

Laparoscopic D2+ lymph node dissection in patients with obesity and gastric cancer: A retrospective study

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Abstract. D2 lymph node dissection is widely used in laparoscopic radical gastrectomy for gastric cancer, and its efficacy and safety are known for patients with obesity. Currently, D2+ lymph node dissection is also applied to certain patients with gastric cancer of later stages. Due to the high difficulty of D2+ surgery, it is more challenging to perform on patients with obesity. There is currently limited research on the efficacy and safety of D2+ surgery in obese patients with gastric cancer. The present study aimed to retrospectively analyze the clinical data of patients undergoing laparoscopic radical gastrectomy for gastric cancer admitted to a single gastroenterology department. Patients with a body mass index ≥ 25 kg/m² were included in the study. A total of 149 patients were selected as the research subjects and divided into two groups. The observation group comprised 74 patients who underwent D2+ lymph node dissection, while the control group comprised 75 patients who underwent standard D2 lymph node dissection. The surgical performance, postoperative recovery and postoperative complications of the two groups were compared. The results showed that the rates of conversion to open surgery in the D2+ and D2 groups were 5.4% (4/74) and 2.7% (2/75), respectively, and were not significantly different. The duration of surgery in the D2+ group (282.55 ± 23.02 min) was significantly longer than that in the D2 group (271.45 ± 20.05 min). The mean number of lymph node dissections in the D2+ group was 28.57 ± 7.19 , which was significantly higher than that in the D2 group (25.29 ± 6.41). No statistically significant differences in intraoperative blood loss, time to first flatus, postoperative hospitalization days, total hospitalization expenses or postoperative complications was detected between the two groups. There were no deaths in either group within the 30-day perioperative period. In addition, there was no significant

difference in the 3-year overall survival rate between the two groups, while the 5-year overall survival rate of the D2+ group was significantly higher than that of the D2 group. For obese patients with gastric cancer, D2+ surgery may increase the duration of surgery and slightly increase intraoperative blood loss compared with standard D2 radical surgery, but does not increase the incidence of postoperative complications. Moreover, D2+ surgery increases the number of lymph node dissections and improves the 5-year survival rate of patients. Therefore, it may be concluded that laparoscopic D2+ lymph node dissection is safe and feasible for obese patients with gastric cancer.

Introduction

Obesity has become a worldwide public health problem. According to a report from the World Health Organization (WHO), over 650 million people worldwide were diagnosed with obesity in 2016 (1). With the improvement of living standards, increased dietary intake and decreased physical activity, the number of people with obesity in China has significantly increased in recent years. The prevalence of obesity in adults in China more than doubled between 2004 (3.1%) and 2018 (8.1%). 85 million adults in China were obese in 2018, which was three times as many as in 2004 (2). Obesity not only causes a number of health, social and psychological problems but also significantly increases the risk of various malignant tumors (3). Gastric cancer is a malignant tumor with high morbidity and mortality worldwide, and its morbidity (5.6%) and mortality (7.7%) are among the highest of all malignant tumors (4). Standardized lymph node dissection is crucial to improving the long-term prognosis of patients with advanced gastric cancer (5). D2 lymph node dissection, as the standard treatment for advanced gastric cancer, has been unanimously recommended in Japanese Classification of Gastric Carcinoma (6) and the US National Comprehensive Cancer Network Gastric Cancer Guidelines (7), and a consensus has been reached regarding its use. However, as yet there is no conformity of opinion on the precise range of lymph node dissection for different stages of gastric cancer. In theory, the prognosis of patients should improve as more lymph nodes are dissected. Therefore, reasonably expanding the scope of lymph node dissection by performing D2+ lymph node dissection may improve the prognosis and survival rate of

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patients. In addition, some studies have found that D2+ lymph node dissection, which is the removal of lymph nodes with an elevated risk of metastasis beyond the specified range of D2, can improve the prognosis and survival rate of patients (8,9). However, due to the difficulty in exposing the surgical field of view in patients with obesity, it is challenging to perform standardized D2 lymph node dissection, and even more difficult to perform D2+ lymph node dissection in patients with obesity. The safety and efficacy of D2+ compared with D2 surgery requires further confirmation. The present study retrospectively analyzed the clinical data of patients with obesity with gastric cancer in a single hospital, with the aim of exploring whether laparoscopic-assisted radical gastrectomy combined with D2+ lymph node dissection is feasible in patients with obesity and gastric cancer and to provide a basis for clinical surgical decision-making.

Materials and methods

Data collection. The clinical data of patients who underwent laparoscopic radical gastrectomy in Henan Provincial People's Hospital (Zhengzhou, China) from January 2016 to January 2018 were collected and analyzed. The inclusion criteria were as follows: i) Age between 18-75 years, either sex, body mass index (BMI) ≥ 25 kg/m²; ii) American Society of Anesthesiologists (ASA) grade I-III; iii) postoperative conventional pathological diagnosis of adenocarcinoma, where the tumor is located in the proximal, middle or distal area; iv) pathological tumor-node-metastasis (pTNM) stage after surgery of II-III, according to the TNM staging criteria for gastric cancer in the 8th edition of the American Joint Committee on Cancer (AJCC) in 2017 (10); and v) underwent laparoscopic radical gastrectomy or conversion to laparotomy. The exclusion criteria were as follows: i) Severe mental illness; ii) previous upper abdominal surgery; iii) combined thoracoabdominal surgery; iv) other malignant tumors in the past 5 years; v) severe cardiopulmonary disease in preoperative evaluation, including myocardial infarction, cerebral infarction, severe coronary heart disease and chronic pulmonary disease within the past year; vi) chemotherapy, radiotherapy or other targeted or immunotherapy before surgery; and vii) distant metastasis of the tumor.

The 485 patients with gastric cancer who underwent laparoscopic radical gastrectomy from January 2016 to January 2018 were screened for the study. The flow chart and reasons for exclusion from the study are shown in Fig. 1. Following the exclusion of 336 patients, 149 patients were ultimately enrolled in the study.

