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GRIm Score Predicts Curative Conversion Surgery in Unresectable Gastric Cancer

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Abstract

Background/Aim: Conversion surgery can prolong survival in initially unresectable gastric cancer when curative (R0) resection is achieved; however, pre-treatment predictors of R0 conversion remain limited. We investigated whether the Gustave Roussy Immune (GRIm) score predicts R0 resection and survival in patients considered for conversion surgery.
Patients and Methods: We retrospectively analyzed 57 patients with unresectable advanced gastric cancer treated with systemic chemotherapy from January 2019 to July 2025. Patients were classified as achieving conversion (AC; conversion surgery with R0 resection) or non-conversion (NC). The GRIm score (albumin, lactate dehydrogenase, and neutrophil-to-lymphocyte ratio) and clinicopathological variables were evaluated as predictors of R0 resection using univariate and multivariate logistic regression. Overall survival (OS) was assessed using the Kaplan–Meier method.
Results: Ten patients (17.5%) achieved R0 resection. The AC group had lower GRIm scores and a more favorable Yoshida classification than the NC group, and intestinal-type histology was more frequent in the AC group. In multivariate analysis, a low GRIm score (0-1) and Yoshida classification C1-2 were independently associated with R0 resection. OS was significantly longer in patients with low GRIm scores than in those with high scores.
Conclusion: The GRIm score is an accessible pre-treatment biomarker associated with successful R0 conversion surgery and improved survival in unresectable gastric cancer and may complement the Yoshida classification in candidate selection.

Keywords: Gastric cancer, conversion surgery, GRIm score, biomarker, R0 resection.

Introduction

Gastric cancer is one of the leading causes of cancer-related mortality worldwide (1). Although systemic chemotherapy remains the standard treatment for unresectable advanced gastric cancer, a subset of patients can achieve long-term survival through conversion surgery when curative (R0) resection becomes feasible after chemotherapy (2-5); radiological imaging plays a crucial role in staging and response evaluation. However,

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conventional imaging modalities often show limited accuracy in predicting surgical resectability and long-term outcomes, and discrepancies between radiological findings and pathological responses are frequently observed (6,7). Consequently, accurate selection of candidates for conversion surgery remains one of the most challenging aspects of gastrointestinal surgical practice.

Recent advances in systemic therapy, including immune checkpoint inhibitors combined with chemotherapy, have improved survival outcomes and achieved higher objective response rates with more durable tumor shrinkage in advanced gastric cancer (8, 9). Nevertheless, imaging-based criteria alone are often insufficient for determining surgical feasibility, highlighting the need for additional clinically applicable biomarkers to guide decision-making.

The Gustave Roussy Immune (GRIm) score, which incorporates serum albumin, lactate dehydrogenase, and the neutrophil-to-lymphocyte ratio, was originally developed as a prognostic index for patients receiving immune checkpoint inhibitors (10). Subsequent studies have suggested its prognostic value across several malignancies, including lung and esophageal cancers (11-13), and emerging evidence is also available in gastric cancer (14). However, its utility for predicting outcomes specifically in patients with initially unresectable gastric cancer considered for conversion surgery remains unclear. Beyond immunotherapy, the GRIm score reflects systemic inflammation and nutritional status, which may influence treatment tolerance and oncological outcomes.

For gastrointestinal surgeons, an ideal predictive tool should be readily accessible, cost-effective, and interpretable without specialized testing. The GRIm score fulfills these criteria because all its components are routinely measured in daily clinical practice. However, the clinical utility of the GRIm score in predicting successful conversion surgery and curative R0 resection in unresectable gastric cancer has not been fully explored.

This study aimed to evaluate whether the GRIm score could serve as a practical biomarker for predicting R0 resection achievement and survival outcomes in patients with initially unresectable gastric cancer undergoing conversion surgery. If validated, the GRIm score could be used at baseline to stratify candidates for intensive systemic therapy with the intent of conversion surgery and to prompt closer multidisciplinary re-evaluation in patients with favorable scores.

Patients and Methods

Patients. This retrospective study included patients with initially unresectable advanced gastric cancer who received systemic chemotherapy at Omihachiman Community Medical Center between January 2019 and July 2025. Among 59 screened patients, two were excluded: one because of participation in a clinical trial and one because no follow-up information after chemotherapy initiation was available (loss to follow-up). Consequently, 57 patients were included in the final analysis. Patients were categorized into two groups: the achieved conversion (AC) group, defined as patients who underwent conversion surgery with R0 resection, and the non-conversion (NC) group, which included all remaining patients.

