

Original Article

Analysis of the efficacy and safety of extended lymph node dissection in gastric cancer surgery: association with dissection quantity, inflammatory response, and complications

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Abstract: Objective: To evaluate the comparative efficacy and safety of standard lymphadenectomy (D2) versus extended lymphadenectomy (D2+) in gastric cancer surgery. Additionally, we explored the relationship between the number of dissected lymph nodes, the magnitude of postoperative inflammatory response, and long-term survival outcomes. Methods: A retrospective cohort was conducted on clinical data from 421 patients diagnosed with gastric cancer and treated between April 2019 and January 2022. Among them, 189 underwent standard D2 dissection and 232 received extended D2+ lymph node dissection. All patients received neoadjuvant chemotherapy followed by radical gastrectomy. Baseline characteristics, intraoperative and postoperative outcomes, inflammatory markers including C-reactive protein (CRP), tumor necrosis factor-alpha (TNF- α), and interleukin-6 (IL-6), complication rates, and survival metrics (3-year overall survival (OS) and progression-free survival (PFS)) were compared between groups. Univariate and multivariate Cox proportional hazards models were applied to identify survival-associated factors. Kaplan-Meier survival curves were constructed for subgroup analysis by TNM (tumor-node-metastasis) stage. Results: There were no significant differences in baseline characteristics between the D2 and D2+ groups ($P > 0.05$). Compared to the D2 group, the D2+ group exhibited significantly longer operative times, greater intraoperative blood loss, and more lymph nodes dissected (all $P < 0.001$), while the length of hospital stay remained similar between the two groups ($P = 0.708$). Postoperative levels of CRP, TNF- α , and IL-6 were significantly elevated in the D2+ group (all $P < 0.001$), correlating positively with the number of lymph nodes removed (all $P < 0.001$). The incidence of postoperative complications did not differ between groups ($P > 0.05$). Notably, the D2+ group demonstrated a superior 2-year OS rate ($P = 0.002$) and significantly improved 3-year OS in patients with stage II disease ($P = 0.018$). However, no significant differences were observed in 1-year OS ($P = 0.067$), 3-year OS ($P = 0.699$), or 3-year OS for stage III patients ($P = 0.428$). Multivariate Cox regression analysis identified extended D2+ dissection, younger age, lower TNM stage, and higher tumor differentiation as independent protective factors for PFS (all $P < 0.05$). Conclusion: Extended D2+ lymph node dissection improves survival outcomes, particularly in stage II gastric cancer patients, without increasing postoperative complication risk. However, it induces a more robust inflammatory response. These findings suggest that D2+ dissection should be selectively considered, weighing the oncological benefits against the potential inflammatory burden, particularly in stage II patients.

Keywords: Gastric cancer, D2 lymph node dissection, D2+ lymph node dissection, inflammatory response, survival outcomes, neoadjuvant chemotherapy

Introduction

Gastric cancer is among the most common malignancies of the digestive system and remains a leading cause of cancer-related morbidity and mortality globally [1]. According to

recent estimates from the World Health Organization (WHO) and the International Agency for Research on Cancer (IARC), approximately 960,000 new cases and 650,000 deaths occurred worldwide in 2022, underscoring the significant public health burden of gas-

tric cancer [2]. The incidence of gastric cancer is particularly high in East Asian countries, including China, Japan, and South Korea, which is attributed to dietary habits, high prevalence of *Helicobacter pylori* infection, and genetic susceptibility [3]. Despite progress in early detection and treatment strategies, the prognosis for advanced-stage gastric cancer remains poor, with the 5-year survival rate rarely exceeding 30% [4]. Therefore, refining surgical treatment approaches is crucial for improving patient survival.

Radical gastrectomy combined with lymphadenectomy remains the cornerstone of curative therapy for gastric cancer [5]. As lymphatic spread is a principal route for tumor progression and an important prognostic factor, the extent of lymph node involvement significantly influences staging and outcomes [6]. It is estimated that 50%-70% of patients present with lymph node metastasis at diagnosis. Accordingly, the thoroughness of lymph node dissection is directly linked to surgical efficacy and long-term survival. Standard lymphadenectomy, known as D2 dissection, involves the removal of perigastric and major vessel-associated lymph nodes and is widely endorsed as the standard approach for resectable locally advanced gastric cancer by both Eastern and Western guidelines [7, 8]. However, based on evolving insights into tumor biology, some experts advocate for an extended approach - D2+ dissection - which additionally targets more distant nodal basins, including para-aortic lymph nodes (station No. 16), to eliminate possible micrometastases [9].

Nonetheless, whether D2+ dissection confers a definitive survival advantage over D2 remains debated. Supporters argue that more extensive clearance may reduce local recurrence and improve prognosis, particularly in patients with high-risk nodal disease [10]. Retrospective studies have reported improved 5-year survival rates in select patient subsets following D2+ procedures [11, 12]. Conversely, randomized controlled trials conducted in western countries have failed to demonstrate significant survival benefits from D2+ dissection and have highlighted increased surgical risks, including prolonged operative duration, greater blood loss, and a higher incidence of complications such as anastomotic leakage, pancreatic fistula, and postoperative infections [13].

Beyond oncologic outcomes and perioperative safety, the systemic inflammatory response following surgery has emerged as a critical factor in postoperative recovery and prognosis. Surgical trauma provokes acute inflammation, with elevated circulating levels of markers such as C-reactive protein (CRP), tumor necrosis factor-alpha (TNF- α), and interleukin-6 (IL-6) [14]. These markers not only reflect the degree of surgical stress but are also associated with postoperative complications, delayed recovery, and worse long-term survival [15]. Given that the extent of lymph node dissection correlates with tissue trauma, D2+ procedures may intensify the inflammatory response. Prior studies have suggested that elevated CRP and IL-6 are predictive of increased risk for tumor recurrence and metastasis [16]. However, direct comparisons of inflammatory profiles between D2 and D2+ lymphadenectomy remain scarce, and the clinical implications of this difference are not yet fully understood.

In light of these considerations, the present study aims to systematically compare D2 and D2+ lymph node dissection in terms of clinical efficacy, postoperative inflammatory response, and survival outcomes. By integrating surgical data with biomarker data and long-term follow-up, we seek to inform evidence-based decisions regarding lymphadenectomy strategy, ultimately optimizing the therapeutic balance between efficacy and safety in gastric cancer management.

Patients and methods

Sample size calculation

Based on the study by Meng et al. [17], which compared survival differences between D2 and D2+ groups, sample size was calculated using the Schoenfeld formula ($D = \frac{(Z_{\alpha/2} + Z_{\beta})^2}{p_1 p_2 (\ln(HR))^2}$). Assuming a significance level of 0.05 and a power of 80%, a hazard ratio (HR) of 0.69 required a minimum of 98 patients per group, totaling 196 patients. The final sample size was dependent on actual case screening.

General information

This retrospective study finally included 421 gastric cancer patients treated at our institution between April 2019 and January 2022, satisfying statistical requirements. The study

was approved by the institutional Baoji Central Hospital ethics committee.

Inclusion and exclusion criteria

Inclusion criteria: Diagnosis of gastric adenocarcinoma was made by preoperative endoscopic biopsy and pathologic examination; At least two cycles of neoadjuvant chemotherapy, including regimens such as oxaliplatin combined with fluoropyrimidine-based drugs; Radical gastrectomy with documented standard (D2) or extended (D2+) lymph node dissection; Complete preoperative, intraoperative, and postoperative clinical data, including inflammatory markers and follow-up records. Pathological stage II or III according to the 8th edition of the AJCC staging system [18].

Exclusion criteria: Distant metastases (M1) indicated by preoperative imaging (CT, PET-CT, etc.) or intraoperative findings; Concurrent primary malignancies or a history of other cancers; Failure to complete the prescribed neoadjuvant chemotherapy cycles or receiving non-standard regimens; Unresectable tumors identified intraoperatively or intolerance to surgery, resulting in palliative surgery or exploratory procedures.

Surgical procedures

D2 dissection: *The D2 dissection* involved the removal of lymph nodes Nos. 1, 3, 4sb, 4d, 5, 6, 7, 8a, 9, 11p, and 12a, covering the lesser and greater curvature of the stomach, pylorus, left gastric artery, common hepatic artery, celiac axis, proximal splenic artery, and hepatoduodenal ligament. The surgical procedure included abdominal exploration, partial or total gastrectomy, systematic lymph node dissection by station, digestive tract reconstruction (e.g., Billroth I/II or Roux-en-Y), and abdominal closure.

D2+ dissection: In addition to D2 dissection, D2+ included clearance of para-aortic lymph nodes (Nos. 16a2 and 16b1). If necessary, lymph nodes at the splenic hilum and distal splenic artery were removed, with splenectomy performed as required. Lymph nodes Nos. 13 and 14v were selectively cleared based on tumor location. The procedure was followed by digestive tract reconstruction and abdominal closure.