Research methods. The standard scope of D2 lymph node dissection is stipulated in the Chinese Society of Clinical Oncology (CSCO) Guidelines for the Diagnosis and Treatment of Gastric Cancer (11) as follows: In cases of distal gastrectomy, node stations 1, 3, 4sb, 4d, 5, 6, 7, 8a, 9, 11p and 12a; for proximal gastrectomy, node stations 1, 2, 3, 4sa, 4sb, 7, 8a, 9, 10 and 11; during total gastrectomy, node stations 1-7, 8a, 9, 10, 11 and 12a. Patients who underwent laparoscopic radical gastrectomy and standard D2 lymph node dissection were included in the control group. Patients who underwent laparoscopic radical gastrectomy and standard D2 lymph

node dissection, as well as the clearance of least one of lymph node stations 13, 14v, 8p, 12b, 12p and 16 had undergone D2+ lymph node dissection and were included in the observation group. Postoperative complications were classified according to the Clavien-Dindo complication classification (12), with grades I-II as minor complications and grades III-IV as severe complications. Classification of macroscopic types of gastric cancer according to Borrmann classification method, including four types: I, II, III, and IV (13).

Follow-up. All patients were followed up by telephone. Patients were followed up every 3 months for 2 years after surgery, every 6 months for the next 3-5 years, and once a year thereafter. The deadline for final follow-up was February 2023.

Statistical analysis. SPSS 26.0 statistical software (IBM Corp.) was used for data processing. The enumeration data are expressed as the mean \pm standard deviation, and an independent sample t-test was used for comparison. Categorical data are expressed as n (%), and the two-sided χ^2 test or Fisher's exact probability method was used for comparison. Overall survival rates were plotted using the Kaplan-Meier method and compared by the log-rank test. $P < 0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics. A total of 149 patients with gastric cancer were included in the study, including 74 patients in the D2+ group and 75 patients in the D2 group. There was no difference in sex composition between the two groups, with 52 males (70.3%) and 22 females (29.7%) in the D2+ group and 55 males (73.3%) and 20 females (26.7%) in the D2 group. There was also no difference in age between the D2+ group (57.24 ± 10.38 years) and the D2 group (55.75 ± 10.81 years). In addition, no difference in BMI was detected between the D2+ group (27.35 ± 1.03 kg/m²) and the D2 group (27.37 ± 1.04 kg/m²). Furthermore, no difference in ASA grade, preoperative complications, tumor location, tumor size, Borrmann type, cancer-associated thrombus or pTNM staging was identified between the two groups. The data are shown in Table I.

Comparison of surgical conditions between the two groups. The duration of surgery in the D2+ group (282.55 ± 23.02 min) was longer than that of the D2 group (271.45 ± 20.05 min), and the difference was statistically significant ($P < 0.05$). The number of lymph nodes dissected in the D2+ group (28.57 ± 7.19) was more than that in the D2 group (25.29 ± 6.41), with a statistically significant difference between groups ($P < 0.05$). The intraoperative blood loss in the D2+ group (117.55 ± 28.02 ml) was more than that in the D2 group (109.37 ± 22.78 ml), albeit not significantly. The rate of conversion to open laparotomy was 4/74 (5.4%) and 2/75 (2.7%) in the D2+ and D2 groups, respectively. The time to first flatus in the D2+ group (4.49 ± 1.32 days) was slightly earlier than that in the D2 group (4.84 ± 1.10 days), and the postoperative hospital stay in the D2+ group (10.46 ± 2.39 days) was similar that in the D2 group (10.69 ± 2.27 days). The total cost of hospitalization in the D2+ group ($8.64 \pm 1.25 \times 10^4$ yuan) was slightly more than

