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ORIGINAL RESEARCH

Intraoperative Diastolic Hypotension-Prolonged Postoperative Hospital Stay in Patients with Gastric Cancer: A Retrospective Cohort Study with Propensity Score Matching

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Purpose: In patients undergoing surgical resection for gastric cancer, perioperative hemodynamic fluctuations may affect organ perfusion, increase the incidence of postoperative complications, and prolong hospital stay.

Patients and Methods: We retrospectively identified patients who underwent resection for gastric cancer at our institution from April 1, 2015 to October 30, 2018. Demographic information, perioperative data, and information on postoperative recovery were recorded. The primary outcome was length of postoperative hospital stay; the secondary outcome was incidence of postoperative complications. Propensity score matching was performed. The associations between perioperative factors and postoperative hospital stay were analyzed using multivariable logistic regression models in the full and matched cohorts.

Results: In total, 933 patients were included; of these, 676 had diastolic hypotension (defined as diastolic blood pressure <60 mmHg for >10 min). In both cohorts, patients with diastolic hypotension had statistically significantly longer postoperative hospital stay (full: mean 14.5 ± standard deviation 10.2 vs 11.6 ± 6.5 days, P < 0.001; matched: 13.7 ± 9.9 vs 11.7 ± 6.6 days, P = 0.009) and a higher incidence of postoperative complications (full: 170 [25.1%] vs 27 [10.5%] cases, P < 0.001; matched: 60 [24.4%] vs 33 [13.4%] cases, P = 0.003), compared with patients without diastolic hypotension. After correction for confounding factors, intraoperative diastolic hypotension was associated with longer postoperative hospital stay in both the full and the matched cohort (full: HR, 1.535 [95% CI, 1.115–2.114], P = 0.009; matched: HR, 1.532 [95% CI, 1.032–2.273], P = 0.034).

Conclusion: For patients with gastric cancer, intraoperative diastolic hypotension may increase the incidence of postoperative complications and prolong postoperative hospital stay.

Keywords: gastric cancer, diastolic hypotension, postoperative complications, hospital stay

Introduction

Surgical resection remains the primary treatment for gastric cancer, one of the most common and lethal cancers worldwide.[1,2] The perioperative period is often accompanied by hemodynamic fluctuations, which can affect organ perfusion, increase the incidence of postoperative complications, and prolong postoperative hospital stay.[3,4]

Studies have shown that intraoperative hypotension can cause an imbalance between oxygen supply and demand and can increase the incidence of postoperative cardiovascular complications,[3,5] acute renal injury,[6,7] and other postoperative complications.[5] Blood pressure is a complex signal that varies considerably over time and includes several components, including diastolic, mean, systolic, and pulse pressures.[8,9] Studies have suggested that diastolic, mean, and systolic pressures from radial arterial catheters can be used comparably to predict perioperative myocardial and renal injury and other postoperative complications.[5] However, most recent studies on the impact of perioperative hemodynamic fluctuations on postoperative

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recovery have focused on systolic blood pressure (SBP) and mean arterial pressure (MAP), with few studies investigating the effect of diastolic blood pressure (DBP). For example, in a review that investigated the relationship between intraoperative hypotension and postoperative adverse outcomes after noncardiac surgery, of the 42 studies included, 29 (69%) used a definition of intraoperative hypotension that was based on an absolute MAP threshold, 17 (40%) used a definition that was based on an absolute SBP threshold, and no studies used a definition that was based on DBP.[10]

Therefore, based on the fact that DBP also plays an important role in organ perfusion,[11] the present study sought to explore the relationship between intraoperative diastolic hypotension and postoperative recovery after gastrectomy.

Methods

This study is a retrospective cohort study that included propensity score matching. The study protocol was approved by the clinical research ethics committee of Peking University Cancer Hospital (Approval No. 2018YJZ71). The study was designed and conducted in accordance with the Helsinki Declaration. As the study was observational, the ethics committee waived the requirement for written informed consent.

Participants

We used the hospital's electronic medical record to retrospectively identify patients who underwent resection for gastric cancer in the Department of Gastrointestinal Surgery at Peking University Cancer Hospital from April 1, 2015, to October 30, 2018. Exclusion criteria were reoperation for postoperative recurrence of gastric cancer and missing data (tumor stage, differentiation grade, patient follow-up information, etc.).

Anesthesia, Surgery, and Perioperative Management

All patients underwent general anesthesia with endotracheal intubation and received invasive arterial pressure monitoring. Anesthesia was induced by intravenous anesthetics (propofol and/or etomidate) and opioids (fentanyl or sufentanil). Inhalational anesthetics (sevoflurane or isoflurane) and opioids (fentanyl and/or sufentanil and/or oxycodone and/or dizocine and/or pentazocine and/or remifentanil) were used to maintain anesthesia. Some patients received combined epidural block (lidocaine and/or ropivacaine) or intravenous nonsteroidal anti-inflammatory drugs (NSAIDs; including flurbiprofen axetil and parecoxib) for supplemental analgesia during anesthesia maintenance. Glucocorticoids (dexamethasone or methylprednisolone) were given to some patients to prevent postoperative nausea and vomiting before induction of anesthesia and/or during postoperative analgesia, in accordance with the guidelines for postoperative nausea and vomiting management.[12] Vasoactive drugs were used in accordance with relevant guidelines.[13,14]

Some patients received tumor-related treatment, such as neoadjuvant chemotherapy, before their operation. Depending on the location of the tumor, total gastrectomy, proximal gastrectomy, distal gastrectomy, or palliative surgery alone was performed.[15] Reconstruction methods (Roux-en-Y esophagojejunostomy, gastroduodenostomy, gastrojejunostomy, or dual-channel reconstruction) and methods (in vitro or in vitro) were selected in accordance with the surgeon's preference.

Patients were given patient-controlled analgesia for 3 days postoperatively. Ropivacaine was used for epidural analgesia, and opioids were used for intravenous analgesia. Intravenous analgesia included dexamethasone, serotonin-3 receptor antagonist, and/or metoclopramide, at the anesthesiologist's discretion, to prevent postoperative nausea and vomiting.[12] Other perioperative treatments were performed in accordance with routine clinical practice. Patients were discharged when they were able to move independently and without surgery-related comorbidities.

