JBUON 2016; 21(4): 903-908
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
E-mail: editorial_office@jbuon.com

ORIGINAL ARTICLE

Laparoscopic versus open total gastrectomy for advanced proximal gastric carcinoma: a matched pair analysis

Yi Lu, Baocheng Jiang, Tao Liu

Department of General Surgery, Suzhou Kowloon Hospital, Suzhou, People's Republic of China

Summary

Purpose: *Laparoscopic total gastrectomy for advanced proximal gastric carcinoma is a complex and challenging procedure, limited to a few expert centers. This study analyzed the short- and long-term outcomes of laparoscopic total gastrectomy for advanced proximal gastric carcinoma compared with open gastrectomy.*

Methods: *From January 2008 to January 2015, 61 patients underwent laparoscopic total gastrectomy for advanced proximal gastric carcinoma. They were matched and compared to 61 patients who underwent a conventional open operation. Short-term operative and postoperative outcomes as well as long-term outcomes, including overall survival and disease-free survival rates, were assessed.*

Results*: Patients were well matched for several preoperative factors. Overall postoperative 30-day complication rates were significantly higher for the open group. No significant difference was seen in 5-year overall survival and 5-year disease-free survival between the open and laparoscopic groups. The same result was seen in subgroup analyses of TNM stage.*

Conclusion: *This study shows the feasibility of laparoscopic total gastrectomy for advanced proximal gastric carcinoma compared to open resection in regard to both short- and long-term outcomes. Laparoscopic surgery offers many advantages commonly attributed to laparoscopy and is well suited for proximal gastric carcinoma when performed by experienced surgeons.*

Key words: *laparoscopic total gastrectomy, minimally invasive surgery, proximal gastric carcinoma, survival*

Introduction

Radical gastrectomy with D2 lymphadenectomy is one of the most challenging and complex procedures encountered by the gastrointestinal surgeon, requiring considerable expertise and surgical skill [1-5]. Laparoscopic gastrectomy requires additional advanced skills. Despite the technical difficulties, more centers have been using laparoscopy in gastric surgery in the last decade [6-10]. Significant advantages of laparoscopic distal gastrectomy versus open procedure have been widely reported, especially with regard to decreased incision, postoperative pain, intraoperative blood loss, surgical complication, and length of hospital stay [11,12]. In contrast, laparoscopic total gastrectomy has been limited to a few centers due to the technical demands of the procedure. Laparoscopic total gastrectomy is perceived as the most complex of all laparoscopic procedures and is limited to a surgical team experienced in both laparoscopic and gastric surgery. Laparoscopic total gastrectomy was first performed in the 2000s [13-15].

This study assessed the feasibility and results of laparoscopic total gastrectomy for advanced proximal gastric carcinoma with regard to both short- and long-term outcomes through a concurrent case-matched comparison with open total gastrectomy.

Methods

This study complied with the Declaration of Helsinki rules and was approved by local ethics committee.

Correspondence to: Yi Lu, MD. Department of General Surgery, Suzhou Kowloon Hospital, 118 Wansheng Street, 215021, Suzhou, People's Republic of China. Tel & Fax: +86 512 6262 9999, E-mail: yilujs@163.com
Received: 02/10/2015; Accepted: 30/10/2015

The need for informed consent from all patients was waived because this was a retrospective study.

From January 2008 to January 2015, 61 patients underwent laparoscopic total gastrectomy for advanced proximal gastric carcinoma and were included in this retrospective study. A control group undergoing open total gastrectomy for advanced proximal gastric carcinoma was 1:1 case-matched for age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score and clinical TNM stage. Medical records were retrospectively reviewed for demographics, clinical presentation, operative results, hospital course, postoperative 30-day complications and postoperative 30-day mortality, pathological findings, and long-term follow-up results. Postoperative 30-day complications were stratified according to the Clavien- Dindo classification [16,17], and complications of grade 3 or greater were considered severe.

The routine preoperative evaluation included history taking, physical examination, routine biochemical examination, blood coagulation test, tumor marker, upper gastrointestinal endoscopy, endoscopic ultrasonography, computed tomographic scans of brain, chest, and abdomen, and abdominal ultrasonography. Positron emission tomography-computerized tomography (PET-CT) and bone scanning were performed in selected cases when necessary. The clinical stage of gastric carcinoma was based on the 7th edition of the TNM classification of gastric carcinoma which was proposed by Japanese Gastric Cancer Association (JGCA), Union for International Cancer Control (UICC), and American Joint Committee on Cancer (AJCC) [18,19].