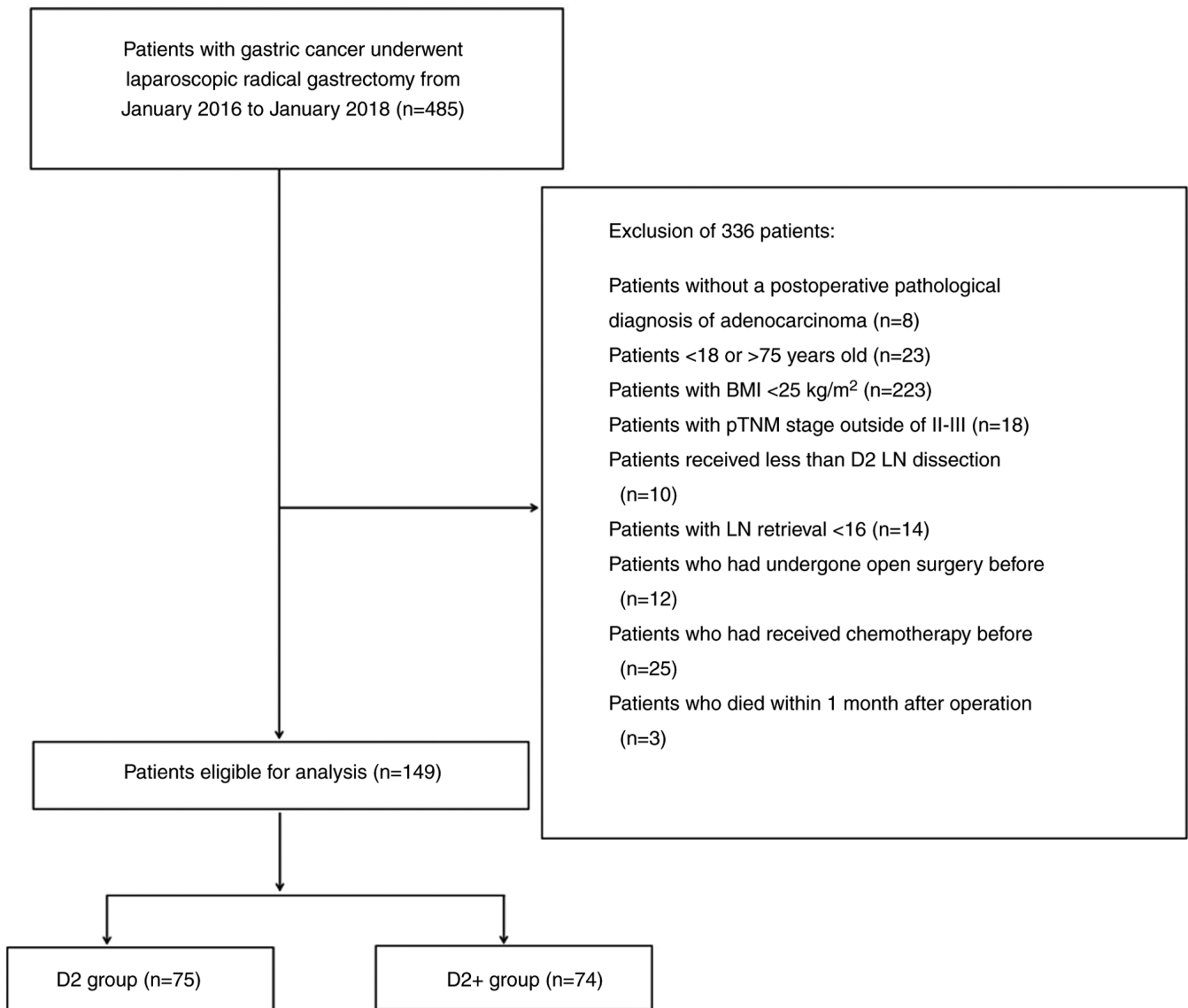


Figure 1. Criteria for inclusion and exclusion of patients in the present study. BMI, body mass index; pTNM, pathological tumor-node metastasis; LN lymph node.

that in the D2 group ($8.42 \pm 1.16 \times 10^4$ yuan), but the difference was not significant. The data are shown in Table II.

In a subgroup analysis according to the type of gastrectomy, for patients with proximal gastrectomy, the duration of surgery was the only factor that was found to be significantly different, with the D2+ group having a longer operation time than the D2 group. For patients undergoing distal gastrectomy, no statistically significant difference was detected in any of the surgery-associated data. For patients undergoing total gastrectomy, the duration of surgery of the D2+ group was longer than that of the D2 group and the number of lymph nodes dissected in the D2+ group was greater than that in the D2 group; these differences were statistically significant ($P < 0.05$). The data are presented in Table III.

Comparison of postoperative complications. Among all the patients included in the study, 31 had postoperative complications, accounting for 20.8% of cases. These included 19 cases (25.7%) in the D2+ group and 12 cases (16%) in the D2 group.

In the D2+ group, there were 16 cases of minor complications (21.6%) and 3 cases of severe complications (4.1%). All minor complications were resolved by conservative treatment. Two cases of severe complications comprised anastomotic fistula, which were resolved by a second operation. There was also 1 case of anastomotic bleeding, which was resolved by endoscopic hemostasis. In the D2 group, there were 10 cases of minor complications (13.3%) and 2 cases of severe complications (2.7%). All minor complications were resolved by conservative treatment. One patient experienced the severe complication of abdominal bleeding, and hemostasis was achieved after a second operation. The patient with severe heart failure was transferred to the intensive care unit for tracheal intubation, cardiac intubation, diuretics and other treatments. Following relief of the symptoms, the patient was transferred back to the general ward, and the patient was finally cured and discharged. Further analysis of the complications of the two groups revealed that the postoperative complications comprised a relatively high proportion of incision and

Table I. Comparison of clinical data and pathological features of patients in the two groups.

Characteristic	D2+ group (n=74)	D2 group (n=75)	P-value
Sex			0.678
Male	52 (70.3)	55 (73.3)	
Female	22 (29.7)	20 (26.7)	
Age, years	57.24±10.38	55.75±10.81	0.390
BMI, kg/m ²	27.35±1.03	27.37±1.04	0.903
ASA grade			0.828
I	12 (16.2)	14 (18.7)	
II	48 (64.9)	45 (60.0)	
III	14 (18.9)	16 (21.3)	
Preoperative complications			
Diabetes	10 (13.5)	8 (10.7)	0.594
Anemia	37 (50.0)	46 (61.3)	0.164
Hypoproteinemia	23 (31.1)	17 (22.7)	0.247
Tumor location			0.323
Upper	37 (50.0)	35 (46.7)	
Central	19 (25.7)	14 (18.7)	
Lower	18 (24.3)	26 (34.7)	
Tumor size, cm	5.87±1.45	5.56±1.22	0.153
Borrmann type			0.179
I	0 (0)	3 (4.0)	
II	9 (12.2)	7 (9.3)	
III	45 (60.8)	52 (69.3)	
IV	20 (27.0)	13 (17.3)	
Cancer-associated thrombus			0.155
Yes	47 (63.5)	39 (52.0)	
No	27 (36.5)	36 (48.0)	
pTNM staging			0.289
II	10 (13.5)	15 (20)	
III	64 (86.5)	60 (80)	

Results are presented as n (%) or mean ± standard deviation. BMI, body mass index; ASA, American Society of Anesthesiologists; pTNM, pathological tumor-node-metastasis.

pulmonary infections. The incidence rates of total, minor and severe complications in the D2+ group were slightly higher than those in the D2 group, but analysis indicated that there was no significant difference. The data are shown in Table IV. In the subgroup analysis, no statistically significant difference in postoperative complications was detected between the D2+ and D2 groups for any gastrectomy type (Table III).

Clinical outcomes. The 3-year overall survival rate of patients in the D2+ group was 54.1%, and that of patients in the D2 group was 46.7%. The difference in 3-year overall survival rates between the two groups was not found to be significant (Fig. 2). In addition, in the subgroup analysis, no statistically significant differences were observed in the 3-year overall survival between the D2+ and D2 groups (Table III).

The 5-year overall survival rate of patients in the D2+ group was 37.8%, and that of patients in the D2 group was 28.0%. The difference in 5-year overall survival rates between

the two groups was statistically significant ($P < 0.05$; Fig. 3). However, in the subgroup analysis, no statistically significant differences were found in 5-year overall survival between the D2+ and D2 groups (Table III).

Discussion

The WHO defines adults with a BMI ≥ 30 kg/m² as obese. However, the healthy BMI of the Asian population is lower than that of the Western population, and the body fat of Asian individuals is greater than that of Western individuals with the same BMI. Therefore, adults of the Asian population with a BMI ≥ 25 kg/m² have an elevated risk of weight-associated diseases. Based on the characteristics of the Asia-Pacific population and of obesity-related diseases, the obesity expert consultant of the WHO proposed that Asian individuals with a BMI ≥ 25 kg/m² should be considered obese (14). Therefore, a BMI ≥ 25 kg/m² was used as an obesity indicator in the

Table II. Comparison of surgical treatment between the two groups of patients.

