

Multicenter Randomized Comparison of LigaSure Versus Conventional Surgery for Gastrointestinal Carcinoma

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Abstract

Purpose. We conducted this randomized trial to compare the LigaSure Vessel Sealing System with conventional methods in gastrointestinal carcinoma surgery at five specialty cancer hospitals.

Methods. Patients with resectable stomach or colorectal cancers were randomized to the LigaSure ($n = 100$) or conventional surgery ($n = 74$) groups according to sealed envelopes. The operative data were compared.

Results. There were no significant differences in operating times, blood loss, postoperative complications, or hospital stay. However, at the hospital where most of the procedures took place, the LigaSure was associated with a shorter operating time (173 ± 43 min for gastric carcinoma and 157 ± 43 min for colorectal carcinoma vs 211 ± 55 min and 202 ± 55 min for conventional surgery; $P = 0.0046$ and $P = 0.0200$, respectively) and less blood loss (300 ± 196 ml and 150 ± 133 ml, respectively, vs 453 ± 387 ml and 382 ± 444 ml; $P = 0.0482$ and $P = 0.0465$, respectively).

Conclusions. The LigaSure is safe for both gastric and colorectal cancer surgery with extended lymph node dissection. Used effectively, the device appears to reduce operating times and blood loss, although this requires confirmation in a larger series.

Key words Colorectal carcinoma · Gastric carcinoma · LigaSure

Introduction

Tumor resection with systematic dissection of the lymph nodes is indispensable to the treatment of gastrointes-

tinal carcinoma.^{1,2} In conventional surgery, most lymphatic channels, vessels, and tissue bundles are ligated easily with suture material or thread to prevent bleeding and lymphatic leakage.

The LigaSure (Covidien, Mansfield, MA, USA) is a new hemostatic system based on pressure and bipolar electrical energy, which seals vessels as large as 7 mm in diameter. The device delivers a controlled high-power current at a low voltage to melt collagen and elastin, permanently fusing the vascular layers and obliterating the vessel lumen. The collagen and elastin re-form to create a “seal zone,” which appears as a distinctive, translucent area with plastic resistance to deformation.³

Many reports suggest the utility of LigaSure, not only for digestive surgery, but also for urologic⁴ and gynecologic⁵ procedures, although Cipolla et al. reported that LigaSure did not reduce the incidence of complications or the operating time compared with traditional hemostasis in total thyroidectomy.⁶ Thus, we sought to clarify the efficacy of the LigaSure as compared with conventional hemostatic methods in gastrointestinal cancer surgery.

Patients and Methods

Patient Selection

With the approval of the ethics committee at each participating hospital, patients were enrolled from June 2007 to August 2008 at five cancer specialty hospitals in Chiba Prefecture. Patients undergoing primary operations for gastric or colorectal cancer for disease in clinical stages I–III were eligible after giving informed consent. Patients were excluded if they had blood vessels with severe calcification, serious preoperative complications, multiple cancers, or a history of cancer. Randomization to surgery with the LigaSure or

Table 1. Clinical characteristics and surgical outcomes of the patients with gastric carcinoma

	LigaSure (<i>n</i> = 55)	Conventional (<i>n</i> = 42)	<i>P</i> value
Mean age	68.8 ± 9.7	65.8 ± 9.2	NS
M:F	40:15	28:14	NS
Distal/total resection	32/23	24/18	NS
TNM stage: I/II/III/IV	23/11/14/7	19/10/8/4	NS
Level of node dissection: 1/2/3	14/41/0	11/30/1	NS
Combined resection	19	7	NS
Preoperative complication	22	9	NS
Body mass index	22.10 ± 4.5	22.25 ± 3.2	NS
Operating time (min)	218.6 ± 75.3	230.6 ± 56.3	NS
Blood loss (ml)	350.1 ± 255.0	418.4 ± 330.1	NS
Number of ties (by threads)	9.98 ± 12.0	45.4 ± 26.4	<0.0001
Start of drinking (days)	6.2 ± 3.2	7.8 ± 13.1	NS
Resumption of eating (days)	8.1 ± 3.9	9.6 ± 13.3	NS
Blood transfusion	1	1	NS
Postoperative stay (days)	17.1 ± 18.4	17.7 ± 20.1	NS
Postoperative complications			NS
Ileus	1	0	
Cardiac disorder	1	1	
Wound infection ^a	4	3	
Anastomotic leakage ^a	1	2	
Pancreatic fistula ^a	1	1	
Intra-abdominal abscess ^a	0	1	

NS, not significant

^aTotal number of patients with surgical site infection (SSI): 6 in the LigaSure group and 7 in the conventional surgery group (*P* = 0.6003)

conventional methods was carried out with sealed envelopes. Of the patients with stomach cancer, 55 were assigned to the LigaSure group and 42 to the conventional surgery group, and of those with colorectal cancer, 45 were randomized to the LigaSure group and 32 to the conventional surgery group. The primary endpoints were operating time and intraoperative blood loss. The secondary endpoints were postoperative complications, including surgical site infection (SSI), and postoperative hospital stay.