Clinical data collection

Clinical data were retrieved from the hospital's electronic medical record system, including baseline characteristics, laboratory markers, and follow-up information. Baseline data consisted of demographic features (age, sex, BMI), lifestyle factors (smoking and alcohol history), clinical characteristics (comorbidities, TNM stage, T stage, N stage), and pathologic features (tumor location, size, differentiation, lymphovascular and neural invasion). Laboratory markers included inflammatory indicators (CRP, TNF- α , and IL-6) measured preoperatively and on postoperative day 7. Follow-up data covered a 3-year period post-surgery and included intraoperative and postoperative features (operative time, intraoperative blood loss, number of lymph nodes dissected, hospital stay). Postoperative complications, including wound infection, pulmonary infection, bleeding, anastomotic leakage, and intestinal obstruction - were recorded within 30 days after surgery. Survival outcomes included 1-, 2-, and 3-year overall survival (OS) and progression-free survival (PFS). All patients received at least two cycles of neoadjuvant chemotherapy, and data completeness met inclusion and exclusion criteria, enabling comprehensive analysis of baseline characteristics, inflammatory responses, complications, and survival outcomes.

Follow-up

A 3-year follow-up was conducted for the included patients who underwent radical gastric cancer surgery. Follow-up data were obtained through the hospital's electronic medical record system and telephone interviews to ensure completeness and accuracy. The follow-up period began on the date of surgery and continued until 36 months post-surgery, patient death, or disease progression, whichever occurred first. The last patient was enrolled in January 2022, and the final follow-up was completed in January 2025. Follow-up assessments included survival status, disease progression (e.g., local recurrence or distant metastasis), and postoperative complications (e.g., wound infection, pulmonary infection, bleeding, anastomotic leakage, intestinal obstruction). Follow-up visits were scheduled at 3, 6, 12, 18, 24, 30, and 36 months post-surgery, with additional

visits arranged as needed based on patient condition.

Outcome measures

Primary outcomes: The primary outcomes included 3-year OS and 3-year PFS to assess the long-term efficacy of D2 versus D2+ lymph node dissection.

Secondary outcomes: Secondary outcomes included intraoperative features (operative time, intraoperative blood loss, number of lymph nodes dissected), postoperative inflammatory markers (CRP, TNF- α , IL-6), postoperative complications (wound infection, pulmonary infection, bleeding, anastomotic leakage, intestinal obstruction), and hospital stay. These outcomes were analyzed to assess surgical safety.

Statistical analysis

Statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA) and R version 4.3.3 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were assessed for normality using the Kolmogorov-Smirnov test. Normally distributed data were expressed as mean $\pm$ standard deviation and compared between groups using the independent t-test, with paired t-tests for pre- and post-treatment comparisons. Non-normally distributed data were presented as median (interquartile range, IQR) and analyzed using the Mann-Whitney U test for intergroup comparisons and the Wilcoxon signed-rank test for paired comparisons. Categorical variables were reported as frequencies (percentages) and compared using the χ^2 test, with continuity correction or Fisher's exact test applied when expected frequencies were < 5 .

Univariate and multivariate Cox proportional hazards regression models were used to identify risk factors for OS and PFS, with hazard ratios (HR) and 95% confidence intervals (CI) calculated. Kaplan-Meier survival curves and cumulative incidence function (CIF) curves were generated in R software to compare OS and PFS between groups, with differences assessed via the log-rank test. Correlation analyses between lymph node clearance and postoperative inflammatory markers (CRP, TNF- α , IL-6) were visualized using scatter plots and

lollipop charts in R. Missing data were handled using right-censoring for loss to follow-up or non-tumor-related deaths. A two-sided P -value < 0.05 was considered significant.

Results

Comparison of baseline characteristics between the D2 and D2+ groups

This study compared baseline characteristics between gastric cancer patients undergoing standard (D2) and extended (D2+) lymph node dissection. No statistically significant differences were found between the two groups in terms of age ($P = 0.376$), sex ($P = 0.174$), BMI ($P = 0.363$), smoking history ($P = 0.380$), alcohol consumption history ($P = 0.480$), comorbidities ($P = 0.245$), TNM stage ($P = 0.470$), T stage ($P = 0.716$), N stage ($P = 0.249$), tumor location ($P = 0.992$), tumor size ($P = 0.678$), differentiation grade ($P = 0.431$), lymphovascular invasion ($P = 0.877$), or neural invasion ($P = 0.883$) (**Table 1**).

Comparison of intraoperative and postoperative features between the D2 and D2+ groups

Intraoperative and postoperative features were compared between the two groups. The D2+ group exhibited significantly longer operative time ($P < 0.001$), greater intraoperative blood loss ($P < 0.001$), and more lymph nodes dissected ($P < 0.001$) than the D2 group. However, there was no significant difference in hospital stay between the groups ($P = 0.708$) (**Table 2**).

Comparison of inflammatory response between the D2 and D2+ groups

Differences in preoperative and postoperative inflammatory markers were evaluated between the two groups. Preoperative levels of CRP ($P = 0.760$), TNF- α ($P = 0.635$), and IL-6 ($P = 0.857$) did not differ significantly between the two groups, indicating comparable preoperative inflammatory status. After treatment, both groups demonstrated significantly elevated levels of CRP, TNF- α , and IL-6 compared to their preoperative levels (all $P < 0.001$). Notably, postoperative levels of CRP ($P < 0.001$), TNF- α ($P < 0.001$), and IL-6 ($P < 0.001$) were significantly higher in the D2+ group compared to the D2 group, suggesting that extended lymph node dissection induces a more pronounced postoperative inflammatory response (**Table 3**).

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Table 1. Comparison of baseline characteristics between standard and extended lymph node dissection groups

Factor	Total (n = 421)	Standard Dissection Group (n = 189)	Extended Dissection Group (n = 232)	χ^2 Value	P Value
Age					
≥ 65 years	262 (62.23%)	122 (64.55%)	140 (60.34%)	0.784	0.376
< 65 years	159 (37.77%)	67 (35.45%)	92 (39.66%)		
Sex					
Male	284 (67.46%)	134 (70.90%)	150 (64.66%)	1.850	0.174
Female	137 (32.54%)	55 (29.10%)	82 (35.34%)		
BMI					
≥ 24 kg/m ²	123 (29.22%)	51 (26.98%)	72 (31.03%)	0.826	0.363
< 24 kg/m ²	298 (70.78%)	138 (73.02%)	160 (68.97%)		
Smoking History					
Yes	303 (71.97%)	132 (69.84%)	171 (73.71%)	0.772	0.380
No	118 (28.03%)	57 (30.16%)	61 (26.29%)		
Alcohol History					
Yes	148 (35.15%)	63 (33.33%)	85 (36.64%)	0.499	0.480
No	273 (64.85%)	126 (66.67%)	147 (63.36%)		
Comorbidities					
≥ 1	126 (29.93%)	62 (32.80%)	64 (27.59%)	1.352	0.245
< 1	295 (70.07%)	127 (67.20%)	168 (72.41%)		
TNM Stage					
II	242 (57.48%)	105 (55.56%)	137 (59.05%)	0.521	0.470
III	179 (42.52%)	84 (44.44%)	95 (40.95%)		
T Stage					
T1-T2	121 (28.74%)	56 (29.63%)	65 (28.02%)	0.132	0.716
T3-T4	300 (71.26%)	133 (70.37%)	167 (71.98%)		
N Stage					
N0	121 (28.74%)	49 (25.93%)	72 (31.03%)	1.327	0.249
N1-N3	300 (71.26%)	140 (74.07%)	160 (68.97%)		
Tumor Location					
Antrum	182 (43.23%)	82 (43.39%)	100 (43.10%)	0.017	0.992
Body	135 (32.07%)	60 (31.75%)	75 (32.33%)		
Cardia	104 (24.70%)	47 (24.87%)	57 (24.57%)		
Tumor Size					
≥ 4 cm	198 (47.03%)	91 (48.15%)	107 (46.12%)	0.172	0.678
< 4 cm	223 (52.97%)	98 (51.85%)	125 (53.88%)		
Differentiation					
Poor	196 (46.56%)	92 (48.68%)	104 (44.83%)	0.620	0.431
Moderate/High	225 (53.44%)	97 (51.32%)	128 (55.17%)		
Lymphovascular Invasion					
Yes	200 (47.51%)	89 (47.09%)	111 (47.84%)	0.024	0.877
No	221 (52.49%)	100 (52.91%)	121 (52.16%)		
Neural Invasion					
Yes	191 (45.37%)	85 (44.97%)	106 (45.69%)	0.022	0.883
No	230 (54.63%)	104 (55.03%)	126 (54.31%)		

Note: BMI: Body Mass Index, TNM: Tumor Node Metastasis.

