J Gastric Cancer. 2022 Oct;22(4):395-407
https://doi.org/10.5230/jgc.2022.22.e32
pISSN 2093-582X·eISSN 2093-5641

Journal of Gastric Cancer

Original Article

Safe Discharge Criteria After Curative Gastrectomy for Gastric Cancer

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Received: Jul 1, 2022
Revised: Aug 16, 2022
Accepted: Aug 29, 2022
Published online: Sep 23, 2022

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Funding
This research was supported by a grant of the

ABSTRACT

Purpose: This study aimed to investigate the relationship between clinical and laboratory parameters and complication status to predict which patients can be safely discharged from the hospital on the third postoperative day (POD).
Materials and Methods: Data from a prospectively maintained database of 2,110 consecutive patients with gastric adenocarcinoma who underwent curative surgery were reviewed. The third POD vital signs, laboratory data, and details of the course after surgery were collected. Patients with grade II or higher complications after the third POD were considered unsuitable for early discharge. The performance metrics were calculated for all algorithm parameters. The proposed algorithm was tested using a validation dataset of consecutive patients from the same center.
Results: Of 1,438 patients in the study cohort, 142 (9.9%) were considered unsuitable for early discharge. C-reactive protein level, body temperature, pulse rate, and neutrophil count had good performance metrics and were determined to be independent prognostic factors. An algorithm consisting of these 4 parameters had a negative predictive value (NPV) of 95.9% (95% confidence interval [CI], 94.2–97.3), sensitivity of 80.3% (95% CI, 72.8–86.5), and specificity of 51.1% (95% CI, 48.3–53.8). Only 28 (1.9%) patients in the study cohort were classified as false negatives. In the validation dataset, the NPV was 93.7%, sensitivity was 66%, and 3.3% (17/512) of patients were classified as false negatives.
Conclusions: Simple clinical and laboratory parameters obtained on the third POD can be used when making decisions regarding the safe early discharge of patients who underwent gastrectomy.

Keywords: Gastric cancer; Gastrectomy; Postoperative complications; Discharge; Readmission

INTRODUCTION

Gastric cancer surgery is a high-risk procedure associated with high surgical stress responses and potential risk for morbidity and mortality [1-5]. Postoperative complications may necessitate weeks of hospital stay, which is longer than that required for conventional gastrointestinal surgery. However, with the implementation of enhanced recovery after

Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number:HI22C0767).

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Author Contributions
Conceptualization: K.H.I.; Data curation: C.M., K.Y.M., G.A.; Formal analysis: G.A., K.H.I.; Funding acquisition: K.H.I.; Investigation: K.Y.K., P.S.H., K.H.I.; Methodology: G.A., K.H.I.; Visualization: G.A., K.H.I.; Writing - original draft: G.A., K.H.I.; Writing - review & editing: G.A., H.W.J., K.H.I.

surgery programs and minimally invasive surgical techniques, including laparoscopy and robotic surgery, the length of hospital stay has been shortened to 4–6 days [5-8]. Moreover, we recently demonstrated that hospital stays can be shortened to as few as 3–4 days [9]. These improvements have led to the question of how discharge decisions can be safely made in the early postoperative period.

During the past decade, attempts have been made to define safe early discharge criteria for patients [10-12]. Although several studies aimed to predict the "presence of complications," few studies were able to predict the "absence of complications," which is a critical component of safe discharge [13,14]. Studies attempting to determine the absence of complications have mainly investigated inflammatory parameters such as C-reactive protein (CRP) and procalcitonin as decisive markers [14,15]. Some studies have also integrated disease-specific laboratory markers or clinical parameters, including bowel function and pain scores, into the decision-making process [10-12].

Similar efforts have been made for gastric cancer surgery, with several approaches aimed at making a discharge decision on postoperative day (POD) 3–5 [14,16-18]. However, because some algorithms use combinations of clinical and laboratory values, complex calculation procedures are required for decision making. In addition, some algorithms require special tests (e.g., procalcitonin) that are not routinely used in clinical practice.

We hypothesized that safe early discharge criteria after gastric cancer surgery could be developed using simple and routinely used parameters obtained on POD 3. To test this hypothesis, we investigated the relationship between POD 3 clinical and laboratory parameters and delayed complication status to predict which patients could be safely discharged from the hospital.

MATERIALS AND METHODS

Data from a prospectively maintained database of 2,110 consecutive patients with gastric adenocarcinoma who underwent surgery by a single surgeon at Severance Hospital, Yonsei University Health System (Seoul, Korea) between March 2009 and April 2021 were retrospectively reviewed for the study cohort. Data for patients treated by other surgeons at the same hospital between January 1, 2015 and December 31, 2015, were reviewed for the validation cohort. Patients were excluded if they had the following: metastatic or an undetermined stage of disease, non-curative surgery, other organ malignancies, neoadjuvant treatment, remnant gastric cancers, American Society of Anesthesiologists (ASA) physical status score of IV, missing data for important postoperative parameters, cardiac arrhythmia, history of transplantation, Clavien-Dindo grade III or higher complications before or on the decision day (i.e., 3 days after surgery), or unresolved grade II or higher complications within 3 days after surgery. If a patient experienced grade II complications within 3 days after surgery that resolved before the decision day without further complications, the patient was considered to have no delayed complications. This study was approved by the institutional review board of Severance Hospital (4-2021-1708).