Perioperative Data

We used the hospital's electronic medical record to collect the following data: basic preoperative data (sex, age, height, weight, smoking history, drinking history, combined preoperative diseases, preoperative laboratory results, American Society of Anesthesiologists [ASA] grade, and preoperative chemotherapy); anesthesia-related information (type of anesthesia, type and dose of anesthetic drugs, intraoperative blood transfusion and rehydration volume, occurrence and duration of intraoperative systolic or diastolic hypotension [as hypotension is defined as blood pressure below 90/60 mmHg, we defined systolic hypotension of 90 mmHg and diastolic hypotension of 60 mmHg], use of intraoperative vasoactive drugs, postoperative analgesia, and use of perioperative glucocorticoids, NSAIDs, and opioids [equivalent doses of perioperative glucocorticoids,[16] NSAIDs,[17] and opioids[18–20] were calculated]); operation-related information (type of procedure, range of gastrectomy, duration of surgery, and estimated intraoperative bleeding); tumor-related information and postoperative information (tumor pathological diagnosis, tumor differentiation, tumor pTNM stage, incidence of complications during hospitalization, and length of postoperative hospital stay).

Outcomes

The primary outcome was length of postoperative hospital stay (LOS), defined as the time from postoperative day 1 to the first discharge. The secondary outcome was incidence of postoperative complications, which were defined as new medical events that were harmful to the patient's recovery during the hospital stay and that required interventional therapy (ie, class II–V on the Clavien-Dindo classification[21]).

Data Analysis

To conduct the analyses, we divided the patients into two groups: those with intraoperative diastolic hypotension (defined in this study as DBP <60 mmHg for >10 min) and those without intraoperative diastolic hypotension (DBP >60 mmHg or DBP <60 mmHg for ≤10 min). Between-group differences in the baseline and intra- and postoperative variables used for propensity score matching were compared using the absolute standardized difference (ASD), which is defined as the absolute difference in means, mean ranks, or proportions, divided by the pooled standard deviation, and calculated using the formula published by Austin.[22] An ASD ≥0.109—that is, $1.96\times\sqrt{(n1+n2)/(n1\times n2)}$ was considered imbalanced between the two groups in the present study.

All baseline and intra- and postoperative variables for the two groups were used for propensity score matching. Baseline data included age, sex, body mass index, smoking history, drinking history, ASA classification, preoperative comorbidities, preoperative laboratory test results, preoperative chemotherapy, pathological diagnoses, pathological tumor-node-metastasis (pTNM) stage of gastric cancer, and degree of cancer differentiation. Intra- and postoperative data included type of procedure; range of gastrectomy; duration of surgery; type of anesthesia; type and dose of anesthetic drugs; estimated blood loss; intraoperative blood transfusion and rehydration volume; the use of intraoperative vasoactive drugs; equivalent doses of perioperative glucocorticoids, NSAIDs, and opioids; and the occurrence of SBP <90 mmHg for >10 min. Patients were matched in a 1:1 ratio using nearest-neighbor matching, with caliper widths equal to 0.2 of the standard deviation of the logit of the propensity score.

For both the full cohort and the matched cohort, continuous data (ie, length of postoperative hospital stay) were compared using Student's *t*-test (normal distribution) or the Mann–Whitney *U*-test (nonnormal distribution); categorical data (ie, postoperative complications) were analyzed using the χ^2 test. Missing data were not replaced. Univariable associations between baseline and perioperative variables and postoperative hospital stay were analyzed using logistic regression models. Variables with *P*<0.20 on univariable analysis and variables that were considered clinically important were included in the multivariable models to assess the adjusted association between diastolic hypotension and postoperative hospital stay.

Statistical analyses were performed using SPSS 25.0 software (IBM SPSS, Chicago, IL) and the free software package "R" (version 2.15.3), including the "Matchit" and "ROC" plug-ins. A two-sided *P*<0.05 was considered statistically significant.

Results

Patient Recruitment

From April 1, 2015, to October 30, 2018, a total of 943 patients underwent surgery for gastric cancer. After data review, 10 patients were excluded, including 8 who underwent reoperation for recurrence of gastric cancer and 2 for whom data were missing (1 was missing pathological cancer stage and 1 was missing tumor differentiation grade). The remaining 933 patients were included in the final analysis: 676 with diastolic hypotension, with a median (IQR) duration of DBP <60 mmHg for 45 (25–65) min, and 257 without diastolic hypotension. After propensity score matching, 246 patients remained in each group (Table 1, Figure 1).

Table 1 Baseline and Perioperative Data and the Results of Propensity Score Matching

