


# Perioperative Use of Glucocorticoids and Intraoperative Hypotension May Affect the Incidence of Postoperative Infection in Patients with Gastric Cancer: A Retrospective Cohort Study

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**Background:** In patients undergoing surgical resection for gastric cancer, postoperative complications—in particular, postoperative infections—remain an important problem and can result in delayed recovery and increased postoperative mortality.

**Objective:** To investigate the association between perioperative anesthesia management and postoperative infectious complications in patients undergoing resection for gastric cancer.

**Design:** Retrospective cohort study.

**Setting:** A single-center study performed from April 1, 2015, to June 30, 2018, at Peking University Cancer Hospital.

**Patients:** Patients who underwent resection for gastric cancer.

**Main Outcome Measures:** Demographic information, perioperative data (including anesthesia-related data, surgery-related data, and cancer diagnosis), and information on postoperative recovery were recorded. The primary outcome was incidence of postoperative infection; the secondary outcome was length of hospital stay. The associations between perioperative factors and postoperative infectious complications were analyzed using multi-variable logistic regression models and the classification tree method.

**Results:** A total of 880 patients were included in the study; of these, 111 (12.6%) had postoperative infectious complications during hospitalization, including 78 surgical site infections and 62 remote infections. After correction for confounding factors on logistic multivariable analysis, perioperative use of glucocorticoids was associated with a lower incidence of postoperative infection (hazard ratio 0.968, 95% confidence interval 0.939 to 0.997,  $P=0.029$ ), and intraoperative systolic blood pressure  $<90$  mmHg for  $>10$  min was associated with a higher incidence of postoperative infection (hazard ratio 2.112, 95% confidence interval 1.174 to 3.801,  $P=0.013$ ). In addition, older age, preoperative hypoproteinemia, and total gastrectomy were identified as independent predictors of postoperative infection.

**Conclusion:** For patients with gastric cancer, perioperative use of glucocorticoids and avoiding intraoperative hypotension may decrease the incidence of postoperative infectious complications.

**Keywords:** gastric cancer, surgery, glucocorticoids, hypotension, infection

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## Introduction

Gastric cancer remains one of the most deadly cancers.<sup>1</sup> According to the latest global cancer statistics, gastric cancer ranked as the fifth most frequently diagnosed and the third most fatal cancer.<sup>2</sup> At present, surgical resection accompanied by

systemic adjuvant chemotherapy is the only treatment approach associated with prolonged survival in patients with gastric cancer.<sup>3</sup> However, postoperative complications—in particular, postoperative infections—remain an important problem and can lead to delayed recovery and increased postoperative mortality.<sup>4,5</sup>

Prolonged operative duration,<sup>6</sup> older age,<sup>7</sup> use of total gastrectomy,<sup>8</sup> and body mass index  $\geq 30$  kg/m<sup>2</sup><sup>9</sup> are all known predictors of postoperative infectious complications. In recent years, it has been shown that perioperative anesthesia management may affect the occurrence of postoperative complications—in particular, infectious complications.<sup>10</sup> For instance, patients who received intravenous propofol anesthesia had a lower incidence of serious postoperative complications and faster asymptomatic recovery after esophageal surgery, compared with patients who received inhalational sevoflurane.<sup>11</sup> Another study found that, among 3081 patients who underwent total hip or knee replacement, general anesthesia was associated with a higher risk of surgical site infection, compared with general anesthesia combined with epidural or spinal anesthesia.<sup>12</sup> Furthermore, it has been shown that perioperative use of low-dose dexamethasone can reduce the incidence of postoperative infectious complications in patients with pancreatic cancer.<sup>13</sup>

Studies attempting to identify predictors of infection after gastrointestinal surgery have mainly focused on colorectal surgery, and scant research has been performed on gastric surgery—even more rarely on the association between anesthesia management and postoperative infectious complications after resection for gastric cancer.<sup>14,15</sup> As for the important role of anesthesia on patients' postoperative recovery,<sup>10–13</sup> this retrospective cohort study was designed to explore the relationship between perioperative anesthesia management and postoperative in-hospital infectious complications in patients who underwent resection for gastric cancer.

## Materials and Methods

This retrospective cohort study was approved by the Clinical Research Ethics Committee of Peking University Cancer Hospital, Beijing, China (approval no. 2018YJZ71, Jie Li, December 25, 2018). Our study was designed and conducted in accordance with the Helsinki declaration. As the study was purely observational, the Ethics Committee of Peking University Cancer Hospital waived the need for written informed patient consent; however, all patients or

their family members had provided oral consent to participate in this study before the collection of data.

## Participants

Potential participants were screened using the electronic medical record system of the hospital. Eligible patients underwent gastrectomy for gastric cancer at the First Department of Gastrointestinal Surgery, Peking University Cancer Hospital, from April 1, 2015, to June 30, 2018. Exclusion criteria included (1) reoperation for recurrence of gastric cancer, (2) clinical signs of infection before operation, (3) combined diseases requiring long-term glucocorticoid treatment (eg, rheumatoid arthritis, vasculitis, or systemic lupus erythematosus),<sup>16</sup> or (4) lack of key clinical data (eg, tumor stage, differentiation grade, or patient follow-up data).

