

Supplementary Online Content

Zheng C, Xu Y, Zhao G, et al. Outcomes of laparoscopic total gastrectomy combined with spleen-preserving hilar lymphadenectomy for locally advanced proximal gastric cancer: a nonrandomized clinical trial. *JAMA Netw Open*. 2021;4(12):e2139992. doi:10.1001/jamanetworkopen.2021.39992

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Eligibility Criteria of the Trial

Inclusion Criteria
(1) Age between 18 and 75 years
(2) Advanced upper third gastric adenocarcinoma (cT2-4a, N-/+, M0) at preoperative evaluation according to the American Joint Committee on Cancer (AJCC) Cancer Staging Manual Seventh Edition
(3) Heart, lungs, kidneys and other vital organs function well, with no obvious surgical contraindications
(4) Preoperative examination with no distant metastasis, no significantly enlarged lymph nodes around abdominal main artery, and tumor not a direct violation of the pancreas, spleen and other surrounding organs
(5) American Society of Anesthesiology (ASA) score class I, II, or III
(6) Written informed consent
Exclusion Criteria:
(1) Women during pregnancy or breast-feeding
(2) Severe mental disorder
(3) History of previous upper abdominal surgery (except laparoscopic cholecystectomy)
(4) Enlarged splenic hilar lymph nodes with integration into a mass and surrounding the blood vessels
(5) History of unstable angina or myocardial infarction within past six months
(6) History of cerebrovascular accident within past six months
(7) History of continuous systematic administration of corticosteroids within one month
(8) History of previous neoadjuvant chemotherapy or radiotherapy
(9) T4b tumors
(10) Emergency surgery due to complication (bleeding, obstruction or perforation) caused by gastric cancer
(11) FEV1(Forced expiratory volume in one second)<50% of predicted values
(12) Peritoneal lavage cytology is positive for cancer cells*
Abbreviations: AJCC, American Joint Committee on Cancer; ASA, American Society of Anesthesiology FEV1, forced expiratory volume in 1 second.

* The peritoneal lavage was performed intraoperatively.

eTable 2. Distribution of Early and Late Complications

Complication	All Population (n=246)
Total early complications	35(14.2%)
Local complications	21(8.5%)
Abdominal infection	12(4.9%)
Wound infection	2(0.8%)
Anastomotic leakage	7(2.8%)
Lymphatic leakage	1(0.4%)
Anastomotic bleeding	2(0.8%)
Abdominal bleeding	3(1.2%)
Systemic complications	17(6.9%)
Pulmonary	13(5.3%)
Cardiac	2(0.8%)
Renal	3(1.2%)
Hepatic	1(0.4%)
Other	3(1.2%)
Total late complications	4(1.6%)
Intestinal obstruction	2(0.8%)
Anastomotic stenosis	1(0.4%)
Malabsorption	1(0.4%)
Clavien-Dindo complication grade	
I or II	29(11.8%)
≥ III	9(3.7%)
90-d mortality	1(0.4%)

eTable 3. Univariable Analysis for Predicting Overall Survival and Disease-Free Survival

Clinicopathologic Characteristics	OS			DFS	
	HR (95% CI)	P		HR (95% CI)	P
Age	1.02(0.99-1.05)	.32		1.02(0.99-1.05)	.18
Sex					
Men	Reference			Reference	
Women	0.80(0.43-1.49)	.48		0.79(0.45-1.39)	.41
BMI	0.98(0.89-1.08)	.65		0.99(0.91-1.08)	.81
ECOG					
0	Reference			Reference	
1	1.19(0.69-2.05)	.53		1.05(0.64-1.73)	.85
Comorbidity					
None	Reference			Reference	
One or more	2.73(1.58-4.71)	<.001		2.44(1.48-4.01)	<.001
Tumor size	1.13(1.03-1.24)	.007		1.13(1.05-1.23)	.002
Histology					
Other	Reference			Reference	
SRC or poorly differentiated AC	2.49(1.34-4.65)	.004		2.17(1.27-3.72)	.005
Cross-sectional part					
Non-greater curvature	Reference			Reference	
Greater curvature	2.06(1.01-4.20)	.05		1.62(0.80-3.26)	.18
No. of retrieved lymph nodes	0.98(0.97-1.00)	.08		1.00(0.99-1.02)	.84
No.10 lymph node metastasis	3.06(1.50-6.26)	.002		2.70(1.38-5.29)	.004
Vascular invasion	2.56(1.50-4.37)	.001		2.74(1.69-4.44)	<.001
Lymphatic invasion	1.86(1.08-3.21)	.03		1.84(1.12-3.01)	.02
Perineural invasion	1.78(1.01-3.16)	.05		1.78(1.06-2.97)	.03
Pathologic TNM stage					
I	NA			NA	
II	Reference			Reference	
III	3.55(1.74-7.27)	.001		3.32(1.78-6.21)	<.001
Received adjuvant chemotherapy	0.64(0.37-1.13)	.13		0.82(0.48-1.40)	.47