Variable	All Patients (N=933)	Full Cohort (N=933)			Matched Cohort (N=492)		
		Diastolic Hypotension (n=676)	No Diastolic Hypotension (n=257)	ASD[a]	Diastolic Hypotension (n=246)	No Diastolic Hypotension (n=246)	ASD[a]
Age, years	59.18 ± 10.83	60.10 ± 10.78	56.75 ± 10.60	**0.310**	56.40 ± 12.00	57.02 ± 10.49	0.057
Male sex	685 (73.4)	508 (75.1)	177 (68.9)	**0.145**	171 (69.5)	169 (68.7)	0.019
Body mass index, kg/m^2	23.39 ± 3.21	23.36 ± 3.22	23.49 ± 3.19	0.041	23.60 ± 3.37	23.51 ± 3.21	0.028
Smoking history	416 (44.6)	311 (46.0)	105 (40.9)	0.103	112 (45.5)	103 (41.9)	0.073
Drinking history	282 (30.2)	209 (30.9)	73 (28.4)	0.054	73 (29.7)	70 (28.5)	0.026
Preoperative comorbidities							
Previous stroke	40 (4.3)	33 (4.9)	7 (2.7)	0.100	5 (2.0)	6 (2.4)	0.019
HBP	255 (27.3)	188 (27.8)	67 (26.1)	0.039	67 (27.2)	64 (26.0)	0.027
Coronary heart disease	53 (5.7)	37 (5.5)	16 (6.2)	0.033	12 (4.9)	16 (6.5)	0.071
COPD[b]	27 (2.9)	21 (3.1)	6 (2.3)	0.044	5 (2.0)	6 (2.4)	0.023
Diabetes	105 (11.3)	82 (12.1)	23 (8.9)	0.097	19 (7.7)	23 (9.3)	0.050
Renal dysfunction[c]	14 (1.5)	12 (1.8)	2 (0.8)	0.075	1 (0.4)	1 (0.4)	0.000
Hepatic dysfunction[d]	31 (3.3)	25 (1.0)	6 (2.3)	0.079	4 (1.6)	5 (2.0)	0.021
ASA grade				0.099			0.034
I	56 (6.0)	47 (7.0)	9 (3.5)		8 (3.3)	9 (3.7)	
II	823 (88.2)	590 (87.3)	233 (90.7)		223 (90.7)	224 (91.1)	
III	54 (5.8)	39 (5.8)	15 (5.8)		15 (6.1)	13 (5.3)	
Preoperative lab test							
Preoperative WBC count >10×10^9/L	126 (13.5)	98 (14.5)	28 (10.9)	0.102	29 (11.8)	28 (11.4)	0.012
Preoperative albumin <35 g/L	49 (5.3)	42 (6.2)	7 (2.7)	**0.144**	10 (4.1)	7 (2.8)	0.050
Preoperative anemia[e]	5 (0.5)	5 (0.7)	0 (0.0)	0.086	0 (0.0)	0 (0.0)	0.000
Preoperative chemotherapy	357 (38.3)	262 (38.8)	95 (37.0)	0.037	108 (43.9)	91 (37.0)	0.142
Pathological diagnosis				0.027			0.024
Adenocarcinoma	819 (87.8)	600 (88.8)	219 (85.2)		216 (87.8)	210 (85.4)	
Signet-ring cell carcinoma	46 (4.9)	28 (4.1)	18 (7.0)		12 (4.9)	17 (6.9)	
Adenocarcinoma combined signet-ring cell carcinoma	34 (3.6)	22 (3.3)	12 (4.7)		10 (4.1)	11 (4.5)	
Neuroendocrine tumor	24 (2.6)	18 (2.7)	6 (2.3)		5 (2.0)	6 (2.4)	
Lymphoid stromal carcinoma	1 (0.1)	1 (0.1)	0 (0.0)		1 (0.4)	0 (0.0)	
Melanoma	2 (0.2)	1 (0.1)	1 (0.1)		0 (0.0)	1 (0.4)	
Squamous cell carcinoma	7 (0.8)	6 (0.9)	1 (0.4)		2 (0.8)	1 (0.4)	
pTNM stage[f]				**0.176**			0.049
IA	232 (24.9)	152 (22.5)	80 (31.1)		72 (29.3)	74 (30.1)	
IB	101 (10.8)	78 (11.5)	23 (8.9)		32 (13.0)	22 (8.9)	
IIA	132 (14.1)	95 (14.1)	37 (14.4)		34 (13.8)	36 (14.6)	
IIB	123 (13.2)	89 (13.2)	34 (13.2)		33 (13.4)	32 (13.0)	
III	312 (33.4)	235 (34.8)	77 (30.0)		70 (28.5)	76 (30.9)	
IV	33 (3.5)	27 (4.0)	6 (2.3)		5 (2.0)	6 (2.4)	
Differentiation grade				0.042			0.026
NA	433 (46.4)	311 (46.0)	122 (47.5)		109 (44.3)	115 (46.7)	
Low	451 (48.3)	333 (49.3)	118 (45.9)		120 (48.8)	114 (46.3)	
Moderate	28 (3.0)	21 (3.1)	7 (2.7)		9 (3.7)	7 (2.8)	
High	21 (2.3)	11 (1.6)	10 (3.9)		8 (3.3)	10 (4.1)	
Range of gastrectomy				**0.149**			0.006
Total gastrectomy	423 (45.3)	326 (48.2)	97 (37.7)		105 (42.7)	95 (38.6)	
Distal gastrectomy	461 (49.4)	313 (46.3)	148 (57.6)		124 (50.4)	142 (57.7)	
Proximal gastrectomy	34 (3.6)	26 (3.8)	8 (3.1)		14 (5.7)	7 (2.8)	
Palliative resection	15 (1.6)	11 (1.6)	4 (1.6)		3 (1.2)	2 (0.8)	
Type of procedure				0.012			0.011
Laparoscopic surgery	254 (27.2)	153 (22.6)	101 (39.3)		64 (26.0)	95 (38.6)	
Open surgery	679 (72.8)	523 (77.4)	156 (60.7)		182 (74.0)	151 (61.4)	

(*Continued*)

Table 1 (Continued).

Variable	All Patients (N=933)	Full Cohort (N=933)			Matched Cohort (N=492)		
		Diastolic Hypotension (n=676)	No Diastolic Hypotension (n=257)	ASD[a]	Diastolic Hypotension (n=246)	No Diastolic Hypotension (n=246)	ASD[a]
Duration of surgery, min	215 (180–255)	220 (181–258)	205 (176–240)	**0.222**	210 (180–245)	205 (177–242)	0.034
Type of anesthesia				**0.157**			0.019
Inhalation anesthesia	205 (22.0)	161 (23.8)	44 (17.1)		45 (18.3)	43 (17.5)	
Balance anesthesia	728 (78.0)	515 (76.2)	213 (82.9)		201 (81.7)	203 (82.5)	
Intravenous anesthetics							
Propofol	727 (77.9)	516 (76.3)	211 (82.1)	**0.132**	199 (80.9)	201 (81.7)	0.063
Etomidate	707 (75.8)	498 (73.7)	209 (81.3)	**0.177**	185 (75.2)	199 (80.9)	0.058
Inhalational anesthetics				**0.109**			0.031
Sevoflurane	870 (93.2)	625 (92.5)	245 (95.3)		232 (94.3)	234 (95.1)	
Isoflurane	63 (6.8)	51 (7.5)	12 (4.7)		14 (5.7)	12 (4.9)	
Estimated blood loss, mL	100 (56–150)	100 (64–151)	100 (50–150)	0.102	100 (60–150)	100 (50–150)	0.013
Intraoperative fluid							
Crystalloids, mL	1600 (1200–1800)	1600 (1250–1850)	1600 (1200–1700)	**0.146**	1600 (1200–1750)	1600 (1200–1700)	0.067
Artificial colloid, mL[g,h]	1000 (500–1000)	1000 (500–1000)	1000 (500–1000)	0.020	1000 (500–1000)	1000 (500–1000)	0.038
Blood transfusion							
Volume transfused, mL[g]	600 (400–800)	600 (400–800)	1000 (400–1000)	0.026	600 (400–800)	600 (400–800)	0.053
Perioperative medication							
Opioids	933 (100.0)	676 (100.0)	257 (100.0)		246 (100.0)	246 (100.0)	
Sufentanil equivalent, μg[i,j]	270 (188–405)	263 (188–405)	297 (189–435)	0.102	287 (200–420)	293 (188–435)	0.012
Remifentanil	812 (87.0)	583 (86.2)	229 (89.1)	0.083	219 (89.0)	218 (88.6)	0.012
Glucocorticoids[k]							
DXM equivalent, mg[g,l]	11 (10–20)	11 (10–20)	15 (10–20)	**0.118**	11 (10–20)	15 (10–20)	0.050
NSAIDS[m]							
FA equivalent, mg[g,n]	100 (80–100)	100 (75–100)	100 (90–150)	0.081	100 (67–100)	100 (90–150)	0.030
Vasoactive drugs							
Nitroglycerin	561 (60.1)	390 (57.7)	171 (66.5)	0.003	164 (66.7)	163 (66.3)	0.037
Esmolol	784 (84.0)	564 (83.4)	220 (85.6)	0.031	212 (86.2)	210 (85.4)	0.005
Vasopressors[o]	166 (17.8)	138 (20.4)	28 (10.9)	**0.236**	32 (13.0)	28 (11.4)	0.040
SBP <90 mmHg for >10 min	94 (10.1)	81 (12.0)	13 (5.2)	**0.213**	17 (6.9)	13 (5.3)	0.050
Duration of DBP <60 mmHg, min	30 (10–55)	40 (25–65)	5 (0–5)	—	40 (20–55)	5 (0–5)	—

