



Geriatric nutritional risk index serves as risk factor of surgical site infection after pancreatoduodenectomy: a validation cohort Ageo study

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Background: Surgical site infections (SSIs), which are associated with preoperative malnutrition, are a well-known potential complication of surgery that leads to increased medical costs and longer hospitalizations. Thus, surgeons need to accurately identify patients at high-risk for SSIs. Considering that the Geriatric Nutritional Risk Index (GNRI) was designed to assess the degree of malnutrition specifically among elderly patients, previous evidence (Kawaguchi study) proved that GNRI predicted the risk of SSIs in patients following pancreatoduodenectomy (PD). In this study, we aimed to validate whether that the same index could predict the risk of SSI among patients who underwent PD in our patient cohort (Ageo study).

Methods: The current validation cohort study was retrospectively conducted on 93 patients at the Department of Surgery, Ageo Central General Hospital, Japan, from January 2015 to October 2019. All patients were subjected to nutritional screening using the GNRI and were followed up for the occurrence of postoperative complications. Additionally, risk factors for developing SSI, as well as patient's height, body mass index, and preoperative laboratory values, were recorded.

Results: Patients were divided into the SSI (N=30) and non-SSI (N=63) groups with a determined SSI incidence rate of 32.3% (30/93). The SSI group had significantly lower GNRI than the non-SSI group (P<0.001). Receiver operating characteristic curve analysis determined a cutoff GNRI value of 94 (sensitivity, 83.3%; specificity, 83.6%), similar to that in the previous study. Univariate and multivariate analyses confirmed that a GNRI of <94 was significantly associated with SSI (P<0.001).

Conclusions: The present Ageo study confirmed the consistency of results in Kawaguchi study. Thus, lower GNRI can be a universal marker for SSI risk following PD.

Keywords: Pancreatoduodenectomy (PD); geriatric nutritional risk index (GNRI); surgical site infection (SSI); validation study

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Introduction

Pancreaticoduodenectomy (PD) has been the gold standard surgical procedure for malignant hepatobiliary

pancreatic and periampullary tumors. With advances in the development of surgical techniques, devices, and perioperative managements, surgical-related mortality

rates following PD has decrease to less than 5% (1-3). However, some studies have still reported morbidity rates of 30–65% (4,5). Among the potential complications, the most common have generally been surgical site infections (SSIs), delayed gastric emptying and postoperative pancreatic fistula (POPF). In particular, SSIs, including intra-abdominal abscess and wound infection, are occasionally caused by POPF (6). SSIs have been known to increase medical costs and prolong hospitalization. Thus, to prevent such outcomes, prompt identification and prevention of SSIs are clinically imperative. More recently, the Geriatric Nutritional Risk Index (GNRI) has gained favor in assessing a patient's nutritional status and predicting clinical outcomes among elderly patients, particularly those with chronic kidney disease and heart failure (7,8). More importantly, the GNRI is easily accessible and inexpensive, requiring only data on body weight, height, and serum albumin levels (9). On the other hand, body weight and albumin levels are associated with postoperative complications including SSI. That was why we hypothesized that GNRI could evaluate the risk of SSI for the patients previously. Due to the intimate relationship between preoperative nutritional status and SSI, previous study (Kawaguchi study) had proved that GNRI <94 could predict SSI among patients who underwent PD (10). Thus, the present Ageo study aimed to validate the association between the GNRI and SSI among the patents who underwent PD in our cohort (Ageo study). This is important considering that the identification of predictive markers for SSI may help identify high-risk patients. We herein present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/gs-20-451>).

Methods

Patients

From January 2015 to October 2019, 93 consecutive patients who underwent PD for malignant hepatobiliary pancreatic or duodenal tumors were enrolled. Patients who underwent robotic and laparoscopic PD were excluded. Our protocol had been reviewed and approved by the Ethics Committee of Ageo Central General Hospital in 2019 (approval number: AMG736), and in accordance with the Helsinki Declaration as revised in 2013. All participants, including retrospectively registered patients or their guardians, verbally consented to the use of their medical information for scientific research. Given that the previous study (Kawaguchi study) enrolled 106 patients who

underwent PD at Kawaguchi Municipal Medical Center, a sample size of 86 to 126 patients was planned (Ageo study).

Clinical and laboratory data collection

Clinical data, including demographic variables (gender and age), anthropometric parameters [height, weight, and body mass index (BMI)], comorbidities, smoking history and alcohol intake, American Society of Anesthesiologist (ASA) physical status classification, estimated blood loss, operative time, and laboratory data (albumin, which was chosen from most recent preoperative data), were collected from individual medical records and analyzed until discharge. Anthropometric parameters were rounded off to one decimal place.

Definition of the GNRI

The GNRI was calculated as follows using serum albumin, height, and body weight obtained on admission: $GNRI = [14.89 \times \text{serum albumin (g/L)}] + [41.7 \times \text{present/ideal body weight (kg)}]$. Ideal body weight was defined as $22 \times \text{patient's height (m)} \times \text{patient's height (m)}$. If the present body weight exceeded the ideal body weight, the present/ideal body weight was set to 1. After definition of the GNRI cut-off value, the patients were divided into two groups according to the presence of SSIs.