Abbreviation: ECOG, Eastern Cooperative Oncology Group score; SRC, Signet-ring cell; AC, Adenocarcinoma.
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eTable 4. Clinical and Pathologic Characteristics Between Patients With and Without Adjuvant Chemotherapy

Characteristics	No ACT (n=5)	ACT (n=14)	P
Age, y			
Mean (SD)	61.8(15.4)	55.6(9.3)	.30
Sex			.53
Women	0(0.0%)	3(21.4%)	
Men	5(100.0%)	11(78.6%)	
BMI			
Mean (SD)	23.0(3.3)	20.7(2.7)	.14
ECOG			.13
0	5(100.0%)	8(57.1%)	
1	0(0.0%)	6(42.9%)	
Comorbidity			>.99
None	5(100.0%)	13(92.9%)	
One or more	0(0.0%)	1(7.1%)	
Tumor size, cm			
Mean (SD)	6.6(2.6)	4.8(2.4)	.18
Histology			.53
SRC or poorly differentiated AC	5(100.0%)	11(78.6%)	
Other	0(0.0%)	3(21.4%)	
Cross-sectional part			.06
Non-greater curvature	3(60.0%)	14(100.0%)	
Greater curvature	2(40.0%)	0(0.0%)	
Clinical T stage			.62
T2	0(0.0%)	1(7.1%)	
T3	1(20.0%)	5(35.7%)	
T4a	4(80.0%)	8(57.1%)	
Clinical N stage			>.99
N0	1(20.0%)	2(14.3%)	
N+	4(80.0%)	12(85.7%)	
Clinical TNM stage			.93
II	1(20.0%)	5(35.7%)	
III	4(80.0%)	9(64.3%)	
Vascular invasion	4(80.0%)	9(64.3%)	.93
Lymphatic invasion	3(60.0%)	8(57.1%)	>.99
Perineural invasion	5(100.0%)	12(85.7%)	>.99
Pathologic T stage			.17
T2	0(0.0%)	2(14.3%)	
T3	1(20.0%)	7(50.0%)	
T4a	4(80.0%)	5(35.7%)	
Pathologic N stage			.31
N1	0(0.0%)	3(21.4%)	
N2	1(20.0%)	1(7.1%)	
N3	4(80.0%)	10(71.4%)	

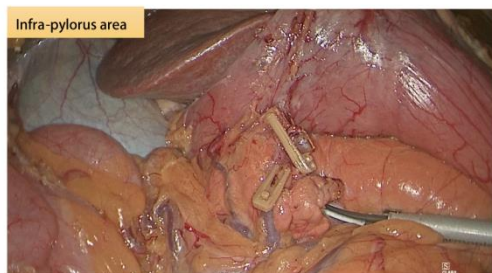
Pathologic TNM stage			.53
II	0(0.0%)	3(21.4%)	
III	5(100.0%)	11(78.6%)	

Abbreviation: ACT, Adjuvant Chemotherapy; ECOG, Eastern Cooperative Oncology Group score; SRC, Signet-ring cell; AC, Adenocarcinoma.

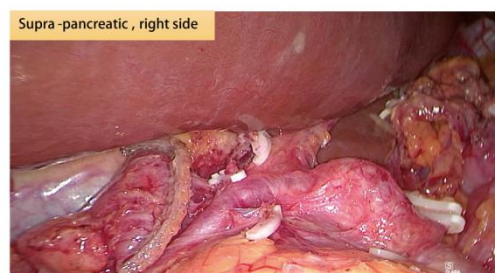
A

Surgeon eligibility	Video evaluation	Photos recorded during operation
<ul style="list-style-type: none"> • experience for > 50 cases in LSTG • the annual no. > 300 cases of gastric cancer surgery in each institute 	<ul style="list-style-type: none"> • three consecutive unedited videos of LSTG • two in each were randomly selected • double-blind peer review • radicality confirmed by 3 reviewers 	<ul style="list-style-type: none"> • Six photos for field of lymph node dissection

