

Title: Feasibility of single-incision laparoscopic cholecystectomy for acute cholecystitis

Authors: Taro Ikumoto, Hidetsugu Yamagishi, Mineo Iwatate, Yasushi Sano, Masahito Kotaka and Yasuo Imai

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We have revised the manuscript according to the comments from editors and reviewers as described below.

We now hope that our paper will be suitable for publication in *World Journal of Gastrointestinal Endoscopy* and look forward to hearing from you concerning your editorial decision.

Sincerely yours,

Taro Ikumoto, MD

Department of Diagnostic Pathology

Dokkyo Medical University

880 Kitakobayashi, Mibu-machi, Shimotuga-gun, Tochigi, 321-0293, Japan.

E-mail: tikumoto@iMEC-Kobe.com

RESPONSE TO REVIEWER 69988:

We wish to express our appreciation to the reviewer for his or her insightful comments on our paper. The comments have helped us significantly improve the paper.

Comment 1: *Please define the equipment used.*

Response: In accordance with the Reviewer's comment, we have added the following section into the MATERIALS AND METHODS section.

"Surgical technique

We performed SILC using a standard technique with conventional trocars and instruments. A 20-mm incision was first made at the umbilicus. An optical port, a 5-mm trocar, and 5-mm forceps were inserted in the incision. These three instruments were placed in a triangle to maximize their spacing. In addition, a 3- or 5-mm instrument was inserted beside the optical port. We did not use any devices specialized for SILS.

It is feasible to perform nearly the same surgical procedure as conventional LC because the potential interference of each device is minimized by direct insertion of two instruments without trocar. We made every effort to create the critical view of safety, as described by Strasberg. To prevent bile duct injury, we

converted to open surgery when we could not create the critical view of safety or could not identify the cystic duct."

Comment 2: *Why is postoperative stay of elective colecystectomies more than 3 days when this operations is in some subgroup of patients a day surgery.*

Response: We appreciate the Reviewer's comment. Our original expression tended to be confusing. However, no elective cholecystectomy was included in this study indeed. In our understanding, elective cholecystectomy means the operation which is performed 6 weeks or more after the onset. All patients in this study were diagnosed with acute cholecystitis according to the criteria and then underwent cholecystectomy as soon as possible. However, as the Reviewer pointed out, we could not have performed cholecystectomy within 72 hours in many cases. Therefore, we have added the following text in DISCUSSION section as one of the limitation of this study.

"Unfortunately, we could not perform early surgery in many cases because of the lack of smooth cooperation with the first-contact physicians, limited availability of operation theater space, and lack of anesthetist availability. Despite our efforts to overcome these issues, some patients were unable to undergo early cholecystectomy."

And in accordance with the Reviewer's indication, we have changed the following text in MATERIALS AND METHODS section from

“This study included all patients who underwent SILC at Sano Hospital (Kobe, Japan) between January 2010 and December 2014.”

to

“This study included all patients who underwent SILC for acute cholecystitis at Sano Hospital (Kobe, Japan) between January 2010 and December 2014.”

Comment 3: *The incidence of suspected common bile ducts is too high. Please explain.*

Response: In accordance with the Reviewer’s comment, we have added the following text in DISCUSSION section.

“Although the incidence of complications related with the bile duct was slightly high, this is likely because our institution specializes in endoscopic treatment. Many patients with suspected common bile duct problems seek treatment at our hospital. In fact, 41% of patients in this study were recommended to our facility for suspected choledocholithiasis and they underwent endoscopic treatment before cholecystectomy. This factor may have contributed to the increased incidence of these complications.”

Thank you again for your valuable comments on our paper. I trust that the revised manuscript is suitable for publication.

RESPONSE TO REVIEWER 2444931:

We wish to express our appreciation to the reviewer for his or her insightful comments on our paper. The comments have helped us significantly improve the paper.