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Table 2. Comparison of intraoperative and postoperative features between standard and extended lymph node dissection groups

Variable	Standard Dissection Group (n = 189)	Extended Dissection Group (n = 232)	Statistic	P Value
Operative Time (min)	236.10 ± 25.41	249.08 ± 26.08	5.139	< 0.001
Intraoperative Blood Loss (mL)	278.27 ± 28.79	295.85 ± 29.41	6.161	< 0.001
Number of Lymph Nodes Dissected	22.00 (6.00)	27.00 (4.00)	12.1	< 0.001
Hospital Stay (days)	9.00 (3.00)	9.00 (3.00)	0.375	0.708

Table 3. Comparison of preoperative and postoperative inflammatory markers between standard and extended lymph node dissection groups

Variable	Standard Dissection Group (n = 189)	Extended Dissection Group (n = 232)	Statistic	P Value
Preoperative CRP	4.72 ± 2.02	4.66 ± 1.93	0.305	0.76
Postoperative CRP	40.20 (10.90)	48.20 (9.45)	9.697	< 0.001
Statistic	92.228	11.921		
P Value	< 0.001	< 0.001		
Preoperative TNF-α	3.78 ± 1.19	3.83 ± 1.16	0.475	0.635
Postoperative TNF-α	24.82 ± 5.45	30.14 ± 4.92	10.515	< 0.001
Statistic	78.129	53.047		
P Value	< 0.001	< 0.001		
Preoperative IL-6	115.49 ± 20.61	115.12 ± 20.99	0.18	0.857
Postoperative IL-6	154.01 ± 34.33	177.21 ± 35.02	6.822	< 0.001
Statistic	23.546	12.794		
P Value	< 0.001	< 0.001		

Note: CRP: C-Reactive Protein, TNF-α: Tumor Necrosis Factor-alpha, IL-6: Interleukin-6. Postoperative measurements were taken on the first day after surgery.

Association between lymph node dissection quantity and postoperative inflammatory response

The study analyzed the relationship between the number of lymph nodes dissected and postoperative inflammatory response. Postoperative CRP, TNF-α, and IL-6 levels were positively correlated with the number of lymph nodes dissected (all $P < 0.001$), indicating that increased lymph node dissection may exacerbate postoperative inflammation. No significant correlation was observed between preoperative CRP ($P = 0.693$), TNF-α ($P = 0.259$), or IL-6 ($P = 0.838$) levels and the number of lymph nodes dissected (**Figures 1, 2**).

Linear regression analysis of lymph node dissection quantity and postoperative inflammatory markers

Linear regression analysis confirmed a significant positive correlation between postopera-

tive CRP ($P < 0.001$), TNF-α ($P < 0.001$), and IL-6 ($P = 0.006$) levels and the number of lymph nodes dissected. This supports the conclusion that greater lymph node clearance intensifies postoperative inflammation. No significant association was found between preoperative CRP ($P = 0.570$), TNF-α ($P = 0.079$), or IL-6 ($P = 0.992$) levels and the number of lymph nodes dissected (**Table 4**).

Comparison of postoperative complications between the D2 and D2+ groups

Postoperative complication rates were compared between the D2 and D2+ groups. No significant differences were observed in the incidence of wound infection ($P = 0.761$), pulmonary infection ($P = 1.000$), bleeding ($P = 0.590$), anastomotic leakage ($P = 1.000$), or intestinal obstruction ($P = 0.330$). These results suggest that extended lymph node dissection does not significantly increase the risk of postoperative

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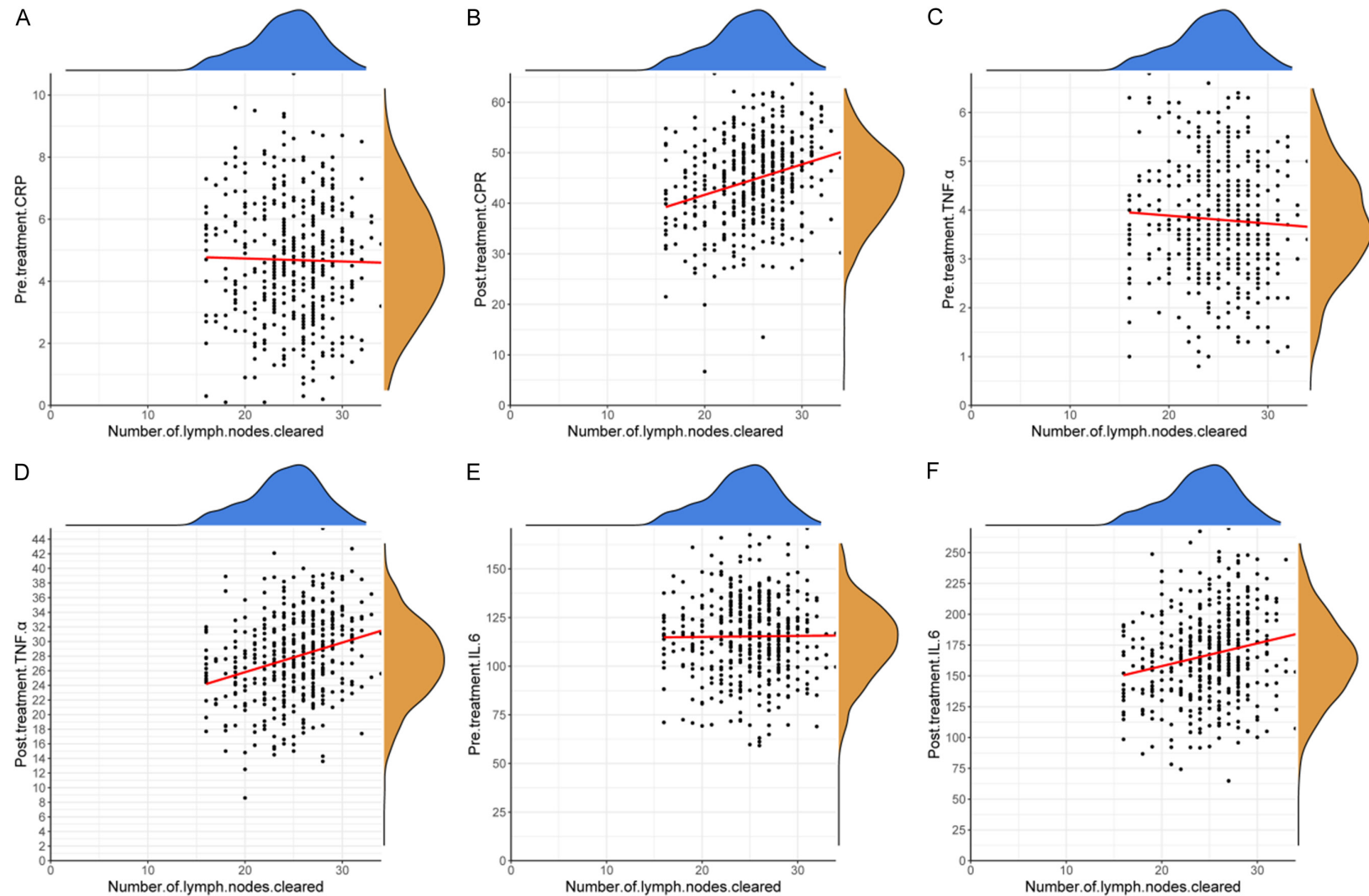


Figure 1. Correlation analysis of intraoperative lymph node dissection quantity and inflammatory markers. A, B. Correlation analysis of preoperative and postoperative CRP with the number of lymph nodes dissected. C, D. Correlation analysis of preoperative and postoperative TNF- α with the number of lymph nodes dissected. E, F. Correlation analysis of preoperative and postoperative IL-6 with the number of lymph nodes dissected. Note: CRP: C-Reactive Protein, TNF- α : Tumor Necrosis Factor-alpha, IL-6: Interleukin-6.

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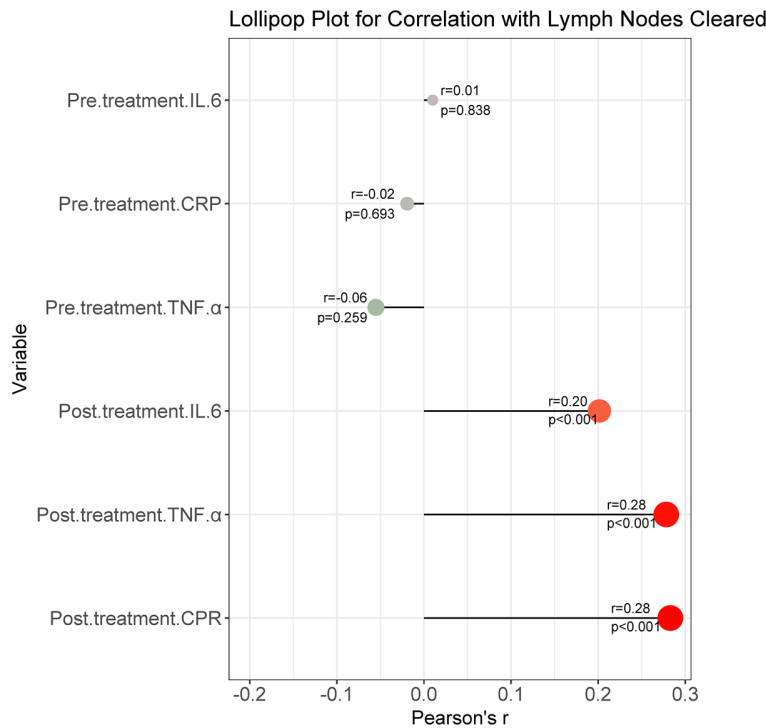


Figure 2. Correlation findings of intraoperative lymph node dissection quantity and inflammatory markers. Note: CRP: C-Reactive Protein, TNF-α: Tumor Necrosis Factor-alpha, IL-6: Interleukin-6.

complications when compared to standard dissection (Table 5).

