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学　位　論　文

Novel approach of laparoscopic and endoscopic cooperative surgery (LECS) for cholecystectomy

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ORIGINAL ARTICLE

Novel approach of laparoscopic and endoscopic cooperative surgery (LECS) for cholecystectomy

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ABSTRACT

Background: Endoscopic submucosal dissection (ESD) techniques, such as generating an artificial space between digestive tract layers for safer dissection, were thought to be safer for the resection of organs in cholecystectomy. We investigated whether combinations of endoscopic techniques and laparoscopic techniques could be performed more safely and rapidly.

Material and methods: Laparoscopic and endoscopic cooperative-cholecystectomy (LEC-chole) and conventional laparoscopic cholecystectomy (Lapa-chole) were performed in six dogs. Operation time was defined as the time from the creation of the first port to the retrieval of the resected gallbladder (GB); and GB bed dissection time was the time from local injection of natural saline to the clipping of the cystic duct. The main roles of the endoscope in LEC-chole were to obtain a sufficient cutting space via local injection of natural saline to the GB bed and to monitor the operative view without laparoscopic camera, thus omitting the umbilical port.

Results: The operation times were 60 ± 18.3 minutes for LEC-chole and 95 ± 7.0 for Lapa-chole ($p=.036$). The GB bed dissection times were 31 ± 8.54 minutes in LEC-chole and 50.6 ± 7.37 minutes in Lapa-chole ($p=0.048$). There were significant differences in liver damage and bleeding ($p=0.116$), but there were no significant differences in one-month survival.

Conclusions: The application of LEC-chole may be expanded to cholecystectomy.

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KEYWORDS
Endoscopic submucosal dissection; laparoscopic and endoscopic cooperative surgery; safer cholecystectomy; reduced port; operation time

Introduction

Laparoscopic and endoscopic cooperative surgery (LECS) was developed in Japan in 2008 and is now covered by Japanese health insurance for gastrointestinal stromal tumor dissection [1–5]. The advantage of LECS is that both endoscopists and laparoscopists cooperate with each other to contribute their technical advantages to achieve a minimally invasive surgery for patients. To date, various surgical procedures related to LECS have been reported [6–9]. The development of flexible endoscopic devices and treatments, such as endoscopic submucosal dissection (ESD), has contributed to the development of LECS.

ESD has made it possible to perform the selective dissection of a thin digestive tract layer to create an artificial space within submucosal layer by local injection; thus, an incision can be safely made [10]. This concept of making an artificial space between organs for safer dissection might be applied to a surgical technique such as LECS. The most applicable surgical procedure for the dissection of the gallbladder (GB) may be laparoscopic cholecystectomy (Lapa-chole), which requires a total of four ports for a safe and efficient surgery.

Based on the concept of LECS, the present study reports on *in vivo* experiments that were performed in six dogs to verify whether this procedure can reduce the number of ports, increase the safety of the cholecystectomy procedure, and shorten the operation time.

Material and methods

In this study, laparoscopic and endoscopic cooperative-cholecystectomy (LEC-chole) and conventional laparoscopic cholecystectomy (Lapa-chole) were performed in six dogs. Six female beagle dogs (Hokuzan Rabesu Co., Nagano, Japan) approximately ten

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Supplemental data for this article can be accessed here.