Surgical Procedure

The handpiece of the LigaSure was the Atlas20, which maintains a constant seal width and shortens the time required for knife function. The main artery of the resected organ was ligated by a thread on the patient side, then sealed and cut using the LigaSure. Other blood vessels, lymphatics, and tissues were likewise cut with the LigaSure. Patients randomized to the conventional surgery group underwent the usual method of thread and suture ligation used at each institution. Standard electrosurgical dissection was used. The methods of reconstruction and anastomosis (instrumental or hand-sewn) were consistent within each institution.

Statistical Analysis

Comparisons of patient characteristics and outcomes were performed using the chi-square test or Mann–Whitney *U*-test. Differences with values of *P* < 0.05 were considered significant. Multivariate analysis of factors influencing the operating time was performed including variables such as LigaSure, institution, body mass index (BMI), blood loss, and surgeons' experience, by using Cox's proportional hazard model. Differences with *P* < 0.05 were considered significant.

Results

The two groups of gastric cancer patients were well matched (Table 1). The differences in the operating time, intraoperative blood loss, blood transfusion, number of SSIs, postoperative complications combined with SSI, and postoperative hospital stay were not significant (Table 1). The two groups of patients with colorectal cancer also were well matched (Table 2). There were no significant differences in operating time, blood transfusion, SSI, postoperative complications combined with SSI, or postoperative hospital stay (Table 2). There were no deaths after surgery for either cancer.

Table 2. Clinical characteristics and surgical outcomes of the patients with colorectal carcinoma

	LigaSure (<i>n</i> = 45)	Conventional (<i>n</i> = 32)	<i>P</i> value
Mean age	66.3 ± 11.0	63.3.8 ± 10.6	NS
M:F	22:23	22:10	NS
Type of resection			
Right hemicolectomy	11	5	
Transverse	2	1	
Left hemicolectomy	2	2	
Sigmoidectomy	9	4	
High anterior	3	6	
Low anterior	9	8	
Abdominoperineal	6	4	
Other	3	2	
TNM stage: I/II/III/IV	9/13/20/3	1/11/18/2	NS
Level of node dissection: 1/2/3	0/16/29	0/5/27	NS
Preoperative complications	20	10	NS
Body mass index	24.07 ± 2.9	24.16 ± 4.2	NS
Operating time (min)	187.5 ± 70.7	208.3 ± 70.4	NS
Blood loss (ml)	217.3 ± 225.9	304.5 ± 365.7	NS
Number of ties (by threads)	4.5 ± 4.0	21.7 ± 15.1	<0.0001
Start of drinking (days)	3.8 ± 1.9	4.2 ± 14.0	NS
Resumption of eating (days)	5.39 ± 1.98	5.75 ± 1.87	NS
Blood transfusion	1	1	NS
Postoperative stay (days)	14.2 ± 11.2	14.1 ± 7.1	NS
Postoperative complications			NS
Ileus	1	1	
Pneumonia	1	0	
Cardiac disorder	0	1	
Renal dysfunction	1	0	
Wound infection ^a	3	2	
Anastomotic leakage ^a	2	1	
Wound dehiscence ^a	0	1	
Pelvic abscess ^a	1	2	

^aTotal number with SSI: 6 in both groups (*P* = 0.7436)

Table 3. Operative outcomes of patients who underwent LigaSure versus conventional surgery at Facility A (largest number of patients)

	LigaSure	Conventional	<i>P</i> value
Gastric carcinoma	<i>n</i> = 28	<i>n</i> = 24	
Operating time (min)	173.0 ± 42.8	210.6 ± 54.6	0.0046
Blood loss (ml)	300.2 ± 196.0	453.0 ± 387.1	0.0482
Postoperative stay (days)	12.6 ± 2.6	13.9 ± 7.6	NS
Colorectal carcinoma	<i>n</i> = 22	<i>n</i> = 15	
Operation time (min)	156.5 ± 42.7	202.3 ± 55.4	0.0200
Blood loss	150.0 ± 132.8	381.9 ± 443.5	0.0465
Postoperative stay (days)	11.0 ± 3.96	12.1 ± 5.8	NS

Interestingly, when we examined independently the results from the institution doing the largest number of operations for both gastric and colorectal cancer, we found the LigaSure to be associated with shorter operating times and less blood loss (Table 3). The postoperative hospital stay was not significantly different, possibly because of the Japanese practice of allowing patients to remain in hospital for several days after

surgery. At the second most used facility, there were no significant differences in primary or secondary endpoints.