Definition of unresectable disease at baseline. At baseline, "unresectable" gastric cancer was defined as (i) technical unresectability due to T4b invasion and/or (ii) distant metastatic disease. Unresectable factors were identified retrospectively based on imaging findings and chart review; multiple factors could coexist in the same patient. Yoshida biological category was assigned retrospectively by two investigators using imaging and medical records; staging laparoscopy was not performed in all patients, and peritoneal metastasis was diagnosed radiologically in some cases (Table I).

Data collection. Clinical data included age, sex, body mass index, medication burden, G8 score, and laboratory indices such as lymphocyte count, albumin level, neutrophil-to-lymphocyte ratio, prognostic nutritional index, and geriatric nutritional risk index. All laboratory data, including the components of the GRIm score, were

Table I. *Baseline unresectable factors and metastatic sites.*

Unresectable factors (n=57)	n (%)
T4b alone	3 (5.3)
Distant metastasis alone	48 (84.2)
Both	6 (10.5)
Number of metastatic organs (n=54)	**n (%)**
1 organ	20 (37.0)
≥2 organs	34 (63.0)
Metastatic sites (n=54)	**n (%)**
Peritoneum	26 (48.1)
Liver	25 (46.3)
Lymph node (PAN)	18 (33.3)
Lymph node (Non-PAN)	9 (16.7)
Ascites	16 (29.6)
Lung	9 (16.7)
Bone	3 (5.6)

Unresectable factors were assessed in all patients (n=57). Metastatic sites and number of metastatic organs were assessed among patients with distant metastasis (n=54); multiple metastatic sites could coexist in the same patient. PAN: Para-aortic lymph node.

obtained at the initial evaluation before chemotherapy. Tumor-related variables included Yoshida classification, number of unresectable factors, histological type (Lauren classification), HER2 status, macroscopic type, and treatment details, including the use of trastuzumab and immune checkpoint inhibitors.

GRIm score. The GRIm score was calculated using serum albumin, lactate dehydrogenase (LDH), and neutrophil-to-lymphocyte ratio (NLR). One point was assigned for each of the following: albumin <3.5 g/dl, LDH > the upper limit of normal (ULN), and NLR >6, for a total score of 0-3. The ULN for LDH in our hospital laboratory was 222 U/l. Patients were grouped as low GRIm score (0-1) and high GRIm score (2-3).

Chemotherapy regimens. Systemic chemotherapy was mainly based on SOX (S-1 plus oxaliplatin) administered every 3 weeks (q3w) or FOLFOX (5-fluorouracil/leucovorin plus oxaliplatin) administered every 2 weeks (q2w). Regimen selection was made at the treating physician's discretion. In general, SOX was preferentially selected for outpatient treatment in patients without renal dysfunction and without frailty, whereas FOLFOX was selected for patients with renal dysfunction and/or frailty and was often administered with intermittent hospitalization. Anti-HER2 therapy (trastuzumab) and immune checkpoint inhibitors were added to chemotherapy as appropriate based on tumor characteristics and the treating physician's discretion.

Surgical evaluation. All patients were evaluated by a multidisciplinary team consisting of gastrointestinal surgeons, medical oncologists, and radiologists. All surgical procedures were performed by experienced gastrointestinal surgeons according to institutional protocols. R0 resection was defined as complete macroscopic and microscopic tumor removal with negative surgical margins. Conversion surgery was considered after systemic chemotherapy for patients with a favorable response when the multidisciplinary team judged that macroscopic complete resection was technically feasible. The decision incorporated (i) objective response on contrast-enhanced CT, (ii) no evidence of progression or new lesions, and (iii) the patient's performance status and treatment tolerability.