Notes: Data are presented as median (interquartile range) or no. (%). ASDs in bold indicate those ≥0.109. [a]An ASD ≥0.109 was considered unbalanced.[22] [b]Includes chronic bronchitis and emphysema. [c]Serum creatinine >133μmol/L. [d]Alanine transaminase, aspartate transaminase and/or total bilirubin 2 times higher than the upper normal limit. [e]For adult men, hemoglobin <120 g/L; for adult women, hemoglobin <110 g/L. [f]According to the 8th Edition of the American Joint Committee on Cancer/Union for International Cancer Control Staging System. [g]Results for patients who received the medication. [h]Includes hydroxyethyl starch 130/0.4, hydroxyethyl starch 200/0.5, and succinylated gelatin. [i]Includes morphine, fentanyl, sufentanil, oxycodone, and dezocine. [j]1 mg of morphine (iv) = 15 μg of fentanyl = 1.5 μg of sufentanil = 1 mg of oxycodone = 1 mg of dezocine.[18–20] [k]Includes methylprednisolone and dexamethasone. [l]1 mg of methylprednisolone = 0.2 mg of dexamethasone.[16] [m]Includes flurbiprofen axetil and parecoxib sodium. [n]40 mg of parecoxib sodium = 50 mg of flurbiprofen axetil.[17] [o]Includes ephedrine, norepinephrine, and norepinephrine.

Abbreviations: ASA, American Society of Anesthesiologists; ASD, absolute standardized difference; CA, cancer antigen; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; DXM, dexamethasone; FA, flurbiprofen axetil; HBP, high blood pressure; NA, not available; NSAID, nonsteroidal anti-inflammatory drug; pTNM, pathological tumor-node-metastasis; SBP, systolic blood pressure; WBC, white blood cell.

Baseline and Perioperative Data

In the full cohort, patients with diastolic hypotension were older, more likely to be male, and had higher pTNM stage, compared with patients without diastolic hypotension. The following variables were also more frequent among patients with diastolic hypotension: hypoproteinemia (albumin <35 g/L), total gastrectomy, receipt of inhalation anesthesia and inhalational isoflurane, receipt of vasopressors, and intraoperative SBP <90 mmHg for >10 min. In addition, patients with diastolic hypotension were less likely to receive propofol/etoposide and received a lower median volume of intraoperative blood transfusion, a lower median dose of perioperative glucocorticoids, and a higher median volume of intraoperative crystalloids. After propensity score matching, there were no statistically significant differences between the two groups (Table 1; Supplement Tables 1–3).

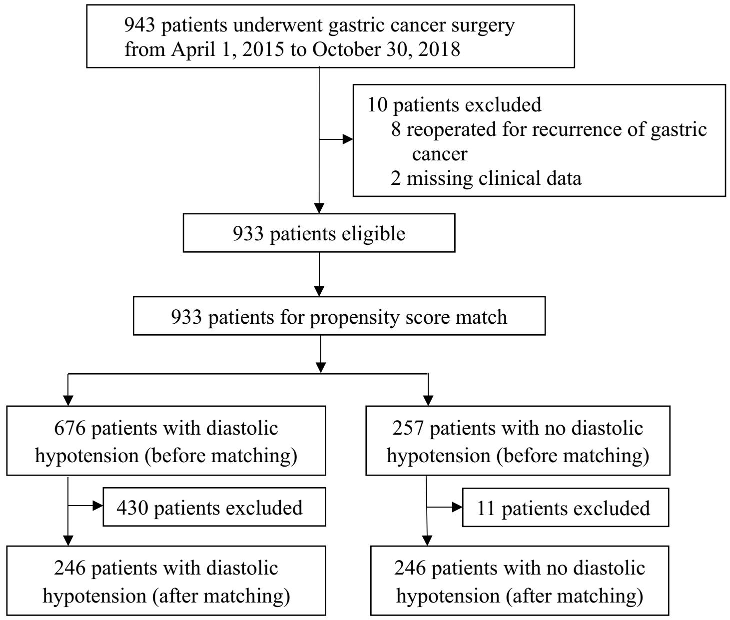

Figure 1 Flowchart of the study.

Postoperative outcomes

In both the full and the matched cohort, diastolic hypotension was associated with longer postoperative hospital stay (full cohort: mean 14.5 ± standard deviation 10.2 vs 11.6 ± 6.5 days, *P*<0.001; matched cohort: 13.7 ± 9.9 vs 11.7 ± 6.6 days, *P*=0.009) and a higher incidence of postoperative complications (full cohort: 170 [25.1%] vs 27 [10.5%] cases, *P*<0.001; matched cohort: 60 [24.4%] vs 33 [13.4%] cases, *P*=0.003).