Clinical data, pathologic characteristics according to the 8th edition of the American Joint Committee on Cancer staging system, operative details following Korean and Japanese guidelines, and postoperative data, including laboratory/clinical data and complications classified using the Clavien-Dindo system, were extracted from the database [19-22]. Adverse events occurring within 30 days after surgery (or within the hospitalization period for patients whose hospital stay was >30 days) were considered postoperative complications.

Patients were followed-up during the postoperative period according to routine protocols. Patient-controlled analgesia was used to manage postoperative pain until POD 2. Oral analgesics were initiated on POD 3. Sips of water on POD 2 were followed by clear liquids and soft diet on POD 3. Patients were allowed to mobilize on the day of surgery. Blood pressure, pulse rate, body temperature, and hemogram were frequently checked, and CRP levels were measured on POD 1, 3, 5, and 7. Postoperative laboratory test results were obtained by analyzing morning blood samples. The highest body temperature and pulse rate during the day were used as day values.

The prerequisite conditions for safe discharge were the following: 1) able to tolerate oral intake, 2) with generally good condition, and 3) has adequate pain control. A total of 1,438 and 512 patients were selected for the study and validation cohorts, respectively (**Fig. 1**). We defined an event as the occurrence of grade II or higher complication after POD 3. Patients without an event were considered to have no delayed complications, and those with an event were considered to have delayed complications and were not suitable for discharge on POD 3.

Statistical analysis

Data are presented as median and 1st–3rd quartiles or mean and standard deviation for continuous variables, and as frequencies and percentages for categorical variables. For comparisons between groups, t-tests or Mann-Whitney tests were used for continuous variables, and χ^2 tests or Fisher tests were used for categorical variables.

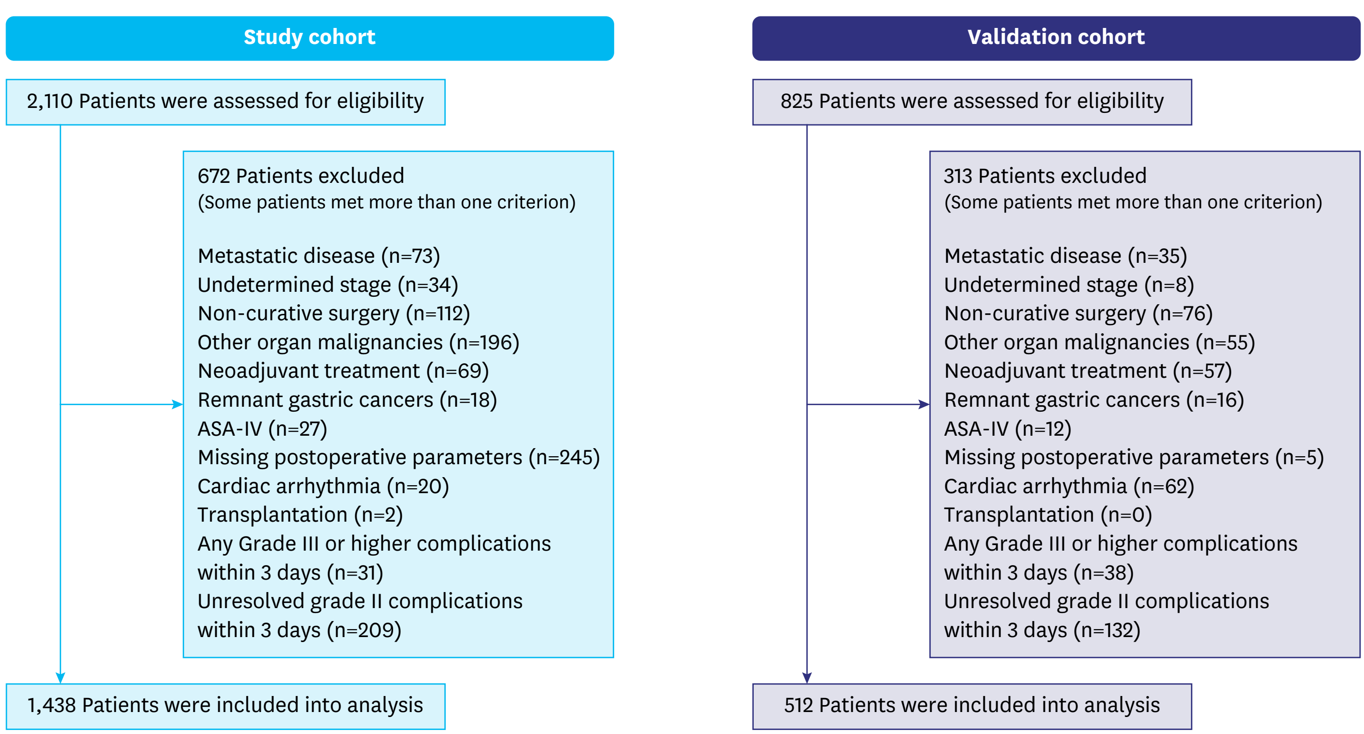

Fig. 1. Flow diagram showing the number of patients who were included in the study and validation cohorts.
ASA = American Society of Anesthesiologists.