Surgical factor	D2+ group (n=74)	D2 group (n=75)	P-value
Operation time, mins	282.55±23.02	271.45±20.05	0.002
Intraoperative blood loss, ml	117.55±28.02	109.37±22.78	0.053
Lymph nodes dissected, n	28.57±7.19	25.29±6.41	0.004
Conversion to open laparotomy	4 (5.4)	2 (2.7)	0.665
Surgical method			0.266
Proximal gastrectomy	30 (40.5)	32 (42.7)	
Distal gastrectomy	16 (21.6)	23 (30.7)	
Total gastrectomy	28 (37.8)	20 (26.7)	
Time to first flatus, days	4.49±1.32	4.84±1.10	0.078
Postoperative hospital stay, days	10.46±2.39	10.69±2.27	0.542
Total hospitalization expenses, x10 ⁴ yuan	8.64±1.25	8.42±1.16	0.263

Results are presented as n (%) or mean ± standard deviation.

present study, and all 149 patients included had a BMI of this magnitude. Obesity is a state involving the excessive accumulation or abnormal distribution of fat in the body. It may cause a series of health, social and psychological problems. A large-sample meta-analysis found that obesity increases the risk of gastric cancer, and a higher BMI is associated with a higher risk. In addition, a subgroup analysis conducted on gastric cancer at different sites found that obesity increases the risk of adenocarcinoma of the esophagogastric junction but is not associated with the incidence of distal gastric cancer (15). The subjects included in the present study all had obesity and gastric cancer. Proximal gastric cancer accounted for 50 and 46.7% of the D2+ and D2 groups, respectively, which is a relatively high proportion of patients, and is consistent with the findings of the meta-analysis. Previous research has also found that a high BMI significantly increases the risk of lymph node metastasis in patients with gastric cancer (16).

As changes in the lifestyles of the Chinese population have occurred, such as reductions in physical activity and changes in diet, the proportion of the population that is obese has been increasing. Therefore, the opportunities for gastrointestinal surgeons to treat patients with obesity and gastric cancer are also increasing. Laparoscopic technology is widely used in clinical radical gastrectomy, but laparoscopic surgery is more difficult in patients with obesity, and is challenging for gastrointestinal surgeons. As well as having increased quantities of intra-abdominal fat, obese patients have fragile blood vessels, so they are more prone to bleeding during surgery. In addition, large amounts of fat and omentum occupy the surgical space, making it difficult to expose the visual field, which may influence the effectiveness of surgery and postoperative recovery. However, due to improvements achieved through increased experience of laparoscopic surgery, the efficacy and feasibility of applying this surgical technique to patients with obesity and gastric cancer have been confirmed in a number of studies conducted in various countries (17-19).

At present, the principal treatment for advanced gastric cancer is surgery-based comprehensive treatment, and sufficient gastrectomy and standardized lymph node dissection

are crucial to improving the long-term prognosis of patients with advanced gastric cancer. After years of clinical research, a global consensus has been reached on the use of D2 lymph node dissection for patients with locally advanced gastric cancer (20). Appropriate lymph node dissection is important for improving the prognosis of patients and reducing surgical complications. In addition, for lymph nodes with a high risk of metastasis outside the scope of D2 lymph node dissection, whether it is advantageous to perform selective D2+ lymph node dissection is a topic of debate for those researching gastric cancer surgery. There has been a prolonged dispute about the benefit of extended lymph node dissection for gastric cancer. In theory, the removal of a larger area of lymph nodes by extended lymphadenectomy should increase the likelihood of cure (21,22). According to a previous report, the number of dissected lymph nodes is an important indicator of the accuracy of pathological staging and can predict the prognosis of patients; every additional 10 lymph node dissections can increase the 5-year survival rate by 5.7-10.9% (23). In addition, a long-term multicenter study conducted in the USA showed that the dissection of a sufficient number of lymph nodes can significantly improve the long-term survival rate of patients (24). Furthermore, a study performed in China by Liang *et al* (25) found that standard D2+ para-aortic lymph nodal dissection surgery with the removal of ≥30 lymph nodes for N3-stage disease can significantly improve the prognosis of patients (25). Some studies have also confirmed this finding in Western populations. Based on their research results, Ozmen *et al* (26) suggested that D2+ lymph node dissection should be preferred for advanced gastric cancer (IIIA-IIIB) as it increases the rate of survival, and that D2+ lymph node dissection can be performed as safely as standard D2 dissection by experienced surgeons without any increase in postoperative morbidity and mortality. In addition, numerous studies have confirmed the safety of D2+ lymph node dissection in terms of surgical conditions and postoperative complications (27-35). Based on these research results, it is feasible to perform D2+ lymph node dissection in patients with advanced gastric cancer. However, it is challenging for gastrointestinal surgeons

Table III. Subgroup analysis of the two groups of patients.

Surgical factor	Proximal gastrectomy			Distal gastrectomy			Total gastrectomy		
	D2+ (n=30)	D2 (n=32)	P-value	D2+ (n=16)	D2 (n=23)	P-value	D2+ (n=28)	D2 (n=20)	P-value
Operation time, mins	282.87±14.80	272.28±16.74	0.011	275.81±25.59	273.22±21.65	0.734	286.07±28.17	268.10±23.45	0.024
Intraoperative blood loss, ml	120.67±25.72	117.56±19.97	0.123	110.50±31.24	107.91±28.33	0.789	118.25±28.78	107.55±20.68	0.141
Lymph nodes dissected, n	26.80±7.73	25.81±6.40	0.585	27.94±6.49	25.48±6.64	0.258	30.82±6.57	24.25±6.37	0.001
Conversion to open surgery	2 (6.7)	0 (0)	0.230	0 (0)	1 (4.3)	1.000	2 (7.1)	1 (5.0)	1.000
Exhaust time, days	4.43±1.36	4.97±1.00	0.084	4.44±1.37	4.57±1.12	0.751	4.57±1.29	4.95±1.23	0.313
Postoperative hospital stay, days	10.63±2.31	10.69±1.96	0.921	10.06±1.81	11.13±2.85	0.194	10.50±2.80	10.20±1.99	0.683
Total hospitalization expenses, ×10 ⁴ yuan	8.82±1.34	8.69±1.34	0.698	8.49±1.20	8.17±0.85	0.322	8.52±1.20	8.27±1.12	0.455
Complications	10 (33.3)	7 (21.9)	0.312	2 (12.5)	3 (13.0)	1.000	7 (25.0)	2 (10.0)	0.348
OS of 3 years	17 (56.7)	15 (46.9)	0.441	9 (56.3)	11 (47.8)	0.748	14 (50.0)	9 (45.0)	0.732
OS of 5 years	12 (40.0)	10 (31.3)	0.472	6 (37.5)	6 (26.1)	0.498	10 (35.7)	5 (25.0)	0.430

Results are presented as n (%) or mean ± standard deviation.

to perform laparoscopic surgery on patients, and difficult to achieve standard D2 lymph node dissection in patients with advanced stage gastric cancer who are obese. However, there have been few studies on the curative effect and safety of D2+ surgery for patients with obesity.