Comparison of survival rates between the D2 and D2+ groups

The study compared 1-, 2-, and 3-year survival rates between the D2 and D2+ groups. The D2+ group showed a significantly higher 2-year survival rate compared to the D2 group ($P = 0.002$). However, no significant differences were observed in 1-year ($P = 0.067$) or 3-year survival rates ($P = 0.699$) (Table 6).

Univariate Cox regression analysis of factors affecting survival outcomes

During the 3-year follow-up, 188 patients died, resulting in a mortality rate of 44.54%. Univariate Cox regression analysis identified several factors associated with survival outcomes. Extended lymph node dissection (D2+) was associated with a significantly lower mortality risk compared to D2 ($P = 0.017$). Patients aged < 65 years had a significantly lower mortality risk than those ≥ 65 years ($P = 0.001$). Other factors associated with higher mortality

risk included comorbidities (≥ 1 , $P < 0.001$), TNM stage III ($P = 0.022$), T stage T3-T4 ($P < 0.001$), and tumor size ≥ 4 cm ($P < 0.001$). No significant associations were found with sex ($P = 0.471$), BMI ($P = 0.891$), smoking history ($P = 0.102$), alcohol consumption history ($P = 0.707$), N stage ($P = 0.372$), tumor location (gastric body $P = 0.068$, cardia $P = 0.902$), differentiation grade ($P < 0.001$), or lymphovascular invasion ($P = 0.660$) (Table 7; Figure 3).

Impact of standard and extended lymph node dissection on 3-year survival rates by TNM stage

Kaplan-Meier analysis of 3-year survival rates in stage II and III patients revealed that D2+ dissection significantly improved survival in stage II patients ($P = 0.018$), while no

significant survival benefit was observed in stage III patients ($P = 0.428$) (Figure 4).

Multivariate Cox regression analysis of factors affecting survival outcomes

Multivariate Cox regression analysis identified key factors influencing survival outcomes. TNM stage III was associated with a significantly higher mortality risk compared to stage II ($P < 0.001$). Moderately/highly differentiated tumors were associated with a significantly lower mortality risk compared to poorly differentiated tumors ($P = 0.017$). Patients aged < 65 years had a significantly lower mortality risk than those ≥ 65 years ($P = 0.036$). The surgical approach (D2+ vs. D2, $P = 0.057$) and T stage (T3-T4 vs. T1-T2, $P = 0.076$) showed trends toward significance but did not reach statistical significance (Table 8).

Univariate Cox regression analysis of factors affecting progression-free survival (PFS)

Univariate Cox analysis and cumulative incidence function (CIF) curves demonstrated that D2+ significantly reduced the risk of disease

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Table 4. Linear regression analysis of lymph node dissection quantity and preoperative/postoperative inflammatory markers

Factor	Unstandardized Coefficient		Standardized Coefficient	t	P Value	95% CI for B	
	Beta	Std. Error	Beta			lower	upper
(Constant)	15.005	1.809		8.294	< 0.001	11.449	18.56
Preoperative CRP	-0.052	0.092	-0.026	-0.568	0.57	-0.232	0.128
Postoperative CRP	0.105	0.022	0.223	4.781	< 0.001	0.062	0.148
Preoperative TNF- α	-0.272	0.155	-0.08	-1.759	0.079	-0.577	0.032
Postoperative TNF- α	0.147	0.032	0.214	4.596	< 0.001	0.084	0.21
Preoperative IL-6	-8.51E-05	0.009	< 0.001	-0.01	0.992	-0.017	0.017
Postoperative IL-6	0.014	0.005	0.130	2.785	0.006	0.004	0.024

Note: CRP: C-Reactive Protein, TNF- α : Tumor Necrosis Factor-alpha, IL-6: Interleukin-6.

Table 5. Comparison of postoperative complication rates between standard and extended lymph node dissection groups

Group	Standard Dissection Group (n = 189)	Extended Dissection Group (n = 232)	χ^2 Value	P Value
Wound Infection	4 (2.12%)	7 (3.02%)	-	0.761
Pulmonary Infection	3 (1.59%)	4 (1.72%)	-	1
Bleeding	2 (1.06%)	1 (0.43%)	-	0.59
Anastomotic Leakage	3 (1.59%)	4 (1.72%)	-	1
Intestinal Obstruction	3 (1.59%)	1 (0.43%)	-	0.33

Note: Fisher test is used.

Table 6. Comparison of postoperative survival rates between standard and extended lymph node dissection groups

Group	Standard Dissection Group (n = 189)	Extended Dissection Group (n = 232)	χ^2 Value	P Value
1-Year Survival Rate	159 (84.13%)	209 (90.09%)	3.361	0.067
2-Year Survival Rate	121 (64.02%)	181 (78.02%)	10.062	0.002
3-Year Survival Rate	95 (50.26%)	121 (52.16%)	0.149	0.699

progression ($P = 0.009$) (**Figure 5A**). Patients at stage III had a significantly higher risk of disease progression compared to stage II ($P < 0.001$), with a faster progression rate observed in stage III (**Figure 5B**). Similarly, patients with N1-N3 stages had a higher risk of disease progression compared to N0 stage ($P < 0.001$). The CIF curve for the N1-N3 group showed a steeper slope, reflecting faster progression (**Figure 5C**). Patients aged ≥ 65 years had a significantly higher risk of progression ($P = 0.001$) and a notably faster disease progression (**Figure 5D**). For T stage, T3-T4 patients had a higher risk of disease progression compared to T1-T2 ($P = 0.025$) (**Figure 5E**), and poorly differentiated tumors exhibited a significantly higher risk of progression ($P < 0.001$)

(**Figure 5F**). More specific findings are shown in **Table 9**.

Multivariate Cox regression analysis of factors affecting progression-free survival (PFS)

Multivariate Cox regression analysis confirmed that extended lymph node dissection (D2+) significantly reduced the risk of disease progression ($P = 0.035$). Patients aged < 65 years had a significantly lower progression risk than those ≥ 65 years ($P = 0.020$). TNM stage III was associated with a significantly higher progression risk compared to stage II ($P < 0.001$). Tumor differentiation grade also played a role, with moderately/highly differentiated tumors showing a significantly lower progression risk compared

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Table 7. Univariate Cox regression analysis of factors affecting survival outcomes in gastric cancer surgery

Variable	Beta	Std. Err.	P Value	HR	Lower	Upper
Surgical Approach						
D2						
D2+	-0.352	0.147	0.017	0.703	0.527	0.938
Age						
≥ 65 years						
< 65 years	-0.534	0.163	0.001	0.586	0.426	0.806
Sex						
Male						
Female	0.111	0.155	0.471	1.118	0.826	1.513
BMI						
≥ 24 kg/m ²						
< 24 kg/m ²	0.156	0.167	0.348	1.169	0.843	1.621
Smoking History						
Yes						
No	-0.022	0.164	0.891	0.978	0.710	1.347
Alcohol History						
Yes						
No	0.261	0.159	0.102	1.298	0.950	1.773
Comorbidities						
≥ 1						
< 1	0.061	0.162	0.707	1.063	0.774	1.459
TNM Stage						
II						
III	0.988	0.151	< 0.001	2.685	1.996	3.613
T Stage						
T1-T2						
T3-T4	0.403	0.176	0.022	1.496	1.061	2.111
N Stage						
N0						
N1-N3	0.910	0.200	< 0.001	2.484	1.680	3.674
Tumor Location						
Antrum						
Body	0.156	0.175	0.372	1.169	0.830	1.646
Cardia	0.332	0.182	0.068	1.393	0.976	1.989
Tumor Size						
≥ 4 cm						
< 4 cm	0.018	0.147	0.902	1.018	0.763	1.359
Differentiation						
Poor						
Moderate/High	-0.606	0.149	< 0.001	0.546	0.408	0.731
Lymphovascular Invasion						
Yes						
No	-0.217	0.147	0.140	0.805	0.603	1.074
Neural Invasion						
Yes						
No	0.065	0.148	0.660	1.067	0.799	1.427

Note: HR: Hazard Ratio, BMI: Body Mass Index, TNM: Tumor Node Metastasis.