The inclusion criteria for laparoscopic total gastrectomy in this study were: histopathologically proven gastric carcinoma; no neoadjuvant chemotherapy or radiotherapy; patients with preoperatively clinical T2-3N0-1M0 disease [18,19]. Exclusion criteria for this study were palliative resection or requiring multivisceral resection.

All patients were placed in supine position with legs apart, and were under general anesthesia. The surgeon was placed to the right side of the patient, and the first assistant stood on the left side. The camera assistant stood on the same side of the surgeon. Carbon dioxide (CO_2) pneumoperitoneum was established at 15 mmHg after a 12-mm trocar was introduced through an umbilical incision. Two 12-mm trocars were introduced in the left and right lower quadrants, and two 5-mm trocars were inserted in the left and right upper quadrants. Firstly, the operator harvested the lymph node along the greater curvature of the stomach, following which the resection of distal margin was performed. Secondly, the operator harvested the lymph node along the lesser curvature of the stomach and the suprapancreatic area. Thirdly, after lymph node dissection was finished, the resection of proximal margin was done. Finally, Roux-en-Y reconstruction, esophagogastric anastomosis and gastrogastrostomy were performed for the gastrointestinal tract reconstruction. A detailed procedure of laparoscopic or open total gastrectomy has been described elsewhere [20].

Follow-up data were obtained through office visits or telephone interviews. Overall survival was assessed from the date of surgery until the last follow up or death of any cause. Disease-free survival was calculated from the date of surgery until the date of cancer recurrence or death from any cause. Disease recurrence was defined as locoregional, peritoneal, distant lymph node, hematogenous recurrence or mixed recurrence proven by radiology or pathology when available. Locoregional recurrence included the anastomotic site and gastric regional lymph nodes. Extraregional lymph nodes were defined as distal lymph nodes. Hematogenous recurrence included recurrence at remote sites, such as the brain, lung and kidney [21,22]. The follow-up was closed in August 2015.

Statistics

SPSS 14.0 for Microsoft windows version (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. Data were presented as mean and standard deviations for variables following normal distribution and were analyzed by Student's *t* test. For data following non-normal distribution, results were expressed as median and range and were compared by Wilcoxon signed rank test. Differences of semiquantitative results were analyzed by Mann–Whitney *U* test. Differences of qualitative results were analyzed by chi-square test or Fisher's exact test where appropriate. Survival rates were analyzed using the Kaplan-Meier method; differences between two groups were analyzed with the log-rank test. A p value <0.05 was considered statistically significant.

Results

Patient demographics and tumor features are listed in Table 1. The patients were well matched for age, sex, BMI, ASA score and clinical TNM stage. There was no significant difference in comorbidity (Table 1).

Table 2 summarizes the operative outcomes and postoperative courses of the two groups. The operative time was significantly longer in the laparoscopy group (p=0.020). However, patients in the laparoscopy group enjoyed faster recovery, such as less blood loss (p=0.015), less analgesic injections (p=0.018), earlier time to first flatus (p=0.028) and earlier hospital discharge (p=0.011) (Table 2).

The postoperative 30-day complication rates were significantly higher in the open group than in the laparoscopy group (p=0.044) (Table 3). However, the proportions of patients with Cla-

Table 1. Comparison of patient clinical characteristics of the two groups

Characteristics	*Laparoscopy (N=61) N*	*Open (N=61) N*	*p value*
Age, years, median (range)	59 (41-72)	57 (43-70)	0.351
Sex			0.709
Male	39	37	
Female	22	24	
BMI (kg/m2), median (range)	19 (19-24)	22 (19-27)	0.520
Clinical TNM stage (7th AJCC-UICC-JGCA)			0.814
IB	18	18	
IIA	17	19	
IIB	26	24	
ASA grade			0.794
I	45	43	
II	11	15	
III	5	3	
Comorbidity			0.645
0	45	43	
1	8	6	
2	5	11	
3	3	1	

Table 2. Comparison of surgical outcomes of the two groups

Outcomes	*Laparoscopy (N=61)*	*Open (N=61)*	*p value*
Operative time (min)	240 (220-320)	190 (170-260)	0.020
Estimated blood loss (ml)	250 (170-450)	330 (220-470)	0.015
Number of analgesic injections	3 (1-6)	5 (4-10)	0.018
Time to first flatus (days)	2 (1-5)	4 (2-7)	0.028
Hospital stay after surgery (days)	8 (5-18)	10 (7-32)	0.011

Numbers show median (range)

vien–Dindo classification >2 were 18.4% in the open group, and 13.2 % in the laparoscopy group, with no significant difference observed. There was no postoperative 30-day death recorded.