Definition of the SSIs and POPF

SSIs were diagnosed according to the CDC guidelines. In addition, the definition of PPH and POPF were defined and clarified according to the International Study Group for Pancreatic Surgery (ISGPS) in 2016.

Statistical analysis

All statistical analyzes were performed using GraphPad Prism v5.0 (GraphPad Software Inc., La Jolla, CA, USA) and SPSS (SPSS Inc., Chicago, IL, USA). Statistical significance was determined using Fisher's exact test or the Chi-squared test. The optimal cutoff value for GNRI was determined using receiver operating characteristic (ROC) curve analysis. Potential risk factors for SSI were determined using univariate (the Chi-squared test or Fisher's exact) and multivariate analyzes. Independent risk factors for SSI were identified using logistic regression. Odds ratios with 95% confidence intervals were also

Table 1 Results of univariate analysis

Characteristics	SSI group (N=30)	non-SSI group (N=63)	P value
Gender			
Male vs. female	23 vs. 7	36 vs. 27	0.10
Age (years)	73.1±1.7	69.8±1.3	0.16
Smoking habit (%)	4 (13.3)	6 (9.5)	0.72
ASA classification			0.99
1	1 (0.0)	2 (3.2)	
2 or 3	29 (100.0)	61 (96.8)	
Body mass index	21.8±0.4	22.0±0.4	0.69
Alcohol intake (%)	1 (3.3)	3 (4.8)	0.75
Preoperative biliary drainage (%)	19 (63.3)	41 (65.1)	0.87
Diabetes mellitus (%)	6 (20.0)	17 (27.0)	0.63
Preoperative albumin (g/L)	3.2±0.1	4.1±0.1	<0.001
Geriatric nutritional risk index	88.6±1.1	100.4±0.9	<0.001
<94	28	11	<0.001
≥94	2	52	
Time of operation (min)	462.8±21.0	452.4±12.7	0.66
Estimated blood loss (mL)	712.7±103.5	656.2±63.3	0.69
Blood transfusion (%)	9 (30.0)	19 (30.2)	0.91
Postoperative pancreatic fistula (%)			<0.001
Grade B or C (%)	20 (66.7)	10 (15.9)	
Postoperative hospital stays (day)	42.8±3.8	22.7±2.0	<0.001
Rate of organ/space (%)	28 (93.3)	0 (0.0)	<0.001

The analysis revealed significantly higher incidence of SSI in GNRI <94 patients.

calculated. A P value of <0.05 was considered statistically significant. In this study, the difference of measurement data including albumin is considered as a possible bias factor.

Results

Patient characteristics

Patients included herein had a male to female ratio of 1.7:1 (59/34) and a mean age of 70.9±10.1 years. Among them, 30 patients developed SSIs (32.3%).

Univariate analysis for SSI risk following PD

Patients were divided into two groups according to the

presence or absence of SSIs. Clinical and demographic data from each group are summarized in *Table 1*. Although no statistically significant differences in gender, age, smoking habit, ASA classification, BMI, alcohol intake, preoperative biliary drainage, estimated blood loss, operative time, blood transfusions, and postoperative length of hospitalization were observed between the SSI and non-SSI groups, statistically significant differences were observed for preoperative albumin (P<0.001), GNRI values (P<0.001), pancreatic fistula (P<0.001) and postoperative hospital stays (P<0.001). POPF developed in 30 patients (32.3%), 20 of whom (66.7%) developed SSIs. The latest International Study Group of Pancreatic Surgery criteria reported in 2016 (11) defined POPF as grades B and C complications. Moreover, majority of the SSIs were developed at the

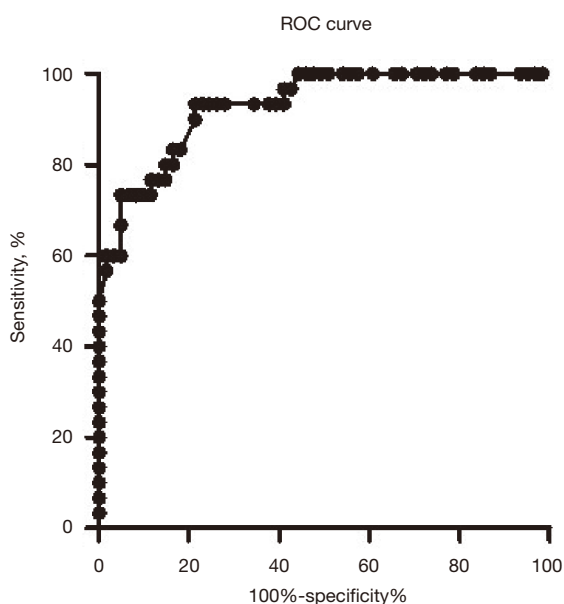


Figure 1 ROC curve analysis. GNRI was chosen by 94 as an optimal cutoff value with sensitivity 83.3% and specificity 83.6%.

organ/space (N=28).