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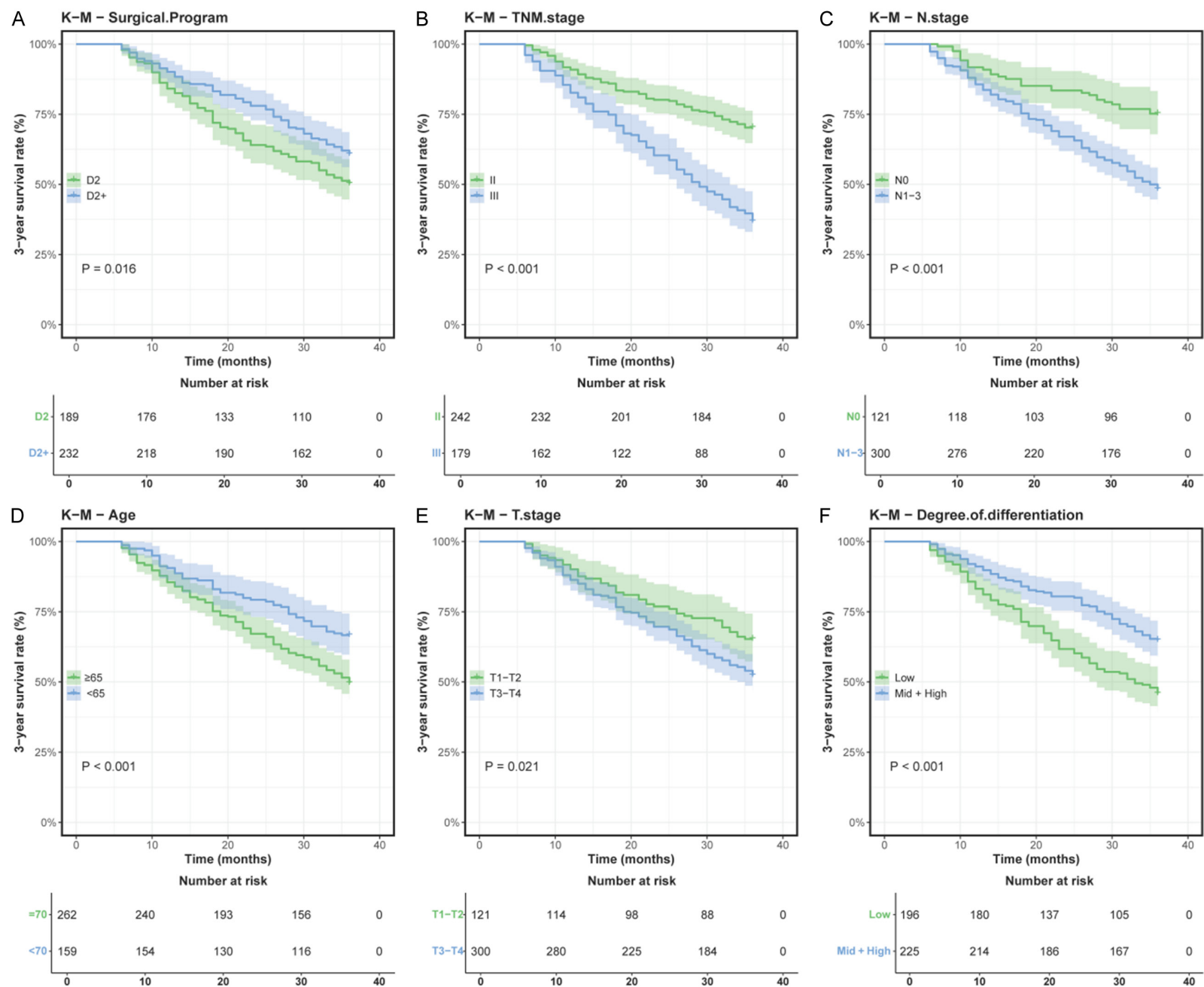


Figure 3. Survival curves for univariate Cox regression significant variables. A. Survival curves for patients with different dissection approaches. B. Survival curves for patients with different TNM stages. C. Survival curves for patients with different N stages. D. Survival curves for patients with different ages. E. Survival curves for patients with different T stages. F. Survival curves for patients with different differentiation grades. Note: TNM: Tumor Node Metastasis.

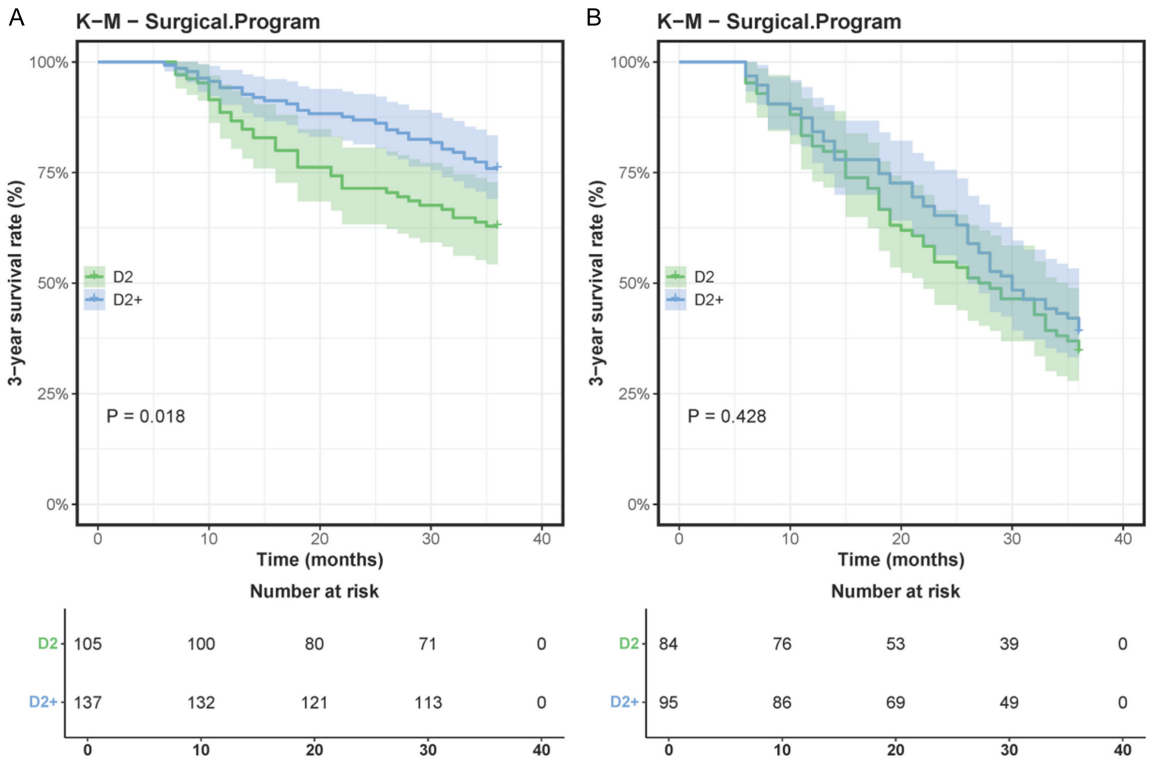


Figure 4. Three-year survival curves for standard and extended lymph node dissection in stage II and III patients. A. Three-year survival curves for standard and extended lymph node dissection in stage II patients. B. Three-year survival curves for standard and extended lymph node dissection in stage III patients.

to poorly differentiated tumors ($P = 0.024$). T stage (T3-T4 vs. T1-T2, $P = 0.072$) showed a trend toward significance but did not reach statistical significance. These results highlight that surgical approach, age, TNM stage, and differentiation grade are independent risk factors for PFS in gastric cancer patients (Table 10).

Discussion

The cornerstone of gastric cancer surgical treatment lies in achieving a balance between radical resection and lymph node dissection. While D2 lymph node dissection is widely regarded as the standard approach for locally advanced gastric cancer, the use of extended D2+ dissection remains controversial, since its potential survival benefits must be weighed against increased surgical risks [19]. Kung et al. [20] reported that in a Swedish national gas-

tric cancer surgery cohort, D1+/D2 lymph node dissection achieved a significantly higher 5-year survival rate (43.7%) compared to D0/D1 (38.5%), without increasing postoperative mortality, suggesting a survival advantage for D2 dissection in western populations. Moreover, studies have shown that laparoscopic distal gastrectomy combined with D2 dissection in locally advanced gastric cancer is associated with lower early complication rates (16.6% vs. 24.1%) and faster recovery, supporting the safety of standardized D2 procedures [21]. Recent advances in neoadjuvant chemotherapy and molecular subtyping have steered gastric cancer treatment toward more personalized approaches. However, there is still limited evidence comparing the efficacy of D2 versus D2+ across different TNM stages, particularly regarding the postoperative inflammatory

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Table 8. Multivariate cox regression analysis of factors affecting survival outcomes in gastric cancer surgery

Variable	Beta	Std. Err.	P Value	HR	Lower	Upper
Surgical Approach						
D2						
D2+	-0.280	0.148	0.057	0.755	0.566	1.009
Age						
≥ 65 years						
< 65 years	-0.350	0.167	0.036	0.705	0.508	0.978
TNM Stage						
II						
III	1.075	0.209	< 0.001	2.929	1.946	4.409
T Stage						
T1-T2						
T3-T4	-0.426	0.240	0.076	0.653	0.408	1.045
N Stage						
N0						
N1-N3		< 0.001 ^a				
Differentiation						
Poor						
Moderate/High	-0.369	0.154	0.017	0.691	0.511	0.935

Note: ^aDue to constant or linearly dependent covariates, degrees of freedom were reduced. HR: Hazard Ratio, TNM: Tumor Node Metastasis.

response and its effect on long-term prognosis.