Pathological data showed comparable results between the two groups (Table 4).

The overall survival and disease-free rates of the two groups are shown in Figure 1 and 2. With a median follow-up of 38 months, no significant difference was seen in 5-year overall survival and disease-free rates between the two groups (p=0.444 and 0.561 respectively). Subset analyses by pathological TNM stage for overall survival and disease-free rates are shown in Table 5. There were no significant differences in the disease-free survival and overall survival rates between the open and laparoscopy group in relation to pathological TNM stage.

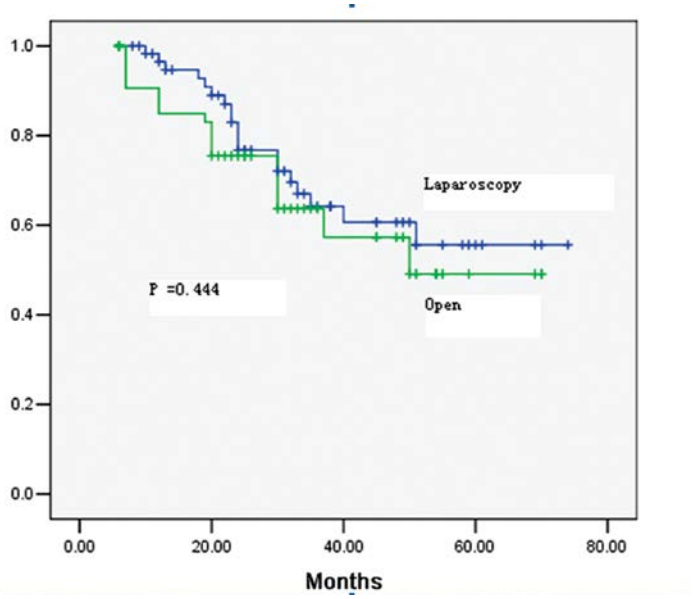

Figure 1. Comparison of overall survival rate between laparoscopy and open groups.

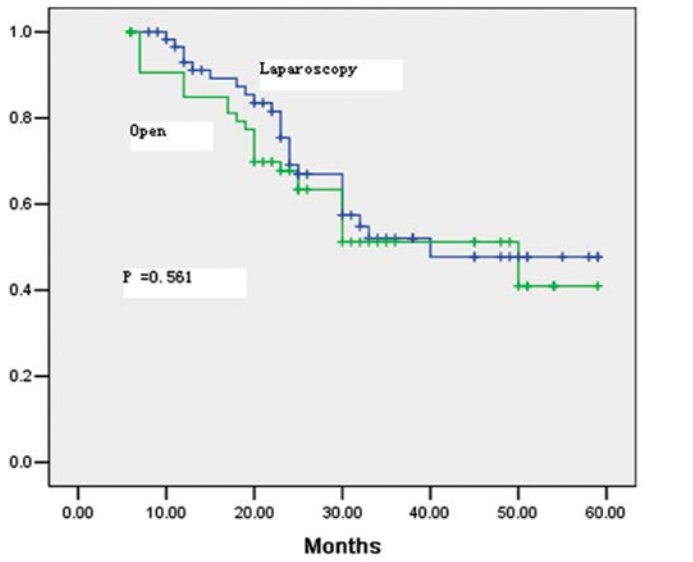

Figure 2. Comparison of disease-free survival rate between laparoscopy and open groups.

