heart failure (14). Features of the GNRI are objective, simple, and easily available in clinical practice because this index only requires measurements of height, weight, and serum albumin level (12).

There are no reports about the relationship between GNRI and the short-term outcomes of elderly patients with GC undergoing radical gastrectomy. The aim of this study was to investigate whether preoperative GNRI is associated with postoperative complications in elderly patients with GC.

## Patients and Methods

*Patients.* This study reviewed 348 patients >75 years of age undergoing curative gastrectomy for GC at the Department of Gastroenterological surgery of Osaka City General Hospital (Osaka, Japan) between January 2006 and December 2015. All patients were diagnosed with GC histopathologically before operation. Patients with other cancers and those undergoing bypass surgery or probe laparotomy were eliminated from the study. Clinicopathological features, perioperative factors and postoperative complications were extracted from medical records, operative records, anesthetic records and pathology reports. Pathological features were recorded according to the 14th edition of the Japanese Classification of Gastric Carcinoma (15). Comorbidity was classified into the following categories as previously reported, ischemic heart disease, cerebrovascular disease, diabetes mellitus, respiratory disease, liver disease, and renal dysfunction (16). Postoperative complications were graded according to the Clavien Dindo (CD) classification (17) and were defined as those of grade ≥II. These complications were divided into either surgical field complications or extra-surgical field complications.

*Assessment of nutritional status.* GNRI formula used was as follows (12): GNRI=1.489 × albumin (g/l) + 41.7 × present/ideal body weight (PBW/IBW)=1.489 × albumin (g/l) + 41.7 × BMI/22. Serum albumin level and PBW were adopted on admission, namely one or two days before operation. Patients were assigned to either the low GNRI (GNRI <92: moderate or major risk) or the high GNRI (GNRI ≥92; no or low risk) group according to previous reports (12, 14).

*Statistical analysis.* Categorical variables were expressed as numerical values and percentages, and group data were compared *via* the $X^2$ test. Fisher's exact test was used if the expected frequency was ≤5. Continuous variables with normal distributions were expressed as means and standard deviations, and mean values were compared using the Mann–Whitney *U*-test. Univariate and multivariate hazard ratios were calculated *via* the Cox proportional hazard model, and all significant variables in the univariate analysis were entered into the multivariate analysis. In univariate and multivariate analysis, the cut-off value of blood loss and operation time set each median value, respectively. All reported *p*-values were two-sided, setting statistical significance at $p<0.05$. The above computations relied on standard software (JMP v10; SAS Institute, Inc., Cary, NC, USA).

## Results

*Distribution of geriatric nutritional risk index.* GNRI distribution is shown in Figure 1. GNRI ranged from 62.8 to 110.2 and the mean GNRI was 91.9. The median GNRI was 92.7. This value had a normal distribution. The cut off value of GNRI was set at 92, 158 patients were assigned to the low GNRI group and 190 patients to the high GNRI group.