## Anesthesia, Surgery, and Perioperative Management

All patients underwent general anesthesia with endotracheal intubation. Anesthesia was induced by intravenous anesthetics (propofol and/or etomidate) and opioids (fentanyl or sufentanil) and maintained with inhalational anesthetics (sevoflurane or isoflurane) and opioids (fentanyl, sufentanil, oxycodone, and/or dezocine). Low-dose glucocorticoids (dexamethasone or methylprednisolone) were administered at the discretion of the anesthesiologist to prevent postoperative nausea and vomiting.<sup>17,18</sup> The indications for administration of glucocorticoids were selected in accordance with the consensus guidelines for perioperative nausea and vomiting management.<sup>19</sup>

All patients received antibiotics (Cefuroxime sodium, 1.5 g per time) 30 mins before operation and when patients went back to the ward. Depending on the location of the tumor, total gastrectomy, proximal gastrectomy, distal gastrectomy, or palliative surgery was performed in accordance with the 2014 Japanese guidelines for the treatment of gastric cancer.<sup>20</sup> The method of reconstruction (Roux-en-Y esophagojejunostomy, gastroduodenostomy, gastrojejunostomy, or dual-channel reconstruction) was selected at the discretion of the operating surgeon.

Postoperative patient-controlled analgesia was provided for up to 3 days. Opioids were used for intravenous analgesia. Antiemetics (dexamethasone, 5-HT<sub>3</sub> receptor antagonist, and/or metoclopramide) were administered when considered necessary.<sup>21</sup> Other perioperative treatments were performed in accordance with routine practice.

## Perioperative Data Collection

Patient data were collected from the hospital's electronic medical record system. Baseline data included age, sex, height, weight, drinking and smoking history, preoperative comorbidities, preoperative laboratory test results, American Society of Anesthesiologists classification, and receipt of preoperative chemotherapy. Anesthesia-related data included anesthetic method, types and doses of anesthetics, intraoperative fluid infusion and blood transfusion, occurrence and duration of intraoperative hypotension (systolic blood pressure <90 mmHg for >10 min), postoperative analgesia, and perioperative receipt of glucocorticoids. Equivalent doses were calculated for glucocorticoids<sup>22</sup> and opioids.<sup>23–25</sup> Surgery-related data included duration and type of surgery (laparoscopic or open gastrectomy), surgical range (total, distal, or proximal gastrectomy or palliative resection), and estimated intraoperative blood loss. Tumor-related data and postoperative data included pathological diagnoses, degree of tumor differentiation, pathologic tumor-node-metastasis stage of gastric cancer, occurrence of postoperative infectious complications, and length of hospital stay.

## Outcomes

The primary outcome was the incidence of postoperative, in-hospital infection, which was defined as any clinical-related infection after gastrectomy and before first discharge. Each specific type of infection was diagnosed in accordance with clinical criteria, recorded in the patient's clinical history, and confirmed by two independent researchers. Surgical site infections and remote infections were included. The criteria used to define and classify surgical site infections (incision infection, ascites or abscess, and anastomotic fistula combined infection) were established in accordance with the guidelines of the American Committee of Disease Control.<sup>26–28</sup> Remote infections included respiratory tract infections, urinary tract infections, catheter-related infections, and primary bacteremia, in accordance with American National Healthcare Safety Network infection criteria.<sup>29</sup> The secondary outcome was the length of the hospital stay.

## Data Analysis

Continuous data were compared using Student's *t*-test (normal distribution) or the Mann–Whitney *U*-test (non-normal distribution); categorical data were analyzed using the  $\chi^2$  test. Missing data were not replaced. Univariable associations between baseline or perioperative variables and postoperative infection were assessed using logistic

regression models. Variables with  $P < 0.20$  on univariable analyses were included in multivariable models to assess the adjusted association between perioperative anesthesia management and postoperative infection.

We also built a model using a classification tree method. A classification tree is a nonlinear discrimination method that uses a set of independent variables to split a sample into progressively smaller subgroups. The procedure, iterative at each branch of the tree selects the independent variable that has the strongest association with the dependent variable according to a specific criterion.<sup>30</sup> In our analysis, the target variable was the postoperative infection rate. The analysis begins with the root node, which contains all the observations in the sample; then the computer program for the classification tree will select another node based on the database, and each node depicted in the classification tree can then be expressed in terms of an “if-then” rule. An individual moves through the tree in the direction determined by the answer to a question at each branch, and the infection rate changes accordingly in order to illustrate the association between the selected independent variables and the dependent variable more clearly.<sup>31</sup>