We analyzed the factors regulating operating time by multivariate analysis; including LigaSure, hospital, BMI, blood loss, and surgeon experience (Table 4). For both gastric and colorectal cancer, the factors regulating operating time were hospital, blood loss, and surgeon

Table 4. Multivariate analysis of the factors regulating operation time

Factor	Level	Risk ratio (95% CI)	P value
Gastric carcinoma			
Hospital ^a	B/A	4.88568 (2.88327–8.52515)	<0.0001
	C/A	0.74754 (0.38655–1.59130)	
LigaSure ^b	L/C	0.70085 (0.44915–1.08595)	0.1118
Blood loss (ml)		1.00264 (1.00150–1.00390)	<0.0001
Body mass index		1.05276 (0.99348–1.12230)	0.084
Surgeon experience ^c	–6Y/7Y–	1.72745 (1.08680–2.70808)	0.0213
Colorectal carcinoma			
Hospital ^a	B/A	2.5754 (1.50558–4.50098)	0.0006
	C/A	0.69637 (0.30505–1.80351)	
LigaSure ^b	L/C	0.87163 (0.52498–1.43498)	0.59
Blood loss (ml)		1.00253 (1.00142–1.00383)	<0.0001
Body mass index		1.05346 (0.97056–1.14068)	0.21
Surgeon experience ^c	–6Y/7Y–	1.91516 (1.09288–3.30023)	0.0237

CI, confidence interval

^aComparison of Facilities A, B, and C

^bLigaSure vs conventional surgery

^c<6 years' surgeon experience vs >7 years' surgeon experience

experience. LigaSure use and BMI were not independent influences.

Discussion

The LigaSure is a new hemostatic system, which can seal vessels as large as 7 mm in 2–7 s.^{3,7} The LigaSure was released in Japan in 2000, and has been used widely in open and laparoscopic surgery. It is usually faster than conventional suture ligation and is operator-independent. Experimental and clinical studies have confirmed its efficacy and safety in many general surgical,^{8–11} urologic, and gynecologic^{12–15} procedures.

Prolonged operating time, greater blood loss, and poor preoperative status are thought to be associated with morbidity in gastrointestinal surgery. Although many surgeons report a shorter operating time with the LigaSure, there are no reports of multicenter randomized trials being carried out to evaluate its usefulness in gastrointestinal carcinoma. In our trial, the primary and secondary endpoints for both gastric and colorectal cancer surgery did not differ for the entire series, but at the institution doing the most procedures, the LigaSure was associated with significantly shorter operating times and less blood loss, suggesting value in the hands of experienced surgeons.

In randomized trials of surgical procedures, unexpected results are often encountered. The differences among the institutions and surgeon experience were major factors in evaluating surgical techniques and speed. Despite the simplicity of the controlled trial, this result was unexpected, demonstrating the difficulty of a

multicenter randomized controlled trial of surgical procedures.

The cost of the LigaSure is ¥78 000, whereas the cost of the silk thread and the absorbable thread used in conventional surgery was ¥1250 (¥25 × 50) and ¥7500 (¥150 × 50), respectively. Conversely, the LigaSure may reduce staff costs (an operator, two assistant physicians, two nurses, and an anesthesiologist) and the anesthesia price if it shortens the operation time. Indeed, in Facility A, the LigaSure shortened the operating time by 38 min in gastric cancer surgery and by 45 min in colorectal cancer surgery. We believe that the reduction in personnel expenses and the anesthesia fee may compensate for the cost of the LigaSure.

According to the results of a randomized trial comparing D2 and extended para-aortic lymphadenectomy (JCOG 9501) reported by Sano et al.,¹⁶ the former entailed an operating time of 237 min and a blood loss of 430 ml. Moreover, the complication rate was 20.1%, and transfusion was given to 14.1% of the patients.¹⁶ In our patients undergoing gastric cancer surgery, the bleeding volume of the conventional treatment group at our facility, where most of the operations were performed, was within the range found in JCOG 9501, and the morbidity rate was similar. However, the operating time was shortened by using the LigaSure, perhaps as a result of greater surgeon experience.

Prevention of SSI is vital for optimizing patient care, minimizing costs, and shortening hospitalization. Suspected risk factors are long operating times, significant blood loss, colorectal surgery, and comorbid conditions such as diabetes.^{17–19} The use of closed drains and prophylactic antibiotics has been studied, and avoiding the

use of nonabsorbable thread and preventing lymphatic leakage are believed to be important. In our study, there was no difference in postoperative complications or length of hospital stay between the LigaSure and conventional surgery groups.

Our results highlight the difficulty of evaluating clinical trials of surgical procedures. Even in specialty hospitals, there can be differences in techniques, learning curves, and experience with particular devices. In recent years, the number of obese and elderly (>75 years) patients with gastrointestinal cancer has been increasing in Japan, so advancing surgical skills and discerning employment of devices is becoming more and more important. In this trial, the superiority of the LigaSure was not proven in this series as a whole, but its benefit was seen at the most active hospital, suggesting its superiority if problems with the learning curve and the technical gap between institutions are resolved. Further exploration of this hypothesis is warranted.

Conflict of Interest Statement. None of the authors has a financial interest in the LigaSure device.

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