 https://doi.org/10.5230/jgc.2022.22.e32

Journal of Gastric Cancer

Important POD 3 variables were selected based on the receiver operating characteristic (ROC) curves. Continuous predictors were dichotomized for further modelling and clinical usability. Youden's index (sensitivity+specificity−1) was used to determine the optimal cut-off value of each continuous parameter, and patients were divided into 2 groups: low- and high-risk. To evaluate the prognostic effects of laboratory values on the primary outcome (i.e., the presence of grade II or higher complications after POD 3), we analyzed all clinicopathological variables and important POD 3 variables using logistic regression. In the univariate models, the variables were tested individually. In the multivariate model, all variables were entered into the model. Variables known to be clinically relevant or identified in the multivariate model were entered into a reduced multivariate model. The model with the lowest Akaike information criterion and highest C-statistic was selected as the final model. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). The assumptions of the model were verified. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were used as performance metrics for POD 3 independent variables. Independent variables were evaluated both individually and in combination. When all evaluated variables were at low risk simultaneously, it was defined as a low risk for delayed complications. As we aimed to rule out the presence of complications, we mainly focused on parameters with high NPV, high sensitivity, and low false negative results [23]. Statistical analysis was performed using R software (R version 4.0.4; R Foundation for Statistical Computing, Vienna, Austria) with R packages, including tidyverse, finalfit, rms, cutpointr, and epiR. Statistical significance was defined as a 2-sided P-value of <0.05.

RESULTS

Of the 1,438 patients with gastric cancer in the study cohort, 900 (62.6%) were male and 538 (37.4%) were female. The median patient age was 60 years (range, 51–68 years). From the total cohort, 1,046 (72.7%) patients had stage I cancer, 176 (12.2%) had stage II cancer, and 216 (15%) had stage III cancer. A total of 142 patients (9.9%) experienced delayed grade II or higher complications and were considered unsuitable for safe early discharge. The demographic and clinical characteristics of the patients according to their complication status are presented in **Table 1**. The daily changes in laboratory values are presented in **Supplementary Fig. 1**.

Among the POD 3 variables, the ROC curves showed that CRP, body temperature, pulse rate, and neutrophil count had a higher area under curve (**Supplementary Fig. 2**). Univariate logistic regression analysis of clinicopathological and laboratory variables (age, sex, ASA classification, approach, extent of gastrectomy and lymphadenectomy, combined resection, operation time, intraoperative blood loss, pathological stage, POD 3 factors [body temperature, pulse rate, CRP, and neutrophil count]) were significantly associated with delayed complications (**Table 2**). In the reduced multivariate model, approach (0.49, 95% CI, 0.32–0.76, P=0.001), extent of gastrectomy (2.42, 95% CI, 1.59–3.67, P<0.001), POD 3 body temperature (3.25, 95% CI, 2.06–5.11, P<0.001), POD 3 pulse rate (2.05, 95% CI, 1.34–3.11, P=0.001), POD 3 CRP (2.07, 95% CI, 1.35–3.19, P=0.001), and POD 3 neutrophil count (2.23, 95% CI, 1.50–3.33; P<0.001) were identified as independent prognostic factors. The relationships between the POD 3 parameters and the probability of delayed complications are shown in **Fig. 2**. The optimal cut-off values derived from Youden's index for body temperature, pulse rate, CRP, and neutrophil count were 38°C, 90/min, 110 mg/L, and 6.7×10^3 cells, respectively.

Table 1. Demographic and clinical characteristics of patients in the study and validation cohorts