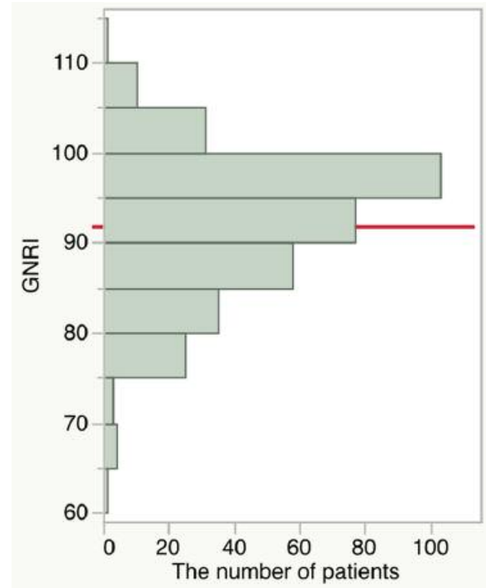


Figure 1. *Distribution of GNRI. GNRI: Geriatric nutritional risk index.*

*Clinicopathological features.* Clinicopathological features are shown in Table I. Mean age in the low GNRI group was significantly higher than that in the high GNRI group ($p=0.001$). BMI in the low GNRI group was significantly lower than that in the high GNRI group ($p<0.001$). Regarding comorbidity, ischemic heart disease, cerebrovascular disease, diabetes mellitus, pulmonary disease, liver disease, and renal disease, were not significantly different between the groups. The proportion of undifferentiated tumor histotype in the low GNRI was significantly higher than that in the high GNRI group ($p=0.008$). Depth of tumor in the low GNRI group was significantly more advanced than that in the high GNRI group ($p<0.001$). Lymph node metastasis in the low GNRI group was significantly more advanced than those in the high GNRI group ($p<0.001$). Pathological stages were more advanced in the low GNRI group as well ($p<0.001$). The proportion of open surgery in the low GNRI group was significantly higher than that in the high GNRI group (35.4 *vs.* 18.4%, $p<0.001$), but the two groups were similar in the range of gastrectomy. The mean number of lymph nodes resected did not differ significantly by pathological stage. Operative blood loss in the low GNRI group was greater, but statistical significance was not reached (224 *vs.* 193 ml, $p=0.062$). Operative time tended to be shorter in

Table I. *Clinicopathological characteristics in the low- and high-GNRI groups.*

| | All patients N=348 N (%) | Low GNRI group N=158 N (%) | High GNRI group N=190 N (%) | *p*-Value |
|---|---|---|---|---|
| Age | 79.6±3.8 | 80.3±3.8 | 79.0±3.6 | 0.001 |
| Gender (Male) | 230 (66.1) | 105 (66.5) | 125 (65.8) | 0.896 |
| BMI | 22.5±3.5 | 21.2±3.1 | 23.6±3.4 | <0.001 |
| Comorbidity | | | | |
| Ischemic heart disease | 38 (11.0) | 19 (12.0) | 19 (10.0) | 0.533 |
| Cerebrovascular disease | 32 (9.2) | 16 (10.1) | 16 (8.4) | 0.571 |
| Diabetes mellitus | 59 (17.0) | 24 (15.2) | 35 (18.4) | 0.439 |
| Pulmonary disease | 42 (12.1) | 21 (13.3) | 21 (11.1) | 0.509 |
| Liver disease | 11 (3.2) | 5 (3.2) | 6 (3.2) | 0.989 |
| Renal disease | 140 (40.2) | 67 (42.4) | 73 (38.4) | 0.451 |
| Histology | | | | |
| Differentiated | 192 (55.2) | 75 (47.5) | 117 (61.6) | 0.008 |
| Undifferenciated | 156 (44.8) | 83 (52.5) | 73 (38.4) | |
| Depth of tumor (pT) | | | | |
| 1 | 163 (46.8) | 57 (36.1) | 106 (55.8) | <0.001 |
| 2 | 51 (14.7) | 20 (12.7) | 31 (16.3) | |
| 3 | 67 (19.3) | 41 (26.0) | 26 (13.7) | |
| 4 | 67 (19.3) | 40 (25.3) | 27 (14.2) | |
| Lymph node metastasis (pN) | | | | |
| 0 | 197 (56.6) | 69 (43.7) | 128 (67.4) | <0.001 |
| 1 | 66 (19.0) | 35 (22.2) | 31 (16.3) | |
| 2 | 39 (11.2) | 28 (17.7) | 11 (5.8) | |
| 3 | 46 (13.2) | 26 (16.5) | 20 (10.5) | |
| pStage | | | | |
| 1 | 175 (50.3) | 58 (36.7) | 117 (61.6) | <0.001 |
| 2 | 88 (25.3) | 48 (30.4) | 40 (21.1) | |
| 3 | 66 (19.0) | 39 (24.7) | 27 (14.2) | |
| 4 | 19 (5.5) | 13 (8.2) | 6 (3.2) | |
| Approach | | | | |
| Laparoscopic | 257 (73.9) | 102 (64.6) | 155 (81.6) | <0.001 |
| Open | 91 (26.1) | 56 (35.4) | 35 (18.4) | |
| Gastrectomy | | | | |
| Total | 78 (22.4) | 37 (23.4) | 41 (21.6) | 0.682 |
| Partial | 270 (77.6) | 121 (76.6) | 149 (78.4) | |
| Number of harvested lymph nodes | | | | |
| pStage 1 | 26.6±13.7 | 26.5±13.9 | 26.6±13.6 | 0.994 |
| pStage 2 | 31.0±14.0 | 30.8±14.5 | 31.2±13.6 | 0.923 |
| pStage 3 | 32.4±14.1 | 33.0±12.2 | 31.5±16.8 | 0.273 |
| pStage 4 | 21.6±10.0 | 20.3±11.1 | 24.3±7.3 | 0.236 |
| Operative blood loss (ml) | 207±345 | 224±390 | 193±301 | 0.062 |
| Operative time (min) | 256±102 | 267±101 | 283±102 | 0.050 |
| Postoperative day | 19.5±17.5 | 21.3±21.5 | 18.0±13.1 | 0.069 |