This study found that the D2+ group exhibited a significantly higher 2-year overall survival (OS) compared to the D2 group, though no significant differences were observed in 1-year or 3-year OS. Notably, in stage II patients, the D2+ group demonstrated a significant improvement in 3-year OS ($P = 0.018$), whereas no benefit was observed in stage III patients ($P = 0.428$). These findings suggest that D2+ may offer a survival advantage in stage II patients by more thoroughly eliminating potential lymph node micrometastases. Stage II gastric cancer typically presents with a lower tumor burden and more localized lymph node metastasis, and the extended lymph node clearance in D2+ (e.g., No. 16 para-aortic lymph nodes) may effectively reduce local recurrence, thereby prolonging survival [22]. Li et al. [23] found that D2+ dissection, including No. 14v lymph nodes, improved survival in distal gastric cancer patients, particularly in those with No. 6 lymph node metastasis. Similarly, Dai et al. [24] reported that D2+ dissection (including Nos. 12a, 12b, and 12p) significantly improved 3-year PFS (67.0% vs. 55.9%) and 5-year OS

(66.2% vs. 54.0%) in advanced distal gastric cancer, further supporting the survival benefit of D2+ in patients with lower tumor burden. In contrast, stage III patients often present with more extensive lymph node metastasis or sub-clinical distant metastases, and the extended scope of D2+ may not be sufficient to alter the disease's biological progression, explaining the limited survival benefit observed in this group [5].

Multivariate Cox regression analysis identified D2+ as an independent protective factor for PFS, indicating that it may reduce local recurrence or delay disease progression. The broader scope of D2+ likely enhances the clearance of residual tumor cells, lowering recurrence risk, particularly in patients with high risk of lymph node metastasis. This finding aligns with the Japanese Gastric Cancer Treatment Guidelines (JCGC), which recommend extended dissection, although the benefits of D2+ may vary based on patient stage and biological characteristics [25, 26]. Studies have also shown that D2+ with complete mesogastric excision (CME) significantly reduces local recurrence rates ($RR = 0.51$) and improves 3-year OS ($RR = 1.16$) in advanced gastric cancer, fur-

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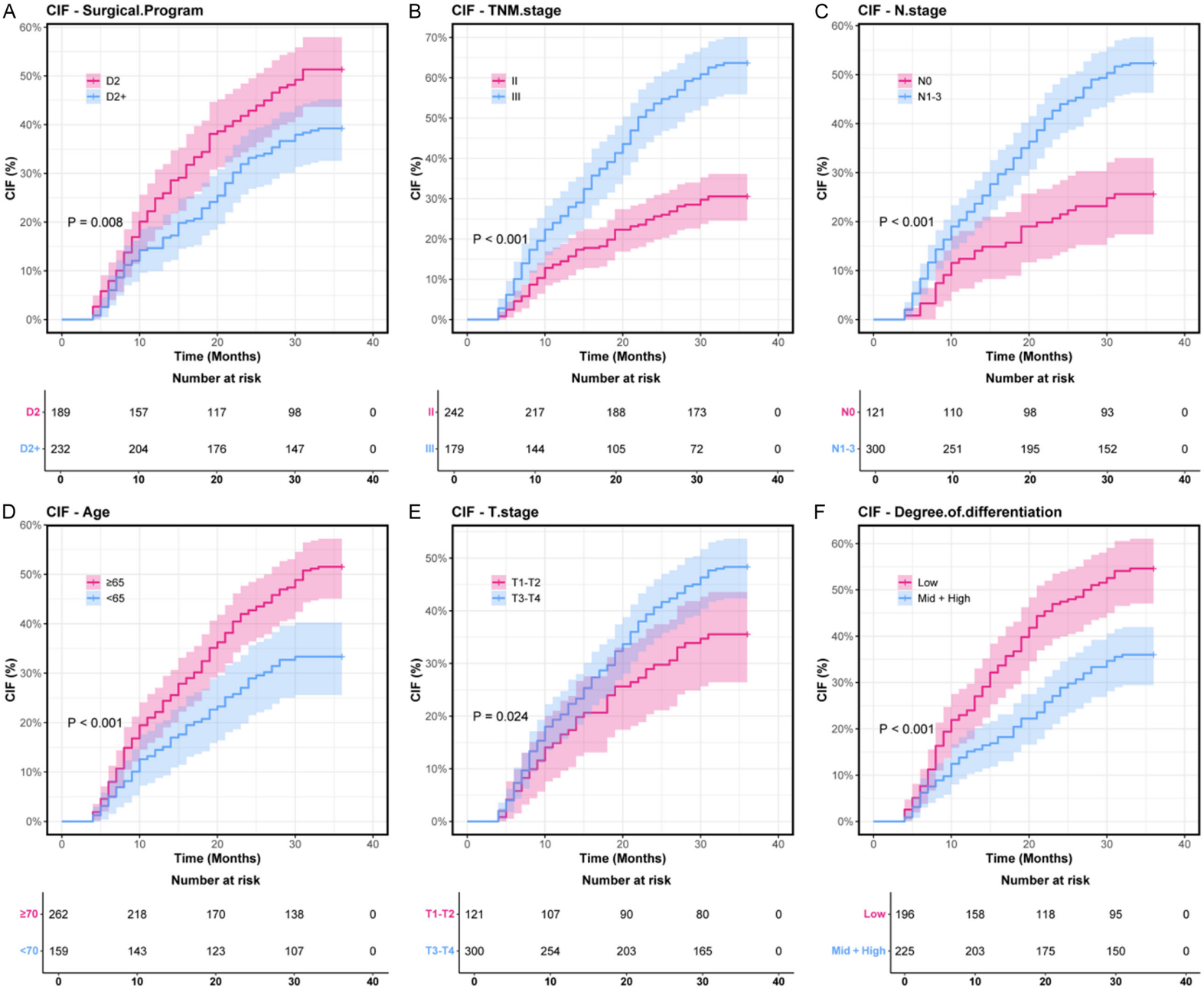


Figure 5. Cumulative incidence function (CIF) curves for univariate Cox regression significant variables. A. CIF curves for patients with different dissection approaches. B. CIF curves for patients with different TNM stages. C. CIF curves for patients with different N stages. D. CIF curves for patients with different T stages. E. CIF curves for patients with different differentiation grades. Note: CIF: Cumulative Incidence Function, TNM: Tumor Node Metastasis.

ther supporting the role of D2+ in improving local control [17]. Additionally, the lymph node ratio (LNR) has been identified as a critical prognostic marker in gastric cancer, highlighting the effect of staging and the extent of metastasis on dissection outcomes [27]. This study emphasizes the importance of TNM stage, age, and differentiation grade on PFS, reinforcing the need for personalized treatment. The differential response to D2+ between stage II and III patients suggests that tumor burden and the extent of lymph node metastasis are key determinants of the efficacy of extended dissection. Stage II patients, with less advanced disease, are more likely to benefit from the thorough clearance offered by D2+, whereas stage III patients, with higher recurrence risk, may require more aggressive systemic therapies, such as postoperative chemotherapy or immunotherapy, to address the limitations of D2+ [28]. Chen et al. [29] demonstrated that totally laparoscopic D2 gastrectomy following neoadjuvant chemotherapy optimizes surgical outcomes, suggesting that neoadjuvant chemotherapy may enhance the efficacy of D2+. Future studies should further refine the appropriate scope of D2+ based on disease stage and molecular markers (e.g., HER2, MMR status) to provide more individualized treatment approaches.

The D2+ group exhibited significantly longer operative time, greater intraoperative blood loss, and a higher number of lymph nodes dissected compared to the D2 group, reflecting the increased complexity of D2+ surgery. Removing lymph nodes from the para-aortic area or splenic hilum requires more extensive dissection, which increases surgical difficulty and technical demands. However, no significant difference in hospital stay was observed, indicating that D2+ did not substantially prolong postoperative recovery. This may be due to the beneficial effects of neoadjuvant chemotherapy on patients' systemic condition, as well as standardized intraoperative techniques and optimized postoperative care. D2+ surgery requires significant expertise and should be

performed at high-volume centers to ensure safety. Kulig et al. [30] reported no significant differences in complication rates or mortality between D2+ (including para-aortic lymph nodes) and D2, confirming the safety of D2+ when performed in experienced centers. Studies also suggest that removing more than 35 lymph nodes in D2 dissection increases complication risks without affecting mortality, indicating that the increased lymph node resected in D2+ may heighten postoperative burden [31]. This study also found that postoperative CRP, TNF- α , and IL-6 levels were significantly higher in the D2+ group and positively correlated with the number of lymph nodes dissected. Linear regression analysis confirmed this association. The extended scope of D2+ likely induces more tissue damage and vascular exposure, triggering an acute inflammatory response marked by elevated inflammatory markers [32]. CRP, as an acute-phase reactant, reflects systemic inflammation, while TNF- α and IL-6 play critical roles in tissue injury and immune responses [16]. The higher number of lymph nodes dissected in D2+ may exacerbate inflammation by prolonging operative time and expanding the trauma area [33, 34]. The heightened inflammatory response associated with D2+ may increase postoperative burden in elderly or frail patients, potentially offsetting its survival benefits. Therefore, preoperative evaluation of inflammatory status (e.g., baseline CRP levels) and systemic tolerance is crucial. For stage II patients, the survival benefits of D2+ likely outweigh the risks of inflammatory burden, but for stage III patients, careful consideration is needed, particularly in cases where inflammation is exacerbated. Future studies could investigate preoperative immunomodulation or postoperative anti-inflammatory therapies (e.g., NSAIDs or immunosuppressants) to reduce inflammation and optimize clinical outcomes following D2+.