Since surgery in patients with obesity is onerous, a number of studies have confirmed that obesity increases the duration of laparoscopic surgery. A meta-analysis of >20,000 patients with gastric cancer showed that in patients with obesity the duration of surgery was significantly longer than that of patients with a normal BMI, and the occurrence of surgery-related complications increased (36). In addition, a Korean study showed that although patients with obesity had prolonged surgery and fewer lymph nodes to be dissected, the short- and long-term surgical effects were not significantly different from those of patients with a normal BMI (37). In the present study, the BMI baselines of the two groups of patients were very similar, which excluded inconsistency of BMI as the cause of the difference in surgical duration and simultaneously excluded the impact of BMI differences on the research results. The present study showed that the duration of surgery for D2+ lymph node dissection was longer than that of D2 lymph node dissection for obese patients. Regarding the reason for this, the lymph nodes around the stomach of patients with obesity are often surrounded by larger quantities of fat. When cleaning the lymph nodes, it is necessary to separate and clean greater amounts of fat tissue from around the blood vessels. It is challenging to obtain a clear surgical field of view and the space for surgery in the abdominal cavity is limited. The surgical assistant may not be able to apply sufficient force when pulling the tissue, and tissues such as the greater omentum and the lesser omentum may slide back and forth repeatedly to obscure the surgical field of view. During surgery, the surgeon and assistants require additional time to adjust the forceps. Also, to maintain sufficient tension, assistants must apply greater force to resist the gravitational pull of fat and gastric tissue. In addition, the tissues of patients with obesity tend to be brittle and bleed easily, particularly when stretched and exposed. Larger volumes of intraoperative bleeding prolong the time required to achieve hemostasis, requiring the use of gauze for compression and to clean the accumulated blood, or the use of suction to remove the accumulated blood. This prolongs the surgical duration even more. Therefore, if lymph node groups in addition to those of D2 are dissected, the operation will be more difficult and the duration of surgery and volume of intraoperative blood loss will increase. In the present study there was no significant difference in postoperative pathological stages between the two groups because the clinical baselines of the two groups were consistent when screening the enrolled cases. Notably, the present study is a retrospective analysis, so patients who decided to undergo D2+ dissection during surgery may have had a later intraoperative clinical stage. For example, if the serosal surface of a patient with distal gastric cancer is smooth and node station 6 is free from metastasis and duodenal invasion, it would be decided during the surgery to perform D2 dissection. However, if the serosa is violated, node station 6 has enlarged lymph nodes or the duodenum is invaded, it may be decided to perform D2 plus node station 13 or 14v excision during the surgery. Therefore, the study has certain limitations

Table IV. Comparison of postoperative complications between the two groups of patients.

Postoperative complications	D2+ group (n=74)	D2 group (n=75)	P-value
Total complications	19 (25.7)	12 (16)	0.146
Clavien-Dindo complication classification I-II	16 (21.6)	10 (13.3)	0.183
Delayed gastric emptying	3	2	
Incision infection	5	2	
Lymphorrhagia	1	0	
Intra-abdominal infection	2	2	
Pancreatic leakage	0	1	
Intestinal obstruction	2	0	
Duodenal stump leakage	0	1	
Pulmonary infection	3	1	
Deep vein thrombosis	0	1	
Clavien-Dindo complication classification III-IV	3 (4.1)	2 (2.7)	0.988
Abdominal bleeding	0	1	
Anastomotic fistula	2	0	
Anastomotic bleeding	1	0	
Pulmonary embolism	0	0	
Heart failure	0	1	
Death within 30 days after surgery	0	0	

Data are presented as n or n (%).

due to its retrospective design. The indications for D2 or D2+ dissection during surgery are not clearly defined, so patients in the D2+ group may generally have a higher clinical stage. This will also increase the difficulty of surgery, leading to an increase in the duration of surgery and intraoperative blood loss in the D2+ group. Therefore, the results may be affected by tumor stage. To avoid this, the pTNM staging of the groups was kept consistent to prevent it from influencing the research results. In addition, the D2+ group underwent the dissection of groups of lymph nodes other than those of standard D2 surgery, so it is expected that the number of lymph node dissections would be significantly increased in the D2+ group compared with the D2 group. The present study suggests that additional lymph node dissections can improve the long-term survival of patients, which is confirmed by the survival analysis. The 3-year overall survival rate of the D2+ group was slightly, but not significantly, higher than that of the D2 group. However, the 5-year overall survival rate of the D2+ group was significantly higher than that of the D2 group. In the subgroup analysis, no statistically significant difference in 5-year overall survival was found between the D2+ and D2 groups. However, in all three subgroups, the 5-year overall survival of the D2+ group was higher than that of the D2 group. The lack of statistical significance may be due to the small sample size of the three subgroups, particularly the distal gastrectomy subgroup with only 39 cases. If a larger number of research cases are included in future studies, statistically significant differences may be obtained.

The present study found that the 3-year overall survival rate of patients in the D2+ and D2 groups was 54.1 and 46.7%, respectively. In the JACCRO GC-07 clinical trial, the 3-year

relapse-free survival rate was 49.6-65.9% in patients with stage III gastric cancer (38). The present study mostly included patients with stage III gastric cancer, with 86.5% of patients in the D2+ group and 80% in the D2 group having stage III disease. However, the 3-year overall survival rate in the present study was markedly lower than that in the JACCRO GC-07 study. It must be noted that education and economic levels differ among provinces, and the compliance of patients in Henan is poor. In addition, some patients have insufficient understanding of gastric cancer, and consider that surgery alone is sufficient treatment and that postoperative adjuvant chemotherapy is unnecessary and expensive. Therefore, some patients did not complete postoperative adjuvant chemotherapy, while others completely refused it. However, in the JACCRO GC-07 study, patients all received postoperative adjuvant chemotherapy. This may be the reason why the 3-year overall survival rate in the present study is lower than that of the JACCRO GC-07 clinical trial. In addition, poor compliance leads to a higher rate of patients being lost to follow-up, which also reduces the 3-year overall survival rate.