Statistical analysis. Univariate analyses were performed to identify factors associated with R0 resection. Variables clinically relevant to surgical decision-making were entered into the multivariate logistic regression model. Given the limited number of R0 resection events, the multivariate model was restricted to two clinically essential variables to reduce the risk of overfitting. Accordingly, the results were interpreted primarily based on the direction and statistical significance of associations rather than on point estimates alone. Yoshida classification was dichotomized as C1-2 *versus* C3-4. Overall survival (OS) was defined as the time from initiation of chemotherapy to death from any cause or last follow-up. Survival curves were generated using the Kaplan–Meier method and compared using the log-rank test. For survival analyses, patients who were alive at the

Table II. *Clinicopathological characteristics of patients in the AC and NC groups.*

Variable	AC group (n=10)	NC group (n=47)	*p*-Value
Background			
Age, years (mean±SD)	69.1±10.4	72.2±10.3	0.407
Sex (Female/Male)	2/8	12/35	1.000
BMI (kg/m^2, mean±SD)	21.3±3.8	21.6±4.1	0.822
Medications (<5/≥5)	4/6	22/25	0.741
G8 score (≤14/≥15/Missing)	2/7/1	20/18/0	0.144
Blood test indices			
Lymphocyte (/μl, mean±SD)	1358±528	1358±528	0.998
Albumin (g/dl, mean±SD)	3.5±0.6	3.1±0.7	0.063
NLR (mean±SD)	3.43±3.32	5.05±3.29	0.164
PNI (mean±SD)	42.2±7.6	37.6±7.5	0.078
GNRI (mean±SD)	90.9±12.3	84.4±12.3	0.132
LDH (U/l, mean±SD)	169.0±30.3	371.9±465.4	0.177
GRIm score (0-1/2-3)	10/0	24/23	0.0037*
Treatment			
Courses (mean)	8.4	11.8	0.364
Regimen (Doublet/Triplet)	5/5	12/35	0.145
Trastuzumab (Absent/Present)	7/3	41/6	0.184
ICI (Absent/Present)	8/2	24/23	0.160
Metastatic status			
Yoshida classification (C1/C2/C3/C4)	5/3/2/0	1/22/8/16	0.0003*
Number of unresectable factors (1/2/≥3)	7/3/0	17/18/12	0.081
Pathological factors			
Histology (Diffuse/Intestinal)	5/5	39/7	0.028*
HER2 status (Positive/Negative/Missing)	3/5/2	6/39/0	0.124
Macroscopic type (Borrmann 4/Others)	0/10	14/32	0.052

Values are presented as mean±SD unless otherwise stated. AC, Achieved conversion group (conversion surgery with R0 resection); NC, non-conversion group; SD, standard deviation; BMI, body mass index; NLR, neutrophil-to-lymphocyte ratio; PNI, prognostic nutritional index; GNRI, geriatric nutritional risk index; ICI, immune checkpoint inhibitor.

last confirmed contact were right censored at that date. To mitigate potential immortal time bias, we additionally performed a 180-day landmark analysis, redefining overall survival from day 180 among patients alive and under follow-up at day 180, comparing patients who had undergone R0 conversion surgery by day 180 with those who had not. All analyses were conducted using JMP version 7.0.1 (SAS Institute Inc., Tokyo, Japan), and a two-sided *p*-Value <0.05 was considered statistically significant.

Ethics statement. This study was approved by the Institutional Review Board of Omihachiman Community Medical Center (Approval No. R7-24). Written informed consent was obtained from all patients prior to treatment.

Results

Baseline characteristics. At baseline (*n*=57), unresectable factors were distributed as follows: T4b alone in 3 patients (5.3%), distant metastasis alone in 48 (84.2%), and both in 6 (10.5%). Among patients with distant metastasis (*n*=54), the most frequent sites were peritoneal metastasis (48.1%), liver metastasis (46.3%), para-aortic lymph node (PAN) metastasis (33.3%), and multi-organ metastasis (≥2 organs) was observed in 63.0% (Table I).

Fifty-seven patients were included in the study, with 10 patients in the AC group and 47 in the NC group. Baseline clinicopathological characteristics are summarized in Table II. There were no significant differences between groups in age, sex, body mass index, or treatment regimen, although some variables contained missing data. The AC

Table III. *Multivariate logistic regression analysis of factors associated with R0 resection.*

Variable	OR	*p*-Value
GRIm score (0-1 *vs.* 2-3)	2.6×10^5	0.0004
Yoshida classification (C1-2 *vs.* C3-4)	5.6	0.0358

GRIm: Gustave Roussy immune; OR: odds ratio.

group demonstrated significantly lower GRIm scores, more favorable Yoshida classification, and a higher proportion of intestinal-type histology compared with the NC group. Multiple unresectable factors (≥2) were more frequently observed in the NC group.