Comment 1: *Abbreviations in key words should be deleted;*

Response: In accordance with the Reviewer's comment, we have replaced the abbreviations in key words with the long form.

from

"Key words: acute cholecystitis; single incision laparoscopic cholecystectomy; SILC; SILS; SPS; SPA"

to

"Key words: acute cholecystitis; single incision laparoscopic cholecystectomy; single incision laparoscopic surgery; single-port access surgery; laparo-endoscopic single-site surgery"

Comment 2: *TG13 recommends performing cholecystectomy within 72 hours. Authors should show the mean time from the onset of the disease to the operation in this study;*

Response: In accordance with the Reviewer's comment, we have added the following text in Patient characteristics section.

"The mean time from the onset of acute cholecystitis to cholecystectomy was 7.7 days."

We have also added the mean time to Table1.

<u>Mean time from onset (days \pm SD)</u>	<u>7.7 \pm 4.1</u>
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TG13 certainly recommends performing cholecystectomy within 72 hours, and we have recognized the usefulness of early cholecystectomy. However, we could not have performed early surgery in many cases. We have also added the following text in DISCUSSION section.

"Unfortunately, we could not perform early surgery in many cases because of the lack of smooth cooperation with the first-contact physicians, limited availability of operation theater space, and lack of anesthetist availability. Despite our efforts to overcome these issues, some patients were unable to undergo early cholecystectomy."

We regret that the mean time from onset in Table 4 was incorrect. With and without conversion were replaced. We have already corrected it.

Comment 3: *Authors should introduce the SILC operation procedure and used devices;*

Response: In accordance with the Reviewer's comment, we have added the following section into the MATERIALS AND METHODS section.

"Surgical technique

We performed SILC using a standard technique with conventional trocars and instruments. A 20-mm incision was first made at the umbilicus. An optical port, a 5-mm trocar, and 5-mm forceps were inserted in the incision. These three instruments were placed in a triangle to maximize their spacing. In addition, a 3- or 5-mm instrument was inserted beside the optical port. We did not use any devices specialized for SILS.

It is feasible to perform nearly the same surgical procedure as conventional LC because the potential interference of each device is minimized by direct insertion of two instruments without trocar. We made every effort to create the critical view of safety, as described by Strasberg. To prevent bile duct injury, we converted to open surgery when we could not create the critical view of safety or could not identify the cystic duct."

Comment 4: *It is unnecessary to compare the parameters of SILC in acute cholecystitis patients with those without acute cholecystitis, including the mean operative time, volume of estimated blood loss, Clavien-Dindo grade and duration of postoperative hospital stay.*

Response: In accordance with the Reviewer's comment, we have removed the comparison from our manuscript. Accordingly, we have changed the following texts in DISCUSSION section;

from

"The operative time was significantly longer in patients with cholecystitis than in those without; this can be assumed to reflect the difficulty in operative maneuvers. Moreover, the volume of intraoperative blood loss was also significantly increased; this may be attributable to the facts that (1) the gallbladder and its surrounding tissue affected by acute inflammation are more likely to bleed because they are congested and become edematous and (2) that the hepatic parenchyma is easily damaged because of inflammatory adherence of the gallbladder to the liver bed."

to

"The operative time was tended to be longer in patients with cholecystitis; this likely reflects the difficulty of operative maneuvers. Moreover, the volume of intraoperative blood loss was also tended to be higher; this may be attributable to the facts that (1) the gallbladder and its surrounding tissue affected by acute inflammation are more likely to bleed because they are congested and become

edematous, and (2) that the hepatic parenchyma is easily damaged because of inflammatory adherence of the gallbladder to the liver bed.”

and from

“Moreover, because no significant difference in complication rates was observed between patients with and without cholecystitis, we consider this to suggest that SILC for acute cholecystitis is as safe as SILC for other diseases under the conditions used in this study.”

to

“Moreover, because the complication rate in this study is not higher than that reported in another study^[23], we believe that SILC for acute cholecystitis is as safe as other surgical procedures under the conditions described in this study.”