Variables	Study cohort (n=1,438)			Validation cohort (n=512)		
	No delayed complications (n=1,296, 90.1%)	Delayed complications (n=142, 9.9%)	P-value	No delayed complications (n=462, 90.2%)	Delayed complications (n=50, 9.8%)	P-value
Age (yr)	59 (51–68)	63 (55.2–72.8)	<0.001	56.5 (49–65)	63 (56.0–70.5)	0.007
Sex			<0.001			0.334
Male	790 (61.0)	110 (77.5)		278 (60.2)	26 (52.0)	
Female	506 (39.0)	32 (22.5)		184 (39.8)	24 (48.0)	
BMI (kg/m^2)	23.5 (21.6–25.8)	22.6 (20.6–25.4)	0.020	23.6 (21.3–25.4)	23.7 (21.3–25.7)	0.937
Previous abdominal surgery	481 (37.1)	57 (40.1)	0.538	87 (18.8)	10 (20.0)	0.992
ASA			0.013			0.608
I	406 (31.3)	42 (29.6)		88 (19.0)	10 (20.0)	
II	671 (51.8)	62 (43.7)		321 (69.5)	32 (64.0)	
III	219 (16.9)	38 (26.8)		53 (11.5)	8 (16.0)	
Comorbidity	689 (53.2)	85 (59.9)	0.153	215 (46.5)	24 (48.0)	0.962
Approach			<0.001			0.010
Open	196 (15.1)	48 (33.8)		175 (37.9)	30 (60.0)	
Laparoscopy	697 (53.8)	59 (41.5)		198 (42.9)	14 (28.0)	
Robotic	403 (31.1)	35 (24.6)		89 (19.3)	6 (12.0)	
Extent of gastrectomy			<0.001			0.002
Subtotal	1,104 (85.2)	84 (59.2)		397 (85.9)	34 (68.0)	
Total	192 (14.8)	58 (40.8)		65 (14.1)	16 (32.0)	
Extent of lymphadenectomy			0.004			0.006
D1+	847 (65.4)	75 (52.8)		220 (47.6)	13 (26.0)	
D2	449 (34.6)	67 (47.2)		242 (52.4)	37 (74.0)	
Combined resection	131 (10.1)	26 (18.3)	0.005	27 (5.8)	9 (18.0)	0.004
Operation time (min)	159 (131–198)	181 (147.2–236.8)	<0.001	173 (143.2–205.0)	178 (160.5–221.8)	0.053
Intraoperative bleeding (mL)	40 (20–79)	70 (30–125.2)	<0.001	70 (35–160)	125 (51.8–215)	0.039
T classification			<0.001			0.016
T1	908 (70.1)	73 (51.4)		310 (67.1)	23 (46.0)	
T2	129 (10.0)	15 (10.6)		46 (10.0)	10 (20.0)	
T3	125 (9.6)	22 (15.5)		54 (11.7)	7 (14.0)	
T4	134 (10.3)	32 (22.5)		52 (11.3)	10 (20.0)	
N classification			<0.001			0.013
N0	974 (75.2)	84 (59.2)		343 (74.2)	28 (56.0)	
N1	131 (10.1)	21 (14.8)		46 (10.0)	5 (10.0)	
N2	84 (6.5)	12 (8.5)		38 (8.2)	8 (16.0)	
N3	107 (8.3)	25 (17.6)		35 (7.6)	9 (18.0)	
Pathological stage			<0.001			0.005
Stage I	968 (74.7)	78 (54.9)		334 (72.3)	27 (54.0)	
Stage II	150 (11.6)	26 (18.3)		67 (14.5)	8 (16.0)	
Stage III	178 (13.7)	38 (26.8)		61 (13.2)	15 (30.0)	

Data are presented as number (%) or median (1st–3rd quartile).
BMI = body mass index; ASA = American Society of Anesthesiologists.

The NPV for ruling out delayed grade II or higher complications was 93.1% for temperature alone, 93.2% for pulse alone, 94.8% for CRP alone, and 93.8% for neutrophil count alone (**Supplementary Table 1**). The sensitivity of these 4 parameters alone ranged from 38.0% to 63.4%. Using the 4-parameter algorithm (when all 4 of these parameters were low risk) across all patients in the study cohort, the NPV was 95.9% (95% CI, 94.2–97.3), sensitivity was 80.3% (95% CI, 72.8–86.5), specificity was 51.1% (95% CI, 48.3–53.8), PPV was 15.2% (95% CI, 12.7–18.0), and the overall accuracy was 54% (95% CI, 51.3–56.6). When the 4-parameter algorithm was tested in various subgroups of patients, the NPV was consistent across subgroups (**Table 3**).

The false negative rate in the study cohort was 1.9% (28/1,438). The median duration to complications was 5.5 (5–7) days for false negative patients. Among the 28 patients, 24 patients experienced grade II complications, 3 patients experienced grade IIIa complications

Table 2. Univariate and multivariate analyses of risk factors for delayed grade II or higher complications