the low GNRI group (267 *vs*. 283 min, *p*=0.050). Patients in the low GNRI group stay longer postoperatively (21.3 *vs*. 18.0 days), albeit not to a statistically significant extent (*p*=0.069).

Table II. *Postoperative complications in the two groups.*

| | All patients N=348 N (%) | Low GNRI group N=158 N (%) | High GNRI group N=190 N (%) | *p*-Value |
|---|---|---|---|---|
| Surgical field complication | | | | |
| All | 52 (14.9) | 27 (17.1) | 25 (13.2) | 0.306 |
| Leakage | 22 (6.3) | 11 (7.0) | 11 (5.8) | 0.655 |
| Pancreatic fistula | 9 (2.6) | 4 (2.5) | 5 (2.6) | 0.953 |
| Abscess | 8 (2.3) | 4 (2.5) | 4 (2.1) | 1.000 |
| Ileus | 7 (2.0) | 4 (2.5) | 3 (1.6) | 0.706 |
| Dumping syndrome | 1 (0.3) | 1 (0.6) | 0 | 0.454 |
| RY stasis | 1 (0.3) | 0 | 1 (0.5) | 1.000 |
| Anastomotic stenosis | 1 (0.3) | 1 (0.6) | 0 | 0.454 |
| Cholecystitis | 1 (0.3) | 1 (0.6) | 0 | 0.454 |
| Bleeding | 1 (0.3) | 1 (0.6) | 0 | 0.454 |
| Colitis | 1 (0.3) | 0 | 1 (0.5) | 1.000 |
| Extra-surgical field complication | | | | |
| All | 19 (5.5) | 15 (9.5) | 4 (2.1) | 0.003 |
| Pneumonia | 9 (2.6) | 8 (5.1) | 1 (0.5) | 0.013 |
| Arrhythmia | 1 (0.3) | 1 (0.6) | 0 | 0.454 |
| Liver dysfunction | 3 (0.9) | 2 (1.3) | 1 (0.5) | 0.593 |
| Delirium | 2 (0.6) | 2 (1.3) | 0 | 0.503 |
| Pancytopenia | 1 (0.3) | 1 (0.6) | 0 | 0.454 |
| Cerebral infarction | 1 (0.3) | 1 (0.6) | 0 | 0.454 |
| Renal failure | 1 (0.3) | 1 (0.6) | 0 | 0.454 |
| Urinary infection | 1 (0.3) | 1 (0.6) | 0 | 0.454 |
| Hives | 1 (0.3) | 1 (0.6) | 0 | 0.454 |
| Consciousness disorder | 1 (0.3) | 0 | 1 (0.5) | 1.000 |
| Prolonged inflammation | 2 (0.6) | 1 (0.6) | 1 (0.5) | 1.000 |
| Clavien Dindo Grade | | | | |
| II | 30 (8.6) | 19 (12.0) | 11 (5.8) | |
| III | 32 (9.2) | 16 (10.1) | 16 (8.4) | |
| IV | 3 (0.9) | 2 (1.3) | 1 (0.5) | |
| V | 5 (1.4) | 4 (2.5) | 1 (0.5) | |
| CD grade ≥II | 70 (20.1) | 41 (26.0) | 29 (15.3) | 0.013 |

*Complications*. Postoperative complications are shown in Table II. Postoperative morbidity rates according to the CD classification by group are as follows (low *vs*. high GNRI): grade II, 12.0 *vs*. 5.8%; grade III, 10.1 *vs*. 8.4%; grade IV, 1.3 *vs*. 0.5%; grade V 2.5 *vs*. 0.5%. Postoperative morbidity rates (≥CD grade II) in the low GNRI group were significantly higher than those in the high GNRI group (26.0 *vs*. 15.3%, *p*=0.013). According to surgical field complications, the incidence of leakage, pancreatic fistula, intraabdominal abscess, wound infection and others did not differ significantly between the groups. On the other hand, extra-surgical complications were significantly greater in the low (*vs*. high) GNRI group (*p*=0.003). The incidence of pneumonia was significantly greater in the low (*vs*. high) GNRI group (*p*=0.013).