Thank you again for your valuable comments on our paper. I trust that the revised manuscript is suitable for publication.

RESPONSE TO REVIEWER 3035920:

We wish to express our appreciation to the reviewer for his or her insightful comments on our paper. The comments have helped us significantly improve the paper.

Comment 1: *You should briefly mention the method of single incision laparoscopic cholecystectomy(SILC) This is the first important point in this article.*

Response: In accordance with the Reviewer's comment, we have added the following section into the MATERIALS AND METHODS section.

"Surgical technique

We performed SILC using a standard technique with conventional trocars and instruments. A 20-mm incision was first made at the umbilicus. An optical port, a 5-mm trocar, and 5-mm forceps were inserted in the incision. These three instruments were placed in a triangle to maximize their spacing. In addition, a 3- or 5-mm instrument was inserted beside the optical port. We did not use any devices specialized for SILS.

It is feasible to perform nearly the same surgical procedure as conventional LC because the potential interference of each device is minimized by direct insertion of two instruments without trocar. We made every effort to create the critical view of safety, as described by Strasberg. To prevent bile duct injury, we

converted to open surgery when we could not create the critical view of safety or could not identify the cystic duct."

Comment 2: *Can you get visualization of critical view of safety in all cases? How can you have it?*

Response: In accordance with the Reviewer's comment, we have added the text which is described in Response for Comment 1. Furthermore, we have also added the following text into Surgical outcomes section and Table 2.

"The critical view of safety was achieved in 89 patients (89%), although anterograde dissection of the gall bladder starting from the fundus was required for 42 of these patients."

<u>Achievement of critical view of safety</u>	<u>89 (89%)</u>
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Comment 3: *Did you place the drain after SILC in your eight necrotizing cholecystitis patients? IF you place the drain after operation, from where and how do you insert a drain in SILC? What is your policy about drain placement during SILC and conventional laparoscopic cholecystectomy in patient with acute cholecystitis including necrotizing cholecystitis?*

Response: In accordance with the Reviewer's comment, we have added the following text into the Surgical outcomes section.

“A drainage tube was placed in 13 patients (13%), including four patients with necrotizing cholecystitis.”

We have also added the following text into the MATERIALS AND METHODS section. This is our policy about drain placement.

“Drainage tubes were not routinely placed, even in cases of severe inflammation. However, we placed a drainage tube from the right lateral abdomen to the liver bed in cases of suspected remnant abscess or bile leakage.”

Comment 4: *How many patients necessitate the learning curve? This is the second important point.*

Response: In accordance with the Reviewer’s comment, we have added the following section and figure into the RESULTS section.

“Learning curve

The mean operative times of every five consecutive cases of SILC performed by a chief surgeon are shown in Figure 2. There were no obvious trends suggestive of a learning curve.”