For specific postoperative complications, diastolic hypotension was associated with a higher incidence of postoperative surgical site infections (full cohort: 70 [10.4%] vs 89 [3.1%], *P*<0.001; matched cohort: 23 [9.3%] vs 7 [2.8%], *P*=0.004), respiratory infections (full cohort: 47 [7.0%] vs 5 [1.9%], *P*=0.002; matched cohort: 16 [6.5%] vs 5 [2.0%], *P*=0.024), and anastomotic leakage (full cohort: 31 [4.6%] vs 1 [0.4%], *P*<0.001; matched cohort: 13 [5.3%] vs 1 [0.4%], *P*=0.002) in both the full and the matched cohort. In the full cohort, diastolic hypotension was associated with a higher incidence of postoperative renal injury (11 [1.6%] vs 0 [0%], *P*=0.041); this association was not present in the matched cohort (2 [0.8%] vs 0 [0%], *P*=0.499). Other complications were not statistically significantly different on the basis of diastolic hypotension (Table 2).

Intraoperative Diastolic Hypotension and Postoperative Hospital Stay

The median length of postoperative hospital stay was 11 days. Prolonged postoperative hospital stay was defined as >11 days. Multivariate logistic regression analysis was used to analysis the relationships between length of postoperative hospital stay and potential risk factors. LOS>11 days was used as a dependent variable. For the full cohort, 17 factors were included in the multivariable logistic model, including 14 factors with *P*<0.20 on univariable analysis (diastolic hypotension, age, history of hypertension, history of diabetes, preoperative hypoproteinemia, ASA grade, pTNM stage, range of gastrectomy, duration of surgery, type of procedure, use of vasopressors, dose of perioperative opioids, intraoperative crystalloids infusion, and intraoperative artificial colloid infusion) and 3 factors that were considered to be clinically important (*P*<0.20 in matched cohort, including use of etomidate, use of nitroglycerin, and intraoperative SBP <90 mmHg for >10 min).

After correction for confounding factors, intraoperative diastolic hypotension was associated with longer postoperative hospital stay (HR, 1.535 [95% CI, 1.115–2.114], *P*=0.009). Among other factors, older age, preoperative hypoproteinemia, total gastrectomy, longer duration of surgery, open surgery, higher perioperative opioids dose, and higher volume of intraoperative artificial colloid infusion were associated with longer postoperative hospital stay (Table 3).

Table 2 Postoperative Outcomes

Variables	All Patients (N=933)	Full Cohort (N=933)			Matched Cohort (N=492)		
		Diastolic Hypotension (n=676)	**No Diastolic Hypotension (n=257)**	***P* value**	**Diastolic Hypotension (n=246)**	**No Diastolic Hypotension (n=246)**	***P* value**
Primary outcome							
Length of hospital stay[a] (mean)	13.7 ± 9.4	14.5 ± 10.2	11.6 ± 6.5	**<0.001[b]**	13.7 ± 9.9	11.7 ± 6.6	**0.009[b]**
Length of hospital stay[a] (median)	11 (9–14)	11 (9–14)	10 (8–13)	**<0.001[c]**	11 (9–13)	10 (8–13)	**0.002[c]**
Secondary outcome							
Postoperative complications[d]	197 (21.1)	170 (25.1)	27 (10.5)	**<0.001**	60 (24.4)	33 (13.4)	**0.003**
Postoperative stroke[e]	5 (0.5)	4 (0.6)	1 (0.4)	>0.999	1 (0.4)	1 (0.4)	>0.999
Acute coronary syndrome[f]	11 (1.2)	9 (13.3)	2 (0.8)	0.737	2 (0.8)	2 (0.8)	>0.999
Respiratory infection[g]	52 (5.8)	47 (7.0)	5 (1.9)	**0.002**	16 (6.5)	5 (2.0)	**0.024**
Delayed gastric emptying[h]	34 (3.6)	27 (4.0)	7 (2.7)	0.437	10 (4.1)	7 (2.8)	0.623
Hepatic insufficiency[i]	37 (4.0)	26 (3.8)	11 (4.3)	0.712	10 (4.1)	10 (4.1)	>0.999
Anastomotic fistula[j]	32 (3.4)	31 (4.6)	1 (0.4)	**<0.001**	13 (5.3)	1 (0.4)	**0.002**
Acute kidney injury[k]	11 (1.2)	11 (1.6)	0 (0)	**0.041**	2 (0.8)	0 (0)	0.499
Postoperative bleeding[l]	39 (4.2)	27 (4.0)	12 (4.7)	0.714	10 (4.1)	10 (4.1)	>0.999
Deep venous thrombosis[m]	6 (0.6)	6 (0.9)	0 (0)	0.196	0 (0)	0 (0)	>0.999
Surgical site infection[n]	78 (8.4)	70 (10.4)	89 (3.1)	**<0.001**	23 (9.3)	7 (2.8)	**0.004**
In-hospital death	0 (0)	0 (0)	0 (0)	>0.999	0 (0)	0 (0)	>0.999

Notes: Data are mean ± SD or median or no. (%). P values in bold indicate those <0.05. ctg. [a]The time between the day of surgery and the first discharge. [b]*t*-test. [c]Mann–Whitney *U*-test. [d]Newly occurred medical events that were harmful to the patients' recovery during postoperative hospitalization and required interventional therapy (ie, class II–V on Clavien-Dindo classification).[21] [e]Confirmed by clinical symptoms and medical imaging examination. [f]Confirmed by clinical symptoms, electrocardiographic changes, and elevated cardiac troponin I levels. [g]New infiltration on chest X-ray with fever and treated with intravenous antibiotics. [h]Gastric tube drainage >800 mL/d, with no other obvious reasons. [i]Prolonged prothrombin time (>18 s) and elevated serum total bilirubin concentration (>30 μmol/L or 1.7 mg/dL) within 7 days after surgery, requiring interventions. [j]Gastric juice–like fluid in the abdominal drainage fluid with a volume >100 mL per day after surgery or gastric juice–like fluid extracted from the local peritoneal effusion under ultrasound and computed tomography positioning. [k]Increased serum creatinine ≥0.3 mg/dL (≥26.5 μmol/L) within 7 days after surgery. [l]Required second surgery for hemostasis. [m]Confirmed by lower limbs venous ultrasonography and treated with anticoagulants. [n]Pus expressed from the incision and bacteria cultured from the pus or purulent puncture extract.