Variables	Univariate	Multivariate	Reduced multivariate
Age (yr)			
≤60	-	-	-
>60	1.47 (1.04–2.09, P=0.030)	1.17 (0.75–1.81, P=0.493)	1.21 (0.80–1.86, P=0.369)
Sex			
Male	-	-	-
Female	0.45 (0.30–0.68, P<0.001)	0.67 (0.41–1.05, P=0.087)	0.71 (0.45–1.11, P=0.146)
BMI (kg/m^2)			
≤27.3	-	-	-
>27.3	1.27 (0.77–2.03, P=0.326)	1.10 (0.62–1.90, P=0.731)	-
Previous abdominal surgery			
No	-	-	-
Yes	1.14 (0.79–1.61, P=0.479)	1.41 (0.93–2.12, P=0.107)	-
ASA			
I	-	-	-
II	0.89 (0.59–1.35, P=0.590)	0.71 (0.44–1.16, P=0.171)	0.70 (0.44–1.12, P=0.137)
III	1.68 (1.05–2.68, P=0.031)	0.97 (0.51–1.83, P=0.934)	0.97 (0.54–1.72, P=0.922)
Comorbidity			
No	-	-	-
Yes	1.31 (0.93–1.88, P=0.130)	0.97 (0.62–1.54, P=0.911)	-
Approach			
Open	-	-	-
MIS	0.35 (0.24–0.51, P<0.001)	0.50 (0.29–0.87, P=0.013)	0.49 (0.32–0.76, P=0.001)
Extent of gastrectomy			
Subtotal	-	-	-
Total	3.97 (2.74–5.73, P<0.001)	2.08 (1.31–3.29, P=0.002)	2.42 (1.59–3.67, P<0.001)
Extent of lymphadenectomy			
D1+	-	-	-
D2	1.69 (1.19–2.39, P=0.003)	0.81 (0.50–1.29, P=0.376)	-
Combined resection			
No	-	-	-
Yes	1.99 (1.23–3.12, P=0.003)	1.08 (0.60–1.87, P=0.797)	-
Operation time (min)			
≤210	-	-	-
>210	2.89 (2.01–4.14, P<0.001)	1.32 (0.82–2.11, P=0.252)	-
Intraoperative bleeding (mL)			
≤70	-	-	-
>70	2.48 (1.75–3.53, P<0.001)	1.01 (0.63–1.61, P=0.971)	-
Pathological stage			
Stage I	-	-	-
Stage II	2.15 (1.32–3.42, P=0.002)	1.43 (0.78–2.58, P=0.236)	-
Stage III	2.65 (1.73–4.01, P<0.001)	1.47 (0.79–2.70, P=0.220)	-
Body temperature (POD 3, °C)			
≤38	-	-	-
>38	6.75 (4.55–9.97, P<0.001)	3.17 (1.99–5.02, P<0.001)	3.25 (2.06–5.11, P<0.001)
Pulse (POD 3, /min)			
≤90	-	-	-
>90	3.85 (2.68–5.51, P<0.001)	1.96 (1.28–2.99, P=0.002)	2.05 (1.34–3.11, P=0.001)
CRP (POD 3, mg/L)			
≤110	-	-	-
>110	4.71 (3.29–6.81, P<0.001)	2.03 (1.31–3.16, P=0.002)	2.07 (1.35–3.19, P=0.001)
Neutrophil count (POD 3)			
≤6.7×10^3 cells	-	-	-
>6.7×10^3 cells	3.83 (2.69–5.47, P<0.001)	2.21 (1.48–3.31, P<0.001)	2.23 (1.50–3.33, P<0.001)

The first row of each variable represents the reference level. Data are presented as odds ratio, 95% confidence interval, and P-value.
BMI = body mass index; ASA = American Society of Anesthesiologists; MIS = minimally invasive surgery; CRP = C-reactive protein; POD = postoperative day.

(2 patients had pleural effusion requiring thoracentesis or pigtail insertion on POD 7 and POD 8, and one patient had biliary injury requiring biliary stenting on POD 7), and one patient experienced a grade IVa complication (esophagojejunostomy leakage managed with