The sites of recurrence and recurrence-free interval from surgery to the first cancer recurrence were not significantly different between the two groups (Table 6). There was no port-site recurrence in patients undergoing laparoscopic total gastrectomy for advanced

Table 3. Comparison of complications of the two groups

Complications	*Laparoscopy (N=61) N*	*Open (N=61) N*	*p value*
Overall complications	8	17	0.044
Major complications	7	14	0.093
Minor complications	1	3	0.611
Pneumonia	4	6	0.509
Anastomotic leakage	2	3	1.000
Wound infection	1	3	0.611
Ileus	1	1	1.000
Atelectasis	0	1	-
Intra-abdominal bleeding	0	1	-
Intra-abdominal abscess	0	1	-

Table 4. Comparison of pathological data of the two groups

Pathology	*Laparoscopy (N=61) N*	*Open (N=61) N*	*p value*
Histological type			0.703
Differentiated	22	20	
Undifferentiated	39	41	
Lauren classification			0.765
Intestinal	28	29	
Diffuse	21	23	
Mixed	12	9	
Retrieved lymph nodes, median (range)	18 (17-23)	19 (16-24)	0.548
Pathological TNM stage (7th AJCC-UICC- JGCA)			0.616
IB	6	8	
IIA	15	16	
IIB	24	20	
IIIA	8	11	
IIIB	3	2	
IIIC	5	4	
Residual tumor (R0/R1/R2)	61/0/0	61/0/0	1.000

Table 5. Comparison of five-year overall survival and disease-free survival rates with regard to pathological stage

Pathological stage	*Laparoscopy (%)*	*Open (%)*	*p value*
Overall survival			
I	87	88	0.550
II	74	78	0.098
III	46	40	0.250
Disease-free survival			
I	69	65	0.280
II	59	64	0.189
III	29	20	0.190

Table 6. Comparison of cancer recurrence data of the two groups

Recurrence	*Laparoscopy (N=61) N*	*Open (N=61) N*	*p value*
Tumor recurrence	21	24	0.573
Locoregional	7	8	0.783
Peritoneal	6	7	0.769
Distant lymph node	3	3	1.000
Hematogenous	3	2	1.000
Mixed	2	4	0.675
Time to recurrence (median, months)	17	13	0.102
Treatment for recurrence			
Metastasectomy	7	4	0.343
Chemotherapy	9	12	0.472
Supportive care	5	8	0.379

Table 7. Comparison of morbidity and prognosis data of the conversion and complete group

Morbidity/Prognosis	*Conversion group (N=6) N*	*Complete group (N=55) N*	*p value*
Postoperative 30-day morbidity	1	7	1.000
Five-year overall survival	54	61	0.820
Five-year disease-free survival	47	53	0.507

proximal gastric carcinoma.

Of the 61 patients in the laparoscopy group, 6 required conversion to laparotomy (conversion group), and the procedure was completed in the remaining 55 with laparoscopy alone (complete group). The reasons for conversion were as follows: severe adhesions in 2 patients, uncontrollable bleeding in 4 patients. There was no difference between the conversion and complete groups in terms of postoperative 30-day morbidity, disease-free survival and overall survival (Table 7).

Discussion

Although previous studies suggested the feasibility of laparoscopic total gastrectomy [23-29], this procedure remains challenging and demands both laparoscopic and gastric surgery expertise. There is also insufficient evidence to determine whether laparoscopic total gastrectomy is more suitable than an open resection for the treatment of advanced proximal gastric carcinoma without compromising the oncologic efficacy.

Laparoscopic total gastrectomy was introduced in the 2000s, and more than 400 procedures have been performed [13-15]. A previous report [25] describing this novel conceptual technique showed that laparoscopic total gastrectomy is performed using essentially the same steps and principles used in the open procedure. This setting is ideal and appropriate for comparative studies of open and laparoscopic total gastrectomy. The main findings of this study are: (1) the short-term outcomes of laparoscopic total gastrectomy for advanced proximal gastric carcinoma appeared to be superior than the open procedure; (2) the technical feasibility of laparoscopic total gastrectomy has been proven; and (3) oncological outcomes including overall and disease-free survival rates after laparoscopic total gastrectomy were comparable to those after the open procedure for advanced proximal gastric carcinoma.

To the best of our knowledge, there were only two reports demonstrating the feasibility and safety of laparoscopic total gastrectomy for proximal gastric carcinoma in comparison with the open resection [20,30].