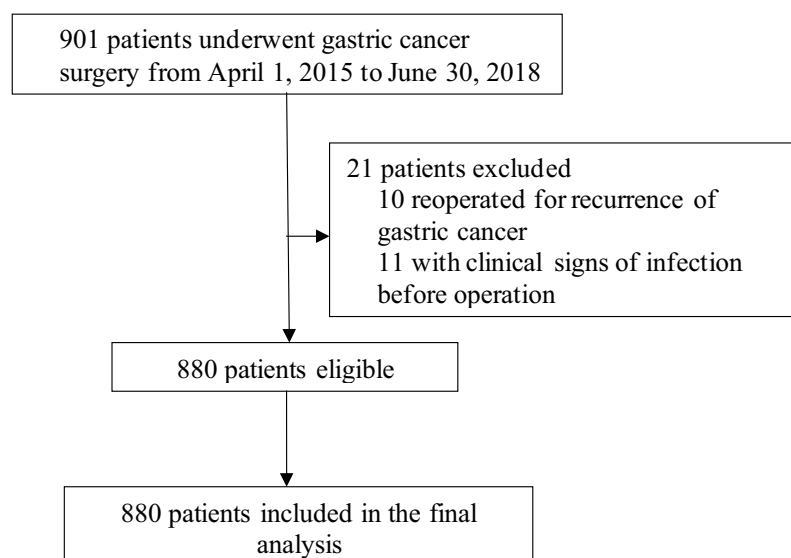
Statistical analyses were performed using SPSS 25.0 software (IBM SPSS, Chicago, IL) and the rpart package of R (<http://www.r-project.org>). Two-sided  $P < 0.05$  was considered to indicate statistical significance.

## Results

A total of 901 patients underwent surgery for gastric cancer between April 1, 2015, and June 30, 2018. Of these, 21 were excluded after data review, including 10 who underwent reoperations for recurrence of gastric cancer and 11 with clinical signs of infection before operation. In total, 880 patients were enrolled and were ultimately considered in the final analysis (Figure 1).

## Baseline and Perioperative Data

Of the 880 patients included in the analysis, 111 (12.6%) had postoperative infections—78 infections (8.9%) were surgical site infections (14 surgical wound infections, 59 peritoneal effusions or abscess, and 10 anastomotic fistula infections) and 62 (7.0%) were remote infections (46 respiratory tract infections, 7 urinary tract infections, 15 catheter-related infections, and 11 primary bacteremia) (Table 1). Compared with patients without infection, patients with postoperative infection were older ( $P = 0.002$ ); more likely to have preoperative arrhythmia ( $P = 0.026$ ), have preoperative hypoproteinemia (albumin <35 g/L) ( $P = 0.003$ ), have intraoperative hypotension



**Figure 1** Study flow chart.

(systolic blood pressure <90 mmHg for >10 min) ( $P=0.004$ ), and undergo total gastrectomy ( $P=0.000$ ); and less likely to receive perioperative glucocorticoids ( $P=0.002$ ). Furthermore, patients with postoperative infection had longer operation duration ( $P=0.001$ ) and longer length of hospital stay ( $P=0.000$ ). Other factors analyzed were not statistically significantly different between the two groups (Table 2, Supplemental Tables 1 and 2).

## Univariable Analysis of Risk Factors for Postoperative Infection

Univariable analysis identified 12 factors that may be related to postoperative infection during hospitalization ( $P<0.20$ ), including age, sex, history of coronary heart disease, history of hypertension, history of arrhythmia, preoperative hypoproteinemia, surgical resection range, operative duration, estimated intraoperative blood loss, intraoperative crystalloids infusion, dose of perioperative glucocorticoids, and intraoperative systolic blood pressure <90 mmHg for >10 min (Table 3). There was no collinearity among the above factors.

## Multivariable Analysis of Risk Factors for Postoperative Infection

After correction for confounding factors by logistic multivariable analysis, perioperative use of glucocorticoids was associated with a lower incidence of postoperative infection (hazard ratio 0.968, 95% confidence interval 0.939 to 0.997,  $P=0.029$ ), and intraoperative systolic blood pressure <90 mmHg for >10 min was associated with a higher

incidence of postoperative infection (hazard ratio 2.112, 95% confidence interval 1.174 to 3.801,  $P=0.013$ ). Among the other factors, older age, preoperative hypoproteinemia, and total gastrectomy were independent predictors of postoperative infection (Table 3).

**Table 1** Infection Sites of Postoperative, in-Hospital Infections (N=880)

Infection Site	No. (%)
Total infections	111 (12.6)
Surgical site infection <sup>a</sup>	78 (8.9)
Surgical wound infection	14 (1.6)
Ascites or abscess	59 (6.7)
Anastomotic fistula combined infection	10 (1.1)
Remote infection <sup>b</sup>	62 (7.0)
Respiratory tract infection <sup>c</sup>	46 (5.2)
Urinary tract infection <sup>d</sup>	7 (0.8)
Catheter-related infection <sup>e</sup>	15 (1.7)
Primary bacteremia <sup>f</sup>	11 (1.3)

**Notes:** <sup>a</sup>According to the guidelines of the Committee of Disease Control.<sup>16–18</sup>

<sup>b</sup>According to the National Healthcare Safety Network infection criteria.<sup>19</sup>

<sup>c</sup>Defined as new infiltration on chest X-ray, fever and cough, leukopenia <4000 cells/mm<sup>3</sup>, or leukocytosis >12,000 cells/mm<sup>3</sup>. <sup>d</sup>Defined as fever (>38°C), no other causes, urgency, frequent urination, dysuria, suprapubic tenderness, 10<sup>5</sup> CFU/mL bacteria in urine culture, or urinary tract infection diagnosed by a physician.

<sup>e</sup>Defined as 1 case of positive blood culture, identification of pathogens in the catheter, and no pathogen infection detected in the blood culture except the catheter.