Univariate and multivariate analyses. In the univariate analysis, the GRIm score, Yoshida classification, number of unresectable factors, and histological type were significantly associated with R0 resection. In the multivariate logistic regression analysis, a low GRIm score (0-1) was identified as a strong independent predictor of R0 resection (p=0.0004). Yoshida classification C1-2 was also independently associated with R0 resection compared with C3-4 (p=0.0358) (Table III).

Survival analyses. The median follow-up period was 9.9 months. Overall survival was significantly longer in the AC group than in the NC group (unadjusted analysis). The median OS was not reached in the AC group, whereas it was 9.43 months in the NC group (p=0.0008; Figure 1). Patients with low GRIm scores had significantly better OS than those with high GRIm scores. The median OS was 26.2 months in the low-score group and 5.2 months in the high-score group (p=0.0004; Figure 2). A stepwise decline in OS was observed with increasing GRIm scores. When OS was further stratified by individual GRIm scores (0, 1, 2, and 3), a stepwise decrease in survival was observed with increasing GRIm scores (Figure 3). Median OS was 28.4, 18.3, 6.3, and 2.5 months for GRIm scores 0, 1, 2, and 3, respectively (p=0.0003, log-rank test). In the 180-day landmark cohort (n=34), 6 patients had undergone R0 conversion surgery by day 180, and overall survival from day 180 differed between groups (log-rank p=0.0327).

Discussion

This study demonstrated that the GRIm score was associated with both the feasibility of conversion surgery and survival outcomes in patients with initially unresectable gastric cancer. Patients with lower GRIm scores were more likely to achieve R0 resection and had significantly better OS. In the multivariate analysis, a low GRIm score and Yoshida classification C1-2 independently predicted R0 resection, indicating that host-related biological factors and disease burden both contribute to operability.

The GRIm score was originally proposed as a prognostic index for patients receiving immune checkpoint inhibitors (10). In addition, the GRIm score has been evaluated as one of several prognostic scoring systems used for patient stratification in advanced cancer populations, including early phase clinical trial cohorts (15). While few studies have addressed its role in advanced gastric cancer, our findings support the potential clinical relevance of the GRIm score in this setting, extending emerging observations in gastric cancer to a cohort of patients considered for conversion surgery (14). Beyond immunotherapy, the GRIm score reflects systemic inflammation and nutritional status, which affect chemotherapy tolerance and treatment outcomes. Consistently, body weight loss during chemotherapy has been reported to be clinically significant in patients undergoing conversion surgery for advanced gastric cancer, supporting the relevance of host nutritional status during systemic treatment (16). In the present cohort, the strong association between low GRIm score and R0 resection suggests that baseline host condition may be a critical determinant of whether patients can tolerate systemic therapy sufficiently to achieve effective downstaging and subsequently undergo curative surgery. The extremely large odds ratio observed for the GRIm score likely reflects the absence of high GRIm