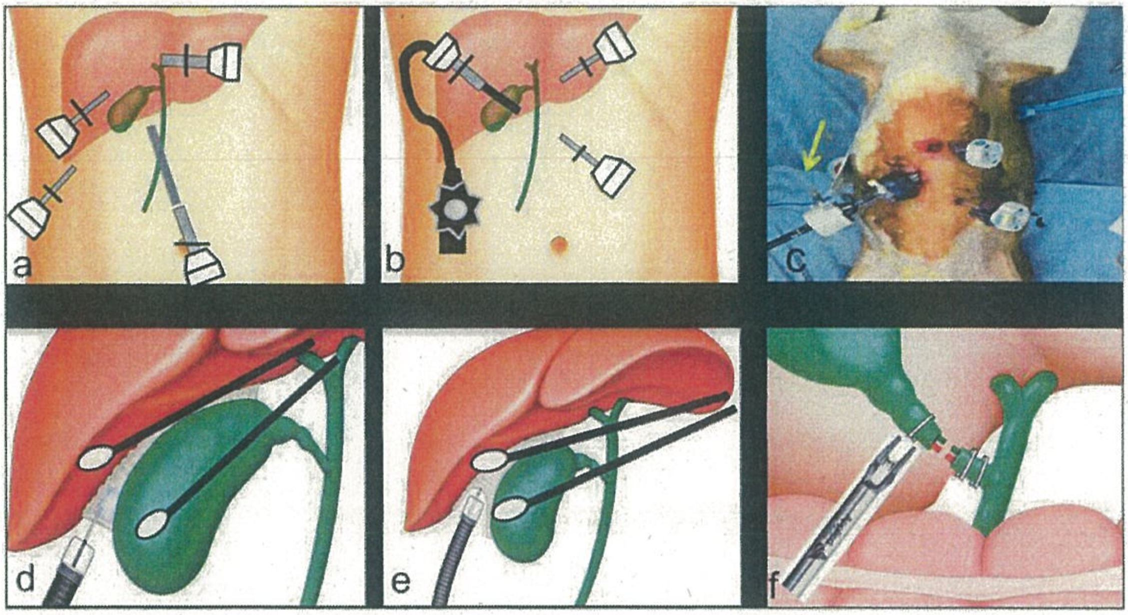

Figure 1. Schema of port placements and LEC-chole procedures. (a) In standard Lapa-chole, a total of four ports are created for safer surgery. (b) In LEC-chole, only three ports were created: a 12-mm blunt port at the right hypochondriac region just above the GB for the flexible endoscope, and two 5-mm ports at the epigastric region and 5 cm caudal to that region. (c) For the experiments in dogs, a flexible endoscope was inserted into the peritoneal cavity via the 12-mm blunt port at the right hypochondriac region in a parallel direction between the liver and the GB bed and connected to the pneumoperitoneum system (yellow arrow). (d) Local injection of natural saline to the GB bed through the endoscope channel made it possible to create a sufficient space between the liver and the GB. (e) Dissection of the GB bed from the GB fundus to the neck was performed smoothly, safely and rapidly using a Dual knife and an IT knife 2. (f) After dissecting the cystic duct and the GB artery in the Calot triangle, two to three clips were applied to the cystic duct using an Endo Clip® and one clip was applied to the cystic duct to be resected; then, the cystic duct was resected using a Sono Surge®.

months old were used in this study. The animal experiments were performed at the Preclinical Animal Laboratory of Kagawa University according to the guidelines on animals of Kagawa University. The dogs were maintained under controlled temperature (23 ± 1 °C) and humidity (54 ± 3%). After they underwent cholecystectomy, dogs were cared for and kept by special breeding staff in the Animal Experimentation Facility of Kagawa University in accordance with the Preclinical Animal Declaration Guidelines approved by the animal institutional review board committee of Kagawa University.

Schema of the standard method of lapa-chole and LEC-chole

The standard method of Lapa-chole requires a total of four ports to conduct a safe and efficient surgery (Figure 1(a)). In Lapa-chole, laparoscopic rigid devices are placed vertical to the GB bed. Therefore, Sono Surge® or other electric scalpels can damage the liver, causing oozing bleeding (Supplementary Video 1). In contrast, only three ports are sufficient for LEC-chole surgery (Figure 1(b,c)). In this surgery, the following three ports are created: a 12-mm blunt port at the right hypochondriac region just above the GB for the flexible endoscope, which was created by the open method to avoid damaging other organs, and two ports that are 5 mm in diameter at the epigastric region and 5 cm caudal to the epigastric port (Figure 1(b)). In only one case, a 12-mm port was added at the umbilicus for a laparoscopic camera to monitor the LEC-chole (total four ports). A flexible endoscope was inserted into the peritoneal cavity through the 12-mm blunt port at the right hypochondriac region and connected to the pneumoperitoneum system (Figure 1(c)). Laparoscopic surgical support was provided via the two 5-mm ports, one at the epigastric region and the other at 5 cm caudal to the epigastric port, Tupfer forceps (Endo Peanuts®) helped to create sufficient counter traction between the liver and the GB bed (Figure 1(d,e)). Natural saline was locally injected to the GB bed to create sufficient space between the liver and the GB (Figure 1(d)). Dissection of the GB bed from the GB fundus to the neck was performed using a Dual knife and an IT knife 2 (Figure 1(e)). To transect the GB artery in the Calot triangle, two to three clips were applied to the cystic duct using an Endo