<sup>f</sup>Defined as fever (>38°C), no other causes, hypotension (systolic blood pressure <90 mmHg) or oliguria (<20 mL/h), and diagnosis of sepsis by a physician regardless of blood culture results.

**Table 2** Baseline and Perioperative Variables

Variables	All Patients (n=880)	Any Infection (n=111)	No Infection (n=769)	P value
Age, years	58.9 ± 10.7	61.8 ± 10.8	58.5 ± 10.6	<b>0.002</b>
Male sex	653 (73.4)	88 (79.3)	565 (73.5)	0.191
Body mass index, kg/m <sup>2</sup>	23.5 ± 3.1	23.5 ± 3.3	23.5 ± 3.1	0.947
Smoking history	404 (45.9)	56 (50.5)	348 (45.3)	0.304
Drinking history	274 (31.1)	31 (27.9)	243 (31.6)	0.453
Preoperative comorbidities				
Previous stroke	39 (4.4)	6 (5.4)	33 (4.3)	0.594
Coronary heart disease	50 (5.7)	10 (9.0)	40 (5.2)	0.105
Hypertension	241 (27.4)	37 (33.3)	204 (26.5)	0.133
Arrhythmia	21 (2.4)	6 (5.4)	15 (2.0)	<b>0.026</b>
COPD <sup>a</sup>	25 (2.8)	0 (0.0)	25 (3.3)	0.054
Diabetes	102 (11.6)	9 (8.1)	93 (12.1)	0.220
Renal dysfunction <sup>b</sup>	13 (1.5)	1 (0.9)	12 (1.6)	>0.999
Hepatic dysfunction <sup>c</sup>	31 (3.5)	6 (5.4)	25 (3.3)	0.266
ASA grade				0.805
I	56 (6.4)	8 (7.2)	48 (6.2)	
II	770 (87.5)	95 (85.6)	675 (87.8)	
III	54 (6.1)	8 (7.2)	46 (6.0)	
Preoperative lab test				
Preoperative WBC count >10×10 <sup>9</sup> /L	126 (14.3)	13 (11.7)	113 (14.7)	0.402
Preoperative albumin <35 g/L	49 (5.6)	13 (11.7)	36 (4.7)	<b>0.003</b>
Preoperative anemia <sup>d</sup>	5 (0.6)	0 (0.0)	5 (0.7)	0.395
Preoperative chemotherapy	338 (38.4)	36 (32.4)	302 (39.3)	0.166
Pathological diagnosis				0.229
Adenocarcinoma	781 (88.8)	97 (87.4)	684 (88.9)	
Signet-ring cell carcinoma	43 (4.9)	2 (1.8)	41 (5.3)	
Adenocarcinoma combined signet-ring cell carcinoma	22 (2.5)	3 (2.7)	19 (2.5)	
Neuroendocrine tumor	24 (2.7)	8 (7.2)	16 (2.1)	
Lymphoid stromal carcinoma	1 (0.1)	0 (0.0)	1 (0.1)	
Melanoma	2 (0.2)	1 (0.9)	1 (0.1)	
Squamous cell carcinoma	7 (0.8)	0 (0.0)	7 (0.9)	
pTNM stage <sup>e</sup>				0.511
IA	224 (25.5)	21 (18.9)	203 (26.4)	
IB	97 (11.0)	13 (11.7)	84 (10.9)	
IIA	121 (13.8)	20 (18.0)	101 (13.1)	
IIB	117 (13.3)	17 (15.3)	100 (13.0)	
III	290 (33.0)	36 (32.4)	254 (33.0)	
IV	31 (3.5)	4 (3.6)	27 (3.5)	
Differentiation grade				0.800
NA	19 (2.2)	2 (1.8)	17 (2.2)	
Low	406 (46.1)	47 (42.3)	359 (46.7)	
Moderate	429 (48.8)	59 (53.2)	370 (48.1)	
High	26 (3.0)	3 (2.7)	23 (3.0)	

(Continued)