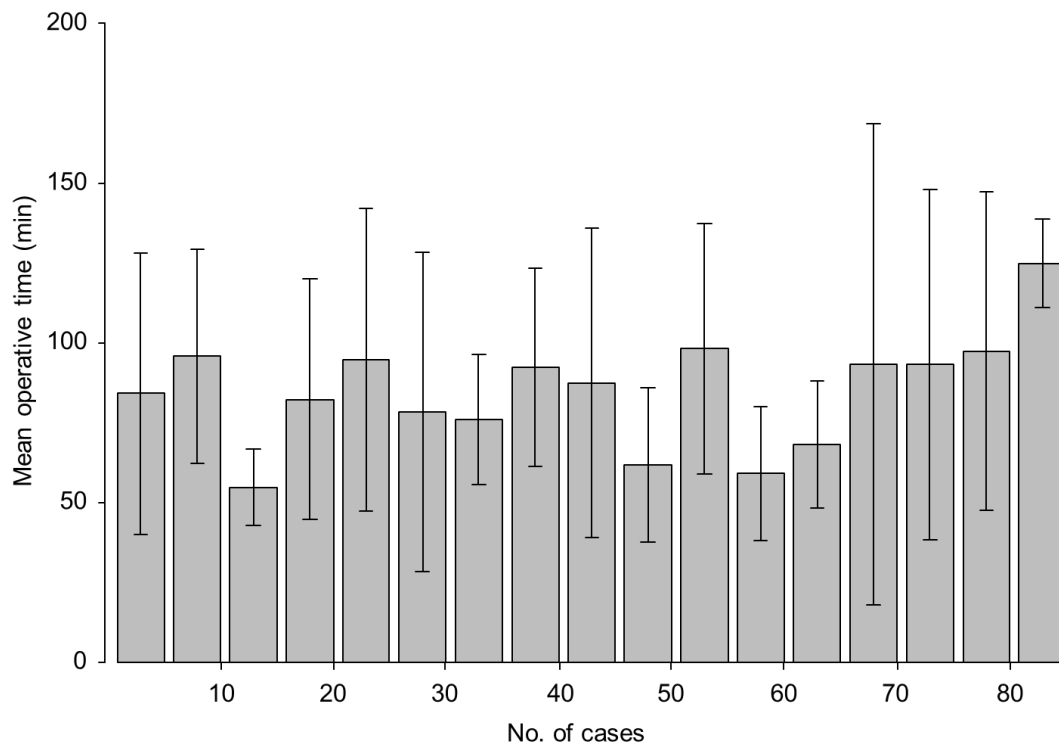


Figure 2 Mean operative time for every five consecutive cases of SILC for acute cholecystitis. All 85 cases performed by a chief surgeon are shown above. The standard deviation of each group is also shown. There are no obvious trends suggestive of a learning curve.

We have also added the following text into the DISCUSSION section.

“New procedures typically have learning curves. However, there was no evidence of a learning curve for SILC for acute cholecystitis in this study. This observation may be owing to the quality of the surgeons in our study. All surgeons who participated in this study were experienced and skilled in laparoscopic surgery and had each experienced more than 10 cases of SILC. Moreover, our SILC surgical procedure can be learned in a short time because

of its similarity to conventional LC. However, the learning curve may be more obvious in less experienced surgeons."

Comment 5: *If you want comparative study, I think that you should compare with conventional laparoscopic cholecystectomy in acute cholecystitis not with others.*

Response: In accordance with the Reviewer's comment, we have removed the comparison between patients with and without acute cholecystitis from our manuscript. Accordingly, we have changed the following texts in DISCUSSION section;

from

"The operative time was significantly longer in patients with cholecystitis than in those without; this can be assumed to reflect the difficulty in operative maneuvers. Moreover, the volume of intraoperative blood loss was also significantly increased; this may be attributable to the facts that (1) the gallbladder and its surrounding tissue affected by acute inflammation are more likely to bleed because they are congested and become edematous and (2) that the hepatic parenchyma is easily damaged because of inflammatory adherence of the gallbladder to the liver bed."

to

“The operative time was tended to be longer in patients with cholecystitis; this likely reflects the difficulty of operative maneuvers. Moreover, the volume of intraoperative blood loss was also tended to be higher; this may be attributable to the facts that (1) the gallbladder and its surrounding tissue affected by acute inflammation are more likely to bleed because they are congested and become edematous, and (2) that the hepatic parenchyma is easily damaged because of inflammatory adherence of the gallbladder to the liver bed.”

and from

“Moreover, because no significant difference in complication rates was observed between patients with and without cholecystitis, we consider this to suggest that SILC for acute cholecystitis is as safe as SILC for other diseases under the conditions used in this study.”

to

“Moreover, because the complication rate in this study is not higher than that reported in another study^[23], we believe that SILC for acute cholecystitis is as safe as other surgical procedures under the conditions described in this study.”

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