With regard to the short-term results of overall complications, which were the most important outcome, laparoscopic total gastrectomy was superior to the open resection. There was no difference between the two groups with regard to the severity of complication, defined as Clavien–Dindo classification. Clavien- Dindo classification >2 status was significantly less frequent in the laparoscopic group. Most complications were pneumonia and anastomotic leakage requiring treatment. These complications represent significant disadvantages of the open procedure. The apparent benefit of laparoscopy may be explained by the lack of damage to the abdominal wall, avoiding less inflammatory cytokines releasing and exposure of the abdominal viscera.

This study suggests comparable oncological outcomes of laparoscopic total gastrectomy compared with open resection. In total, TNM staging was comparable between the two groups. Other pathological findings, including histology, tumor-free margin, and the results of D2 lymphadenectomy, which could significantly influence disease-free and overall survival, also were comparable between the two groups. Both groups were therefore well matched with regard to tumor behavior, suggesting the reliability of long-term outcomes analysis. The long-term outcome was similar in the two groups. Furthermore, subgroup analyses by pathological TNM stage showed the same resulsts, indicating that laparoscopic total gastrectomy is associated with similar oncological results.

This is an intention-to-treat analysis; thus, all 6 converted cases in the laparoscopic group were analyzed as laparoscopic cases. We have compared the complete cases (N=55) and conversion cases (N=6) and found no significant differences between the two groups with regard to postoperative 30-day morbidity and prognosis (data not shown). The conversion rate for laparoscopic procedures was nearly 10%, which is similar with previous reports [20,23-30].

The reliability of the current study is limited because of the relatively small sample size and the limitations of the study design. Although well-designed, randomized controlled trials with large sample size would be preferred, when considering the difficulty in designing such a study, our conclusions will nonetheless be very useful in the future development of laparoscopic total gastrectomy for advanced proximal gastric carcinoma.

In conclusion, the present study demonstrated the technical feasibility as well as the comparable short-term and oncological outcomes of laparoscopic total gastrectomy for advanced proximal gastric carcinoma compared with the open resection. Although laparoscopic total gastrectomy offers many advantages commonly attributed to laparoscopy and is thus well suited to treat advanced proximal gastric carcinoma, given the relative high incidence of conversion rate, laparoscopic total gastrectomy should be regarded as a highly complicated procedure.

Acknowledgements

We sincerely thank the patients, their families and our colleagues who participated in this research.

Conflict of interests

The authors declare no confict of interests.