https://doi.org/10.5230/jgc.2022.22.e32

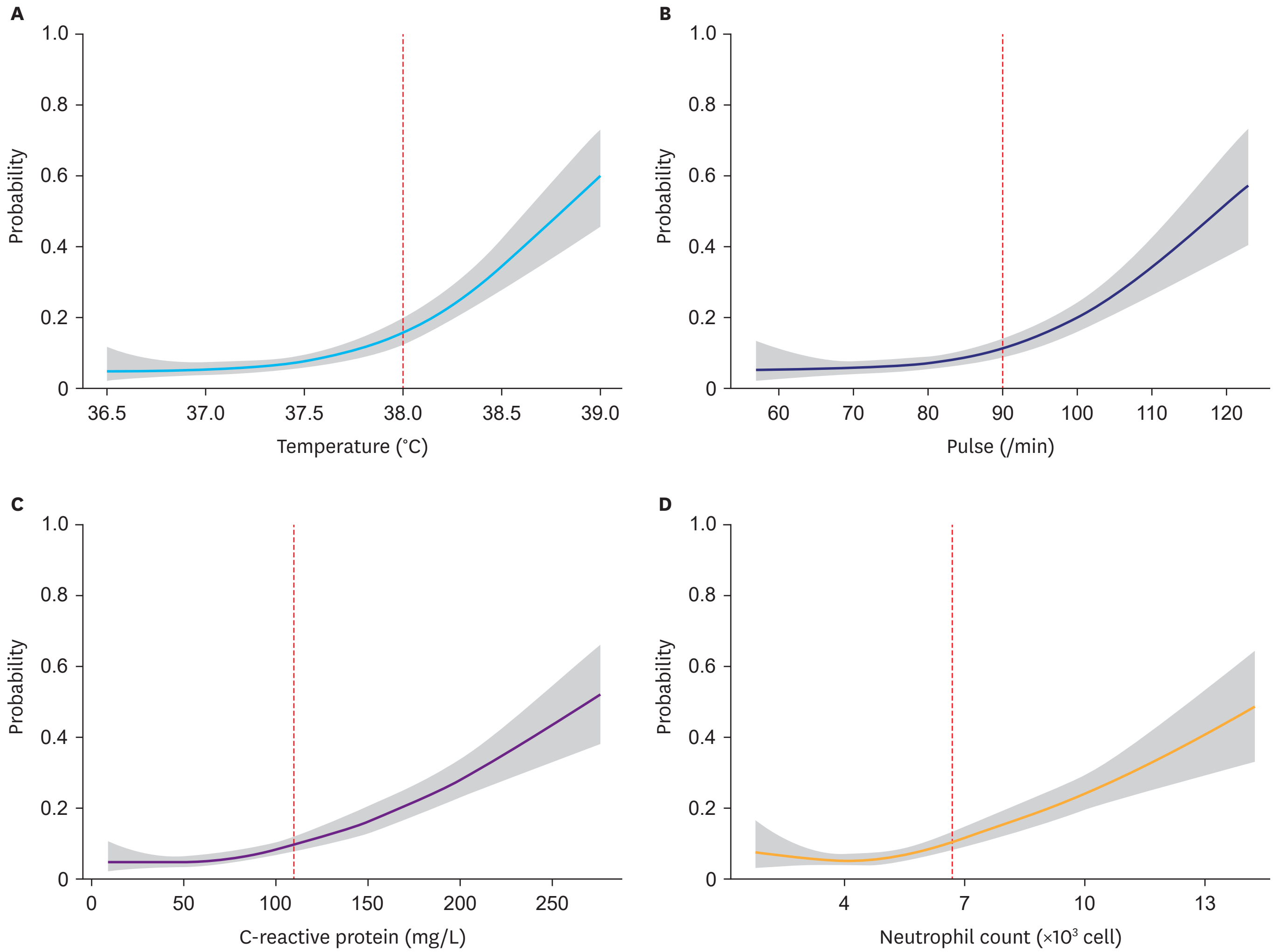

Fig. 2. Relationships between postoperative day 3 variables and the predicted probability of delayed complications. Red dashed lines represent the Youden-based optimal cut-offs (body temperature=38, pulse=90, C-reactive protein=110, neutrophil count=6.7).

conservative Levin tube drainage procedures and intensive care unit management on POD 7). The patient with biliary injury had no symptoms, except for a bilious color change of abdominal drainage and elevated serum bilirubin on POD 3. The patient with leakage had a history of hypertension, stroke, abdominal aortic aneurysm with stenting, brain tumor, and lung emphysema. No 90-day mortality rate was observed.

The 4-parameter algorithm was tested on a separate validation dataset (**Fig. 1**, **Table 1**), with a sensitivity of 66%, specificity of 54.5%, PPV of 13.6%, and NPV of 93.7%. When tested in various subgroups of patients, the NPV was consistent across subgroups, except for approach (**Table 3**).

The false negative rate in the validation cohort was 3.3% (17/512). The median duration to delayed complications was 9 (5–13) days for false negative patients. Among these 17 patients, 12 experienced grade II complications, 4 experienced grade IIIa complications, and one experienced grade V complications. The first patient with grade IIIa complication was discharged on POD 5 without an event, but after 5 days, the patient experienced

https://doi.org/10.5230/jgc.2022.22.e32

Journal of Gastric Cancer

Table 3. Performance metrics of 4-parameter algorithm in patient subgroups in the study and validation cohorts

Variables	Number*	Delayed complications (%)	TP	FP	FN	TN	Prevalence (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
All patients	1,438	9.9	114	634	28	662	52.0	80.3	51.1	15.2	95.9	54.0
	512	9.8	33	210	17	252	47.5	66.0	54.5	13.6	93.7	55.7
ASA												
ASA I/II	1,181	8.8	81	520	23	557	50.9	77.9	51.7	13.5	96.0	54.0
	451	9.3	27	174	15	235	44.6	64.3	57.5	13.4	94.0	58.1
ASA III	257	14.8	33	114	5	105	57.2	86.8	47.9	22.4	95.5	53.7
	61	13.1	6	36	2	17	68.9	75.0	32.1	14.3	89.5	37.7
Sex												
Female	538	5.9	22	210	10	296	43.1	68.8	58.5	9.5	96.7	59.1
	208	11.5	13	75	11	109	42.3	54.2	59.2	14.8	90.8	58.7
Male	900	12.2	92	424	18	366	57.3	83.6	46.3	17.8	95.3	50.9
	304	8.6	20	135	6	143	51.0	76.9	51.4	12.9	96.0	53.6
Approach												
MIS	1,194	7.9	72	515	22	585	49.2	76.6	53.2	12.3	96.4	55.0
	307	6.5	16	115	4	172	42.7	80.0	59.9	12.2	97.7	61.2
Open	244	19.7	42	119	6	77	66.0	87.5	39.3	26.1	92.8	48.8
	205	14.6	17	95	13	80	54.6	56.7	45.7	15.2	86.0	47.3
Pathological stage												
Stage I	1,046	7.5	59	449	19	519	48.6	75.6	53.6	11.6	96.5	55.3
	361	7.5	17	135	10	199	42.1	63.0	59.6	11.2	95.2	59.8
Stage II/III	392	16.3	55	185	9	143	61.2	85.9	43.6	22.9	94.1	50.5
	151	15.2	16	75	7	53	60.3	69.6	41.4	17.6	88.3	45.7
Extent of gastrectomy												
Subtotal	1,188	7.1	64	526	20	578	49.7	76.2	52.4	10.8	96.7	54.0
	431	7.9	19	174	15	223	44.8	55.9	56.2	9.8	93.7	56.1
Total	250	23.2	50	108	8	84	63.2	86.2	43.8	31.6	91.3	53.6
	81	19.8	14	36	2	29	61.7	87.5	44.6	28.0	93.5	53.1