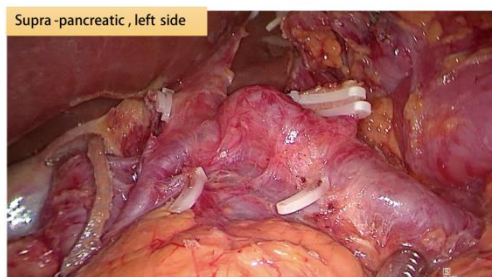
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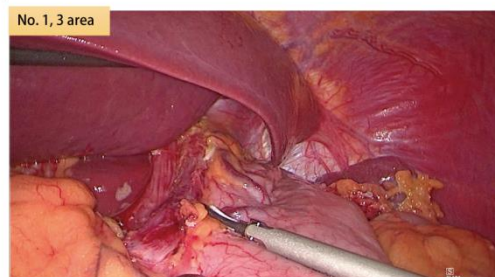
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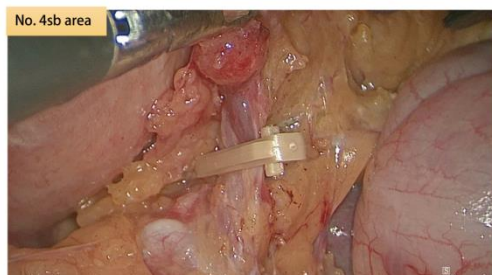
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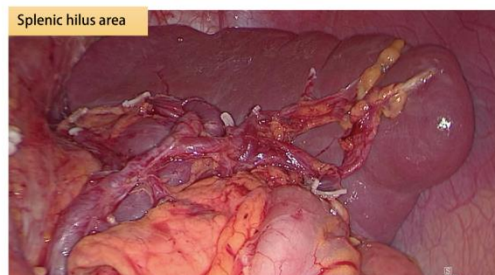
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F