The results of the present study serve as a clinical reference for D2+ lymph node dissection in patients with obesity. The findings require confirmation in studies with a larger sample size and randomized controlled study design. An increased number of lymph node dissections requires a greater surgical scope and increased surgical trauma. However, despite the D2+ group having a prolonged surgical duration and increased intraoperative blood loss, if there is no significant difference in postoperative recovery and complications in comparison with D2 dissection, it is feasible to reasonably expand the scope of lymph node dissection for certain patients with obesity at

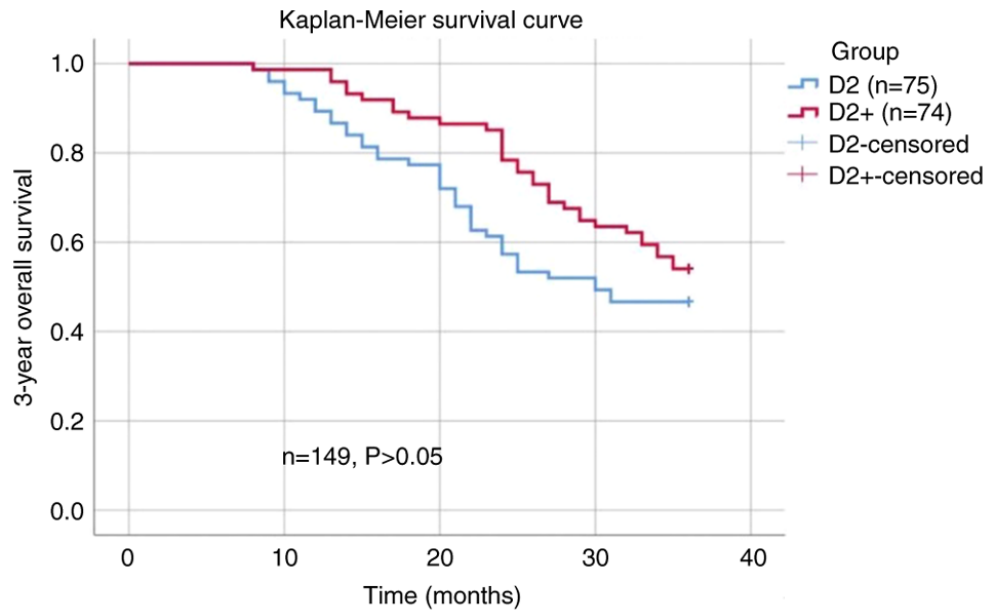


Figure 2. Comparison of the 3-year overall survival rate for the D2+ and D2 groups.

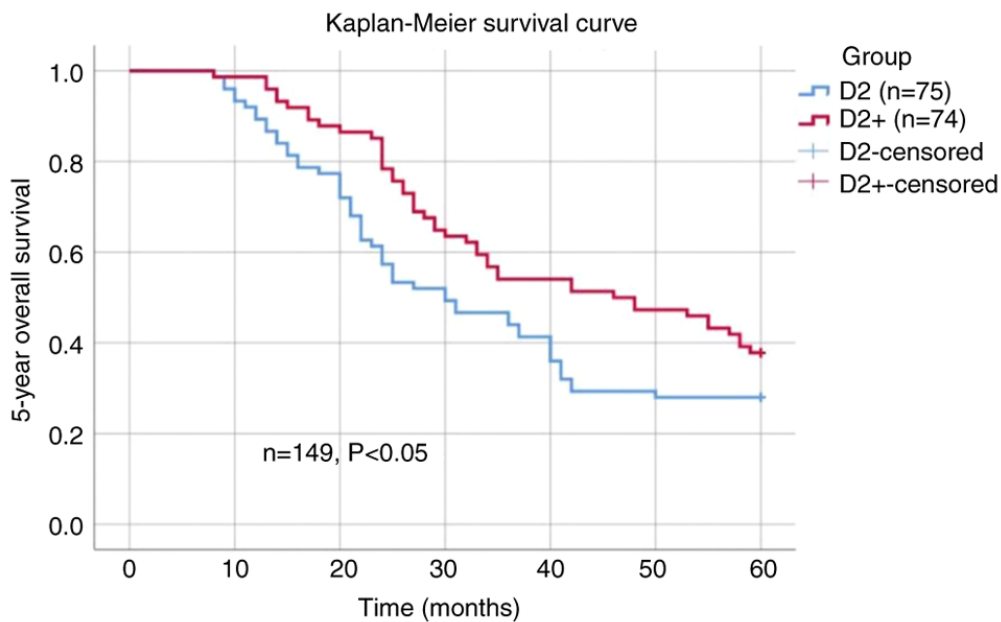


Figure 3. Comparison of the 5-year overall survival rate for the D2+ and D2 groups.

stage II-III. The present study found no significant difference in surgical methods, the rate of conversion to open surgery, postoperative time to first flatus postoperative hospital stay, total hospitalization costs, postoperative complications or mortality within 30 days. Therefore, D2+ lymph node dissection improves the prognosis of patients and increases the long-term survival rate, without affecting postoperative recovery or increasing postoperative complications.

The present study has several limitations. First, as already mentioned, it is a retrospective study, not a prospective randomized controlled study. Second, the sample size of the study is small, and the follow-up time is short. Third, although there was no statistically significant difference in the characteristics

of the two groups of patients, this did not overcome all selection bias. For example, factors associated with the selection of D2+ or D2 lymph node resection remain. D2+ lymph node resection is more likely to be performed in patients with a healthier physical condition and younger average age, which may improve survival and reduce the incidence of complications. Finally, the present study was performed at a single center. The patients enrolled in the study were all operated on by the same team of physicians in the same hospital, including the same chief surgeon, first assistant and mirror supporter. However, the hospital operates on a large scale, performs a large number of surgeries and has a great amount of experience in laparoscopic gastric cancer surgery. It is undeniable

that medical institutions with that perform a larger number of surgeries and have more experienced gastrointestinal surgeons can significantly reduce surgical complications and patient mortality, and can significantly improve the rate of survival (39,40). Although this eliminates the bias caused by different surgeons, it also has certain limitations. Since laparoscopic gastric cancer surgery is more complex than colorectal surgery, the learning curve is longer, and surgery for patients with obesity is particularly challenging. Therefore, it is necessary to collaborate with multicenter medical institutions to obtain a larger sample size and follow up the patients for a longer time. The analysis of data from multiple centers will negate the impact of differences in surgical experience on the research results. In addition, larger-scale prospective randomized clinical trials are necessary to obtain higher-level evidence of the clinical efficacy and safety of this surgery. This should also avoid the influence of selective bias on the research results.