Table 3 Risk Factors for Longer Postoperative Hospital Stay After Elective Surgery for Gastric Cancer: Univariable and Multivariable Logistic Regression Analyses (Full Cohort)

Variable	Univariable Analysis		Multivariable Analysis	
	OR (95% CI)	***P* value**	**OR (95% CI)**	***P* value**
Age, years	1.970 (1.459 to 2.660)	**0.000**	1.020 (1.006 to 1.034)	**0.005**
Male sex	1.049 (0.784 to 1.405)	0.748		
Body mass index, kg/m^2	0.981 (0.942 to 1.021)	0.340		
Smoking history	0.981 (0.757 to 1.272)	0.887		
Drinking history	0.941 (0.711 to 1.246)	0.671		
History of stroke	1.098 (0.578 to 2.083)	0.775		
Coronary heart disease	1.356 (0.766 to 2.401)	0.296		
Hypertension	1.331 (0.993 to 1.784)	**0.056**	1.165 (0.836 to 1.621)	0.367
Diabetes	1.713 (1.116 to 2.628)	**0.014**	1.403 (0.876 to 2.247)	0.159
Hepatic dysfunction	0.858 (0.419 to 1.756)	0.674		
Renal dysfunction	2.041 (0.635 to 6.553)	0.231		
COPD[a]	1.010 (0.468 to 2.183)	0.979		
ASA grade (III vs I and II)	1.613 (0.900 to 2.892)	**0.108**	1.039 (0.542 to 1.993)	0.908
Preoperative WBC count >10×10^9/L	1.132 (0.774 to 1.655)	0.523		
Preoperative albumin <35 g/L	2.331 (1.219 to 4.455)	**0.010**	2.057 (1.041 to 4.067)	**0.038**
Preoperative anemia[b]	1.213 (0.202 to 7.295)	0.833		

(*Continued*)

Table 3 (Continued).

Variable	Univariable Analysis		Multivariable Analysis	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Preoperative chemotherapy	0.889 (0.682 to 1.159)	0.383		
Pathological diagnosis (adenocarcinoma vs others)[c]	1.033 (0.884 to 1.206)	0.685		
pTNM stage (IIB, III, IV vs IA, IB, IIA)[d]	1.409 (1.087 to 1.826)	**0.009**	1.021 (0.764 to 1.365)	0.886
Differentiation grade (low or NA vs moderate or high)	0.884 (0.683 to 1.145)	0.351		
Range of gastrectomy (total vs distal or proximal gastrectomy)	2.689 (2.054 to 3.519)	**0.000**	2.150 (1.609 to 2.872)	**0.000**
Type of procedure (laparoscopic vs. Open gastrectomy)	0.420 (0.313 to 0.564)	**0.000**	0.572 (0.410 to 0.798)	**0.001**
Duration of surgery	1.005 (1.003 to 1.007)	**0.000**	1.004 (1.001 to 1.007)	**0.013**
Type of anesthesia (balance vs inhalation anesthesia)	1.062 (0.778 to 1.449)	0.706		
Use of propofol	1.024 (0.750 to 1.397)	0.883		
Use of etomidate	0.857 (0.634 to 1.158)	0.315	0.747 (0.523 to 1.065)	0.107
Use of nitroglycerin	1.089 (0.837 to 1.418)	0.524	0.952 (0.702 to 1.292)	0.753
Use of esmolol	1.046 (0.736 to 1.488)	0.801		
Use of vasopressors[e]	1.278 (0.908 to 1.799)	**0.159**	1.155 (0.791 to 1.684)	0.456
Use of remifentanil	0.923 (0.628 to 1.357)	0.683		
Inhalational anesthetics (isoflurane vs sevoflurane)	1.247 (0.740 to 2.101)	0.408		
Perioperative opioids (sufentanil equivalent, mg)[f]	1.004 (1.000 to 1.009)	**0.067**	1.001 (1.000 to 1.003)	**0.039**
Estimated blood loss, mL	1.000 (1.000 to 1.001)	0.279		
Intraoperative blood transfusion, mL[g]	1.001 (0.999 to 1.002)	0.485		
Intraoperative artificial colloid, mL	1.001 (1.000 to 1.001)	**0.001**	1.001 (1.000 to 1.001)	**0.018**
Intraoperative crystalloids, mL	1.000 (1.000 to 1.001)	**0.019**	1.000 (1.000 to 1.000)	0.989
Perioperative glucocorticoids (DXM equivalent, mg)[h]	1.003 (0.985 to 1.022)	0.750		
Perioperative NSAIDs (FA equivalent, mg)[i]	1.000 (0.998 to 1.003)	0.685		
SBP <90 mmHg for >10 min	1.050 (0.683 to 1.613)	0.825	1.020 (0.626 to 1.663)	0.935
DBP <60 mmHg for >10 min	2.009 (1.502 to 2.689)	**0.000**	1.535 (1.115 to 2.114)	**0.009**

Notes: *P* values in bold indicate *P*<0.20 on univariable analysis and *P*<0.05 on multivariable analysis. [a]Includes COPD (chronic bronchitis and emphysema), asthma, and old tuberculosis. [b]For adult men, hemoglobin <120 g/L; for adult women, hemoglobin <110 g/L. [c]Includes signet-ring cell carcinoma, adenocarcinoma combined signet-ring cell carcinoma, neuroendocrine tumor, lymphoid stromal carcinoma, melanoma, and squamous cell carcinoma. [d]According to the American Joint Committee on Cancer 8th Edition Cancer Staging System. [e]Includes ephedrine, norepinephrine, and norepinephrine. [f]1 mg of morphine (iv) = 15 μg of fentanyl = 1.5 μg of sufentanil = 1 mg of oxycodone = 1 mg of dezocine.[18–20] [g]Packed red blood cells were transfused. [h]Includes dexamethasone and methylprednisolone; 1 mg of methylprednisolone = 0.2 mg of dexamethasone.[16] [i]40 mg of parecoxib sodium = 50 mg of flurbiprofen axetil.[17]

Abbreviations: ASA, American Society of Anesthesiologists; CI, confidence interval; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; DXM, dexamethasone; FA, flurbiprofen axetil; NA, not available; NSAID, nonsteroidal anti-inflammatory drug; OR, odds ratio; pTNM, pathological tumor-node-metastasis; SBP, systolic blood pressure; WBC, white blood cell.

In the matched cohort, 17 factors were included in the multivariable model, including 14 with *P*<0.20 on univariable analysis (diastolic hypotension, age, history of hypertension, history of diabetes, preoperative hypoproteinemia, ASA grade, range of gastrectomy, duration of surgery, type of procedure, dose of perioperative opioids, intraoperative crystalloids infusion, intraoperative artificial colloid infusion, use of etomidate, and use of nitroglycerin) and 3 that were considered to be clinically important (*P*<0.20 in full cohort, including pTNM stage, use of vasopressors, and intraoperative SBP <90 mmHg for >10 min).