**Table 2** (Continued).

Variables	All Patients (n=880)	Any Infection (n=111)	No Infection (n=769)	P value
Range of gastrectomy				<b>0.000</b>
Total gastrectomy	385 (43.8)	72 (64.9)	313 (40.7)	
Distal gastrectomy	446 (50.7)	31 (27.9)	415 (54.0)	
Proximal gastrectomy	34 (3.9)	6 (5.4)	28 (3.6)	
Palliative resection	15 (1.7)	2 (1.8)	13 (1.7)	
Type of procedure				0.279
Laparoscopic gastrectomy	244 (27.7)	26 (23.4)	218 (28.3)	
Open gastrectomy	636 (72.3)	85 (76.6)	551 (71.7)	
Duration of surgery, min	215 (180 to 255)	235 (193 to 282)	213 (180 to 250)	<b>0.001</b>
Type of anesthesia				0.370
Inhalation anesthesia	193 (21.9)	28 (25.2)	165 (21.5)	
Balance anesthesia	687 (78.1)	83 (74.8)	604 (78.5)	
Intravenous anesthetics				
Propofol	686 (78.0)	80 (72.1)	606 (78.8)	0.113
Etomidate	674 (76.6)	78 (70.3)	596 (77.5)	0.095
Inhalational anesthetics				
Sevoflurane	822 (93.4)	101 (91.0)	721 (93.8)	0.272
Isoflurane	58 (6.6)	10 (9.0)	48 (6.2)	
Estimated blood loss, mL	100 (58 to 150)	100 (80 to 200)	100 (56 to 150)	0.080
Intraoperative fluid				
Crystalloids, mL	1600 (1200 to 1800)	1600 (1200 to 1925)	1600 (1200 to 1750)	0.100
Artificial colloid, mL <sup>f,g</sup>	1000 (500 to 1000)	1000 (500 to 1000)	1000 (500 to 1000)	0.955
Blood transfusion	12 (1.4)	3 (2.7)	9 (1.2)	0.193
Volume transfused, mL <sup>f</sup>	600 (400 to 800)	600 (500 to 700)	600 (400 to 800)	>0.999
Perioperative medication				
Opioids <sup>h</sup>	880 (100)	111 (100)	769 (100)	>0.999
Sufentanil equivalent, µg <sup>i</sup>	255 (120 to 320)	255 (85 to 320)	270 (140 to 320)	0.093
Glucocorticoids <sup>j</sup>	777 (88.3)	91 (82.0)	686 (89.2)	<b>0.027</b>
DXM equivalent, mg <sup>f,k</sup>	15 (10 to 20)	10 (5 to 20)	15 (10 to 20)	<b>0.002</b>
SBP <90 mmHg for >10 min	92 (10.5)	21 (18.9)	71 (9.2)	<b>0.004</b>
Length of hospital stay, days	13.8 ± 9.9	24.7 ± 18.3	12.2 ± 6.7	<b>0.000</b>

**Notes:** Results are presented as no. (%), median (interquartile range), or mean ± SD. P values in bold indicate statistical significance (P<0.05). <sup>a</sup>Includes COPD (chronic bronchitis and emphysema), asthma, and old tuberculosis. <sup>b</sup>Serum creatinine level >133 µmol/L. <sup>c</sup>Alanine transaminase, aspartate transaminase, and/or total bilirubin 2 times the upper limit of normal. <sup>d</sup>For adult men, hemoglobin <120 g/L; for adult women, hemoglobin <110 g/L. <sup>e</sup>According to the American Joint Committee on Cancer 8th Edition Cancer Staging System. <sup>f</sup>Results of patients who received the medication. <sup>g</sup>Includes hydroxyethyl starch 130/0.4, hydroxyethyl starch 200/0.5, and succinylated gelatin. <sup>h</sup>Includes sufentanil, fentanyl, oxycodone, morphine, and dezocine. <sup>i</sup>1 mg of morphine (iv) = 15 µg of fentanyl = 1.5 µg of sufentanil = 1 mg of oxycodone = 1 mg of dezocine. <sup>j</sup>Includes methylprednisolone and dexamethasone. <sup>k</sup>1 mg of methylprednisolone = 0.2 mg of dexamethasone. <sup>18</sup>

**Abbreviations:** ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; DXM, dexamethasone; pTNM, pathologic tumor-node-metastasis; SBP, systolic blood pressure; WBC, white blood cell.

## Classification Tree

We also used a classification tree to further illustrate the effect of the five independent predictors on postoperative infectious complications. As shown in [Figure 2](#), four of the five factors were selected by the computer program for the classification tree: age, range of gastrectomy, dexamethasone equivalent, and

presence of intraoperative hypotension. Beginning with the root node, the infection rate for all patients in the cohort was 13%. The first node depicted was age, with an infection rate of 42% for patients aged ≥77 years and 12% for patients aged <77 years. For patients aged ≥77 years, if the dose of perioperative dexamethasone equivalent was ≥11 mg, the rate of infection



**Table 3** Risk Factors for Early Postoperative Infection After Elective Gastric Cancer Surgery: Univariable and Multivariable Logistic Regression Analyses