Table III. *Univariate and multivariate analyses of factors predicting postoperative complications.*

| | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | HR | 95%CI | *p*-Value | HR | 95%CI | *p*-Value |
| Age (≥80) | 1.73 | 1.01-3.03 | 0.045 | 1.9 | 1.06-3.48 | 0.030 |
| Gender (male) | 1.62 | 0.91-3.00 | 0.099 | - | - | - |
| BMI (<22) | 1.19 | 0.70-2.01 | 0.516 | - | - | - |
| Ischemic heart disease | 1.73 | 0.78-3.60 | 0.170 | - | - | - |
| Cerebrovascular disease | 1.4 | 0.56-4.27 | 0.489 | - | - | - |
| Diabetes mellitus | 1.79 | 0.93-3.35 | 0.080 | - | - | - |
| Pulmonary disease | 1.48 | 0.68-3.04 | 0.314 | - | - | - |
| Liver disease | 2.34 | 0.60-7.98 | 0.206 | - | - | - |
| Renal dysfunction | 1.49 | 0.86-2.62 | 0.155 | - | - | - |
| GNRI (low) | 1.95 | 1.15-3.34 | 0.013 | 2.02 | 1.13-3.66 | 0.017 |
| Histology (undiff) | 0.78 | 0.45-1.33 | 0.362 | - | - | - |
| T3,4 (*vs.* T1,2) | 1.94 | 1.15-3.31 | 0.014 | 1.11 | 0.59-2.07 | 0.744 |
| Lymph node metastasis | 1.21 | 0.71-2.05 | 0.480 | - | - | - |
| Gastrectomy (total) | 2.79 | 1.57-4.93 | 0.001 | 2.31 | 1.22-4.37 | 0.011 |
| Blood loss (>210 ml) | 3 | 1.73-5.21 | <0.001 | 2.3 | 1.26-4.16 | 0.007 |
| Operative time (>280 min) | 1.17 | 0.68-1.98 | 0.575 | | | |

*Univariate and multivariate analysis.* Univariate and multivariate analyses are shown in Table III. Univariate analysis of complications indicated that GNRI (low) ($p$=0.013), age (≥80) ($p$=0.045), depth of tumor (≥T3) ($p$=0.014), gastrectomy (total) ($p$=0.001), and blood loss (>210 ml) ($p$<0.001) were independent predictors. In multivariate analysis of complications, GNRI (low) ($p$=0.017), age (≥80) ($p$=0.030), gastrectomy (total) ($p$=0.011), and blood loss (>210 ml) ($p$=0.007) were independently associated with complications. The hazard ratio for low GNRI was 2.02 [95% confidence interval (CI) 1.13-3.66, $p$=0.017].

## Discussion

Our study demonstrated that preoperative GNRI was an independent predictor of postoperative complications in elderly patients with GC. It has been reported that preoperative malnutrition is a risk factor for postoperative complications (18-20), but this is the first study that examined the relevance between preoperative GNRI and postoperative complications of elderly patients undergoing gastrectomy for GC. Our study showed that the rate of extra-surgical field complications, particularly pneumonia, is significantly higher in the low GNRI group than the high GNRI group. Kiuchi *et al.* reported that preoperative serum albumin level (<3.0) of patients with GC who underwent gastrectomy was an independent risk factor of postoperative pneumonia (21). In addition, Yamana *et al.* reported that postoperative respiratory complications of patients undergoing esophagectomy for esophageal cancer occurred at significantly higher rates in patients with low GNRI than in patients with high GNRI, and furthermore GNRI was an independent risk factor of postoperative respiratory complications (22). Our results agree with theirs and suggest that preoperative malnutrition strongly correlates with postoperative respiratory complications. Thus, preoperative respiratory rehabilitation and nutritional treatment of patients with low GNRI might be useful for prevention of postoperative respiratory complications. To prove this hypothesis, further examination in a prospective study is needed. On the other hand, the incidence of surgical field complications, for example anastomotic leakage and pancreatic fistula, was not significantly different between the two groups in the present study. Our previous study indicated that preoperative nutritional statuses were not associated with anastomotic leakage in gastrectomy for elderly patients with GC (16). Migita *et al.* also reported that preoperative nutritional statuses in patients undergoing total gastrectomy for GC were not associated with anastomotic leakage (23). However, Frasson *et al.* reported that preoperative serum protein level was an independent risk factor of anastomotic leakage in colon cancer patients undergoing colon resection (24). Since various nutritional parameters have been reported, additional studies are needed to examine whether malnutrition of patients with GC is associated with anastomotic leakage.