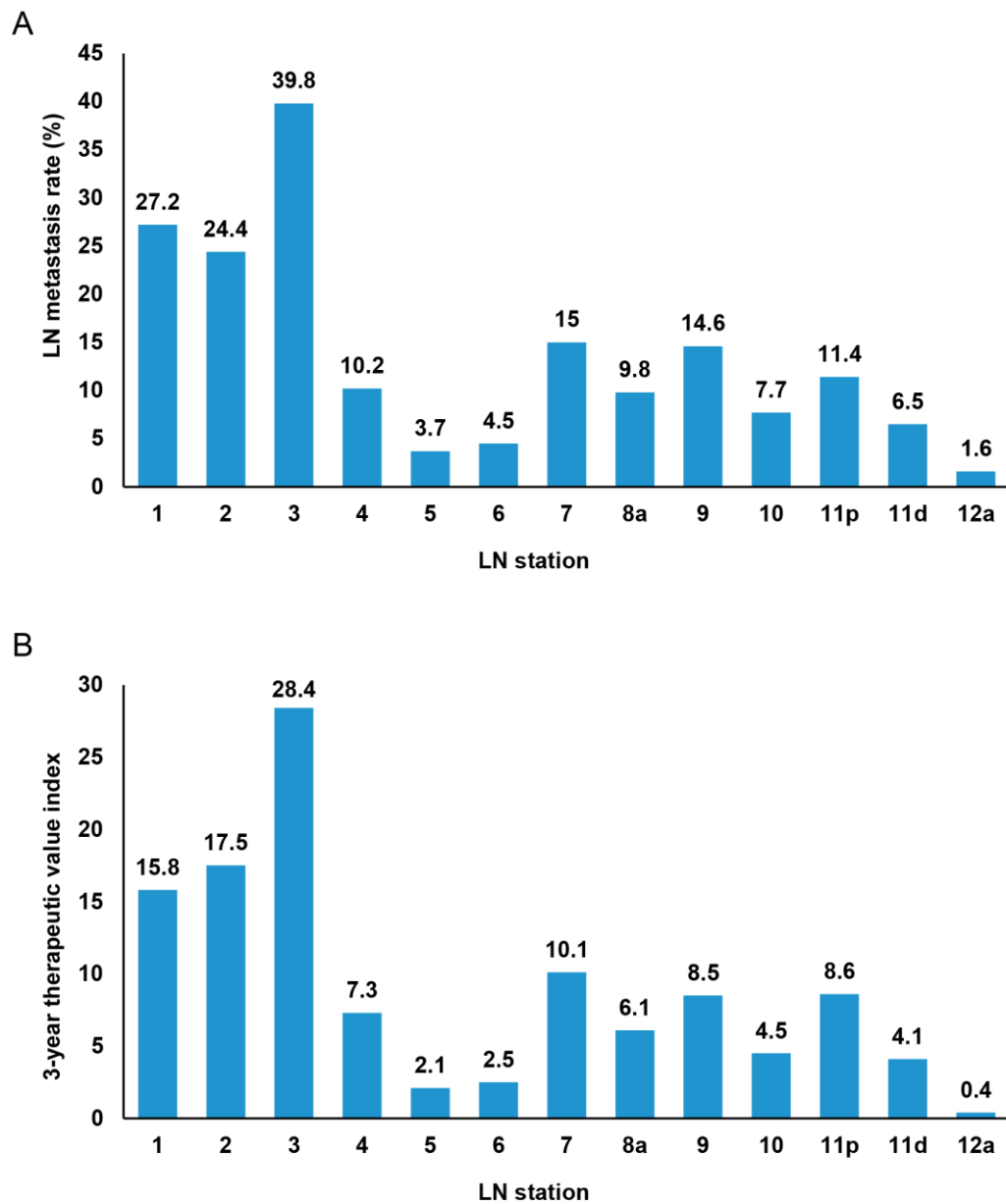


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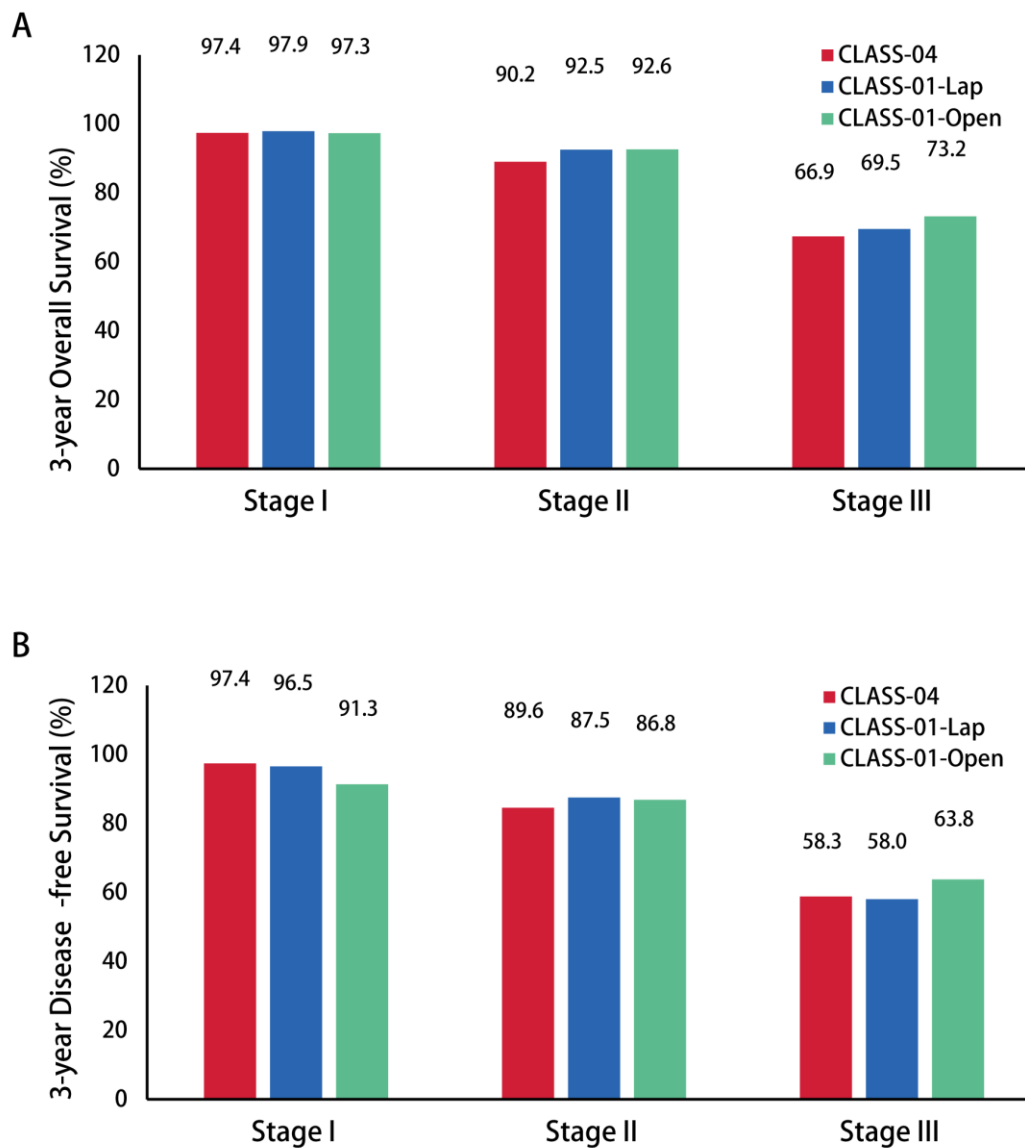