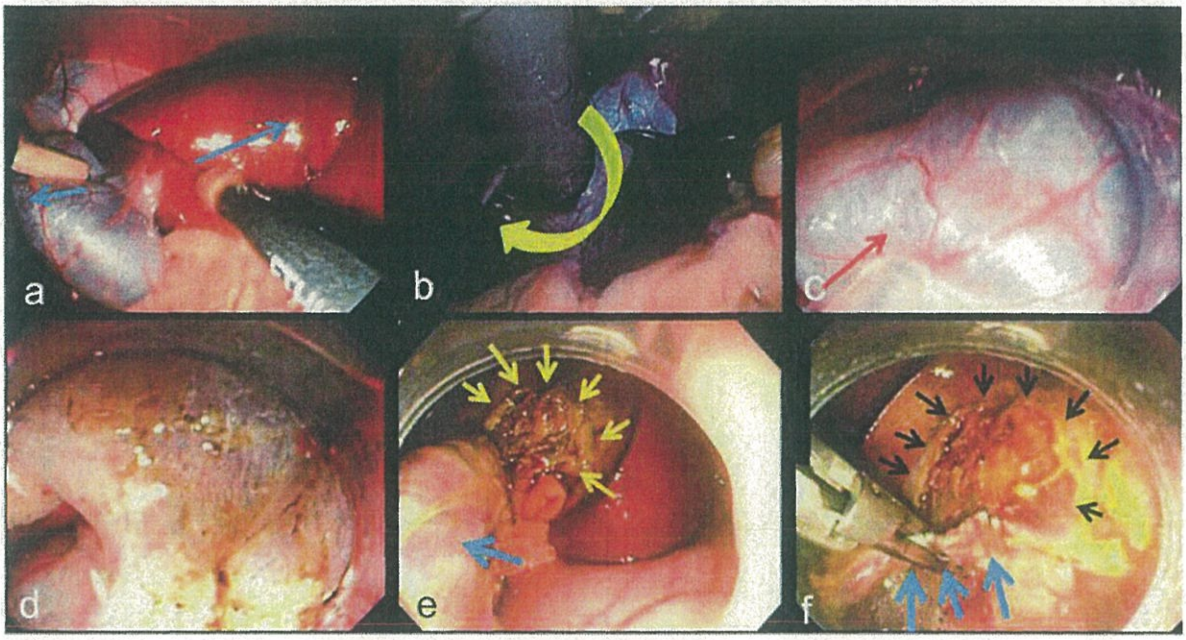

Figure 2. LEC-chole procedures in the *in vivo* dog experiments. (a) Laparoscopic support was provided via 2 5-mm ports at the epigastric region and 5 cm caudal to the epigastric region; Tupfer forceps (Endo Peanuts®) were used to create sufficient counter traction between the liver and the GB bed (blue arrows). (b) An endoscope with a tip attachment was inserted between the liver and the GB bed (yellow curved arrow). (c) Local injection of natural saline was performed through the endoscopic channel (red arrow), and a sufficient space between the liver and the GB bed was created. (d) Dissection of the GB bed from the GB fundus to the neck was performed smoothly using an ESD technique. (e) The GB bed was completely dissected (blue arrow) without any liver damage (yellow arrows). (f) Three clips were applied to the cystic duct using an Endo Clip®, and one clip was applied to the cystic duct to be resected, and then, the cystic duct was resected using a Sono Surge®.

Clip® while one clip was applied to the cystic duct to be resected; then, the duct was resected using a Sono Surge® (Figure 1(f)) (Supplementary Video 2).

N.K, who was an ESD novice, performed the dissection of the GB bed, and H.M, who was a laparoscopic surgery expert, performed Lapa-chole to compare the following items.

The observed items were as follows:

- The operation time from the creation of the first port to the retrieval of the resected GB in both LEC-chole and Lapa-chole.
- The GB bed dissection time from the local injection of saline to the application of clips to the cystic duct in both LEC-chole and Lapa-chole.
- The safety of the procedures, as determined by one-month survival after LEC-chole or Lapa-chole.

Devices

The following devices were used for the procedures:

Endoscopes (disinfected with ethylene oxide (EtO) gas): OLYMPUS GIF TYPE Q260J (OLYMPUS, Tokyo, Japan).

Incisional knife (disinfected with EtO gas): Dual knife® (KD-650 L), IT knife 2® (KD-611 L) (OLYMPUS, Tokyo, Japan) and Sono Surge® (Olympus Co., Tokyo, Japan).

Incisional generator device: ERBE VIO300D (Elektromedizin, Tuebingen, Germany).

CO_2 insufflation device: OLYMPUS UCR (OLYMPUS, Tokyo, Japan).

Laparoscopic clips: Endo Clip® (Covidien co., Tokyo, Japan).