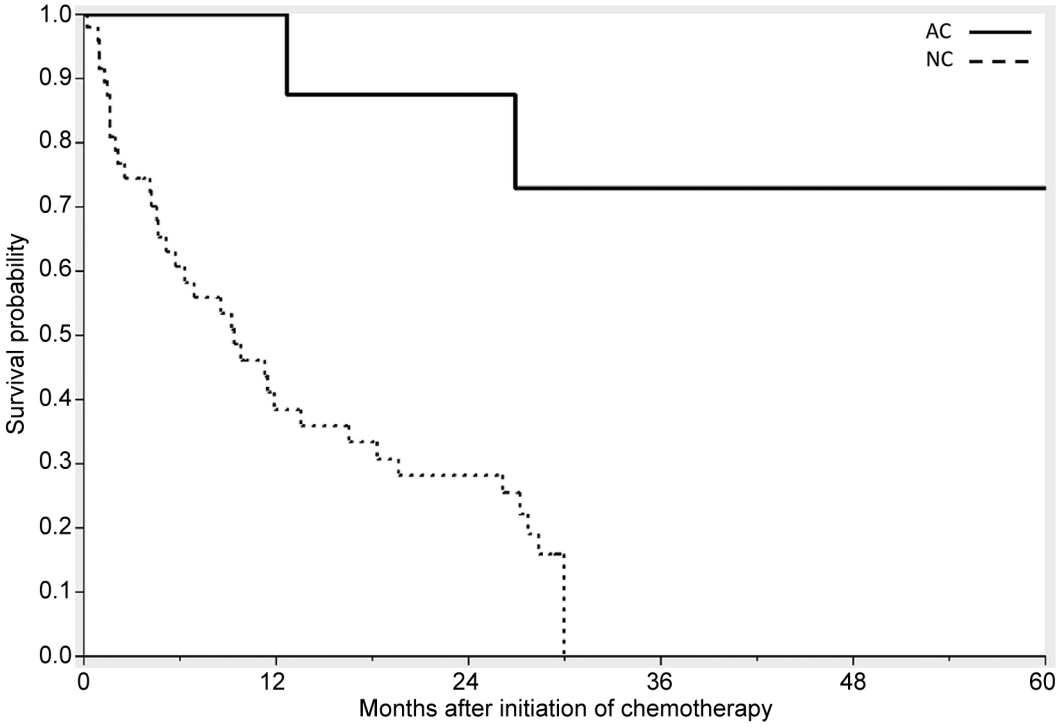

Figure 1. *Kaplan–Meier OS curves according to conversion surgery. Patients in the AC group (n=10) had significantly longer survival than those in the NC group (n=47). The median OS was not reached in the AC group but was 9.43 months in the NC group. The 1-, 2-, and 3-year survival rates were 100.0%, 87.5%, and 72.9%, respectively, in the AC group and 38.4%, 28.2%, and 0%, respectively, in the NC group (p=0.0008, log-rank test). AC, Achieved conversion group (conversion surgery with R0 resection); NC, non-conversion group; OS, overall survival.*

score patients among those who achieved R0 resection, indicating a clear separation between groups rather than an artifact of model instability. The additional analysis by individual GRIm categories further supported a dose–response relationship between worsening host condition and poorer survival.

International series have consistently reported that R0 resection is the strongest determinant of survival in patients with stage IV gastric cancer (3, 5). In our cohort, the R0 resection rate was 17.5%, which was somewhat lower than that reported in larger institutional series. This discrepancy may partly reflect differences in referral patterns and baseline disease burden. Nevertheless, the consistent prognostic advantage of R0 resection across studies underscores its central role in determining survival outcomes. In line with these reports, our survival analysis demonstrated that patients who achieved R0 resection experienced markedly prolonged OS compared with those who did not.

While surgical decision-making for stage IV gastric cancer has traditionally relied on imaging-based tumor characteristics, the Yoshida classification system has introduced a more structured biological framework for this process (2,17). The CONVO-GC-1 registry further clarified the role of conversion surgery by categorizing stage IV gastric cancer using the Yoshida classification (17). In the present study, the Yoshida classification was also a significant predictor of R0 resection. Importantly, the GRIm score complemented the Yoshida classification by incorporating host-related biological factors. While the Yoshida classification primarily reflects anatomical disease burden and metastatic distribution, the GRIm score provides a multifaceted assessment of the host's biological state, including nutritional status and