Multivariate Cox regression analysis revealed that age < 65 years, lower TNM stage (stage II), and higher differentiation grade were independent protective factors for both OS and PFS,

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Table 9. Univariate Cox regression analysis of factors affecting progression-free survival (PFS) in gastric cancer surgery

Factor	Beta	Std. Err.	P Value	HR	Lower	Upper
Surgical Approach						
D2						
D2+	-0.381	0.146	0.009	0.683	0.513	0.909
Age						
≥ 65 years						
< 65 years	-0.563	0.162	0.001	0.570	0.415	0.783
Sex						
Male						
Female	0.119	0.153	0.439	1.126	0.834	1.521
BMI						
≥ 24 kg/m ²						
< 24 kg/m ²	0.151	0.165	0.361	1.163	0.841	1.607
Smoking History						
Yes						
No	-0.036	0.163	0.825	0.965	0.701	1.328
Alcohol History						
Yes						
No	0.256	0.158	0.106	1.291	0.947	1.760
Comorbidities						
≥ 1						
< 1	0.049	0.160	0.760	1.050	0.767	1.438
TNM Stage						
II						
III	0.972	0.150	0.000	2.644	1.971	3.546
T Stage						
T1-T2						
T3-T4	0.389	0.174	0.025	1.476	1.050	2.074
N Stage						
N0						
N1-N3	0.897	0.197	0.000	2.453	1.668	3.607
Tumor Location						
Antrum						
Body	0.130	0.173	0.454	1.139	0.810	1.600
Cardia	0.319	0.180	0.075	1.376	0.968	1.957
Tumor Size						
≥ 4 cm						
< 4 cm	0.032	0.146	0.829	1.032	0.775	1.375
Differentiation						
Poor						
Moderate/High	-0.590	0.148	0.000	0.555	0.415	0.741
Lymphovascular Invasion						
Yes						
No	-0.199	0.146	0.173	0.819	0.616	1.091
Neural Invasion						
Yes						
No	0.089	0.147	0.545	1.093	0.819	1.459

Note: PFS: Progression-Free Survival, HR: Hazard Ratio, BMI: Body Mass Index, TNM: Tumor Node Metastasis.

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Table 10. Multivariate Cox regression analysis of factors affecting progression-free survival (PFS) in gastric cancer surgery

Variable	Beta	Std. Err.	P Value	HR	Lower	Upper
Surgical Approach						
D2						
D2+	-0.309	0.146	0.035	0.734	0.551	0.978
Age						
≥ 65 years						
< 65 years	-0.386	0.167	0.020	0.680	0.490	0.942
TNM Stage						
II						
III	1.056	0.206	0.000	2.875	1.921	4.304
T Stage						
T1-T2						
T3-T4	-0.425	0.236	0.072	0.654	0.411	1.039
N Stage						
N0						
N1-N3		0.000 ^a				
Differentiation						
Poor						
Moderate/High	-0.346	0.153	0.024	0.708	0.524	0.955

Note: ^aDue to constant or linearly dependent covariates, degrees of freedom were reduced. HR: Hazard Ratio, TNM: Tumor Node Metastasis.

with D2+ showing an independent protective effect on PFS ($P = 0.035$) and a trend toward significance for OS ($P = 0.057$). Younger patients, with better systemic conditions, recover faster and tolerate more extensive dissection [35]. Lower TNM stage and higher differentiation grade were associated with reduced tumor invasiveness and metastatic potential, correlating with better prognosis [36]. These findings highlight the importance of patient-specific characteristics in treatment decision-making. The potential benefits of D2+ in younger, stage II, and well-differentiated patients may stem from its enhanced tumor control capabilities. The benefits of D2+ observed in stage II patients in this study may be due to the widespread use of neoadjuvant chemotherapy, which shrinks tumors and controls micrometastases, thereby amplifying the efficacy of D2+. The lack of clear benefits from D2+ in western studies may be due to differences in patient selection, postoperative adjuvant therapies, or insufficient follow-up duration.

However, this study has some limitations. First, its retrospective design may have introduced selection bias, limiting causal inferences. Second, the 3-year follow-up duration

did not assess 5-year survival or long-term prognosis, potentially underestimating the benefits of D2+. Lastly, the study did not assess postoperative quality of life, digestive function, or conduct subgroup analyses of dissection extent, restricting the comprehensiveness of the findings. Future research should include multicenter, prospective randomized controlled trials to validate the efficacy and safety of D2+, extend follow-up to evaluate long-term survival and quality of life, explore inflammatory markers (e.g., CRP, TNF- α , IL-6) as prognostic indicators, and investigate D2+ efficacy across molecular subtypes of gastric cancer using genomic and immunological approaches. The effect of D2+ on postoperative adjuvant therapies (e.g., immune checkpoint inhibitors) should also be further explored.

Conclusion

D2+ lymph node dissection improves 2-year OS and PFS in stage II gastric cancer patients without increasing postoperative complication risk. However, it induces a more pronounced inflammatory response, particularly in elderly or frail patients. D2+ should be prioritized for stage II patients, balancing survival benefits against

inflammation. For stage III patients, careful assessment is needed. Monitoring inflammatory markers can optimize postoperative management. Future studies should focus on long-term follow-up, molecular subtyping, and the role of D2+ in precision medicine to enhance patient outcomes.

Disclosure of conflict of interest

None.

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References

- [1] Thrift AP, Wenker TN and El-Serag HB. Global burden of gastric cancer: epidemiological trends, risk factors, screening and prevention. *Nat Rev Clin Oncol* 2023; 20: 338-349.
- [2] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I and Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024; 74: 229-263.
- [3] Huang J, Lucero-Prisno DE 3rd, Zhang L, Xu W, Wong SH, Ng SC and Wong MCS. Updated epidemiology of gastrointestinal cancers in East Asia. *Nat Rev Gastroenterol Hepatol* 2023; 20: 271-287.
- [4] Cheng X, Dai E, Wu J, Flores NM, Chu Y, Wang R, Dang M, Xu Z, Han G, Liu Y, Chatterjee D, Hu C, Ying J, Du Y, Yang L, Guan X, Mo S, Cao X, Pei G, Jiang J, Lu X, Benitez AM, Waters RE, Pizzi MP, Shanbhag N, Fan Y, Peng F, Hanash SM, Calin G, Futreal A, Song S, Yee C, Mazur PK, Qin JJ, Ajani JA and Wang L. Atlas of metastatic gastric cancer links ferroptosis to disease progression and immunotherapy response. *Gastroenterology* 2024; 167: 1345-1357.
- [5] Hikage M, Fujiya K, Kamiya S, Tanizawa Y, Bando E, Notsu A and Terashima M. Prognostic factors in patients who received paraaortic lymph node dissection for locally advanced gastric cancer with extensive lymph node metastasis. *Langenbecks Arch Surg* 2022; 407: 1027-1037.
- [6] Wang D, Wang Y, Dong L, Zhang X and Du J. Preoperatively predicting the lymph node metastasis and prognosis for gastric cancer patients. *Sci Rep* 2024; 14: 11213.
- [7] Dehal A, Woo Y, Glazer ES, Davis JL and Strong VE; Society of Surgical Oncology Gastrointestinal Disease Site Workgroup. D2 lymphadenectomy for gastric cancer: advancements and technical considerations. *Ann Surg Oncol* 2025; 32: 2129-2140.
- [8] Yang Y, Chen Y, Hu Y, Feng Y, Mao Q and Xue W. Outcomes of laparoscopic versus open total gastrectomy with D2 lymphadenectomy for gastric cancer: a systematic review and meta-analysis. *Eur J Med Res* 2022; 27: 124.
- [9] Xie D, Shen J, Liu L, Cao B, Xiao A, Qin J, Wu J, Yan Q, Hu Y, Yang C, Cao Z, Hu J, Yin P and Gong J. Randomized clinical trial on D2 lymphadenectomy versus D2 lymphadenectomy plus complete mesogastric excision in patients undergoing gastrectomy for cancer (DCGC01 study). *Br J Surg* 2024; 111: znae106.
- [10] Xiang H, Dong Z, Wu H, He Y, Chen Z, Chen S, Yu W and Liang C. Convenient method to improve efficiency of lymph node examination after gastrectomy with D2 lymphadenectomy for gastric cancer. *BMC Gastroenterol* 2023; 23: 428.
- [11] Faiz Z, Hayashi T and Yoshikawa T. Lymph node dissection for gastric cancer: establishment of D2 and the current position of splenectomy in Europe and Japan. *Eur J Surg Oncol* 2021; 47: 2233-2236.
- [12] Kossenas K, Moutzouri O and Georgopoulos F. Evaluating the safety of robotic total gastrectomy with D2 lymphadenectomy for gastric cancer against the conventional laparoscopic approach: a systematic review and meta-analysis. *J Robot Surg* 2025; 19: 59.
- [13] de Steur WO, van Amelsfoort RM, Hartgrink HH, Putter H, Meershoek-Klein Kranenbarg E, van Grieken NCT, van Sandick JW, Claassen YHM, Braak JPBM, Jansen EPM, Sikorska K, van Tinteren H, Walraven I, Lind P, Nordmark M, van Berge Henegouwen MI, van Laarhoven HWM, Cats A, Verheij M and van de Velde CJH; CRITICS investigators. Adjuvant chemotherapy is superior to chemoradiation after D2 surgery for gastric cancer in the per-protocol analysis of the randomized CRITICS trial. *Ann Oncol* 2021; 32: 360-367.
- [14] Wang SB, Chen JY, Xu C, Cao WG, Cai R, Cao L and Cai G. Evaluation of systemic inflammatory and nutritional indexes in locally advanced gastric cancer treated with adjuvant chemoradiotherapy after D2 dissection. *Front Oncol* 2022; 12: 1040495.
- [15] Liu J, Geng Q, Chen S, Liu X, Kong P, Zhou Z, Zhan Y and Xu D. Nomogram based on systemic inflammatory response markers predicting the survival of patients with resectable gastric cancer after D2 gastrectomy. *Oncotarget* 2016; 7: 37556-37565.
- [16] Fu J, Lin F, Zheng S, Hong W and Zhang M. Laparoscopic D2 radical gastrectomy improves