Summarizing the results of the present study, it can be concluded that among obese patients with gastric cancer, although the D2+ group had a longer surgical duration and slightly more intraoperative bleeding than the D2 group, there was no difference in postoperative recovery or complications between the two groups. Moreover, the D2+ group had a greater number of lymph node dissections and a higher 5-year survival rate. Therefore, it is suggested that D2+ lymph node dissection is safe to apply to obese patients with gastric cancer who are treated in medical institutions with a relatively high level of surgical experience.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

YCS and YG were responsible for the conception of the present study. GTZ performed acquisition of data, statistical analysis and revision of the tables and figures. XFS, YY and PZ analyzed and interpreted the data. XDZ analyzed data. All authors drafted the manuscript and revised it critically for important intellectual content. YCS, YG and PZ confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

All procedures performed in the present study involving biological samples, medical record information and data were approved by the Medical Ethics Committee of Henan Provincial People's Hospital (Zhengzhou, China). Written

informed consent was obtained from all patients. All methods were performed in accordance with the relevant guidelines and regulations (Declaration of Helsinki).

Patient consent for publication

Written informed consent for the publication of their data was obtained from all patients.

Competing interests

The authors declare that they have no competing interests.

References

1. World Health Organization: Obesity and overweight. Available from: <http://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>. Accessed June 9, 2021.
2. Wang L, Zhou B, Zhao Z, Yang L, Zhang M, Jiang Y, Li Y, Zhou M, Wang L, Huang Z, *et al*: Body-mass index and obesity in urban and rural China: Findings from consecutive nationally representative surveys during 2004-18. *Lancet* 398: 53-63, 2021.
3. Sung H, Siegel RL, Torre LA, Pearson-Stuttard J, Islami F, Fedewa SA, Goding Sauer A, Shuval K, Gapstur SM, Jacobs EJ, *et al*: Global patterns in excess body weight and the associated cancer burden. *CA Cancer J Clin* 69: 88-112, 2019.
4. Chen WQ, Li H, Sun KX, Zheng RS, Zhang SW, Zeng HM, Zou XN, Gu XY and He J: Report of cancer incidence and mortality in China, 2014. *Zhonghua Zhong Liu Za Zhi* 40: 5-13, 2018 (In Chinese).
5. Lin GT, Chen QY, Zheng CH, Li P, Xie JW, Wang JB, Lin JX, Lu J, Cao LL, Lin M, *et al*: Lymph node noncompliance affects the long-term prognosis of patients with gastric cancer after laparoscopic total gastrectomy. *J Gastrointest Surg* 24: 540-550, 2020.
6. Japanese Gastric Cancer Association: Japanese classification of gastric carcinoma: 3rd English edition. *Gastric Cancer* 14: 101-112, 2011.
7. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology. Gastric cancer (version 2.2023). https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed August 29, 2023.
8. Liang Y, Cui J, Cai Y, Liu L, Zhou J, Li Q, Wu J and He D: 'D2 plus' lymphadenectomy is associated with improved survival in distal gastric cancer with clinical serosa invasion: A propensity score analysis. *Sci Rep* 9: 19186, 2019.
9. Xue L, Chen XL, Zhang WH, Yang K, Chen XZ, Zhang B, Chen ZX, Chen JP, Zhou ZG and Hu JK: Risk factors and prognostic significance of retropancreatic lymph nodes in gastric adenocarcinoma. *Gastroenterol Res Pract* 2015: 367679, 2015.
10. Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, *et al* (eds): *AJCC Cancer Staging Manual*. 8th edition. Springer, New York, NY, 2017.
11. Guidelines Working Committee of Chinese Society of Clinical Oncology: Chinese Society of Clinical Oncology (CSCO) Guidelines for Diagnosis and Treatment of Gastric Cancer (version 1.2023). People's Health Publishing House, Beijing, 2023.
12. Dindo D, Demartines N and Clavien PA: Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 240: 205-213, 2004.
13. Borrmann R: Geschwülste des Magens und Duodenums. In: *Verdauungsschlauch: Rachen und Tonsillen · Speiseröhre Magen und Darm · Bauchfell*. Borchardt H, Borrmann R, Christeller E, Dietrich A, Fischer W, Von Gierke E, Hauser G, Kaiserling C, Koch M, Koch W, *et al* (eds). Springer Berlin Heidelberg, Berlin, Heidelberg, pp812-1054, 1926.
14. Choo V: WHO reassesses appropriate body-mass index for Asian populations. *Lancet* 360: 235, 2002.
15. Yang P, Zhou Y, Chen B, Wan HW, Jia GQ, Bai HL and Wu XT: Overweight, obesity and gastric cancer risk: Results from a meta-analysis of cohort studies. *Eur J Cancer* 45: 2867-2873, 2009.