TP = true positive; FP = false positive; FN = false negative; TN = true negative; PPV = positive predictive value; NPV = negative predictive value; ASA = American Society of Anesthesiologists; MIS = minimally invasive surgery.
*The top row of each item means number of study cohort and the bottom row means number of validation cohort.

abrupt epigastric pain and visited the emergency department. An imaging study detected a hematoma around the gastroduodenal artery, and the patient underwent embolization procedure on POD 12. The second patient with grade IIIa complications underwent pigtail drainage for pneumoperitoneum, which was found on POD 13. The third patient underwent liver abscess drainage on POD 13, and the fourth patient underwent endoscopic stenting on POD 13 for the oedematous anastomosis site after gastroduodenostomy. The patient who experienced a grade V complication was a 91-year-old woman with a urinary tract infection on POD 6 who was treated with antibiotics and discharged on POD 13. One week after discharge, the patient visited the outpatient department as scheduled and booked the next visit for 2 months. No signs of infection were observed. One week later, the patient presented with urinary sepsis and died the next day (POD 27). **Fig. 3** shows the timing and grade of delayed complications among false negative patients in the study and validation cohorts.

DISCUSSION

We investigated the relationship between POD 3 parameters and delayed complication status among patients undergoing curative gastrectomy for gastric cancer and found that CRP level, body temperature, pulse rate, and neutrophil count were the most important independent predictors. When patients were classified as low- or high-risk according to these 4 parameters, the NPV was 95.9% among patients in whom all 4 parameters were low risk. Only 28 of 1,438 patients were classified as false negatives in the study cohort, and the

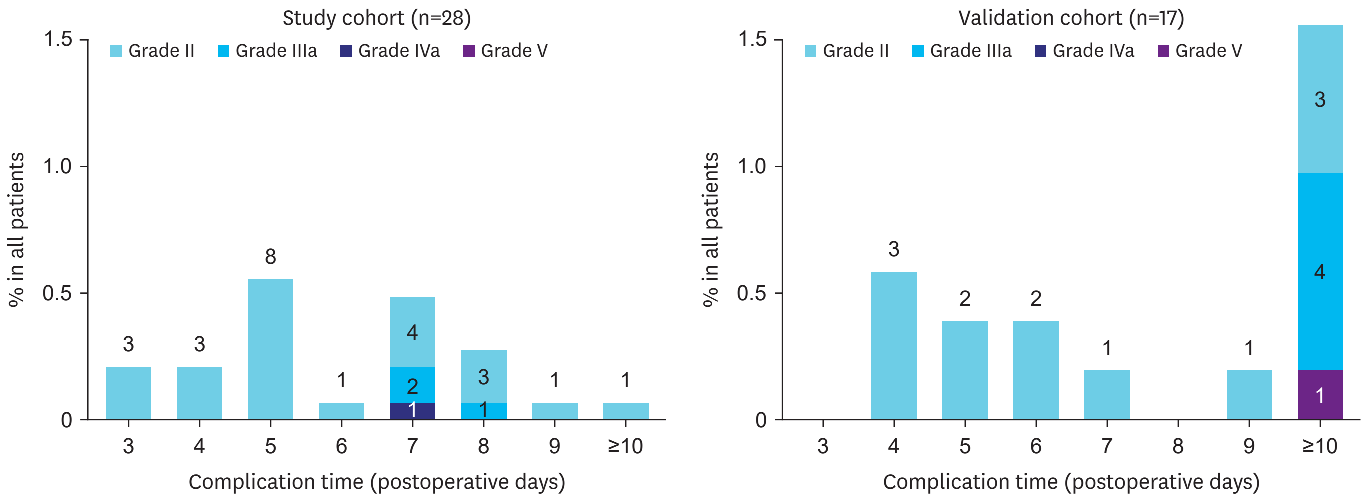

Fig. 3. Timing and grade of delayed complications among false negative patients in the study and validation cohorts.

proposed algorithm demonstrated consistent results across different patient subgroups. In the external validation dataset, the NPV was 93.7%.

Our goal was to develop a simple algorithm consisting of routine follow-up parameters obtained on POD 3 that could be used to predict whether complications requiring treatment would arise within the first postoperative month. A previous study employed a similar approach to predict complications and make safe discharge decisions using the parameters of age, approach, presence of combined resection, POD 5-to-preoperative white blood cell ratio, CRP level on POD 5, and body temperature on POD 4 [18]. For the previous algorithm, the sensitivity was 96.7% and the NPV was 75.5%, which were higher and lower, respectively, than the values obtained in the present study. Another previous study used a 7-parameter nomogram to predict severe postoperative complications among patients who underwent gastrectomy, which included sex, body temperature, amount of oral intake and ambulatory duration on POD 4, pain score, and proportion of neutrophils and defecation status on POD 5 [17]. The NPV was 95.7% for the development dataset and 91.6% for the validation dataset. Although both algorithms appear to be useful and effective, predicting complications on POD 5 has a low value for clinical application, and the algorithms employ too many parameters to be routinely used in daily clinical practice. In addition, a study that examined only procalcitonin measured on POD 3 had a 97.6% NPV and 75% sensitivity in ruling out intra-abdominal infections after gastric cancer surgery [14]. Although procalcitonin is a useful marker for diagnosing bacterial and fungal infections, its lower validity for predicting non-infective complications restricts its use as a safe discharge marker.