Tupfer forceps: Endo Peanuts® (Covidien co., Tokyo, Japan).

Results

The surgical procedures of LEC-chole were as follows (Supplementary Video 1) (Figure 2): LEC-chole was performed under general anesthesia. A flexible endoscope was inserted into the peritoneal cavity through a 12-mm blunt port at the right hypochondriac region and connected to the pneumoperitoneum system. Laparoscopic surgical support was provided via 2 5-mm ports; Endo Peanuts® helped to create sufficient counter traction between the liver and the GB bed

Table 1. Result of 6 beagle dogs' experiments.

	Age (month)	Male/ Female	Total operation time (min)	Dissecting time of GB bed (min)	Liver damage or bleeding	Other complications	1 month survival
Case 1 (LEC-chole)	10	F	80	40	–	–	○
Case 2 (LEC-chole)	10.5	F	56	30	–	–	○
Case 3 (LEC-chole)	11	F	44	23	–	–	○
Case 4 (Lapa-chole)	10	F	100	59	+	–	○
Case 5 (Lapa-chole)	9.5	F	98	48	+	–	○
Case 6 (Lapa-chole)	11	F	87	45	–	–	○

(Figure 2(a)). A flexible endoscope was easily inserted between the liver and the GB via the right hypochondriac port (Figure 2(b)). Local injection of natural saline to the GB bed through the endoscope channel created sufficient space between the liver and the GB (Figure 2(c)). Dissection of the GB bed from the GB fundus to the neck was performed using a Dual knife and an IT knife 2, which made the surgery smooth, safe and rapid (Figure 2(d)). After dissection of the cystic duct (Figure 2e) and the GB artery in the Calot triangle, two to three clips were applied to the cystic duct using an Endo Clip® and resected by Sono Surge® (Figure 2(f)). After retrieval of the resected GB, a peritoneal wash was conducted with 2 L of natural saline. The surgical procedures of Lapa-chole were performed with conventional methods. The operation times were 80, 56 and 44 min (60 ± 18.3) in LEC-chole and 100, 98 and 87 min (95 ± 7.0) in Lapa-chole ($p = .036$) (Mann-Whitney U test). There was a significant difference in the operation time (Table 1). The GB bed dissection times were 40, 30, and 23 min (31 ± 8.54) by LEC-chole and 59, 48, and 45 min (50.6 ± 7.37) by Lapa-chole ($p = .048$) (Mann-Whitney U test). There was a significant difference in the dissection time. There were significant differences in the incidence of liver damage or bleeding ($p = .048$), but no significant differences were observed in one-month survival.

Discussion

In LEC-chole, the main benefits of using an endoscope are as follows: First, the rapid, safe, accurate and efficient resection of the GB bed depends on creating sufficient cutting space by local injection of saline, thus avoiding injury to the liver. Second, monitoring the operation by endoscope without the use of a laparoscopic camera helps to reduce the number of ports required for surgery.

In contrast, the benefits of laparoscopic surgery are as follows: First, creating an appropriate operative field by lifting up the liver and pulling down the GB fundus is helpful for the endoscopic GB resection. Second, the clipping and cutting of the cystic duct is safer. Therefore, the proportion of endoscopic procedures throughout the cholecystectomy is increased.

In this study, LEC-chole was a rapid and safe procedure without any of the complications that sometimes occur in Lapa-chole [11].

From a technical point of view, although laparoscopic rigid devices are approached in a vertical direction to the GB bed in Lapa-chole, rigid electrical scalpels sometimes cause injuries to the liver, such as bleeding, and to the common bile duct by thermal trauma of the liver parenchyma, especially when using the monopolar cutter (Figure 3(a,b,c)) [12]. On the other hand, in LEC-chole, the electric knives for ESD approach in a parallel direction between the liver and the GB bed (Figure 3(d,e,f)). In LEC-chole, as saline injection to the GB bed was performed to detect and pre-coagulate vessels under direct endoscopic view between GB bed and liver bed before GB bed dissection, there was no bleeding, damage and injury of the liver bed. On the other hand, as in Lapa-chole, there were bleedings from the liver bed in two cases, and an electric knife of sprayed mode was used to stop the bleeding.

Even if a bleeding from the liver bed occurs, the bleeding can probably be managed by hemostatic forceps for intraluminal use.

As LECS-related surgical procedures seem to be increasing in prevalence due to their minimal invasiveness and safety assurance, the creation of an artificial space by local injection of saline between organs to promote a safe resection will be applied to more surgical procedures involving both an endoscopist and a surgeon. Isayama et al. reported that pure cholecystectomy via the transgastric route could be performed by injecting hyaluronic acid into the GB bed [13]; however, this may be difficult to apply in clinical procedures due to safety concerns about using only a flexible endoscope.