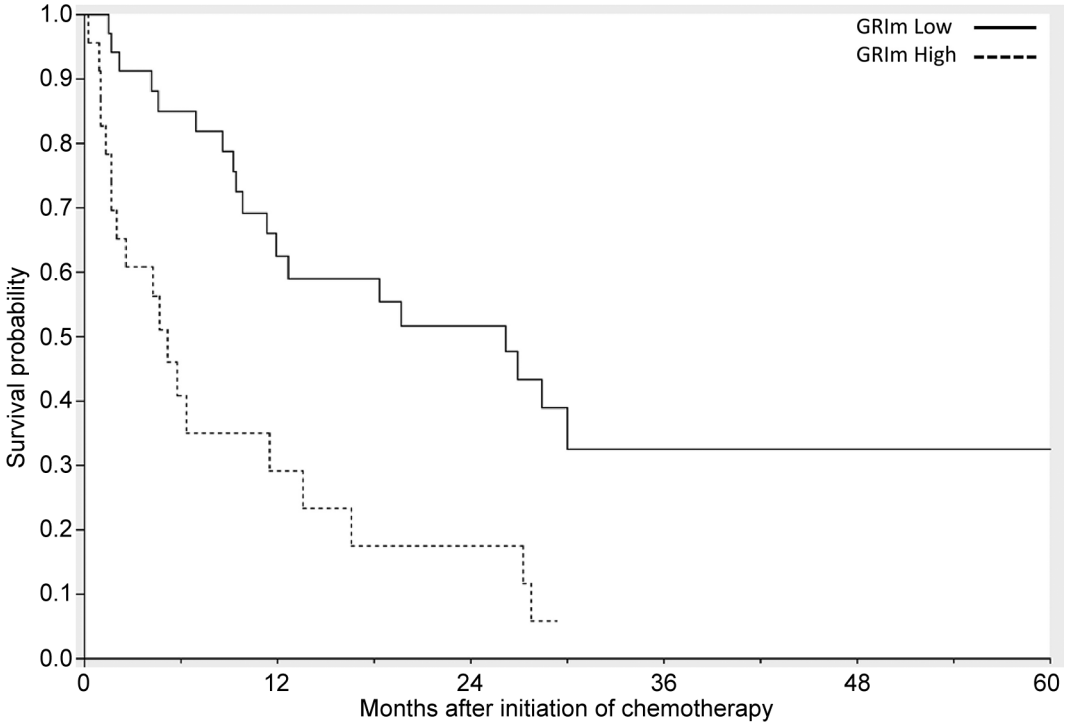

Figure 2. *Kaplan–Meier OS curves based on GRIm score (low: 0-1 points, n=34; high: 2-3 points, n=23). Patients with low scores had a significantly better OS than those with high scores. The median OS was 26.2 months for the low-score group compared to 5.2 months for the high-score group. The 1-, 2-, and 3-year survival rates were 62.5%, 51.6%, and 32.5%, respectively, for the low-score group and 29.2%, 17.5%, and 0%, respectively, for the high-score group (p=0.0004, log-rank test). GRIm, Gustave Roussy Immune score; OS, overall survival.*

systemic inflammation. These host-related factors are critical determinants of chemotherapy tolerance and the eventual transition to curative-intent surgery, paralleling established evidence that markers such as the modified Glasgow Prognostic Score (mGPS), Prognostic Nutritional Index (PNI), neutrophil-to-lymphocyte ratio (NLR), and lymphocyte-to-C-reactive protein ratio (LCR) are independent predictors of survival and short-term surgical outcomes in metastatic gastrointestinal cancers (18,19).

Radiological imaging remains indispensable for evaluating disease extent and treatment response. However, discrepancies between imaging and pathological findings are occasionally observed (6, 7), highlighting the need for complementary clinical indicators. In daily practice, decisions regarding conversion surgery often depend not only on radiological response but also on the patient's overall clinical trajectory, including treatment tolerability and physiological resilience. The GRIm score may serve as an objective and readily available marker reflecting these host-related conditions.

Regarding systemic therapy, immune checkpoint inhibitors have become a standard component of first-line regimens for advanced gastric cancer (8, 9). In our cohort, the use of ICIs was not significantly associated with R0 resection. Recent real-world data in clinical stage IVB HER2-negative gastric cancer have suggested that nivolumab plus chemotherapy may increase conversion surgery rates compared with chemotherapy alone, although external validation and careful patient selection remain essential (20). In addition, early progression during immune checkpoint inhibitor–based therapy has been reported in other malignancies, underscoring heterogeneity in treatment response (21). However,