We found that body temperature, pulse rate, CRP level, and neutrophil count were independent predictors of delayed postoperative complications. All 4 parameters are related to systemic inflammatory response and may reflect different aspects of this response. However, higher levels of these variables are often observed in the very early PODs in patients without complications. Previous studies have sought to determine differences in postoperative parameters between patients with and without complications. CRP on POD 3 and POD 4 show the highest diagnostic accuracy [13,24,25]. Thus, we arbitrarily chose POD 3 during the hypothesis development phase because this day is after the point after which values are initially high during the early postoperative period, but are early enough to reduce

https://doi.org/10.5230/jgc.2022.22.e32

Journal of Gastric Cancer

the length of hospital stay and its associated cost. Vital signs such as body temperature, pulse rate, and markers reflecting the inflammatory response have been frequently investigated [3,11,26,27]. The present study shows that all 4 independent parameters can be used alone based on the NPV. However, combinations of 3 or 4 parameters increased the algorithm sensitivity and decreased the number of false negative results. It should be kept in mind that the purpose of the proposed algorithm is to predict patients who will not have delayed complications; therefore, all performance metrics should be interpreted in this context.

The oral intake status and the general condition of the patient were not included in the algorithm because both are mandatory components for safe early discharge, and they were not used as exclusion criteria because both are signs of complications. It is difficult to evaluate the effect of these 2 parameters on the safe early discharge decision in a retrospective study; however, oral intake status, general condition, and even the patient's willingness to be discharged should be considered prerequisites for applying the proposed safe early discharge criteria.

The outcome measure in the present study was grade II or higher on POD 3. It would also be possible to use grade III or higher (i.e., major) complications. However, because all grade II complications may require specific treatment, such as intravenous antibiotics or parenteral nutrition, we used delayed grade II or higher complications as an outcome measure because they captured all possible unplanned readmissions to the hospital. Our study showed that most patients who were classified as false negative were readmitted to the hospital a week after discharge, largely due to grade II complications. This finding can be used to improve the standardization of home care and to implement closer follow-up programs in the first week for patients who are discharged early.

When developing algorithms for decision-making, care should be taken when selecting cut-off values. We chose cut-offs that maximized the sum of the sensitivity and specificity. The selected optimal cut-off values for temperature and pulse rate were 38°C and 90/min, respectively, which are the same as those used to define systemic inflammatory response syndrome [28]. However, there are several published thresholds for laboratory values of CRP [16]. We identified 110 mg/L as the threshold value for CRP, which is slightly below the cut-off values described in previous studies, possibly because of the high proportion of patients in our cohort who underwent minimally invasive surgery. Therefore, additional thresholds should be examined in future studies.

The main limitation of the present study is its retrospective design. Although we used a prospective, well-organized database, our study was designed based on the hypothetical assumption that the patients were discharged on POD 3. However, the median length of hospital stay was actually 6 (5–7) days. Therefore, we used detailed complication data to reduce the likelihood of potential misinterpretation. Another limitation is that the data reflected the outcomes of a single experienced surgeon from a tertiary, high-volume center. Some site-specific characteristics, including a high proportion of patients with early gastric cancer and frequent use of minimally invasive surgery, may limit the generalizability of the findings. In addition, because of the known relationship between the prevalence of the outcome and NPV/PPV, some performance metrics should be cautiously evaluated. Although we examined the success of the proposed algorithm using an external validation dataset, further validation of this algorithm in centers with distinct patient populations and other characteristics is critically important. The presented algorithm has been shown to have varying performances in patient subgroups. To avoid reducing the simplicity of the decision-making process, separate pathways have not been tested for each subgroup but may be considered for different subgroups in future studies.

In conclusion, simple clinical and laboratory parameters, including CRP, body temperature, pulse rate, and neutrophil count obtained on POD 3 can be used in the decision-making process for safe early discharge of post-gastrectomy patients with gastric cancer. The combination of these 4 parameters yielded an NPV of 95.9% in the study dataset and 93.7% in the validation dataset.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Performance metrics of individual and combined versions of postoperative day 3 parameters for the study cohort (n=1,438, complication rate 9.9%)

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Supplementary Fig. 1

Daily changes in postoperative parameters according to complication status. Points represent median values and error bars represent 1st–3rd quartiles. Because some parameters are not routinely checked on postoperative day 2, these are blank for some parameters.

Click here to view

Supplementary Fig. 2

Receiver operating characteristic curves of postoperative day 3 parameters for delayed grade II or higher complications. The numbers in parentheses represent the area under the curve values for each parameter.

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