Variable	Univariable Analysis		Multivariable Analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Age, years	1.032 (1.011 to 1.053)	<b>0.002</b>	1.027 (1.004 to 1.050)	<b>0.020</b>
Male sex	1.381 (0.850 to 2.246)	<b>0.193</b>	1.177 (0.703 to 1.970)	0.536
Body mass index $\geq 30$ , kg/m <sup>2</sup>	0.943 (0.278 to 3.204)	0.925	1.210 (0.344 to 4.253)	0.767
Smoking history	1.232 (0.827 to 1.834)	0.305		
Drinking history	0.927 (0.600 to 1.431)	0.732		
History of stroke	1.274 (0.521 to 3.115)	0.595		
Coronary heart disease	1.804 (0.875 to 3.720)	<b>0.110</b>	1.725 (0.795 to 3.745)	0.168
Hypertension	1.385 (0.905 to 2.120)	<b>0.134</b>	1.373 (0.864 to 2.183)	0.180
Arrhythmia	2.872 (1.090 to 7.566)	<b>0.033</b>	1.792 (0.612 to 5.252)	0.287
Diabetes	0.641 (0.314 to 1.311)	0.223	0.643 (0.319 to 1.294)	0.215
Hepatic dysfunction	1.701 (0.682 to 4.242)	0.255		
Renal dysfunction	0.573 (0.074 to 4.454)	0.595		
COPD <sup>a</sup>	0	0.998		
ASA grade (III vs I and II)	1.021 (0.582 to 1.793)	0.942		
Preoperative WBC count $>10 \times 10^9/L$	0.770 (0.418 to 1.420)	0.403		
Preoperative albumin $<35$ g/L	2.701 (1.384 to 5.270)	<b>0.004</b>	2.392 (1.163 to 4.920)	<b>0.018</b>
Preoperative anemia <sup>b</sup>	0	0.999		
Preoperative chemotherapy	0.767 (0.502 to 1.171)	0.220		
Pathological diagnosis (adenocarcinoma vs others) <sup>c</sup>	0.829 (0.474 to 1.453)	0.513		
pTNM (IIB, III, IV vs IA, IB, IIA) <sup>d</sup>	1.037 (0.670 to 1.544)	0.858		
Differentiation grade (low or NA vs moderate or high)	0.826 (0.553 to 1.233)	0.350		
Range of gastrectomy (total vs distal or proximal gastrectomy)	2.545 (1.683 to 3.847)	<b>0.000</b>	2.227 (1.443 to 3.437)	<b>0.000</b>
Type of procedure (laparoscopic vs open gastrectomy)	0.773 (0.485 to 1.233)	0.280		
Duration of surgery	1.006 (1.003 to 1.009)	<b>0.000</b>	1.003 (1.000 to 1.007)	0.056
Type of anesthesia (balance vs inhalation anesthesia)	0.810 (0.510 to 1.285)	0.370		
Use of propofol	0.816 (0.514 to 1.295)	0.388		
Use of etomidate	0.801 (0.510 to 1.259)	0.336		
Inhalational anesthetics (isoflurane vs sevoflurane)	1.487 (0.729 to 3.032)	0.275		
Sufentanil equivalent ( $<255$ ug vs $\geq 255$ ug) <sup>e</sup>	0.999 (0.997 to 1.001)	0.212		
Estimated blood loss	1.001 (0.999 to 1.002)	<b>0.140</b>	1.000 (0.999 to 1.001)	0.607
Intraoperative blood transfusion <sup>f</sup>	2.346 (0.625 to 8.799)	0.206		
Intraoperative artificial colloid	1.000 (0.999 to 1.001)	0.941		
Intraoperative crystalloids	1.000 (1.000 to 1.001)	<b>0.041</b>	1.000 (1.000 to 1.001)	0.568
Perioperative glucocorticoids (DXM equivalent) <sup>g</sup>	0.971 (0.944 to 0.998)	<b>0.037</b>	0.968 (0.939 to 0.997)	<b>0.029</b>
SBP $<90$ mmHg for $>10$ min	1.818 (1.040 to 3.178)	<b>0.036</b>	2.112 (1.174 to 3.801)	<b>0.013</b>

**Notes:** P values in bold indicate  $P < 0.20$  on univariable analyses and  $P < 0.05$  on multivariable analyses. <sup>a</sup>Includes COPD (chronic bronchitis and emphysema), asthma, and old tuberculosis. <sup>b</sup>For adult men, hemoglobin  $<120$  g/L; for adult women, hemoglobin  $<110$  g/L. <sup>c</sup>Includes signet-ring cell carcinoma, adenocarcinoma combined signet-ring cell carcinoma, neuroendocrine tumor, lymphoid stromal carcinoma, melanoma, and squamous cell carcinoma. <sup>d</sup>According to the American Joint Committee on Cancer 8th Edition Cancer Staging System. <sup>e</sup>1 mg of morphine (iv) = 15  $\mu$ g of fentanyl = 1.5  $\mu$ g of sufentanil = 1 mg of oxycodone = 1 mg of dezocine. <sup>f</sup>Packed red blood cells were transfused. <sup>g</sup>Includes dexamethasone and methylprednisolone; 1 mg of methylprednisolone = 0.2 mg of dexamethasone. <sup>22</sup>