eFigure 1. Surgical Quality Control for CLASS-04 Trial (A) and Field of Lymph Node Dissection (B-G)

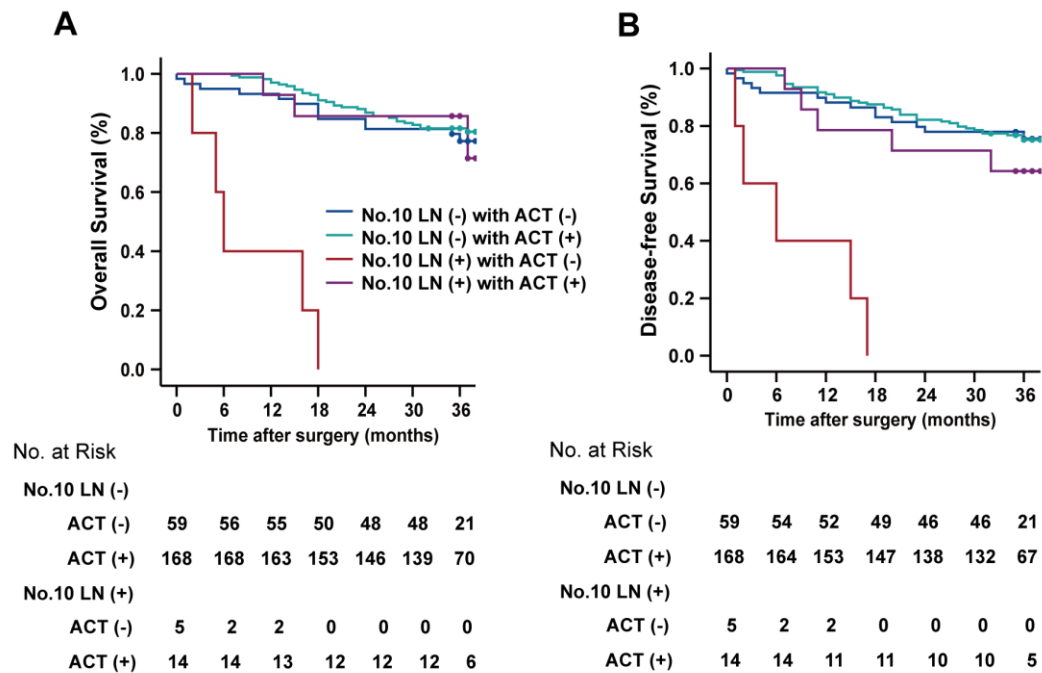
(B) Infra-pylorus area; (C) Supra-pancreatic, right side; (D) Supra-pancreatic, left side; (E) No. 1, 3 area; (F) No. 4sb area; (G) Splenic hilus area.



eFigure 2. The Incidence of Lymph Node (LN) Metastasis (A) and 3-Year Therapeutic Value Index (B) of LN Dissection



eFigure 3. Comparison of the long-term survival of patients with different stages in the CLASS-04 and CLASS-01 studies. Lap, Laparoscopic.



eFigure 4. Kaplan-Meier Curves of Overall Survival (A) and Disease-Free Survival (B) for Patients With No. 10 Lymph Node (LN) Metastasis and Without Metastasis Stratified by Adjuvant Chemotherapy