References

1. Canyilmaz E, Soydemir G, Serdar L et al. Evaluation of prognostic factors and survival results in gastric carcinoma: single center experience from Northeast Turkey. Int J Clin Exp Med 2014;7:2656-2666.
2. Karagulle M, Fidan E, Kavgaci H, Ozdemir F. The effects of environmental and dietary factors on the development of gastric cancer. J BUON 2014;19:1076-1082.
3. Li B, Liu HY, Guo SH et al. The postoperative clinical outcomes and safety of early enteral nutrition in operated gastric cancer patients. J BUON 2015;20:468-472.
4. Varol U, Alacacioglu A, Yildiz I, Kucukzeybek Y, Uslu R. Gastric cancer with diffuse hepatic metastases and complete radiological response to triplet chemotherapy. J BUON 2014;19:1128-1129.
5. Liu ML, Zhang SJ. Effects of resveratrol on the protein expression of survivin and cell apoptosis in human gastric cancer cells. J BUON 2014;19:713-717.
6. Qiu JF, Yang B, Fang L et al. Safety and efficacy of laparoscopy-assisted gastrectomy for advanced gastric cancer in the elderly. Int J Clin Exp Med 2014;7:3562-3567.
7. Huang YL, Lin HG, Yang JW et al. Laparoscopy-assisted versus open gastrectomy with D2 lymph node dissection for advanced gastric cancer: a meta-analysis. Int J Clin Exp Med 2014;7:1490-1499.
8. Tang HN, Hu JH. A comparison of surgical procedures and postoperative cares for minimally invasive laparoscopic gastrectomy and open gastrectomy in gastric cancer. Int J Clin Exp Med 2015;8:10321-10329.
9. Zhang B, Tu JC, Fang J, Zhou L, Liu YL. Comparison of early-term effects between totally laparoscopic distal gastrectomy with delta-shaped anastomosis and conventional laparoscopic-assisted distal gastrectomy: a retrospective study. Int J Clin Exp Med 2015;8:9967-9972.
10. Gong JQ, Cao YK, Wang YH, Zhang GH, Wang PH, Luo GD. Three-step hand-assisted laparoscopic surgery for radical distal gastrectomy: an effective surgical approach. Int J Clin Exp Med 2014;7:2156-2164.
11. Lee J, Kim W. Clinical experience of 528 laparoscopic gastrectomies on gastric cancer in a single institution. Surgery 2013;153:611-618.
12. Deng Y, Zhang Y, Guo TK. Laparoscopy-assisted versus open distal gastrectomy for early gastric cancer: A meta-analysis based on seven randomized controlled trials. Surg Oncol 2015; 24:71-77.
13 Parisi A, Nguyen NT, Reim D et al. Current status of minimally invasive surgery for gastric cancer: A literature review to highlight studies limits. Int J Surg 2015;17:34-40.
14. Emir S, Sözen S, Bali I et al. Outcome analysis of laporoscopic D1 and D2 dissection in patients 70 years and older with gastric cancer. Int J Clin Exp Med 2014;7:3501-3511.
15. Lianos GD, Rausei S, Ruspi L et al. Laparoscopic gastrectomy for gastric cancer: current evidences. Int J Surg 2014;12:1369-373.
16. Xiao H, Xie P, Zhou K et al. Clavien-Dindo classification and risk factors of gastrectomy-related complications: an analysis of 1049 patients. Int J Clin Exp Med 2015;8:8262-8268.
17. Clavien PA, Barkun J, de Oliveira ML et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250:187-196.
18. Yegin EG, Duman DG. Staging of esophageal and gastric cancer in 2014. Minerva Med 2014;105:391-411.
19. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (vers 3). Gastric Cancer 2011;14:113-123.
20. Lin J, Huang C, Zheng C et al. A matched cohort study of laparoscopy-assisted and open total gastrectomy for advanced proximal gastric cancer without serosa invasion. Chin Med J (Engl) 2014;127:403-407.
21. Qu JL, Qu XJ, Li X et al. Early initiation of fluorouracil-based adjuvant chemotherapy improves survival in patients with resectable gastric cancer. J BUON 2015;20:800-807.
22. Uzel M, Sahiner Z, Filik L. Gastric cancer and gallbladder: single center experience. J BUON 2015;20:667-668.
23. Lee SR, Kim HO, Son BH, Shin JH, Yoo CH. Laparoscopic-assisted total gastrectomy versus open total gastrectomy for upper and middle gastric cancer in short-term and long-term outcomes. Surg Laparosc Endosc Percutan Tech 2014;24:277-282.
24. Lee JH, Nam BH, Ryu KW et al. Comparison of outcomes after laparoscopy-assisted and open total gastrectomy for early gastric cancer. Br J Surg 2015. [Epub ahead of print]
25. Lee MS, Lee JH, Park do J, Lee HJ, Kim HH, Yang HK. Comparison of short- and long-term outcomes of laparoscopic-assisted total gastrectomy and open total gastrectomy in gastric cancer patients. Surg Endosc 2013;27:2598-2605.
26. Eom BW, Kim YW, Lee SE et al. Survival and surgical outcomes after laparoscopy-assisted total gastrectomy for gastric cancer: case-control study. Surg Endosc 2012;26:3273-3281.
27. Sato H, Shimada M, Kurita N et al. Comparison of long-term prognosis of laparoscopy-assisted gastrectomy and conventional open gastrectomy with special reference to D2 lymph node dissection. Surg Endosc 2012;26:2240-2246.
28. Bo T, Peiwu Y, Feng Q et al. Laparoscopy-assisted vs. open total gastrectomy for advanced gastric cancer: long-term outcomes and technical aspects of a case-control study. J Gastrointest Surg 2013;17:1202-1208.
29. Kim KH, Kim YM, Kim MC, Jung GJ. Is laparoscopy-assisted total gastrectomy feasible for the treatment of gastric cancer? A case-matched study. Dig Surg 2013;30:348-354.
30. Cai J, Zhang C, Zhang H et al. Open versus laparoscopy-assisted D2 radical gastrectomy in advanced upper gastric cancer: a retrospective cohort study. Hepatogastroenterology 2013;60:1805-1808.