After correction for confounding factors, intraoperative diastolic hypotension was associated with longer postoperative hospital stay (HR, 1.532 [95% CI, 1.032–2.273], *P*=0.034). Among other factors, older age, preoperative hypoproteinemia, total gastrectomy, open surgery, no use of etomidate and higher volume of intraoperative artificial colloid infusion were associated with longer postoperative hospital stay (Table 4).

Table 4 Risk Factors for Longer Postoperative Hospital Stay After Elective Surgery for Gastric Cancer: Univariable and Multivariable Logistic Regression Analyses (Matched Cohort)

Variable	Univariable Analysis		Multivariable Analysis	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age, years	1.024 (1.008 to 1.041)	**0.003**	1.020 (1.001 to 1.039)	**0.038**
Male sex	1.138 (0.776 to 1.668)	0.509		
Body mass index, kg/m^2	0.976 (0.925 to 1.031)	0.386		
Smoking history	1.194 (0.836 to 1.706)	0.329		
Drinking history	1.175 (0.796 to 1.734)	0.418		
History of stroke	1.225 (0.369 to 4.069)	0.740		
Coronary heart disease	1.614 (0.740 to 3.520)	0.229		
Hypertension	1.398 (0.936 to 2.090)	**0.102**	1.0652 (0.670 to 1.694)	0.791
Diabetes	2.167 (1.111 to 4.224)	**0.023**	1.813 (0.848 to 3.874)	0.125
Hepatic dysfunction	2.059 (0.509 to 8.327)	0.311		
Renal dysfunction	1.016 (0.063 to 16.343)	0.991		
COPD[a]	1.225 (0.369 to 4.069)	0.740		
ASA grade (III vs I and II)	1.782 (0.799 to 3.975)	**0.158**	0.832 (0.329 to 2.104)	0.698
Preoperative WBC count >10×10^9/L	0.979 (0.564 to 1.701)	0.940		
Preoperative albumin <35 g/L	4.971 (1.410 to 17.520)	**0.013**	6.041(1.640 to 22.258)	**0.007**
Preoperative anemia[b]	NA	—		
Preoperative chemotherapy	0.945 (0.659 to 1.354)	0.756		
Pathological diagnosis (adenocarcinoma vs others)[c]	0.906 (0.726 to 1.130)	0.380		
pTNM stage (IIB, III, IV vs IA, IB, IIA)[d]	1.214 (0.851 to 1.732)	0.285	0.895 (0.597 to 1.344)	0.593
Differentiation grade (low or NA vs moderate or high)	0.822 (0.577 to 1.171)	0.278		
Range of gastrectomy (total vs distal or proximal gastrectomy)	3.007 (2.067 to 4.375)	**0.000**	2.584 (1.708 to 3.911)	**0.000**
Type of procedure (laparoscopic vs. Open gastrectomy)	0.403 (0.272 to 0.596)	**0.000**	0.476 (0.303 to 0.748)	**0.001**
Duration of surgery	1.005 (1.002 to 1.009)	**0.002**	1.004 (0.999 to 1.008)	0.090
Type of anesthesia (balance vs inhalation anesthesia)	1.158 (0.729 to 1.838)	0.534		
Use of propofol	1.151 (0.731 to 1.812)	0.544		
Use of etomidate	0.627 (0.408 to 0.962)	**0.030**	0.973 (0.955 to 0.991)	**0.004**
Use of nitroglycerin	1.433 (0.984 to 2.089)	**0.061**	1.210 (0.768 to 1.904)	0.411
Use of esmolol	1.372 (0.823 to 2.285)	0.225		
Use of vasopressors[e]	1.099 (0.640 to 1.887)	0.732	0.971 (0.527 to 1.788)	0.924
Use of remifentanil	1.023 (0.584 to 1.792)	0.937		
Inhalational anesthetics (isoflurane vs sevoflurane)	1.017 (0.462 to 2.241)	0.966		
Perioperative opioids (sufentanil equivalent, mg)[f]	1.004 (0.999 to 1.010)	**0.131**	1.001 (0.999 to 1.003)	0.178
Estimated blood loss, mL	1.000 (0.998 to 1.001)	0.523		
Intraoperative blood transfusion, mL[g]	0.998 (0.992 to 1.004)	0.579		
Intraoperative artificial colloid, mL	1.001 (1.000 to 1.002)	**0.011**	1.001 (1.000 to 1.002)	**0.038**
Intraoperative crystalloids, mL	1.000 (1.000 to 1.001)	**0.096**	1.000 (0.999 to 1.001)	0.987
Perioperative glucocorticoids (DXM equivalent, mg)[h]	1.008 (0.983 to 1.034)	0.545		
Perioperative NSAIDs (FA equivalent, mg)[i]	1.001 (0.998 to 1.004)	0.649		
SBP <90 mmHg for >10 min	0.765 (0.363 to 1.610)	0.480	0.956 (0.405 to 2.258)	0.919
DBP <60 mmHg for >10 min	1.633 (1.144 to 2.331)	**0.007**	1.532 (1.032 to 2.273)	**0.034**

Notes: *P* values in bold indicate $P<0.20$ on univariable analysis and $P<0.05$ on multivariable analysis. [a]Includes COPD (chronic bronchitis and emphysema), asthma, and old tuberculosis. [b]For adult men, hemoglobin <120 g/L; for adult women, hemoglobin <110 g/L. There was no preoperative anemia in the matched cohort. [c]Includes signet-ring cell carcinoma, adenocarcinoma combined signet-ring cell carcinoma, neuroendocrine tumor, lymphoid stromal carcinoma, melanoma, and squamous cell carcinoma. [d]According to the American Joint Committee on Cancer 8th Edition Cancer Staging System. [e]Includes ephedrine, norepinephrine, and norepinephrine. [f]1 mg of morphine (iv) = 15 μg of fentanyl = 1.5 μg of sufentanil = 1 mg of oxycodone = 1 mg of dezocine.[18–20] [g]Packed red blood cells were transfused. [h]Includes dexamethasone and methylprednisolone; 1 mg of methylprednisolone = 0.2 mg of dexamethasone.[16] [i]40 mg of parecoxib sodium = 50 mg of flurbiprofen axetil.[17]

Abbreviations: ASA, American Society of Anesthesiologists; CI, confidence interval; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; DXM, dexamethasone; FA, flurbiprofen axetil; NA, not available; NSAID, nonsteroidal anti-inflammatory drug; OR, odds ratio; pTNM, pathological tumor-node-metastasis; SBP, systolic blood pressure; WBC, white blood cell.