16. Xiao J, Shen K, Liu K, Wang Y, Fan H, Cheng Q, Zhou X, Hu L, Wang G, Xu Z and Yang L: Obesity promotes lipid accumulation in lymph node metastasis of gastric cancer: A retrospective case-control study. *Lipids Health Dis* 21: 123, 2022.
17. Kulig J, Sierzega M, Kolodziejczyk P, Dadan J, Drews M, Fraczek M, Jeziorski A, Krawczyk M, Starzynska T and Wallner G; Polish Gastric Cancer Study Group: Implications of overweight in gastric cancer: A multicenter study in a Western patient population. *Eur J Surg Oncol* 36: 969-976, 2010.
18. Son SY, Jung DH, Lee CM, Ahn SH, Ahn HS, Park DJ and Kim HH: Laparoscopic gastrectomy versus open gastrectomy for gastric cancer in patients with body mass index of 30 kg/m² or more. *Surg Endosc* 29: 2126-2132, 2015.
19. Sugimoto M, Kinoshita T, Shibasaki H, Kato Y, Gotohda N, Takahashi S and Konishi M: Short-term outcome of total laparoscopic distal gastrectomy for overweight and obese patients with gastric cancer. *Surg Endosc* 27: 4291-4296, 2013.
20. Songun I, Putter H, Kranenbarg EM, Sasako M and van de Velde CJH: Surgical treatment of gastric cancer: 15-Year follow-up results of the randomised nationwide Dutch D1D2 trial. *Lancet Oncol* 11: 439-449, 2010.
21. Hartgrink HH, van de Velde CJ, Putter H, Bonenkamp JJ, Klein Kranenbarg E, Songun I, Welvaart K, van Krieken JH, Meijer S, Plukker JT, *et al*: Extended lymph node dissection for gastric cancer: Who may benefit? Final results of the randomized Dutch gastric cancer group trial. *J Clin Oncol* 22: 2069-2077, 2004.
22. Ozmen MM, Zulfikaroglu B, Kucuk NO, Ozalp N, Aras G, Koseoglu T and Koç M: Lymphoscintigraphy in detection of the regional lymph node involvement in gastric cancer. *Ann R Coll Surg Engl* 88: 632-638, 2006.
23. Smith DD, Schwarz RR and Schwarz RE: Impact of total lymph node count on staging and survival after gastrectomy for gastric cancer: Data from a large US-population database. *J Clin Oncol* 23: 7114-7124, 2005.
24. Gholami S, Janson L, Worhunsky DJ, Tran TB, Squires MH III, Jin LX, Spolverato G, Votanopoulos KI, Schmidt C, Weber SM, *et al*: Number of lymph nodes removed and survival after gastric cancer resection: An analysis from the US gastric cancer collaborative. *J Am Coll Surg* 221: 291-299, 2015.
25. Liang YX, Liang H, Ding XW, Wang XN, Zhang L, Wu LL, Liu HG and Jiao XG: The prognostic influence of D2 lymphadenectomy with para-aortic lymph nodal dissection for gastric cancer in N3 stage. *Zhonghua Wai Ke Za Zhi* 51: 1071-1076, 2013 (In Chinese).
26. Ozmen MM, Zulfikaroglu B, Ozmen F, Moran M, Ozalp N and Seckin S: D2 vs D2 plus para-aortic lymph node dissection for advanced gastric cancer. *Turk J Surg* 37: 49-58, 2020.
27. Sano T, Sasako M, Yamamoto S, Nashimoto A, Kurita A, Hiratsuka M, Tsujinaka T, Kinoshita T, Arai K, Yamamura Y and Okajima K: Gastric cancer surgery: Morbidity and mortality results from a prospective randomized controlled trial comparing D2 and extended para-aortic lymphadenectomy-Japan clinical oncology group study 9501. *J Clin Oncol* 22: 2767-2773, 2004.
28. Marrelli D, Pedrazzani C, Neri A, Corso G, DeStefano A, Pinto E and Roviello F: Complications after extended (D2) and superextended (D3) lymphadenectomy for gastric cancer: Analysis of potential risk factors. *Ann Surg Oncol* 14: 25-33, 2007.
29. Günther K, Horbach T, Merkel S, Meyer M, Schnell U, Klein P and Hohenberger W: D3 lymph node dissection in gastric cancer: Evaluation of postoperative mortality and complications. *Surg Today* 30: 700-705, 2000.
30. Bostanci EB, Kayaalp C, Ozogul Y, Aydin C, Atalay F and Akoglu M: Comparison of complications after D2 and D3 dissection for gastric cancer. *Eur J Surg Oncol* 30: 20-25, 2004.
31. Sasako M, Sano T, Yamamoto S, Kurokawa Y, Nashimoto A, Kurita A, Hiratsuka M, Tsujinaka T, Kinoshita T, Arai K, *et al*: D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. *N Engl J Med* 359: 453-462, 2008.
32. 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* 193: 10-15, 2007.
33. Danielson H, Kokkola A, Kiviluoto T, Sirén J, Louhimo J, Kivilaakso E and Puolakkainen P: Clinical outcome after D1 vs D2-3 gastrectomy for treatment of gastric cancer. *Scand J Surg* 96: 35-40, 2007.
34. Kunisaki C, Akiyama H, Nomura M, Matsuda G, Otsuka Y, Ono H, Nagahori Y, Hosoi H, Takahashi M, Kito F and Shimada H: Comparison of surgical results of D2 versus D3 gastrectomy (para-aortic lymph node dissection) for advanced gastric carcinoma: A multi-institutional study. *Ann Surg Oncol* 13: 659-667, 2006.
35. Wu CW, Hsiung CA, Lo SS, Hsieh MC, Shia LT and Whang-Peng J: Randomized clinical trial of morbidity after D1 and D3 surgery for gastric cancer. *Br J Surg* 91: 283-287, 2004.
36. Wu XS, Wu WG, Li ML, Yang JH, Ding QC, Zhang L, Mu JS, Gu J, Dong P, Lu JH and Liu YB: Impact of being overweight on the surgical outcomes of patients with gastric cancer: A meta-analysis. *World J Gastroenterol* 19: 4596-4606, 2013.
37. Kim JH, Chin HM, Hwang SS and Jun KH: Impact of intra-abdominal fat on surgical outcome and overall survival of patients with gastric cancer. *Int J Surg* 12: 346-352, 2014.
38. Yoshida K, Koderia Y, Kochi M, Ichikawa W, Kakeji Y, Sano T, Nagao N, Takahashi M, Takagane A, Watanabe T, *et al*: Addition of docetaxel to oral fluoropyrimidine improves efficacy in patients with stage III gastric cancer: Interim analysis of JACCRO GC-07, a randomized controlled trial. *J Clin Oncol* 37: 1296-1304, 2019.
39. Mahar AL, McLeod RS, Kiss A, Paszat L and Coburn NG: A systematic review of the effect of institution and surgeon factors on surgical outcomes for gastric cancer. *J Am Coll Surg* 214: 860-868.e12, 2012.
40. Smith DL, Elting LS, Learn PA, Raut CP and Mansfield PF: Factors influencing the volume-outcome relationship in gastrectomies: A population-based study. *Ann Surg Oncol* 14: 1846-1852, 2007.



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