- postoperative inflammation and gastric function in elderly patients with advanced gastric cancer. *Am J Transl Res* 2022; 14: 8695-8702.
- [17] Meng X, Wang L, Liu G, Zhang J, Wang Y, Yang D, Zheng G, Zhang T, Zheng Z and Zhao Y. D2 lymphadenectomy with complete mesogastrium excision vs. conventional D2 gastrectomy for advanced gastric cancer. *Chin Med J (Engl)* 2022; 135: 1223-1230.
 - [18] Lauricella S, Caricato M, Mascianà G, Caranante F, Carnazza M, Bonaccorso A, Angeletti S, Ciccozzi M, Coppola R and Capolupo GT. Topographic lymph node staging system shows prognostic superiority compared to the 8th edition of AJCC TNM in gastric cancer. A western monocentric experience. *Surg Oncol* 2020; 34: 223-233.
 - [19] Wang G, Tan Y, Jiang Y, Liu J, Su Y, Sun Z and Liu B. Prognostic model of D2 radical gastrectomy combined with neoadjuvant chemotherapy for gastric cancer. *Risk Manag Healthc Policy* 2023; 16: 1259-1271.
 - [20] Kung CH, Tsai JA, Lundell L, Johansson J, Nilsson M and Lindblad M. Nationwide study of the impact of D2 lymphadenectomy on survival after gastric cancer surgery. *BJS Open* 2020; 4: 424-431.
 - [21] Lee HJ, Hyung WJ, Yang HK, Han SU, Park YK, An JY, Kim W, Kim HI, Kim HH, Ryu SW, Hur H, Kong SH, Cho GS, Kim JJ, Park DJ, Ryu KW, Kim YW, Kim JW, Lee JH and Kim MC; Korean Laparo-endoscopic Gastrointestinal Surgery Study (KLASS) Group. Short-term outcomes of a multicenter randomized controlled trial comparing laparoscopic distal gastrectomy with D2 lymphadenectomy to open distal gastrectomy for locally advanced gastric cancer (KLASS-02-RCT). *Ann Surg* 2019; 270: 983-991.
 - [22] Lee H, Song KY, Lee HH and Lee J. Worse survival of patients with T1 stage II gastric cancer following radical gastrectomy. *J Gastric Cancer* 2023; 23: 598-608.
 - [23] Li JQ, He D and Liang YX. Current status of extended 'D2 plus' lymphadenectomy in advanced gastric cancer. *Oncol Lett* 2021; 21: 467.
 - [24] Dai W, Zhai ET, Chen J, Chen Z, Zhao R, Chen C, Yuan Y, Wu H, Cai S and He Y. Extensive dissection at No. 12 station during D2 lymphadenectomy improves survival for advanced lower-third gastric cancer: a retrospective study from a single center in southern China. *Front Oncol* 2022; 11: 760963.
 - [25] Katai H, Ishikawa T, Akazawa K, Fukagawa T, Isobe Y, Miyashiro I, Oda I, Tsujitani S, Ono H, Tanabe S, Nunobe S, Suzuki S and Kakeji Y; Registration Committee of the Japanese Gastric Cancer Association. Optimal extent of lymph node dissection for remnant advanced gastric carcinoma after distal gastrectomy: a retrospective analysis of more than 3000 patients from the nationwide registry of the Japanese Gastric Cancer Association. *Gastric Cancer* 2020; 23: 1091-1101.
 - [26] Nico R, Veiziant J, Chau A, Eveno C and Piessen G. Optimal lymph node dissection for gastric cancer: a narrative review. *World J Surg Oncol* 2024; 22: 108.
 - [27] Wang Y, Wang Y, Wu W, Lu X, An T and Jiang J. Laparoscopic gastrectomy plus D2 lymphadenectomy is as effective as open surgery in terms of long-term survival: a single-institution study on gastric cancer. *World J Surg Oncol* 2021; 19: 102.
 - [28] An JY, Min JS, Hur H, Lee YJ, Cho GS, Park YK, Jung MR, Park JH, Hyung WJ, Jeong SH, Kim YW, Yoon HM, Eom BW, Kook MC, Han MR, Nam BH and Ryu KW; SENTinel Node ORiented Tailored Approach (SENORITA) Study Group. Laparoscopic sentinel node navigation surgery versus laparoscopic gastrectomy with lymph node dissection for early gastric cancer: short-term outcomes of a multicentre randomized controlled trial (SENORITA). *Br J Surg* 2020; 107: 1429-1439.
 - [29] Chen Z, Chen G, Li Y, Kou S, Wang T, Zhang L, Cao Y and Liu L. Comparison of totally laparoscopic and laparoscopic-assisted approach in gastrectomy with D2 lymphadenectomy for advanced gastric cancer after neoadjuvant chemotherapy: a retrospective comparative study. *Ann Surg Treat Res* 2024; 106: 218-224.
 - [30] Kulig J, Popiela T, Kolodziejczyk P, Sierzega M and Szczepanik A; Polish Gastric Cancer Study Group. Standard D2 versus extended D2 (D2+) lymphadenectomy for gastric cancer: an interim safety analysis of a multicenter, randomized, clinical trial. *Am J Surg* 2007; 193: 10-15.
 - [31] Brisinda G, Chiarello MM, Crocco A, Adams NJ, Fransvea P and Vanella S. Postoperative mortality and morbidity after D2 lymphadenectomy for gastric cancer: a retrospective cohort study. *World J Gastroenterol* 2022; 28: 381-398.
 - [32] Liang H. Prevention of surgery-related complications of D2+ lymphadenectomy for gastric cancer. *Zhonghua Wei Chang Wai Ke Za Zhi* 2017; 20: 140-143.
 - [33] Szczepanik AM, Scislo L, Scully T, Walewska E, Siedlar M, Kolodziejczyk P, Lenart M, Rutkowska M, Galas A, Czupryna A and Kulig J. IL-6 serum levels predict postoperative morbidity in gastric cancer patients. *Gastric Cancer* 2011; 14: 266-273.
 - [34] Ling J, Wang X and Ying J. The impact of laparoscopic radical gastrectomy on the inflammatory response and immune function of patients

Extended lymph node dissection in gastric cancer surgery

- with gastric cancer. *Cell Mol Biol (Noisy-le-grand)* 2024; 70: 92-96.
- [35] Matsui R, Inaki N, Tsuji T and Fukunaga T. Preoperative chronic inflammation is a risk factor for postoperative complications independent of body composition in gastric cancer patients undergoing radical gastrectomy. *Cancers (Basel)* 2024; 16: 833.
- [36] Sasako M, Sano T, Yamamoto S, Kurokawa Y, Nashimoto A, Kurita A, Hiratsuka M, Tsujinaka T, Kinoshita T, Arai K, Yamamura Y and Okajima K; Japan Clinical Oncology Group. D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. *N Engl J Med* 2008; 359: 453-462.