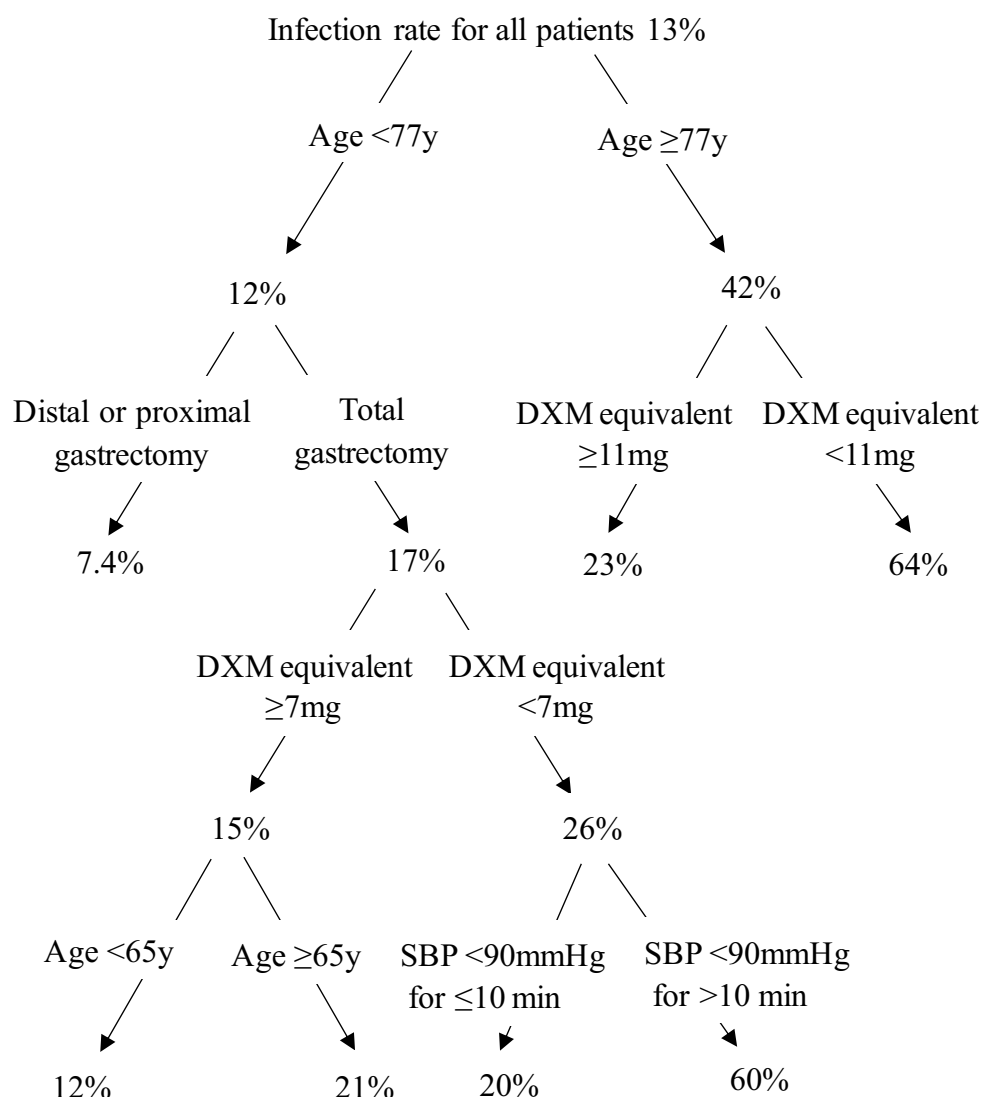
**Abbreviations:** ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; DXM, dexamethasone; NA, not available; pTNM, pathologic tumor-node-metastasis; SBP, systolic blood pressure; WBC, white blood cell.

decreased to 23%; if the dose of perioperative dexamethasone equivalent was  $<11$  mg, the rate of infection increased to 64%. For patients aged  $<77$  years, total gastrectomy, dexamethasone equivalent  $<7$  mg, and systolic blood pressure  $<90$  mmHg for  $>10$  min increased the infection rate, whereas distal or proximal gastrectomy, dexamethasone equivalent  $\geq 7$  mg, and

systolic blood pressure  $<90$  mmHg for  $\leq 10$  min decreased the infection rate.

## Discussion

In this retrospective study comprising 880 patients with gastric cancer, the incidence of postoperative infection was



**Figure 2** Study classification tree. Beginning with the root node, the infection rate for all patients in the cohort was 13%. The first node depicted was age, with an infection rate of 42% for age  $\geq 77$  y and 12% for age  $< 77$  y. For age  $\geq 77$  y, the rate of infection decreased to 23% when DXM equivalent  $\geq 11$  mg, and the rate of infection increased to 64% when DXM equivalent  $< 11$  mg. For age  $< 77$  y, total gastrectomy, dexamethasone equivalent  $< 7$  mg, and systolic blood pressure  $< 90$  mmHg for  $> 10$  min increased the infection rate, whereas distal or proximal gastrectomy, dexamethasone equivalent  $\geq 7$  mg, and systolic blood pressure  $< 90$  mmHg for  $\leq 10$  min decreased the infection rate.

consistent with rates in previous reports.<sup>6,32,33</sup> After correction for confounding factors by logistic multivariable analysis, perioperative use of glucocorticoids was associated with a lower incidence of infectious complications, and intraoperative systolic blood pressure  $< 90$  mmHg for  $> 10$  min was associated with a higher incidence of postoperative infectious complications.

Perioperative glucocorticoids are commonly used to prevent postoperative nausea and vomiting associated with general anesthesia.<sup>19</sup> However, the perioperative use of glucocorticoids has been a matter of controversy.<sup>34,35</sup> Concerns exist that the use of glucocorticoids may lead to peripheral insulin resistance, and postoperative

hyperglycemia may be a risk factor for postoperative infection.<sup>34</sup> However, these studies mainly focused on the long-term use of glucocorticoids,<sup>35,36</sup> and more-recent studies have observed favorable outcomes with the use of glucocorticoids even in long-term use cases.<sup>37</sup> For instance, a randomized controlled study from 2016 found that perioperative application of hydrocortisone for 3 days reduced the incidence of postoperative complications in patients undergoing pancreatoduodenectomy.<sup>37</sup> What is more, in a retrospective cohort study from 2018, patients undergoing resection for pancreatic cancer received a single antiemetic dose of dexamethasone during the perioperative period, which was associated with a lower incidence of postoperative



infectious complications.<sup>13</sup> In line with the previous studies, the present study found that perioperative use of an antiemetic dose of glucocorticoids was associated with a lower incidence of postoperative infections in patients who underwent gastrectomy. Similarly, a randomized controlled study including patients undergoing hepatectomy also found that a single dose of methylprednisolone before surgery reduced postoperative infectious and systemic complications and shortened the length of the hospital stay.<sup>38</sup>