In terms of severity of complications, complications higher than grade II occurred significantly more in the low GNRI group than in the high GNRI group. The rate of complications of each grade was comparatively greater in the low GNRI group. Fukuda *et al.* reported that the rate of total postoperative complications was not different between patients with and without sarcopenia undergoing gastrectomy for GC, but more patients with sarcopenia suffered significantly more from severe complications (CD ≥ IIIa) than patients without sarcopenia (25). Mohri *et al*. reported that patients undergoing resection for colorectal cancer with low PNI (<45) suffer from severe complications significantly more often than patients with high PNI (≥45) (26). Also, in the present study, patients with low GNRI tended to suffer from grade II or more severe complications. Past reports showed that there was a correlation between malnutrition and severe complications, so further study might be needed to prove this relation.

Estimation of Physiological Ability and Surgical Stress (E-PASS) and Physiological and Operative Severity Score, for the en Umeration of Mortality and morbidity (POSSUM), were reported as parameters for predicting the risk of postoperative complications using factors except nutrition. Haga *et al*. reported that the rate of morbidity and mortality after gastrointestinal surgery in patients whose comprehensive risk score (CRS), calculated using E-PASS, was ≥1.0, was higher than in patients whose CRS was <1.0 (27). However, E-PASS cannot evaluate the risk of postoperative complications before operation because E-PASS includes operative factors. POSSUM, which was devised by Copeland *et al*., quantifies the patient's state and the risk of operation and predicts morbidity and mortality after operation (28). However, E-PASS and POSSUM evaluate many parameters, and the calculation formulae are so complicated that they cannot be widely used in daily medical examinations. On the other hand, serum albumin and body weight are usually measured before operation, so extra examinations are not needed to calculate GNRI. GNRI can be measured easily and repeatedly, so there is the advantage that GNRI is easy to use in daily medical examinations.

In past reports, it was reported that GNRI was associated with prognosis in some chronic diseases. Kinugasa *et al*. reported that patients with heart failure with low GNRI (< 92) had significantly higher mortality rates than with high GNRI (≥92), and physical activity on discharge was significantly lower in the low GNRI group (14). Edalat-Nejad *et al*. reported that hemodialysis patients with GNRI <100 had significantly higher mortality than with GNRI ≥ 100 (29). It has recently been reported that GNRI is useful as a prognosis factor for patients with not only chronic disease, but also cancer diseases. Miyake *et al*. reported that patients undergoing surgery for renal cell cancer with GNRI <98 had lower cancer-specific survival than those with GNRI ≥98, and GNRI was useful for predicting prognosis (30). In this study, long-term outcomes after surgery were not examined, but preoperative GNRI might become a useful prognostic factor for elderly patients with GC.

There are some limitations of this study. At first, this study is a retrospective study that used patients records from a single facility. It is essential to perform multicenter prospective studies to confirm these results. Secondly, this study did not evaluate long-term outcomes, especially the prognosis after surgery. Thirdly, factors such as risk factors of postoperative complications that might affect the results were not considered. Finally, the mechanism by which a one-time check before operation affects outcome was unclear.

In conclusion, GNRI may be useful for predicting postoperative complications in elderly patients with GC undergoing gastrectomy. Significantly more patients with low GNRI suffered from extra-surgical complications, especially pneumonia, than patients with high GNRI. There was no relationship between preoperative GNRI and surgical field complications in this setting.

## Conflicts of Interest

There are no conflicts of interest to declare.

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