Optimal GNRI cutoff value calculation

The optimal cutoff value was determined using ROC curve analysis (Figure 1). With an area under the curve of 0.93 (95% confidence interval: 0.88–0.98), the most appropriate cutoff value determined to be 94, which was the same as that in our previous work. This value had a sensitivity of 83.3% and a specificity of 83.6%. Patients were then divided into two groups according to the established cutoff value: group A (GNRI \geq 94, N=52) and group B (GNRI <94, N=41). Accordingly, the observed SSI rate in groups A and B was 3.8% and 68.3%, respectively.

Univariate analysis for SSI risk following PD

Univariate analysis revealed that a GNRI value <94 was able to predict SSIs risk following PD. Group B had a significantly higher incidence of SSI than group A (P<0.001).

Multivariate logistic regression analysis

Logistic regression analysis showed that a GNRI value <94 was an independent risk factor for SSIs as outlined in Table 2.

Discussion

PD is a technically complex and invasive procedure. As such, preventing postoperative complications, including POPF, delayed gastric empty, intra-abdominal bleeding, and SSIs, remain a major priority for surgeons. In particular, SSIs, which are among the most common complications following PD, can lead to decreased survival and delayed adjuvant chemotherapy (6,11). In addition, SSIs prolong hospitalization and increase medical costs by an estimated \$1,400 per patient after PD (12). Additionally, POPF can promote SSIs apart from merely occurring independently. Accordingly, studies have reported that 45–55% of patients with POPFs developed intra-abdominal abscesses (13,14). Recent reports have also revealed an association between nutritional status and POPF among patients who had undergone pancreatic resection (15,16).

Identified risk factors for SSIs following PD generally include preoperative bile drainage, BMI, age, neoadjuvant chemotherapy, operative time, estimated blood loss, pancreatic duct diameter, and nutritional status (17–19). Despite the absence of definitive risk factors for SSIs, but nutritional status must reach a certain level of consensus among risk factors for developing SSIs in abdominal surgery (20). Another study showed that lower albumin level was an independent predictor of SSIs among patients with gastrointestinal cancer (20). Moreover, other studies have shown that sarcopenia was an objective and independent preoperative predictor of infectious complications after PD (21), while preoperative sarcopenia affected liver surgery outcomes (22) even during liver transplantation (23).

Several objective parameters have been developed to assess nutritional status, such as Nutrition Risk Index, Prognostic Nutritional Index (24), Controlling Nutritional Status (25), and the GNRI (26). Among them, the GNRI had been previously identified as a risk factor for SSIs among patients after PD in Kawaguchi study (10). The GNRI had originally been developed to predict prognosis among elderly patients (9). Subsequently, several studies have consistently reported a relationship between the GNRI and postoperative complications. For instance, one study showed that the GNRI criteria may help in the risk stratification of elderly patients undergoing chemoradiation therapy (27), while, Hanada *et al.* showed that the GNRI can predict postoperative complications after abdominal surgery and delay postoperative course (28). Moreover, the GNRI can be useful in predicting postoperative

Table 2 Multivariate analysis by logistical regression

Characteristics	Odds ratio	95% confidence interval	P value
Diabetes mellitus	0.92	0.18–6.78	0.92
Preoperative albumin (g/L)	123.79	4.41–3,472.55	0.005
Postoperative pancreatic fistula	9.63	1.45–63.95	0.019
Geriatric nutritional risk index <94	0.113	0.01–0.9	0.04
Blood transfusion	0.2	0.02–1.8	0.15

GNRI <94 was independent risk factor to predict SSI following PD.

complications among elderly patients with gastric cancer undergoing gastrectomy (29).

The present Ageo study aimed to validate whether the GNRI can predict the incidence of SSI following PD in our patient cohort. Accordingly, results for the validation cohort revealed that a low GNRI value (<94), which was the same as that in previous Kawaguchi study (10), was strongly associated with higher SSI risk, supporting the feasibility of nutritional assessment before surgery. Recent evidence by Sasaki *et al.* also showed that the GNRI could be a useful predictor of SSI after surgery, further supporting our data (30). Thus, we believe that our hypothesis has exhibited relative consistency. The present Ageo study has several limitations worth noting. First, though our hypothesis had been confirmed in two independent cohorts, the relatively small sample size may limit the statistical power of our study. Second, given the retrospective design of this study, a more comprehensive prospective study should be conducted to confirm our findings in the near future.

Conclusions

The present study provided assurance of Kawaguchi study that a lower GNRI, which can be easily calculated using serum albumin level, height, and body weight, can be a potential predictor of SSIs among patients who had undergone PD in clinical practice.

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Footnote

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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. The present study was approved by the Ethics Committee of Ageo Central General Hospital in 2019 (approval number: AMG736) and informed verbal consent obtained from each patient. In addition, approval of the present study was performed according to the Declaration of Helsinki as revised in 2013.

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