Moreover, the advantage of LEC-chole compared to Lapa-chole is the reduction of the umbilical camera port, which is sometimes the cause of surgical site infection (SSI) [14].

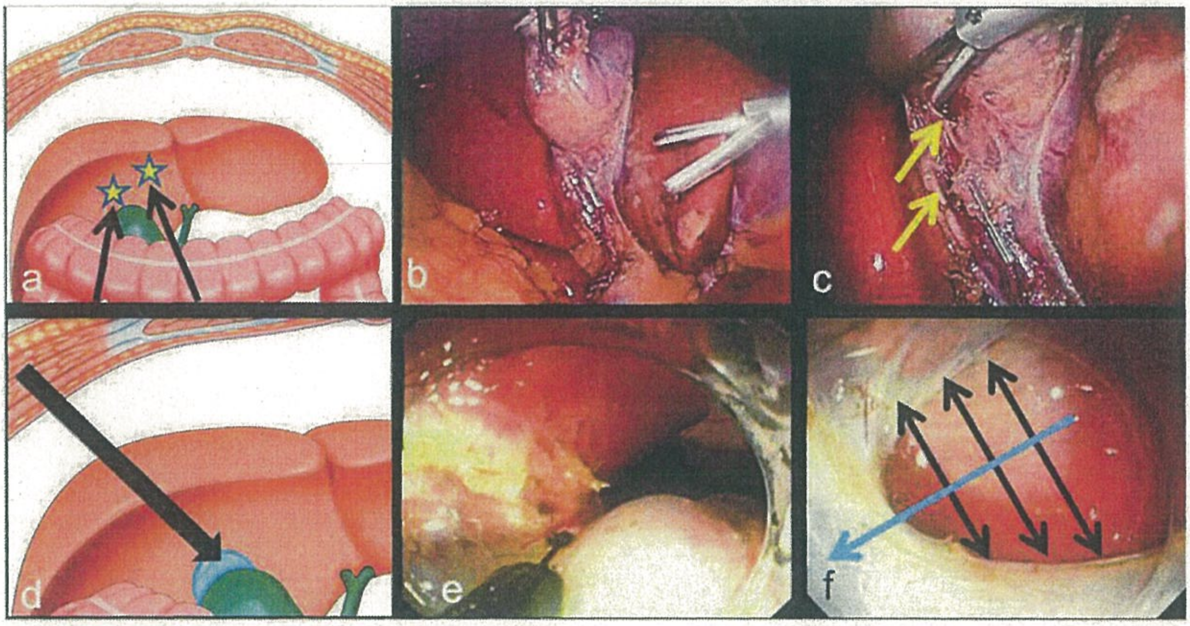

Figure 3. Advantages of LEC-chole compared to conventional Lapa-chole. (a) In Lapa-chole, laparoscopic rigid devices approached in a vertical direction to the GB bed (black arrows). (b) Rigid electrical scalpels sometimes cause injuries to the liver, such as bleeding, and the common bile duct by thermal trauma, especially when using the monopolar scalpel. (c) Sono Surg® damaged the liver, causing oozing bleeding (yellow arrows). (d) In LEC-chole, an endoscope with tip attachments approached the GB bed from a parallel direction between the liver and GB bed prior to the dissection (black arrow). (e) Dissection of the GB bed from the GB fundus to the neck was performed smoothly, safely and rapidly. (f) Creating sufficient artificial space by the local injection of natural saline between the liver and the GB bed (bidirectional black arrows), and the dissection of the GB bed was approached from a parallel direction between the liver and the GB bed (blue arrow).

Hence, using the concept of LECS to first secure the patient's safety, more evidence of minimally invasive surgery for cholecystectomy may be accumulated.

In conclusion, considering the advantages of surgical procedures involving the collaboration of both an endoscopist and a surgeon, the application of LEC-chole may be expanded to cholecystectomy in the near future.

Study limitations

The limitations to the study are as follows: small sample size, single laparoscpic operator and no standardization of the Lapa-chole procedure for dogs.

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Declaration of interest

Drs. Nobuya Kobayashi, Hirohito Mori, Hideki Kobara, Noriko Nishiyama, Masao Fujiwara, Keiichi Okano, Yasuyuki Suzuki and Tsutomu Masaki have no conflicts of interest or financial ties to disclose.

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