The anti-inflammatory effect of glucocorticoids may be the mechanism responsible for reducing the incidence of postoperative infectious complications. Studies have confirmed that perioperative dexamethasone is associated with a lower rate of positive systemic inflammatory syndrome in patients after selective surgery for colorectal cancer.<sup>39</sup> C-reactive protein level has been proved to be a predictor of postoperative infectious complications,<sup>14,40</sup> and a recent study by Laaninen et al found that patients receiving hydrocortisone treatment had lower plasma C-reactive protein levels.<sup>37</sup> Another retrospective analysis based on propensity score matching in patients with colorectal cancer also found that the use of dexamethasone to prevent postoperative nausea and vomiting was associated with lower plasma C-reactive protein levels on postoperative day 3.<sup>39</sup>

Adequate blood pressure is required for suitable wound perfusion. Some studies have suggested that there is an important association between intraoperative hypotension and surgical site infections.<sup>15,41,42</sup> In the present study, we found that systolic blood pressure <90 mmHg for >10 min was associated with an increased incidence of infectious complications during hospitalization in patients who underwent surgical resection for gastric cancer. Similarly, another retrospective study including patients with colon cancer also found that intraoperative hypotension was an independent predictor of postoperative infections.<sup>43</sup> However, there may be some doubt about how intraoperative hypotension can influence postoperative infections, as the duration of intraoperative hypotension is usually short, owing to timely intervention by the anesthetist. Actually, Abdelmalak et al had shown that, although the duration of intraoperative hypotension was short, it was the lowest tissue oxygen saturation that was associated with severe complications, not time-weighted average oxygenation.<sup>44</sup> This is consistent with the findings from more-recent studies, which have observed that even transient hypotension during operation is associated with myocardial injury, acute kidney injury, and death.<sup>45,46</sup> A retrospective study including patients with colon cancer also found that postoperative time-weighted average arterial

pressure was not associated with postoperative surgical site infections, whereas lowest mean arterial pressure was.<sup>47</sup>

Regarding the definition of “intraoperative hypotension,” some studies use the absolute reduction of mean arterial pressure, others use the absolute reduction of systolic arterial pressure,<sup>48</sup> and still others use the proportion of reduction based on baseline blood pressure, such as the traditional 20% reduction.<sup>49</sup> The data on hypotension collected in the present study were based on the absolute decrease in systolic blood pressure. Some studies have shown that, at least for the relationship between hypotension and myocardial and renal injury, the absolute decrease in blood pressure and the decrease ratio of baseline values are both predictive of postoperative infections.<sup>50</sup>

Our other main findings—that preoperative albumin <35 g/L, older age and total gastrectomy were independent predictors of increased incidence of postoperative infection in patients who underwent radical resection for gastric cancer—are consistent with the findings of previous studies.<sup>7,8,51</sup> For instance, a retrospective study of 1798 patients who underwent gastrectomy for gastric adenocarcinoma found that prealbumin concentrations were useful predictors of short-term postoperative outcomes after gastrectomy.<sup>51</sup> Another randomized controlled trial involving 685 patients found that advanced age was identified as a risk factor for superficial incisional surgical site infections after gastrectomy.<sup>7</sup> A retrospective study of 407 patients also showed that total gastrectomy is an independent risk factor for organ/space SSI after gastric surgery.<sup>8</sup>

The limitations of our study include its retrospective design, which may have introduced selection bias, and its single-center nature, limiting the generalizability of the results. What is more, all cases received inhalational anesthesia and no case received combined epidural block during general anesthesia in our patients. This limited our ability to detect any effects of total intravenous anesthesia and epidural block on the outcome of gastric patients, as suggested by previous studies.<sup>11,12</sup> Finally, previous studies reported that body mass index  $\geq 30$  kg/m<sup>2</sup>, perioperative ventilator setting, inspiratory oxygenation fraction, temperature, blood transfusion and postoperative extubation/not extubation were also risk factors for postoperative infection,<sup>9,52–56</sup> but only 25 (2.8%) cases in our patients with body mass index  $\geq 30$  kg/m<sup>2</sup> and 12 (1.4%) cases received blood transfusion, and the present study did not collect data about perioperative ventilator setting, inspiratory oxygenation fraction, temperature, or postoperative extubation/not extubation, which also limited our ability to detect the effect of these factors on the outcome of gastric patients.

## Conclusions

For patients with gastric cancer, perioperative use of glucocorticoids and avoiding intraoperative hypotension may decrease the incidence of postoperative infectious complications. Considering the widespread perioperative use of glucocorticoids and the high incidence of intraoperative hypotension, prospective studies are urgently needed to clarify their effects on infections after gastric cancer surgery.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Disclosure

The authors report no conflicts of interest in this work.

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