Discussion

In this retrospective study that included propensity score matching, 933 patients were enrolled, of whom 676 had intraoperative diastolic hypotension (defined as DBP <60 mmHg for >10 min), with a median (IQR) duration of DBP <60 mmHg for 45 (25–65) min. The incidence of intraoperative diastolic hypotension in the present study was high (72.5%), but it was in line with another retrospective cohort analysis, aiming to explore the associations of intraoperative radial arterial systolic, diastolic, mean, and pulse pressures with myocardial and acute kidney injury after noncardiac surgery,[23] which implied that intraoperative hypotension maybe not a rare thing in our clinical practice. However, most studies on the impact of perioperative hemodynamic fluctuations on postoperative recovery had focused on SBP and MAP, with few studies on DBP,[10] that's also why the present study trying to investigate the significance of intraoperative diastolic hypotension on postoperative recovery.

We chose length of postoperative hospital stay as the primary outcome to comprehensively evaluate the effect of intraoperative diastolic hypotension on postoperative recovery. Length of hospital stay is one of the key performance indicators for hospital management and efficiency of the health care system.[23,24] Previous studies have shown that intraoperative hypotension (MAP <60 mmHg for >10 min or MAP <70 mmHg and a decrease in MAP >30% from the baseline value for >10 min) is a risk factor for postoperative complications and may be associated with prolonged hospitalization and worse outcomes in patients who have undergone elective major abdominal surgery.[25] But there were rare studies focusing on the relationship between intraoperative diastolic hypotension and postoperative hospital stay. In the present study, patients with diastolic hypotension had longer postoperative hospital stay than patients without diastolic hypotension, and after correction for confounding factors, intraoperative diastolic hypotension was associated with longer postoperative hospital stay in both the full and the matched cohort, while systolic hypotension was not an independent factor for more extended hospital stay in the present study.

Previous studies have shown that DBP below a certain threshold may be associated with adverse outcomes, including a higher incidence of coronary events, stroke, heart failure, and all-cause mortality.[26–28] Possible mechanisms underlying this association include lower endocardial perfusion leading to coronary events or coronary stenosis limiting blood flow.[29,30] While some studies also have found that DBP <60 mmHg was not associated with myocardial infarction, acute coronary syndrome without myocardial infarction, stroke, acute decompensated heart failure, or death from cardiovascular causes.[11] In the present study, although the incidence of postoperative complications was higher among patients with diastolic hypotension, the incidence of coronary events or stroke was not statistically significantly different on the basis of hypotension. The lack of a detected difference may be attributable to the low incidence of coronary events or stroke among enrolled patients (stroke, n=5 [0.5%]; coronary heart disease, n=11 [1.2%]) and the small sample size.

Other studies have shown that ischemia and reperfusion injury can be associated with postoperative acute renal injury.[7] In the present study, in the full cohort, the incidence of postoperative renal injury was statistically significantly higher among patients with intraoperative hypotension, but no statistically significant difference was observed between the two groups in the matched cohort, which may be related to the low incidence of renal injury among the patients in the matched cohort (n=2 [0.8%]) and the small sample size.

Adequate blood pressure is important for proper wound perfusion. Although perioperative hypotension occurs for a short time, it may still can cause adverse outcomes, as previous work has shown that, it is the lowest tissue oxygen saturation, rather than overall mean oxygenation, that is associated with serious complications.[31,32] In the present study, we found that in both the full and the matched cohort, patients with diastolic hypotension had a higher incidence of postoperative surgical site infections, respiratory infections, and postoperative anastomotic leakage, compared with patients without diastolic hypotension. That is in line with previous researches which have shown that intraoperative hypotension may be associated with postoperative surgical site infections and other infectious complications.[25,33] Another retrospective study also found that perioperative hypotension was an independent predictor of postoperative infectious complications in patients with colon cancer.[34,35]

In addition, in the present study, other factors, such as older age, preoperative hypoproteinemia, total gastrectomy, longer duration of surgery, open surgery, higher dose of perioperative opioids, and higher volume of intraoperative artificial colloid infusion, were statistically significantly associated with longer postoperative hospital stay, which is consistent with the findings of previous studies.[36,37] For instance, another retrospective study performed on 2033 patients who underwent gastric surgery also found that, age, surgical procedure, extent of resection, degree of incision healing, and perioperative blood transfusion are the independent risk factors for prolonged postoperative LOS.[38] But as for the association between higher dose of perioperative opioids/higher volume of intraoperative artificial colloid infusion and longer postoperative hospital stay, the OR in the present study was of very low level of significance, so further studies are still needed.

The present study has limitations beyond those normally associated with retrospective studies. In previous studies, it has been suggested that general anesthesia combined with epidural anesthesia may improve postoperative recovery, compared with general anesthesia alone.[39] However, in the present study, only 2 (0.2%) patients received general anesthesia combined with epidural anesthesia, and the effect of this factor on postoperative recovery is not known. What' more, as for the sample size calculation, retrospective studies cannot accurately estimate sample size, so we included all patients underwent surgery for gastric cancer from April 1, 2015, to October 30, 2018. Thirdly, the present study is a single-center study, so the scope of application of the results may be limited.

Conclusion

For patients with gastric cancer, intraoperative diastolic hypotension (DBP <60 mmHg for >10 min) was associated with a higher incidence of postoperative complications and longer postoperative hospital stay. Considering the high incidence of intraoperative diastolic hypotension, prospective studies are urgently needed to clarify its effect on patients' recovery after gastric cancer surgery.

Data Sharing Statement

The data sets used and/or analyzed in the present study are available from the corresponding author on reasonable request.

Ethics Approval

The study protocol was approved by the clinical research ethics committee of Peking University Cancer Hospital (Approval No. 2018YJZ71). As the study was observational, the ethics committee waived the requirement for written informed consent. During the study period, the patient's name, gender and other personal data will be replaced by codes or numbers, and will be strictly confidential. Only the relevant doctors know their data, and the patient's privacy will be well protected. When the research results are published, no personal information of patients will be disclosed.

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work.

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The authors declare that they have no conflicts of interest in this work.

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