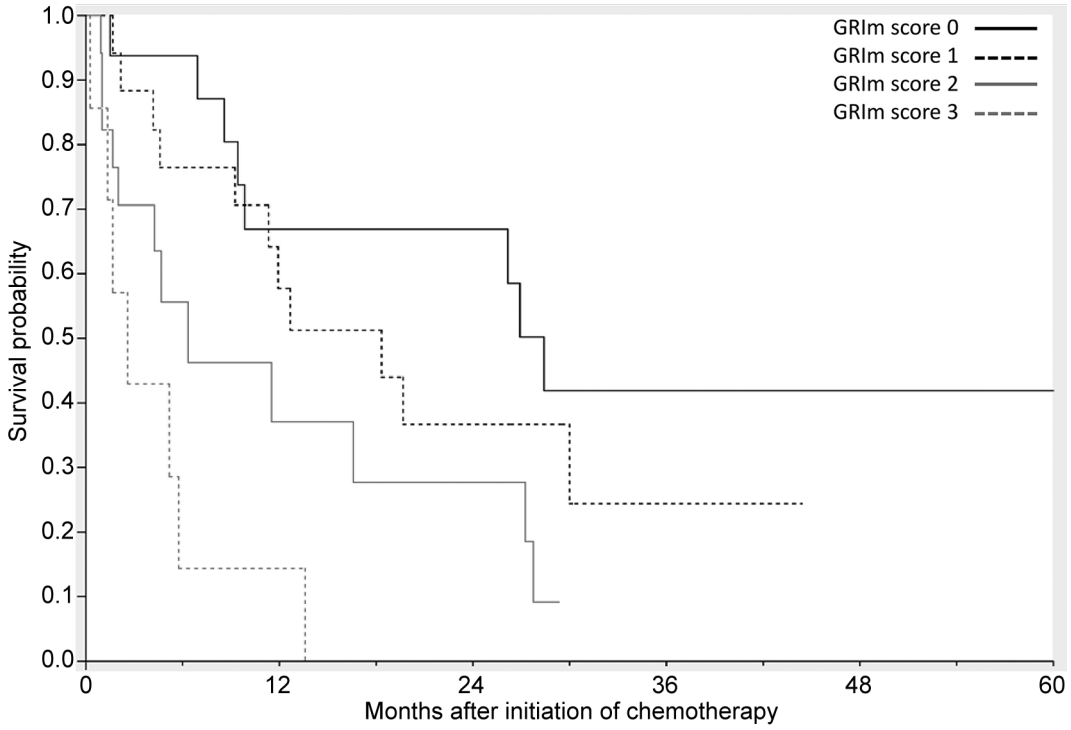

Figure 3. *Kaplan–Meier OS curves according to GRIm score (0, 1, 2, and 3). Median OS was 28.4, 18.3, 6.3, and 2.5 months, respectively, demonstrating a stepwise decrease in survival with increasing scores (p=0.0003, log-rank test). GRIm, Gustave Roussy Immune score; OS, overall survival.*

this analysis may have been underpowered to detect regimen-specific effects on resectability, and the role of ICIs in facilitating conversion surgery warrants validation in larger cohorts. Although ICIs improve survival in advanced disease, these findings suggest that surgical feasibility may be more strongly influenced by baseline host condition and disease distribution than by systemic therapy alone.

This study has several limitations, including its retrospective design, single-center setting, relatively small sample size, heterogeneous treatment regimens, and limited follow-up duration. Because treatment regimens (including the use of ICIs and trastuzumab) were heterogeneous, residual confounding cannot be excluded; therefore, the observed association between baseline GRIm score and R0 conversion should be interpreted as predictive association rather than proof of causality. In particular, the small number of patients achieving R0 resection necessitated restriction of the multivariate analysis to two clinically essential variables to avoid overfitting. Larger prospective multicenter studies are warranted to validate the predictive value of the GRIm score and to clarify its role in standardized conversion surgery strategies. Comparing overall survival from chemotherapy initiation between patients who eventually underwent conversion surgery and those who did not may introduce immortal time bias, potentially overestimating survival differences. Therefore, the survival findings should be interpreted cautiously despite the landmark sensitivity analysis.

Conclusion

The GRIm score is a clinically practical and independent predictor of successful conversion surgery and survival in patients with initially unresectable gastric cancer. Incorporation of the GRIm score into preoperative assessment may enhance patient selection and

complement established classification systems such as the Yoshida classification.

Conflicts of Interest

The Authors declare no conflicts of interest.

Authors' Contributions

Conceptualization was performed by Nagata T and Nakano K. Methodology was developed by Nagata T, Kojo M, and Takemoto K. Formal analysis was conducted by Nagata T, Takemoto K, and Naito K. Investigation was carried out by Kojo M and Takemoto K. Data curation was performed by Morishita S, Fujimoto H, and Kadotani Y. Nagata T wrote the original draft. Nakano K and Naito K reviewed and edited the manuscript. Nakano K supervised the study.

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Artificial Intelligence (AI) Disclosure

During the preparation of this manuscript, a large language model (Genspark AI Workspace 2.0, MainFunc, and ChatGPT 5.2, OpenAI) was used solely for language editing and stylistic improvements in select paragraphs. No sections involving the generation, analysis, or interpretation of research data were produced by generative AI. All scientific content was created and verified by the authors. Furthermore, no figures or visual data were generated or modified using generative AI or machine learning–based image enhancement tools.

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